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Simple and accurate scheme to compute electrostatic interaction: Zero-dipole summation technique for molecular system and application to bulk water

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The zero-dipole summation method was extended to general molecular systems, and then applied to molecular dynamics simulations of an isotropic water system. In our previous paper [I. Fukuda, Y. Yonezawa, and H. Nakamura, J. Chem. Phys. **134**, 164107 (2011)], for evaluating the electrostatic energy of a classical particle system, we proposed the zero-dipole summation method, which conceptually prevents the nonzero-charge and nonzero-dipole states artificially generated by a simple cutoff truncation. Here, we consider the application of this scheme to molecular systems, as well as some fundamental aspects of general cutoff truncation protocols. Introducing an idea to harmonize the bonding interactions and the electrostatic interactions in the scheme, we develop a specific algorithm. As in the previous study, the resulting energy formula is represented by a simple pairwise function sum, enabling facile applications to high-performance computation. The accuracy of the electrostatic energies calculated by the zero-dipole summation method with the atom-based cutoff was numerically investigated, by comparison with those generated by the Ewald method. We obtained an electrostatic energy error of less than 0.01% at a cutoff length longer than 13 Å for a TIP3P isotropic water system, and the errors were quite small, as compared to those obtained by conventional truncation methods. The static property and the stability in an MD simulation were also satisfactory. In addition, the dielectric constants and the distance-dependent Kirkwood factors were measured, and their coincidences with those calculated by the particle mesh Ewald method were confirmed, although such coincidences are not easily attained by truncation methods. We found that the zero damping-factor gave the best results in a practical cutoff distance region. In fact, in contrast to the zero-charge scheme, the damping effect was insensitive in the zero-charge and zero-dipole scheme, in the molecular system we treated. We discussed the origin of this difference between the two schemes and the dependence of this fact on the physical system. The use of the zero damping-factor will enhance the efficiency of practical computations, since the complementary error function is not employed. In addition, utilizing the zero damping-factor provides freedom from the parameter choice, which is not trivial in the zero-charge scheme, and eliminates the error function term, which corresponds to the time-consuming Fourier part under the periodic boundary conditions.
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I. INTRODUCTION

Appropriate treatment of the electrostatic interaction is critical for computational studies of solids, soft matter, and biomolecular systems, including water, proteins, lipids, DNAs, and their complexes.[1–3] In fact, electrostatic interactions play an essential role in a number of systems to maintain physical structures, to generate chemical properties, and to perform biological functions.[4–7] However, since the Coulombic interaction is long ranged and has both positive and negative signatures, its treatment is nontrivial, except for a small, finite system. Despite many studies, the treatment still represents a bottleneck in numerical simulations requiring high accuracy, low computational cost, freedom from artifacts, and ease of implementation.

The monotonic decreasing feature of the Coulombic potential function with increasing atomic distance allows a truncation of the interaction.[8,9] The simplest treatment of the interaction is a straight cutoff procedure. One of the advantages of such a method, which comes from the simple pairwise summation form, is that it avoids a massive computational cost, yielding an $O(N)$ scheme for a large system of N classical particles. This is very demanding, since the explosive growth of computational power over the past three decades now enables a simulation with over $N = 10^6$ particles, typically utilized in biomolecular studies. The issue of the computational cost is also critical, from the viewpoint that a long simulation duration is often required to realistically understand a number of material features, physical phenomena, and biological functions. The other advantage of the truncation method is its simplicity. This results in ease of implementation, which enhances the utility in high-performance computational architectures, including highly parallel protocol and special purpose architectures.[10]

However, the disadvantage of the straight cutoff truncation method, as revealed by many studies, is physical artifacts, which often lead to large discrepancies from the true values.[6,11] One of the most intrinsic artifacts appears in the dielectric properties in, e.g., a pure bulk water system: the dielectric constant was far away from the experiment, and the distance-dependent Kirkwood factor had a deep and wide hole-like structure around the cutoff length, contradicting the reliable results, where the factor shows an almost monotonic increase with increasing the atomic distance.[12] These artifacts should be due to the incorrect orientations of water molecules.[13]

To reduce the artifacts, several modifications of the truncation method have been proposed. For example, deformation of the potential or force function via a shifting or switching procedure[14] was employed, thus keeping the advantage of the pairwise summation form and essentially preserving the simplicity. The other modification appeared in the reaction field (RF) method,[15,16] which assumes that the region outside the cutoff sphere would be seen as a dielectric continuum polarized via reacting with the molecules inside the sphere. These methods actually reduced the artifacts, and often greatly reduced the errors.[14,17] However, the discrepancies[18,19] from the accurate values often remained. For example, for the distance-dependent Kirkwood factor, a hole around the cutoff length still exists, depending on the simulation conditions. This is especially problematic, when one employs the group-based cutoff protocol.

Another approach to calculate the electrostatic interactions is the lattice-sum methods, such as the Ewald summation.[20,21] These methods assume the periodicity of the system and treat the infinite sum, composed of the contributions from infinite copies of the original unit cell system. Due to the slow decay of the Coulombic potential function, in general, the infinite series is not absolutely summable, and thus the limit value completely depends on the ordering of the summation. In the Ewald method, a physically natural ordering, in view of the norm, is adopted, and a highly accurate value can be produced via enhanced convergence. Such methods are quite natural and accurate for applying to an inherently periodic system. In many studies, they are useful to treat an isotropic bulk system, although the system is not necessarily inherently periodic. This is because the periodic boundary condition (PBC) enables us to avoid the creation of an interface, which often causes a significantly large artifact, and to mimic the bulk state.

In contrast, for an intrinsically non-periodic system, the interactions from the infinite copies imposed by the PBC are clearly duplicated.[22,23] For instance, for the system of a protein with water solvent molecules, the interactions between the protein in the original cell and all the image proteins should be calculated through the Fourier part in the Ewald summation. This is an undesirable situation, unless we treat a certain crystal state. The ideal boundary condition would mimic the bulk state, but should not require such unphysical duplicate interactions. In this sense, it may be expedient if we develop methods that are irrelevant to boundary conditions. Thus, cutoff-based approaches, which can be applied to any boundary conditions in principle, would be appealing, if we can reduce the artifacts and improve the accuracy to an acceptable level, with maintaining its advantages.

In the previous study,[24] we developed the zero-dipole (ZD) summation method for evaluating the electrostatic energies of classical particle systems. The summation conceptually prevents the nonzero-charge and nonzero-dipole states artificially generated by a simple cutoff truncation, which causes energetic noise and several artifacts. The derived energy formula is nevertheless represented by a simple pairwise sum form, which utilizes the cutoff procedure but employs a pairwise function modified from the pure Coulombic form into a new form, taking account of the neutrality of the charges and dipoles in the cutoff sphere. We applied this scheme to a sodium ionic system under crystal and liquid phases, and confirmed that it gives good approximations of the energetic and structural properties.

