Molecular dynamics simulations of water with Ewald summation for the long range electrostatic interactions

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The use of a partial charge version of the Ewald sum method to treat long range electrostatic interactions in molecular dynamics simulations of water has been investigated. The orientational structure and energetic properties of the liquid have been studied for several choices of Ewald sum parameters. The results, including the dielectric constant ϵ_0, the radial-dependent Kirkwood factor $G_K(r)$, the orientational projection $H_\Delta(r)$, and the average dipole interaction energy, are compared with those from molecular dynamics simulations of water using the reaction field method. While the orientational structure of the liquid obtained from simulations which treat long range interactions by Ewald summation is different from corresponding results obtained from simulations with a reaction field, consistent values are calculated for the dielectric constant. The sensitivity of the results to variations in the convergence parameter α, the real-space cutoff R_c, and the number of vectors used in the reciprocal space sum was also analyzed.

1. Introduction

For the accurate modeling of aqueous solutions by computer simulations, the dielectric properties of the system must be considered. The question of the dielectric response is particularly crucial for chemical and biochemical simulations in which the electrostatic forces predominate. There are two distinct aspects of liquid simulations which determine the dielectric response: the microscopic model used for the intermolecular potential, and the way in which long range forces are treated in the simulation. There has been considerable confusion about the effects of various boundary conditions on the simulated dielectric response of liquids. The theoretical basis for relating dielectric properties of neat liquids to specific implementations of different boundary conditions in computer simulations has been strengthened recently; we refer the reader particularly to the insightful work of Neumann in this area [1,2].

Most of the systematic studies of the relationship between dielectric response and specific implementations of boundary methods in computer simulations have been carried out for models of simple molecular liquids, notably the Stockmayer point dipole model and closely related systems [3–8]. On the other hand, a large number of laboratories are using simulation methods to study aqueous solutions, of which those working on biochemical simulations make up a substantial portion. The reaction field and Ewald sum methods constitute the two most widely used methods for treating long range forces in liquid state simulations [9]. The study of the dielectric response of various water models using the reaction field method has been reported [10–13]. Water simulations using Ewald summation for the long-range interactions which report the dielectric constant have also appeared [14–19]. In a previous paper, we analyzed the effects of various implementations of the reaction field method on the dielectric response of water computed from simulations. The conventional reaction field method is limited to homogeneous liquids, although we are pursuing a generalization of the reaction field method which can be used for simulations of heterogeneous solute plus solvent systems [20]. Since at the present time the Ewald sum method can more readily be used to simulate heterogeneous systems, we have been studying the implementation of the Ewald sum method for aqueous solutions as well. In this communication, we report

results concerning the use of a partial charge version of the Ewald sum method to treat long range electrostatic interactions in molecular dynamics simulations of water. We analyze the effects of varying the Ewald sum parameters on the computed dielectric constant and compare the orientational structure of the liquid calculated from simulations with the Ewald sum to corresponding results from reaction field simulations.

In the Ewald summation technique, the central simulation box is infinitely replicated in all directions, and the long-range forces are included by evaluating the interaction of all molecules in the central box with all their images in the replicas. The Ewald sum is obtained by rewriting the conditionally convergent sum over Coulomb interactions in terms of two absolutely convergent sums, one in real-space, the other in reciprocal-lattice k-space. We have studied the orientational properties [21] (Kirkwood factor $G_K(r)$, the orientational projection $H_A(r)$, dielectric constant ϵ_0, and the radial dependence of the average dipole interaction energy) of liquid water in molecular dynamics simulations for several choices of the Ewald sum parameters. The results are compared with those from molecular dynamics simulations of water using the reaction field method. The sensitivity of the orientational structure of water in the simulations to variations in the Ewald sum parameters was also analyzed. The Ewald sum method is summarized in section 2. The results are presented and discussed in section 3.