In this paper, first we consider a theoretical treatment of the ZD summation method for applications to general molecular systems. In contrast, from a viewpoint of individual numerical applications, we should take account of the isotropy, homogeneity, characteristic boundary conditions, and objective phenomena of the target molecular system. Here, by limiting our interest to a specific application of the method, we second numerically investigated the accuracy and the artifacts of the method, using a bulk water system. In general, an isotropic bulk system is suitably represented by a non-boundary system, and it is reasonable to impose three-dimensional (3D) PBC to a considerable extent, enabling us to have a reliable reference method, such as the Ewald summation. We treat a bulk water system as an example of such a system for a pragmatic reason—a homogeneous polar molecule system should be the first benchmark test for the electrostatic evaluation—and a scientific reason—its accurate descriptions, including electrostatic properties, are critical, considering the key role played by water in a number of important physical, chemical, and biological processes.[25–27]

In Sec. II, after a brief review of the ZD summation method, we consider the issue of the treatment for the bonding interactions in general molecular systems. This is because the force field in molecular systems is, in general, defined such that two atoms that obey the bonding interactions should not feel the electrostatic interaction, even though they both have charges. By following a simple theoretical idea to harmonize these two kinds of interactions, we present a specific algorithm that is consistently adapted in our scheme to effectively realize it. Following the description of the numerical simulation protocol in Sec. III, the computation results are shown in Sec. IV. We tested the accuracy of the current method by applying it to a molecular system, and comparing the results with those obtained by the conventional methods. The energetic, static, and dielectric properties for the water system were investigated, and the characteristic properties of the current method were analyzed in detail. We also studied the cutoff truncation protocols, including the relationship between the electrostatic and bonding interactions, the truncation mode, and the parameter dependencies. The stability of the molecular dynamics (MD) simulation and the computational timing were investigated. We conclude with remarks in Sec. V.

II. ZERO-DIPOLE SUMMATION METHOD FOR MOLECULAR SYSTEM

A. Basics

First, we will briefly review the ZD summation method,[24] which seeks the total Coulombic energy $E(x)$, for configurations $x \equiv (x_1, \ldots, x_N)$, of a classical system of N point particles, each of which has charge q_j for $j \in \mathcal{N} \equiv \{1, \ldots, N\}$. According to the zero-dipole summation principle, first, for each i we assume the existence of the neutralized subset (*zero-charge zero-dipole subset,* in short, ZD subset) $\mathcal{M}_i \subset \mathcal{N}_i \equiv \mathcal{N} - \{i\}$, consisting of particles in a given cutoff sphere of charge q_i with cutoff length r_{c} such that both the sum (adding i) of the charges and the sum of the dipoles are (nearly) zeros and that the remaining charges (except i) in the sphere are located near the cutoff surface. We consider that to effectively avoid the nonzero-dipole and nonzero-charge state artificially generated in the simple cutoff truncation scheme, the summation is approximated by the zero-dipole summation,

$$\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} q_i q_j V(r_{ij}) \approx \sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{M}_i} q_i q_j V(r_{ij}), \tag{1}$$

where $r_{ij} \equiv \|x_{ij}\|$ $(x_{ij} \equiv x_i - x_j \in \mathbb{R}^3)$ is the atomic distance between atoms i and j. Here, function V, specifically defined by

$$V(r) = \frac{\mathrm{erfc}(\alpha r)}{r}, \tag{2}$$

is utilized in a function decomposition,

$$E(x) = \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} \frac{q_i q_j}{r_{ij}} \tag{3a}$$

$$= \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} q_i q_j V(r_{ij}) + \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} q_i q_j \left[\frac{1}{r_{ij}} - V(r_{ij})\right]. \tag{3b}$$

For the first term in Eq. (3b), we use the right-hand side of Eq. (1), which can be approximated by a formula with an accuracy of the second order with respect to the displacement vectors $h^{(i)}$ $(i \in \mathcal{N})$ designating the excess subset.[24] Namely, we have

$$\frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{M}_i} q_i q_j V(r_{ij}) = \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i\\ r_{ij}<r_{\mathrm{c}}}} q_i q_j V(r_{ij}) - \hat{E}(x) \tag{4}$$

with

$$\hat{E}(x) \equiv \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{J}_i} q_i q_j V(r_{ij}) \tag{5}$$

being the excess energy ($\mathcal{J}_i \equiv \{j \in \mathcal{N}_i - \mathcal{M}_i \mid r_{ij} < r_{\mathrm{c}}\}$ is the excess subset), represented as

$$\hat{E}(x) = \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i\\ r_{ij}<r_{\mathrm{c}}}} q_i q_j \left[V(r_{\mathrm{c}}) - \frac{F(r_{\mathrm{c}})}{2r_{\mathrm{c}}}\left(r_{ij}^2 - r_{\mathrm{c}}^2\right)\right] + \frac{1}{2}\left[V(r_{\mathrm{c}}) + \frac{1}{2}F(r_{\mathrm{c}})r_{\mathrm{c}}\right]\sum_{i\in\mathcal{N}} q_i^2 + \sum_{i\in\mathcal{N}} o(h^{(i)}). \tag{6}$$

For the second term of Eq. (3b), we use an approximation

$$\frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} q_i q_j \left[\frac{1}{r_{ij}} - V(r_{ij})\right] \sim -\frac{\alpha}{\sqrt{\pi}}\sum_{i\in\mathcal{N}} q_i^2, \tag{7}$$

which can be justified for a small damping factor $\alpha(\geq 0)$, as demonstrated by Wolf *et al.*[28] Along with a consistency condition[24] for $\{\mathcal{J}_i\}_{i\in\mathcal{N}}$, we reach an approximation

$$E(x) \simeq E_{\mathrm{ZD}}(x), \tag{8}$$

with the definition,

$$E_{\mathrm{ZD}}(x) = \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i\\ r_{ij}<r_{\mathrm{c}}}} q_i q_j [u(r_{ij}) - u(r_{\mathrm{c}})] - \frac{1}{2}\left[u(r_{\mathrm{c}}) + \frac{2\alpha}{\sqrt{\pi}}\right]\sum_{i\in\mathcal{N}} q_i^2. \tag{9}$$

Here,

$$u(r) \equiv V(r) + \frac{1}{2}\frac{F(r_{\mathrm{c}})}{r_{\mathrm{c}}} r^2 \tag{10}$$

is a redefined pair potential function with

$$F(r) \equiv -DV(r) = \frac{\mathrm{erfc}(\alpha r)}{r^2} + \frac{2\alpha}{\sqrt{\pi}}\frac{\exp(-\alpha^2 r^2)}{r} \tag{11}$$

being the force function of the original pair function, V. The resulting formula for the energy, Eq. (9), is a simple truncated pairwise sum of $u - u(r_{\mathrm{c}})$ with the configuration irrelevant term.