2. Methods

Simulations have been carried out with the SPC water potential [22]. Only intermolecular interactions are included in the model. The model is widely used in simulations of solvated biomolecules and we have previously studied the dielectric properties of this model using the reaction field method [13]. The equations of motion were integrated with the Verlet algorithm using SHAKE constraints to preserve the rigid monomer geometry [23]. Cubic periodic boundary conditions were employed. In our previous study [13] of the dielectric properties of water including reaction field, we found ϵ_0 to be independent of system size for $N \geqslant 126$. In most simulations

reported here the system included 126 molecules enclosed in a cubic box of length $L = 15.52$ Å. The system size dependence of ϵ_0 with Ewald sum boundary conditions was investigated by performing one simulation of 345 molecules in a box with $L = 21.72$ Å. The 126-molecule simulations employed a spherical cutoff with $R_c = 7.75$ Å in some simulations, while a minimum image cutoff with $R_c = 13.423$ Å was used in other simulations. For the 345-molecule system, a spherical cutoff with $R_c = 10.85$ Å was used. The time step used in all simulations was 2×10^{-15} s. The average temperature was 300 K in these simulations.

Several different numerical methods for computing Ewald sums in liquid simulations have been proposed [15,24–26]. Most studies have focused on a dipolar version appropriate for point dipole molecular models. The SPC water model is a three point interaction site model for water with partial charges placed at the atomic centers. We employed a form of the Ewald sum appropriate to interactions between atoms carrying partial charges [9,27]

$$
V = \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} \left[q_i q_j \frac{\mathrm{erfc}(\alpha |r_{ij} + n|)}{|r_{ij} + n|} \right.
$$

$$
+ \frac{1}{\pi L^3} \sum_{k \neq 0} q_i q_j \left(\frac{4\pi^2}{k^2} \right)
$$

$$
\left. \times \exp(-k^2/4\alpha^2) \cos(k \cdot r_{ij}) \right]. \tag{1}
$$

Here, α is a convergence parameter which controls the relative weights of the real space and reciprocal space sums, q_i is the charge on atom i, r_{ij} is the vector between atoms i and j, n is a vector whose components are $(n_x L, n_y L, n_z L)$ (where n_x, n_y, and n_z are integers), and $k = 2\pi n/L^2$. With respect to the convergence parameter, there is to some extent a trade off, in that increasing the value of α necessitates fewer terms be included in the real space sum but more terms in the reciprocal space sum. When a partial charge formulation of the Ewald sum expression is used, there is a self-energy term due to the interaction between partial charges within an individual molecule which must be subtracted from the total energy [27]

$$V^{self} = \frac{1}{2} \sum_i \sum_{a=1}^{n_s} q_{ia} \left(2\alpha q_{ia}/\pi^{1/2} \right.$$

$$\left. + \sum_{b \neq a}^{n_s} q_{ib} \, \text{erf}(\alpha d_{ab}/d_{ab}) \right), \tag{2}$$

where n_s is the number of atoms per molecule (3 for water), and d_{ab} is the intramolecular separation of atoms a and b.

In the simulations reported here, only interactions within the central box are included in the real-space sum ($n=0$); interactions with the periodic images are included in the k-space sum. Two types of truncation of the real-space sum, spherical and minimum image cutoffs, were tested. The convergence of the reciprocal space sum is determined by the number of vectors in k-space that are included; we performed simulations which included 100, 690, and 1000 vectors. Simulations were completed using convergence parameter values of $\alpha = 2.4/L$, $5.0/L$, and $8.0/L$. The investigation of the effects of varying α, N_{vec}, and R_c on the computed dielectric constant was performed using the 126-molecule system.

The dielectric constant ϵ_0 is related to the mean square total dipole moment $\langle M^2 \rangle$ calculated in a simulation through [1]

$$\frac{\epsilon_0 - 1}{\epsilon_0 + 2} = \frac{4\pi\rho\mu^2}{9kT} G_K \left[1 - \left(\frac{3}{4\pi}\right) \frac{\epsilon_0 - 1}{\epsilon_0 + 2} T(0) \right], \tag{3}$$

where $G_K = \langle M^2 \rangle / N\mu^2$, and $T(0) = \int_V dr \, T(r)$, the integral of the dipole–dipole tensor over the basic simulation cell, for zero wavevector. For reaction field simulations,

$$T(0) = \frac{4\pi}{3} \left(\frac{2(\epsilon_{RF} - 1)}{2\epsilon_{RF} + 1} \right), \tag{4}$$

where ϵ_{RF} is the continuum dielectric constant in the reaction field Hamiltonian. For simulations employing the Ewald summation,

$$T(0) = \frac{4\pi}{3} \int_0^{R_c} 4\pi r^2 \, dr \left(\frac{\alpha}{\sqrt{\pi}}\right)^3$$