B. Protocol for applying to molecular system

For a classical molecular system, the total energy can be represented by

$$E^{\mathrm{Tot}} \equiv E_{\mathrm{Bond}} + E_{\mathrm{vdW}} + E_{\mathrm{Ele}}, \tag{12}$$

where E_{Bond} is the energy for the covalent bonding interactions, E_{vdW} is the energy of the van der Waals interactions, and E_{Ele} is the energy relevant to the electrostatic interactions. This last term can be specifically denoted as

$$E_{\mathrm{Ele}}(x) \equiv \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}} \frac{q_i q_j}{r_{ij}} + \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}4}} q_i q_j g_{ij}(r_{ij}), \tag{13}$$

where $\mathcal{N}_i^{\mathrm{B}}$ is the subset of particles that interact with particle i via the bonding interactions; e.g., i and $(\mathcal{N}_i^{\mathrm{B}} \ni) j$ obey the bond ("1-2") interaction or bend ("1 -3") interaction or torsion ("1 -4") interaction; so $j \in \mathcal{N}_i - \mathcal{N}_i^{\mathrm{B}}$ indicates that j does not interact with i through these bonding interactions. Often, the "1-4" pairs, denoted by $\mathcal{N}_i^{\mathrm{B}_4}$ for i, need special care, and the second term of Eq. (13) represents the "1-4 electrostatic" interactions; e.g., $g_{ij}(r) = \nu_{ij}/r$ with a reducing factor $\nu_{ij} < 1$. Below, we evaluate the first term of Eq. (13),

$$E^{(\mathrm{NB})}(x) \equiv \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}}\frac{q_iq_j}{r_{ij}} \tag{14a}$$

$$= \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i}\frac{q_iq_j}{r_{ij}} - \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}}\frac{q_iq_j}{r_{ij}}, \tag{14b}$$

through the ZD summation method.

To do this, we consider that the first term in Eq. (14b) is the electrostatic interactions submitted to all charges in the system in a consistent manner, and thus is irrelevant to the bonding interactions, and consider that the second term in Eq. (14b) is the correction relevant to the bonding interactions (more detailed discussions are in Sec. IV D 1). According to this simple interpretation of Eq. (14b), applying the approximation through the ZD scheme, Eq. (8), to the first term in Eq. (14b) gives

$$E^{(\mathrm{NB})}(x) \simeq E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) \tag{15a}$$

$$\equiv E_{\mathrm{ZD}}(x) - \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}}\frac{q_iq_j}{r_{ij}} \tag{15b}$$

$$= \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i\\ r_{ij}<r_{\mathrm{c}}}} q_iq_j[u(r_{ij})-u(r_{\mathrm{c}})] - \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}} q_iq_j\frac{1}{r_{ij}} - \frac{1}{2}\left[u(r_{\mathrm{c}}) + \frac{2\alpha}{\sqrt{\pi}}\right]\sum_{i\in\mathcal{N}}q_i^2. \tag{15c}$$

Supposing that state x satisfies $\|x_{ij}\| < r_{\mathrm{c}}$ for every $j\in\mathcal{N}_i^{\mathrm{B}}$ for any i (viz., bonding interactions with respect to i occur in the cutoff sphere around i; always true in practical applications), we obtain the following form, which may be convenient for applications,

$$E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) = \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}\\ r_{ij}<r_{\mathrm{c}}}} q_iq_j[u(r_{ij})-u(r_{\mathrm{c}})] + \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}} q_iq_j \times\left[u(r_{ij})-\frac{1}{r_{ij}}\right] - \frac{u(r_{\mathrm{c}})}{2}\sum_{i\in\mathcal{N}}q_i\left(q_i+\sum_{j\in\mathcal{N}_i^{\mathrm{B}}}q_j\right) - \frac{\alpha}{\sqrt{\pi}}\sum_{i\in\mathcal{N}}q_i^2 \tag{16a}$$

$$= \sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}\\ r_{ij}<r_{\mathrm{c}}\\ i<j}} q_iq_j[u(r_{ij})-u(r_{\mathrm{c}})] + \sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i^{\mathrm{B}}\\ i<j}} q_iq_j\left[u(r_{ij})-\frac{1}{r_{ij}}\right] - u(r_{\mathrm{c}})\sum_{i\in\mathcal{N}}q_i\left(\frac{q_i}{2}+\sum_{\substack{j\in\mathcal{N}_i^{\mathrm{B}}\\ i<j}}q_j\right) - \frac{\alpha}{\sqrt{\pi}}\sum_{i\in\mathcal{N}}q_i^2. \tag{16b}$$

In Eq. (16b), we have used the symmetric property between i and j. The first term in Eq. (16b) is the usual nonbonding pairwise-sum cutoff form utilizing the pair function $q_iq_j[u(r_{ij}) - u(r_{\mathrm{c}})]$, and the second term is a bonding pairwise sum form with $q_iq_j[u(r_{ij}) - \frac{1}{r_{ij}}]$. We can evaluate in advance the third term in Eq. (16b), which comes from the image charge terms in the ZD summation. The last term in Eq. (16b) is the self energy term.

The force acting on atom i can be obtained by differentiating Eq. (15c), and, by noticing the fact that $\lim_{r\to r_{\mathrm{c}}}(u(r) - u(r_{\mathrm{c}})) = \lim_{r\to r_{\mathrm{c}}} Du(r) = 0$, we have a continuous gradient of $E_{\mathrm{ZD}}^{(\mathrm{NB})}$,

$$-\nabla_i E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) = \sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}\\ r_{ij}<r_{\mathrm{c}}}} q_iq_je(r_{ij})\frac{x_{ij}}{r_{ij}} + \sum_{j\in\mathcal{N}_i^{\mathrm{B}}} q_iq_j\left[e(r_{ij}) - \frac{1}{r_{ij}^2}\right]\frac{x_{ij}}{r_{ij}}. \tag{17}$$

Here, e is a pair force function defined by

$$e(r) \equiv -Du(r) = F(r) - \frac{F(r_{\mathrm{c}})}{r_{\mathrm{c}}}r. \tag{18}$$