$$\times \exp(-\alpha^2 r^2) = \frac{4\pi}{3} Q . \tag{5}$$

$T(0)$ is therefore a function of the Ewald sum parameters. For the "ideal" simulation, in which all images in real-space and all vectors in k-space are included in the Ewald sum, $Q=1$. In actual simulations, both the real and k-space sums must be truncated. It is usually the case in computer simulations $0.9 \leq Q \leq 1$. Neumann and Steinhauser have shown that in certain cases the failure to account for the deviation of Q from 1 can lead to significant errors in the computed dielectric constant [28]. In the simulations reported in section 3, Q varied between 0.9940 (spherical cutoff) and 1.000 (minimum image cutoff); this very small variation in Q had a small (less than 10%) effect on the calculated dielectric constant. The dielectric constant values reported in table 1 have been calculated using the corrected Q values calculated with eq. (5).

We note that eqs. (3) and (5), which relate the dielectric constant to the finite system Kirkwood factor G_K and an integral involving Ewald sum parameters, were derived for systems where the elec-

Table 1
Ewald sum results for pure water

N	Run [a]	αL	R_c	No. vectors	Time (ps)	G_K	ϵ_0
126	c	5.0	0.87L	690	500	3.45±0.66	63.0±11.6
126	d	5.0	0.50L	100	800	3.29±0.13	66.6± 2.6
126	e	5.0	0.50L	690	500	3.28±0.60	65.8±11.9
126	f	8.0	0.87L	690	500	3.78±0.87	67.6±15.4
126	g	8.0	0.87L	1000	500	3.52±0.48	63.2± 8.5
345	h	5.5	0.50L	200	500	4.14±0.56	77.1±10.9

[a] Simulations a and b used a very small convergence parameter ($\alpha L=2.4$) which results in unphysical Kirkwood factors ($G_K<1$). The errors in the Kirkwood factor G_K and the dielectric constant ϵ_0 were estimated by the method of batch means. Each simulation was divided into five equally spaced segments. The Kirkwood factor and dielectric constant were calculated for each segment and the mean and standard deviation of these values are reported for each simulation.

trostatic interactions are purely dipolar – such as the Stockmayer fluid. In practice however, these relations are commonly applied to interaction site molecular models such as the SPC water model, where the electrostatic interactions between molecules are expressed as a sum of Coulomb interactions between partial charges located on each molecule. At short intermolecular separations, higher electric multipoles contained in the interaction site models affect the solvent structure – for water the quadrupole moment is known to be important [29]. The finite system Kirkwood factor G_K and dielectric constant however, are determined by the long-range electrostatic interactions, which for neutral molecules are dipolar even when the molecules are modeled as a composition of sites with partial charges. The use of eqs. (3)–(5) to analyze the dielectric constant of SPC water is justified on this basis. There are interesting questions concerning the appropriate extension of the equations for the dielectric constant to finite wavevectors when the molecules are viewed as a collection of partial charges rather than point dipoles. We will consider this issue in a future communication.

3. Results and discussion

A summary of the different simulations carried out is presented in table 1. As is apparent from the results, very long simulations are required to obtain converged estimates of the dielectric constant. The cumulative value of the dielectric constant over the course of one of the simulations (simulation d, table 1) is shown in fig. 1. For the first 200 ps, there are large fluctuations in the value of ϵ_0. In this very long simulation (simulation d, 800 ps), the statistics are sufficiently good to estimate the dielectric constant with high precision (4% error bars estimated by batch means); in shorter runs, it is not possible to estimate the dielectric constant with better than $\pm 20\%$ accuracy. Simulation d is used as a reference simulation in the discussion below. Because of the length of the simulation, the orientational properties can be calculated with high precision; the dielectric response is consistent with results calculated for the SPC water model by other methods.

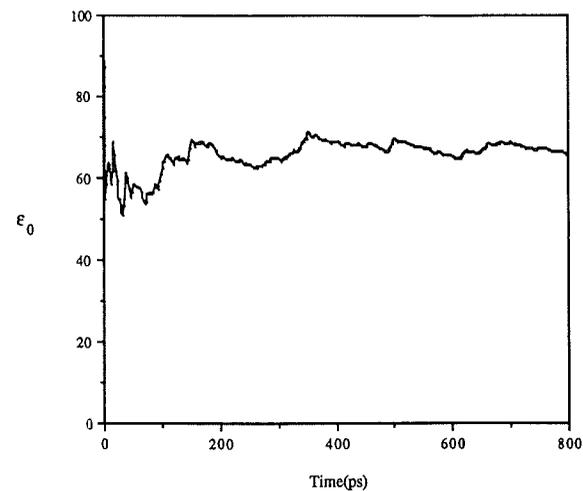Table 1 lists the finite system Kirkwood factor, G_K

Fig. 1. The cumulative dielectric constant for simulation d of table 1. For this simulation, $\alpha = 5.0/L$, $R_c = 7.75$ Å, and 690 vectors were employed for the k-space sum.

and the dielectric constant ϵ_0 calculated from each of the simulations. We have also calculated the radial decomposition of the average cosine between water dipoles in different shells $\langle \cos \theta \rangle_R$, and the integral

$$G_K(R) = 1 + \frac{4\pi\rho}{3} \int_0^R h_\Delta(r) \, r^2 \, dr \, , \qquad (6a)$$

$$h_\Delta(R) = 3g_{OO}(R) \langle \cos \theta \rangle_R \, . \qquad (6b)$$

$G_K(R)$ is a radial decomposition of the Kirkwood factor G_K, and $h_\Delta(r)$ is the leading term in the expansion of the molecular pair correlation function in rotational invariants [21]. These quantities provide a more detailed description of the liquid orientational structure. The results corresponding to simulation d of table 1 are shown in figs. 2 and 3. The general structure of $\langle \cos \theta \rangle_R$ and $G_K(R)$ are in agreement with previous simulations of liquid water that treated the long-range interactions by the Ewald sum method [14–19]. Also shown in the figures are corresponding results from a simulation of SPC water using the reaction field method [13]. The orientational structure of the liquid is clearly different with the two boundary conditions. This has been observed previously for the Stockmayer fluid [2]. Although to our knowledge a direct comparison of the effect of the Ewald sum versus the reaction field method on the orientational structure of liquid water
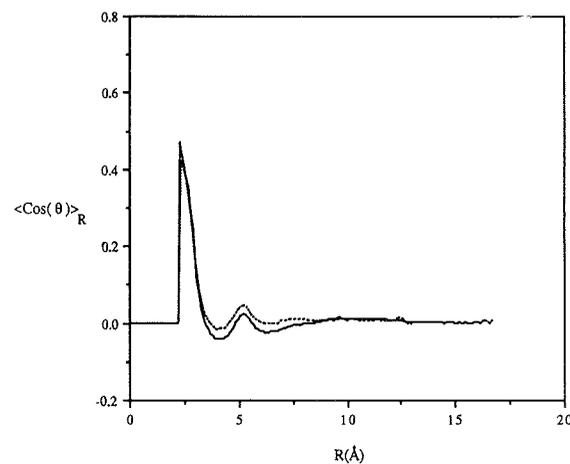
Fig. 2. The average cosine between water dipole vectors, $\langle \cos \theta \rangle_R$ versus the distance R between the water oxygen atoms. The dotted line is the result for simulation d of table 1 (Ewald sum); the solid line is the result for a reaction field simulation with 265 molecules and a cutoff of 9.85 Å.
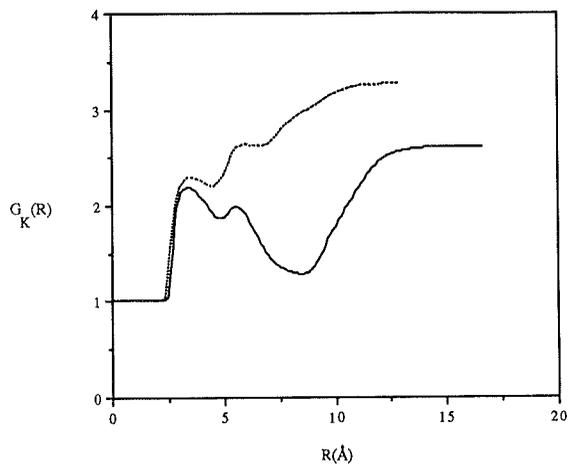

Fig. 3. The radial Kirkwood factor, $G_K(R)$ (given by eq. (6)). The solid and dotted lines are as in fig. 2.