In summary, the current method provides the very simple form of the energy, Eq. (15c) or Eq. (16b), and the atomic force, Eq. (17), which are specifically represented as

$$E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) = \sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}\\ r_{ij}<r_{\mathrm{c}}\\ i<j}} q_iq_j\left[\frac{\mathrm{erfc}(\alpha r_{ij})}{r_{ij}} - \frac{\mathrm{erfc}(\alpha r_{\mathrm{c}})}{r_{\mathrm{c}}} + b\left(r_{ij}^2 - r_{\mathrm{c}}^2\right)\right] + \sum_{i\in\mathcal{N}}\sum_{\substack{j\in\mathcal{N}_i^{\mathrm{B}}\\ i<j}} q_iq_j\left[-\frac{\mathrm{erf}(\alpha r_{ij})}{r_{ij}} + br_{ij}^2\right] - c\sum_{i\in\mathcal{N}}q_i\left(\frac{q_i}{2}+\sum_{\substack{j\in\mathcal{N}_i^{\mathrm{B}}\\ i<j}}q_j\right) - \frac{\alpha}{\sqrt{\pi}}\sum_{i\in\mathcal{N}}q_i^2 \tag{19}$$

and

$$-\nabla_i E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) = \sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}\\ r_{ij}<r_{\mathrm{c}}}} q_iq_j\left[\frac{\mathrm{erfc}(\alpha r_{ij})}{r_{ij}^2} + \frac{2\alpha}{\sqrt{\pi}}\frac{\exp\left(-\alpha^2r_{ij}^2\right)}{r_{ij}} - 2br_{ij}\right]\frac{x_{ij}}{r_{ij}} + \sum_{j\in\mathcal{N}_i^{\mathrm{B}}} q_iq_j\left[-\frac{\mathrm{erf}(\alpha r_{ij})}{r_{ij}^2} + \frac{2\alpha}{\sqrt{\pi}}\frac{\exp\left(-\alpha^2r_{ij}^2\right)}{r_{ij}} - 2br_{ij}\right]\frac{x_{ij}}{r_{ij}}, \tag{20}$$

with constants depending on α and r_c,

$$b \equiv \frac{\operatorname{erfc}(\alpha r_c)}{2r_c^3} + \frac{\alpha}{\sqrt{\pi}} \frac{\exp\left(-\alpha^2 r_c^2\right)}{r_c^2}, \tag{21}$$

$$c \equiv \frac{3}{2} \frac{\operatorname{erfc}(\alpha r_c)}{r_c} + \frac{\alpha}{\sqrt{\pi}} \exp\left(-\alpha^2 r_c^2\right). \tag{22}$$

III. MATERIALS AND METHODS

A. Water system

A water system of 4178 molecules of a simple TIP3P model[29] was studied. A preliminary equilibration MD run (0.1 ns), under the isotropic *NTP* (constant temperature and pressure) ensemble with the temperature of $T = 300$ K and the pressure of $P = 1$ atm, resulted in the MD cell length of 50.48 Å. Using this cell, a 2 ns NTV (constant temperature) MD simulation with $T = 300$ K was performed for configuration sampling: 1000 configurations were sampled during the last 1 ns at every 1 ps, in order to estimate the energy accuracy. The velocity-Verlet integrator with a time step of 1 fs was used. In these sampling-aimed MD simulations, which were performed with the myPresto program,[30] the particle mesh Ewald (PME) (Ref. 31) with the real part cutoff length of 12 Å and the damping factor of 0.35 Å^{-1} was used, under the 3D PBCs for calculating the Coulombic interactions. For the Fourier part, 6th order interpolation with a 64 × 64 × 64 grid was used.

B. Truncation mode and conventional methods

To estimate the energy by the ZD summation method, we have used the atom-based cutoff (AC) mode; i.e., for atom j such that $r_{ij} > r_c$, we simply ignore the contribution $q_i q_j[u(r_{ij}) - u(r_c)]$ in Eq. (15c) or (16), even if atom k that is connected to j via the bonding is of $r_{ik} < r_c$ (while the k's contribution is counted).

For comparisons, we evaluated the first term in Eq. (14b) [viz., Eq. (3a)] with three other methods. First, the straight truncation, viz., the sum of the bare Coulombic potential with the AC mode,

$$E_{\mathrm{ATOM}}(x) = \frac{1}{2} \sum_{i \in \mathcal{N}} \sum_{\substack{j \in \mathcal{N}_i \\ r_{ij} < r_c}} \frac{q_i q_j}{r_{ij}}, \tag{23}$$

was calculated (we denote it by "ATOM cutoff"). Second, the sum of the bare Coulomb with the so called group-based cutoff (GC) mode was evaluated; here, all of the interactions in a molecule are counted if at least one atom in the molecule is inside the cutoff sphere (denoted by "RESA cutoff" which originally abbreviates the residue-based cutoff using minimum atomic distance). Third, in the zero-charge (ZC) scheme with wide applications,[28,32–46] we used the force-switching Wolf (FSw-Wolf) method,[47,48] which was designed in a consistent manner to prevent the nonzero-charge states artificially generated by a simple cutoff truncation. The difference between the ZC and ZD schemes is that, for neutrality, the former takes into account only the charges and the latter considers both the charges and dipoles. The energies defined by these methods were calculated under the 3D minimum image convention, viz., effectively, the 3D PBCs.

C. Accuracy of energy

The error of the Coulombic energy in the ZD summation method at configuration x was estimated through the difference between the energy $E_{\mathrm{ZD}}^{(\mathrm{NB})}(x)$ [Eq. (19)] and the reference energy $E_{\mathrm{Ref}}(x)$. The latter was evaluated by the Ewald method,[20] using the real part cutoff length of 12 Å and the damping factor of 0.35 Å^{-1}, where the Fourier part evaluated all the terms such that the individual contributions fall below the machine precision.[49] The total error was obtained by the average of the error ratio over the $n_x = 1000$ configurations generated by the NTV run described in Sec. III A, as

$$\Delta_{\mathrm{ZD}} \equiv \frac{1}{n_x} \sum_{x} \left| E_{\mathrm{ZD}}^{(\mathrm{NB})}(x) - E_{\mathrm{Ref}}(x) \right| / \left| E_{\mathrm{Ref}}(x) \right|. \tag{24}$$

Similar energy errors were estimated for the bare Coulombic energy, E_{ATOM}, the Coulombic energy with the RESA cutoff, E_{RESA}, and the Coulombic energy by the FSw-Wolf method, E_{FSw}. For these energies, we used formula (14b) [viz., the first term is replaced with the individual energy formula; also with E_{Ref}], and denoted the errors for the three energies by Δ_{ATOM}, Δ_{RESA}, Δ_{FSw}, respectively.

D. *NEV* simulation

To consider the stability of the MD simulation, we investigated the total-energy conservation in a 1 ns NEV MD run of the water system, using the ZD summation methods with $\alpha = 0$ and $\alpha = 0.1$. Initial molecular velocities were set such that the kinetic energy corresponds to the room temperature. The SHAKE algorithm was used to maintain the shape of the TIP3P molecule. We used the AC-mode cutoff with $r_c = 12$ Å for both the electrostatic and vdW interactions in the NEV simulations.

E. Dielectric properties

Since dielectric properties often strongly depend on the simulation conditions, we prepared the samples very carefully. By a preliminary equilibration MD run for 1 ns of the water system under the *NTP* ensemble with $T = 300$ K and $P = 1$ atm, we determined the average value of the MD cell length to be $L_0 \equiv 50.400$ Å. We chose a configuration x_0 at the time when the cell length L is closest to L_0. We then started an NTV MD simulation at $T = 300$ K with the cell length of $L = 50.399$ Å and the initial configuration x_0, for 10 ns. Such a long run is necessary to obtain a reliable value for the dielectric properties, as investigated in Refs. 50–52. The electrostatic calculations were performed by the ZD summation method with the damping parameter of $\alpha = 0$ and the cutoff length of $r_c = 12$ Å, with $\alpha = 0$ and $r_c = 14$ Å, and with $\alpha = 0.1$ and $r_c = 12$ Å. A similar long run was also performed by the PME method[31] with the same parameter values denoted in Sec. III A.

The distance-dependent Kirkwood factor G_K was calculated as follows:[53,54]

$$G_K(r) \equiv \left\langle \frac{1}{m} \sum_{a=1}^{m} \sum_{\substack{b \\ r_{ab}<r}} \frac{(\mu_a \mid \mu_b)}{\|\mu_a\| \|\mu_b\|} \right\rangle, \tag{25}$$

where μ_a $(\in \mathbb{R}^3)$ is the dipole moment of molecule $a = 1, \ldots, m$ [$(\cdot \mid \cdot)$ is the standard inner product on $\mathbb{R}^3$], and the distance between molecule a and b, r_{ab}, was measured by their O–O length. The brackets, which approximate the ensemble (time) average, are the average of the samples that were picked up at every 1000 steps during the 10 ns time series. Namely, (the cosine of) the angle between two dipole moments of water molecules contained in the sphere of radius r is averaged over the molecules and the samples.

The dielectric constant ε was estimated in the direct manner[52,55]

$$\varepsilon \equiv 1 + \frac{1}{3L^3 k_B T \varepsilon_0} (\langle \|M\|^2 \rangle - \|\langle M \rangle\|^2), \tag{26}$$

where k_B is Boltzmann's constant, ε_0 is the vacuum permittivity, and M is the total dipole moment of the system, $M \equiv \sum_{i\in\mathcal{N}} q_i x_i = \sum_a \mu_a$ (note that M and μ_a are independent of the origins of coordinates if the total charge of the system and that of molecule a, respectively, vanish). Brackets are the same average as above.

F. Radial distribution function

Regarding a static property of water, we measured the radial distribution function (RDF), $g(r)$, with respect to the distance, r, of two oxygen atoms, which are the vdW interaction sites of the TIP3P model. Similar to the dielectric properties, the configurations were sampled during the 10 ns at every 1 ps via the NTV run, using the ZD summation and PME methods, respectively. Namely, we calculated

$$g_0(r) \equiv \left\langle \frac{1}{m} \sum_{a=1}^{m} \rho_a(r) \right\rangle = \left\langle \frac{1}{m} \sum_{a=1}^{m} \sum_{\substack{b \\ r<r_{ab}<r+\delta r}} 1/\delta V(r) \right\rangle, \tag{27}$$

and normalized it to obtain $g(r)$ with $\lim_{r\to\infty} g(r) = 1$. Here, $\rho_a(r)$ is the number density for oxygen atoms that exist in the distance with $r < r_{ab} < r + \delta r$ from molecule a, and $\delta V(r)$ is the volume of this spherical shell; the brackets mean the sample average.

IV. RESULTS AND DISCUSSION

A. Accuracy of the energy

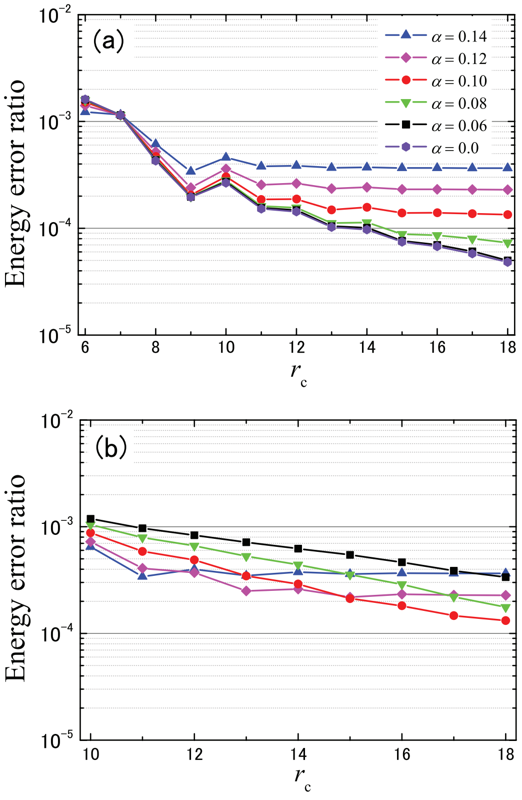

FIG. 1. The error ratio of the electrostatic energy [Eq. (24)], using the reference energy obtained by the Ewald method, in the TIP3P bulk water system. (a) The error ratio for the ZD summation method, Δ_{ZD}, and (b) that for the FSw-Wolf method, Δ_{FSw}, are shown. The parameters r_c (Å) and α (Å^{-1}) indicate the cutoff length and the damping factor, respectively, involved in the energy formulas in both methods.

Figure 1 shows the energy errors calculated for the current ZD summation method and for the scheme of the ZC method, FSw-Wolf method. In both methods, the error was lower for a larger cutoff length, and sufficient accuracies were attained at a practical cutoff distance, e.g., 11–16 Å. In the ZD summation method, the energy error was about 0.015% at $r_c = 11$ Å , 0.01% at $r_c = 13$ Å, and less than 0.01% at $r_c = 15$ Å with $\alpha \le 0.06$. In particular, small α values, e.g., $\alpha < 0.1$, gave superior results in the practical cutoff length region. This is in contrast to the results of the ZC method, where the damping effect is important, viz., a large α value gave a small error, especially for a small r_c. Although we noticed in our previous studies for the sodium chloride system that as α becomes small the ZD summation method is superior to the ZC method,[24] the current clear contrastive behavior between the two methods with respect to the α-parameter dependence was unexpected and surprising. This difference between the two methods can be detected from the fast *crossing* behavior seen in the results of the ZD summation method; i.e., the crossing between the curves with different α values occurs at a very small cutoff length, which is in fact $r_c \cong 7$ Å. In the ZC method, this crossing occurs slowly, i.e., it is observed at $r_c \gtrsim 12$ Å. In other words, for a very large r_c, the ZC with a smaller α would give a superior result, as compared to that with a larger α. Below we consider the reasons and influences regarding the differences in the two methods.