using the same molecular potential has not been explicitly reported, the effects can be seen by comparing the orientational functions $G_K(R)$ and $h_\Delta(R)$ presented as figures in different publications [12,13,17–19]. The distinct structural results corresponding to the different ways of treating the long-range interactions (Ewald sum versus reaction field) are particularly pronounced for the orientational correlations between next-nearest neighbors begin-

ning at $\approx R = 4.5$ Å. In the reaction field simulations there is a larger anticorrelation between orientations of next-nearest neighbors as compared with the Ewald sum simulations [12,14,19,30]. The anticorrelation causes a large depression in $G_K(R)$ between ≈ 5 and 8 Å in the reaction field simulations which is absent in the Ewald sum simulations. We note that the effect of boundary conditions on the orientational structure of the first two shells of nearest neighbors is apparently much greater for water than for the model Stockmayer system. For the Stockmayer system, there is a positive orientational correlation between next-nearest neighbors in both Ewald and reaction field geometry (except for $\epsilon_{RF} = 1$) [4]. Despite the differences between the finite system Kirkwood factors G_K with the different boundary methods (note G_K is just $G_K(R)$ evaluated at $R = \frac{1}{2}\sqrt{3}L$), when the effects of boundary conditions on the orientational structure are correctly accounted for, the dielectric constant for SPC water calculated with the Ewald sum and reaction field methods are very similar. Thus we calculate a dielectric constant for SPC water of between 65 and 75 by either method. In a future communication, we will analyze the effects of the boundary conditions on wavelength-dependent dielectric response functions, the longitudinal and transverse Kirkwood factors $G^L(k)$, and $G^T(k)$.

The effects on average energies of the Ewald sum versus the reaction field method in the water simulations are compared in table 2. The average water binding energy for SPC water calculated from a representative trajectory with Ewald sum is -9.78 ± 0.01, while the corresponding result for a typical reaction field simulation is -9.88 ± 0.01. It is known that for dipolar liquids, the total energy is not sensitive to the use of Ewald sum versus reaction field methods [30,31]. The table also shows that the components of the total energy are essentially the same using either boundary condition. Note that the average electrostatic interaction energy between next-nearest neighbors is very small (the dipole–dipole energy is decreasing as $1/r^3$), so that although next-nearest neighbors are oriented differently in the Ewald and reaction field simulations, the effect on the electrostatic interaction energy is small. It is interesting to note from the results in table 1, that although the quadrupolar moment of the water model

Table 2
Energies [a]

Boundary condition	E_{tot}	E_{LJ}	E_{Coul}	E_{dip}	E_1^{dip}	E_2^{dip}	E_1^{Coul}	E_2^{Coul}
Ewald sum	-9.91	1.73	-11.64	-11.24	-9.05	-1.36	-9.95	-0.94
reaction field	-9.88	1.74	-11.62	-11.36	-9.28	-1.42	-10.17	-0.97

[a] E_{tot}, E_{LJ}, and E_{Coul} are the average total, Lennard-Jones, and Coulomb potential energy per water molecule calculated from a simulation of SPC water. E_{dip} is the average dipolar interaction energy, calculated using the dipole–dipole energy function instead of the Coulomb formula. E_1^{dip} is the average dipolar interaction energy of a typical molecule with its first coordination shell. E_2^{dip} is the average dipolar interaction energy of a typical molecule with its second coordination shell. E_1^{Coul} is the average Coulomb interaction energy of a typical molecule with its first coordination shell. E_2^{Coul} is the average Coulomb interaction energy of a typical molecule with its second coordination shell.

is important for the liquid structure [29], the average Coulomb energy (which includes all moments) per water molecule is very close to the average dipole energy; this observation applies to the pair energies between nearest neighbors as well as to the total binding energy. For example, for the Ewald sum simulation listed in the table, the average dipolar interaction energy of a water molecule with its first coordination shell is -9.05 kcal/mol, whereas the corresponding total Coulomb interaction energy of a water with its first coordination shell is -9.95 kcal/mol.