1. Crossing: Parameter dependencies and comparison with ZC scheme

a. Reason for the crossing We begin with the reason why the crossing between the curves with different α values occurs. Note that the following matters are applicable to both the ZC and ZD summation methods.

As the cutoff length r_c increases, the error tends to decrease. The reasons seem to be trivial but should be reconsidered for further discussions, and thus are provided as follows: (a) the replacement by the ZD summation, Eq. (1), makes a better approximation for a larger r_c, since the members in the neutralized subset ($\mathcal{M}_i$ for each i) are contained in the cutoff sphere; viz., for a larger r_c the subset is larger *relative to the whole system*; and (b) the excess energy approximation [Eq. (6)] is better for a larger r_c, since the neutralized subset can be larger *relative to the cutoff sphere* for a large r_c (by increasing the degrees of freedom for the cancellations; for more detailed discussions, see Sec. IV D 3).

However, in increasing r_c, the error approaches a certain tolerance value (appearing to be the convergent value), which is mainly governed by the approximation ignoring the "Fourier part." This error, measured by the degree of approximation in Eq. (7), is irrelevant to r_c and greater for a larger α; in fact, the minimum α, viz., $\alpha = 0$, gave zero error for this approximation (also see a recent mathematical analysis of the convergence of the Wolf summation with the zero damping factor applied to 3D PBC (Ref. 56)).

Imagine two curves, one corresponding to a small α and the other to a large α. For a smaller r_c, the damping effect by the damping factor α is still effective, so that a larger α gives a smaller error. In contrast, for a large r_c, the Fourier-neglect error remains and becomes prominent as demonstrated above, so that a larger α gives a greater error. These two compensating factors yield the crossing of the curves.

b. Reason for the crossing at a smaller cutoff in the ZD summation method We then provide an explanation for why the crossing occurs at a much smaller r_c in the ZD summation method, as compared with that in the ZC method. First note that the degree of approximation ignoring the Fourier part, Eq. (7), is common between the ZC and ZD summation methods. Also note that the approximation of the replacement by the neutralized summation, Eq. (1), is also common between the two methods, whenever we suppose that almost all of the samples $\{x\}$ are the ZD states (note that the ZC method can be applied to the ZD states, since it can be derived from the same conditions as those in the ZD summation method, ignoring only the zero-dipole condition[24,47]). Thus the difference in the accuracy between the methods appears in the approximation of the excess energy. The excess energy, Eq. (5), can be more accurately evaluated in the ZD summation method than in the ZC method, due to the above supposition regarding the states; and the difference in the accuracy of the excess energy is larger as α becomes smaller, since the difference between the two methods measured by the energy formula is larger as α becomes smaller.[24] Therefore, the energy accuracy refinement by the ZD summation method against the ZC method must be better as α becomes smaller. In fact, whereas the error curves for large α indicate similar values for the ZC and the ZD summation methods (compare the curves with $\alpha \geq 0.12$ in Figs. 1(a) and 1(b)), the degree of lowering the error curve of the ZD summation method in reference to the error curve of the ZC method is high for a smaller α (compare the curves with $\alpha < 0.1$ in the figures). These structures, as well as the appearance of the crossing itself stated above, gave the reason why the crossing occurs at a much smaller r_c for the ZD summation method than for the ZC method.

c. Effects of the fast crossing This significant property of the ZD summation method, viz., the crossing at a smaller cutoff, yields four effects. The first effect is simply the fact that a lower α becomes effective. Namely, as discussed above, in a practical cutoff distance region typically used in an MD simulation, lower α is more accurate and $\alpha = 0$ provides the best results. In other words, the damping is not important, at least for the water system. Considering the fact that the ZD summation method is a kind of extension of the Wolf method,[28,57] this feature is surprising, since one of the appealing points of the Wolf method is the damping effect. The second effect comes from the positive use of $\alpha = 0$, leading to the elimination of the complementary error function, and to the use of just the bare Coulomb function, $V(r) = 1/r$, in Eq. (2), and

$$u(r) = \frac{1}{r} + \frac{r^2}{2r_c^3} \tag{28}$$

in Eqs. (10), (16) and (18). This fact leads to the simplification of the implementation of the method and enhances the speed, even in high-performance computational architectures. Third, from a practical viewpoint, it is important that we can be free from the parameter choice if $\alpha = 0$ is always the best. This point will be discussed again in Sec. IV D 3. For the fourth effect, note that $\alpha = 0$ implies the vanishment of the Fourier part, so that its neglect is no more than the error [viz., Eq. (7) becomes *exact*]. Thus, the factors of the error come from only the replacement by the neutralized sum and the approximation of the excess part. Hence, we can reduce the error without the saturation, as in the use of a larger cutoff length [recall (a), (b) stated in Sec. IV A 1 a].

2. Comparison with conventional methods: ATOM and RESA

As stated, the ZD summation method utilizes the AC mode, but utilizes the pair function $u(r)$ defined by Eq. (10), which is not simply the pure Coulombic function $1/r$, even if $\alpha = 0$ (see Eq. (28)). At the same time, the electrically neutralizing condition is ensured through the functional form of the energy, but not through the GC mode. The protocol of the GC mode usually defines neutrally charged molecular units in each molecule, and the cutoff is done in every unit, which ensures the neutrality for the total "switch-on" interactions. Namely, either the AC mode procedure or the charge neutrality can be taken into account by an individual conventional method, but both of them can be utilized by the ZD summation method alone.