To examine the effect of variations in the convergence parameter α on the orientational properties, three simulations b, c, and f were completed. We observed (simulation b) that $\alpha = 2.4/L$ is too small a convergence parameter to use when the real space sum only includes interactions in the central cell; it leads to unphysical values for the Kirkwood factor ($G_K < 1$). Results corresponding to simulations c and f are shown in table 1. A minimum image cutoff for the non-bonded interactions was employed in simulations c and f, and 690 vectors in the k-space sum were included in each case. Most simulations of dipolar fluids have employed about 100 vectors. The effect of varying the cutoff of the real-space sum was studied by performing simulations c and e of table 1. In these simulations $\alpha = 5.0/L$ and $N_{vec} = 690$. A minimum image cutoff ($R_c = 13.42$ Å) and spherical cutoff ($R_c = 7.75$ Å) were employed respectively in simulations c and e. The dielectric constant calculated from the mean square dipole moment is independent of the type of cutoff used. However, the evaluation of the interactions using a spherical cutoff with $R_c = 7.75$ Å is about twice as efficient computationally as the minimum image cutoff in these simulations. We have also investigated the effect of varying the number of vectors included in the reciprocal space sum between 100 and 1000 vectors (see table 1). We find that it is sufficient to include as few as 100 reciprocal lattice vectors in the reciprocal sum, even when a spherical cutoff with $R_c = 7.75$ Å is used for the real-space sum.

We found in our previous studies of dielectric properties of water using the reaction field method that the dielectric constant reached a limiting value independent of system size for simulations including as few as 126 water molecules [13]. In this series of water simulations using the Ewald sum boundary method, we have carried out one simulation of 500 ps duration with 345 water molecules (simulation h, table 1) to compare with our Ewald sum results for simulations of the smaller system (126 water molecules). Although we calculate a slightly higher dielectric constant for the larger system ($\epsilon_0 = 77 \pm 10.9$), the results agree within error bars with estimates of the dielectric constant obtained from the simulations of the smaller system.

Finally, we comment on the CPU time required to calculate the Ewald sum (eq. (1)) in this molecular dynamics simulation of water. We found that explicit evaluation of the Ewald sum increases the CPU time by about 1.5–2 fold on a Cray YMP as compared with simulations using a spherical cutoff with $R_c = L/2$. Subsequent to completing the simulations reported in table 1, we have implemented look-up tables to accelerate the computation of the Ewald sum. Look-up tables were constructed for $erfc(\alpha r_{ij})$, $exp(-\alpha r_{ij}^2)$, and r^{-n} with $n = 1, 2, 3$. At run time, only r_{ij}^2 is calculated for each atom pair. The index

of a particular r_{ij}^2 is calculated from: index $=$ NINT$[\,(r_{ij}^2 - r_{min})r_{incv}\,] + 1$, where r_{min} is the minimum distance between any two atoms, and r_{incv} is the inverse of the increment of r_{ij}^2 in the table. Choosing $r_{min} = 1.0$ Å, and $r_{incv} = 250$, for a simulation with a non-bonded interaction cutoff $L/2 = 10.85$ Å (345 water molecules), each of the five look-up tables contains approximately 45000 elements. The internal energies and radial distribution functions calculated from simulations with this degree of discretization of the potential and force are indistinguishable from corresponding results obtained from simulations using explicit function evaluation of the potential and force. The use of look-up tables to calculate the Ewald sum potential and force resulted in a substantial increase in the performance of the program; the water molecular dynamics simulations ran four times faster with look-up tables as compared with explicit function evaluations.

4. Conclusions

We have completed a series of molecular dynamics simulations of water using a partial sum version of the Ewald sum method to treat the long-range electrostatic interactions. The orientational structure and energetic properties of the liquid were studied for several choices of Ewald sum parameters. Results for the dielectric constant consistent with those obtained with the reaction field boundary method are obtained with Ewald sum simulations using either a spherical cutoff or a minimum image cutoff for the real-space sum. The dielectric properties calculated from simulations containing 126 molecules and 345 molecules are very similar. A convergence parameter $\alpha = 5/L$ or larger was found to be needed in these simulations in which only interactions in the central cell are included in the real-space sum. The effect of using the Ewald sum on the orientational structure of water was compared with corresponding results obtained from simulations with a reaction field. In the reaction field simulations there is a larger anti-correlation between orientations of next-nearest neighbors as compared with the Ewald sum simulations. The effect of the boundary conditions for the long-range interactions on the orientational structure of liquid water are larger than the corresponding

results for the model Stockmayer fluid. Finally, the partial charge version of the Ewald sum method increased the computational cost per molecular dynamics step by a factor of between 1.5 and 2 compared with simulations which used a simple spherical cutoff truncation for the long-range interactions, but a substantial increase in speed was achieved by substituting look-up tables for function evaluations needed for the Ewald sum.

Acknowledgement

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