We calculated the energies obtained by these conventional basic ideas, as shown in Fig. 2, to confirm the attainment of the $\alpha = 0$ ZD summation method with the AC mode. Namely, in order to see the effect of the current pair function form, we compared the energy error with that obtained by the conventional pure Coulombic function with the AC mode (see "ATOM cutoff"). In addition, to see the effect of the current

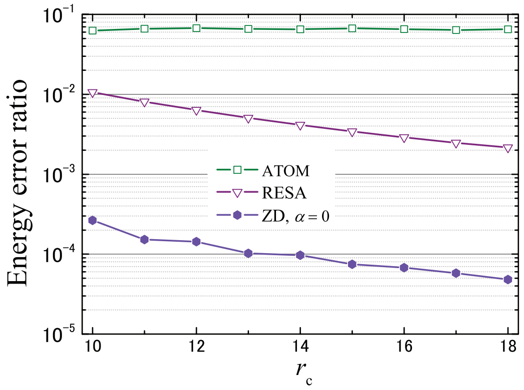

FIG. 2. The error ratio of the electrostatic energy, using the Ewald energy as the reference, in the TIP3P water system. The ratios are shown for the ZD summation method with $\alpha = 0$, Δ_{ZD}, the RESA group-based cutoff method, Δ_{RESA}, and the atom-based cutoff method, Δ_{ATOM}.

neutralizing idea with the aid of AC, we compared the energy error with that obtained by the group-based neutralizing cutoff of the pure Coulombic function (see "RESA cutoff"). In the GC modes, we used the "RESA cutoff" (defined in Sec. III B), which seems to be natural and could avoid the artifact yielded by the other GC modes, as stated in Sec. IV D 2. Figure 2 shows that the error of the ZD summation method is smaller than the group-based "RESA cutoff" by a factor of 100, and also smaller than the "ATOM cutoff" by a factor of 1000. We thus understand that the ideas, the atom-based cutoff and the neutrality, are useful, but their combination with a suitable energy functional form, as in the ZD method, is also important.

B. Radial distribution function

The static factor is important to understand the system, and we calculated the RDF of the water system. As shown in Fig. 3, the results of the ZD summation method within a 25 Å distance are similar to those of the PME method. The discrepancies between the two methods are sufficiently small except near the cutoff distance, where about 1% order errors exist. Considering the fact that this kind of discrepancy, which seems to be oscillating around the cutoff, is also found in another effective truncation method,[58] it appears to be an artifact characteristic of the general truncation method, rather than particular to the ZD summation method. To understand the discrepancy, we investigated the error provided by several α values, other than $\alpha = 0$, which is the best regarding the energetic accuracy. We observed that both a large α and a large r_c give small discrepancies around the cutoff length. A large α or a large r_c gives more damping, so that the pair function is smoother near the cutoff distance [viz., even though the function $u - u(r_c)$ is of class C^1 for any α and r_c, it tends fast to zero at $r = r_c$ for a larger α or larger r_c; in fact the Hessian of u at r_c is positive and strictly monotone decreasing with respect to both α and r_c]. That is, devising a certain smoothing method around the cutoff distance may reduce the discrepancies. To do this, a technique for switching higher order derivatives or a function smoother than u would be useful, in combination with the ZD scheme.

C. Dielectric properties

The dielectric properties require a long simulation duration to yield reliable results, as discussed in Refs. 50–52. For these properties, the dielectric constant ε and the distance-dependent Kirkwood factor $G_K(r)$ were calculated via the 10 ns MD simulation using the ZD summation method and that using the PME method. Figure 4 shows the time-developments of the ensemble (time) averages of the dielectric constants for these methods. Namely, they are cumulative averages, and the averages of the short durations were far from the convergence, even with the PME method. The convergences were seen after 6 ns, consistent with the results reported by Gereben and Pusztai,[52] whereas they used different water models than ours. This suggests that a long duration is also needed to compare the dielectric properties at a reliable level for the TIP3P model. The results of both $r_c = 12$ Å and $r_c = 14$ Å agree well with that generated by the PME method after 6 ns. The final results of ε are described in Table I. Note that the comparison between the experimental and computational results might be done in a more suitable manner, because the value depends on the choice of the potential model of water,[55,59] the system size,[52,60,61] and the ensemble size and kind.[50,52]

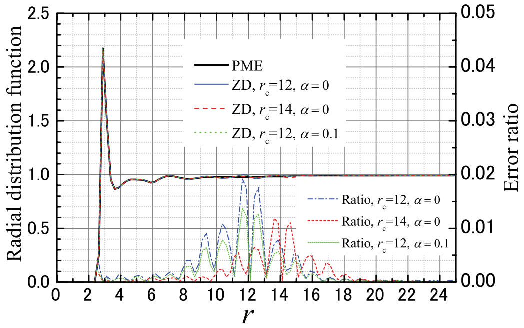

FIG. 3. Radial distribution functions (no dimension) with respect to the distance of two oxygen atoms, r (Å), for the TIP3P water system, obtained by the ZD summation method [with several values of the cutoff length r_c (Å) and the damping factor α (Å^{-1})] and the PME method. The error ratios, in comparison to the results of the PME method, are also shown.

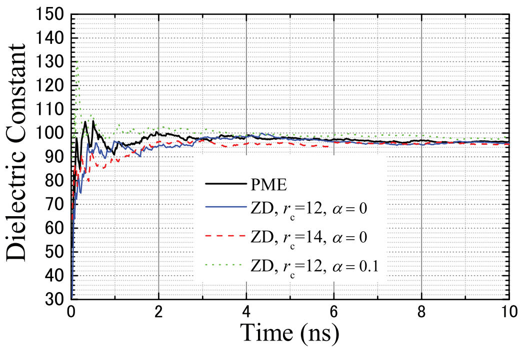

FIG. 4. Cumulative time averages of the dielectric constants [Eq. (26)] for the water system, each obtained by MD runs using the ZD summation method [with several values of the cutoff length r_c (Å) and the damping factor α (Å^{-1})] and that using the PME method.

TABLE I. Dielectric constant ε (no dimension) of the TIP3P water system obtained from the time average of 10 ns MD simulations via the ZD summation method or the PME method, using the parameters, cutoff length r_c (Å) and damping factor α (Å^{-1}). The standard deviations are shown in parentheses.

Method: r_c, α	ZD: 12, 0	ZD: 14, 0	ZD: 12, 0.1	PME: 12, 0.35
ε	95.8 (4.6)	95.2 (4.1)	98.1 (4.8)	96.3 (4.6)

Figure 5 shows $G_K(r)$ for the ZD summation methods with $r_c = 12$ Å and $r_c = 14$ Å and that for the PME method. There is no significant hole, as often seen in conventional cutoff-based methods (see below), and the results of the ZD summation method are similar to those of the PME method in a long range distance. As discussed regarding the RDF, some discrepancies around the cutoff length, which may have originated from the truncation protocol, are observed, and must be properly explained. A similar origin may generate the discrepancies seen in a larger distance, or they may be due to the difference in the boundary conditions used in the two methods.

In general, conventional truncation methods, including the potential deformation method and the RF method, often have significantly large discrepancies from the Ewald method, regarding the dielectric properties. For example, Mark and Nilsson[12] found a hole, located around $r_c = 12$ Å, in $G_K(r)$ via the straight cutoff truncation method in modified TIP3P water. For a larger cutoff length, similar results were also found by Spoel and Maaren[13] ($r_c = 18$ Å) in the TIP3P water model with several system sizes, and by Yonetani[62] ($r_c \leq 19$ Å) who also revealed the nearly periodic structure of the discrepancies. The discrepancies were also found for the RF method in various water models, including TIP3P,[13,63] TIP4P,[13,64,65] SPC,[13,61,65] and MCY[66] models. Such discrepancies are prominent in the GC mode, and will be reconsidered in Sec. IV D.

Although the ZD summation method is of a type of truncation method, the above studies imply that it should be distinguished from the other truncation methods, at least regarding the ability to produce the dielectric properties. The large dielectric constant with the averaged vanishing total dipole moment means that the total dipole moment largely fluctuates around zero in the ensemble. This fact apparently contradicts the assumption in the ZD summation method that the dipole moment is always zero in a certain particle subset. However, such a subset is locally defined, and the most suitable members of the subset can be chosen. Thus, the two issues can be consistent when we consider that such a subset exists at every time and that the members of the subset change depending on time. Otherwise, the correct fluctuations (dielectric constant) cannot be obtained, due to the effect of the assumption break on the dynamics of the system. It is noted that the isotropic periodic sum (IPS) method,[67] which is also a truncation method, produces good results for the dielectric properties of several water models for long cutoff lengths in a 1 ns simulation.[58]

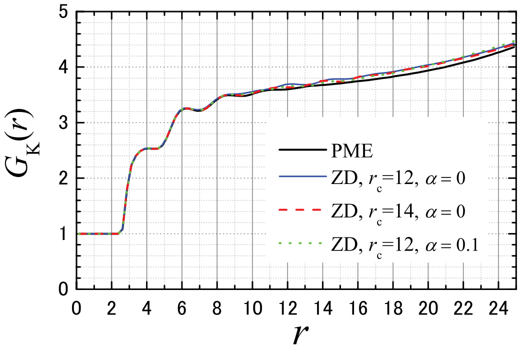

FIG. 5. The distance-dependent Kirkwood factor (no dimension) [Eq. (25)] of the water system, calculated via 10 ns NTV MD simulation using the ZD summation method [with several values of the cutoff length r_c (Å) and the damping factor α (Å^{-1})] and that using the PME method.

D. Truncation protocol

Thus far, we have seen that the properties of bulk water can be realistically produced by the current ZD summation method, if we suitably address the following issues in treating electrostatic interactions: (a) removal of the bonding (1-2,3,4) interactions, (b) use of the truncation mode (atom-based or group-based), (c) assignment of the parameter values. The detailed discussions below on these issues are formally for the ZD summation method, but are expected to be useful for cutoff-based methods closely related to the ZD summation method, such as the Wolf method,[28,57] the RF method[15,16] and the pre-averaging (PA) method.[68,69] The discussions might also be useful for other truncation methods, including the force matching method,[70,71] IPS method,[67,72] and the screening scheme using the Yukawa potential.[73]

1. Removal of the bonding interactions

For issue (a), in the ZD summation method, the removal of the bonding (1-2,3,4) interactions has been done in the manner stated in Sec. II B. This manner is not peculiar, and is also seen in calculating the Ewald summation.[31,74,75] In fact, it is natural if we read Eq. (12) [except E_{vdW}] as

$$E_{\mathrm{Ele}} + E_{\mathrm{Bond}} \tag{29a}$$

$$= \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i-\mathcal{N}_i^{\mathrm{B}}} \frac{q_i q_j}{r_{ij}} + \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}} k_{ij}\left(r_{ij} - r_{ij}^0\right)^2 + \text{etc.} \tag{29b}$$

$$= \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i} \frac{q_i q_j}{r_{ij}} - \frac{1}{2}\sum_{i\in\mathcal{N}}\sum_{j\in\mathcal{N}_i^{\mathrm{B}}}\left[\frac{q_i q_j}{r_{ij}} - k_{ij}(r_{ij} - r_{ij}^0)^2\right] + \text{etc.} \tag{29c}$$

[the second term in Eq. (29b) is the interaction to keep each bond length at the equilibrium value r_{ij}^0, and "etc." is the other bonding interactions plus the "1-4 electrostatic" interactions] and consider the first term in Eq. (29c) as the Coulombic interactions of "bare" N point charges, which can be purely treated by the electromagnetic theory, while the second term describes the interaction for the bonding pairs, which can be treated by the mechanics theory by supposing that $q_i q_j$ is simply a parameter with the physical dimensions of a charge square. This view is the essence of our starting point, Eq. (14b), for applying the ZD summation to molecular systems.

However, another formula may be possible if we employ another consistent calculation idea. In particular, from the viewpoint of the force field consideration in a molecular system, it might be natural to employ just the atomic form of Eq. (9), by simply replacing $\sum_{j\in\mathcal{N}_i,\, r_{ij}<r_\mathrm{c}}$ by $\sum_{j\in\mathcal{N}_i-\mathcal{N}_i^\mathrm{B},\, r_{ij}<r_\mathrm{c}}$ [in other words, in Eq. (16b) or (19), dropping the second term and $\sum_{j\in\mathcal{N}_i^\mathrm{B},\, i<j} q_j$ in the third term; correspondingly, in the force, Eq. (20), dropping the second term]. For example, such a treatment might also have been used in the RF correction protocol. However, we still do not have an interpretation to consistently assess such an idea, according to the neutralized conditions currently considered.

Nevertheless, aside from the theoretical view, to achieve a rough estimation of $E_\mathrm{ZD}^{(\mathrm{NB})}(x)$ [Eq. (16)], the following most simple (*ad hoc*) implementation,

$$\sum_{i\in\mathcal{N}} \sum_{\substack{j\in\mathcal{N}_i-\mathcal{N}_i^\mathrm{B}\\ r_{ij}<r_\mathrm{c}\\ i<j}} q_i q_j [u(r_{ij}) - u(r_\mathrm{c})], \tag{30}$$

meets this requirement, if we use a sufficiently large r_c and if the electric neutrality in each bonding set holds,

$$\sum_{j\in\mathcal{N}_i^\mathrm{B}} q_j = -q_i \quad \forall i \in \mathcal{N}. \tag{31}$$

To see this, it suffices to show in Eq. (16a) that the second term is nearly the negative value of the last term, viz., the bonding term compensates for the self energy term [while the third term vanishes, owing to Eq. (31)]. In the effective range of the bonding interaction, the pair function $u(r) - 1/r = -\mathrm{erf}(\alpha r)/r + br^2$ in the second term of Eq. (16a) [or see Eq. (19)] can be approximated by $-2\alpha/\sqrt{\pi}$: this is because br^2 is nearly zero in the range, since b is small for large r_c, and because $\mathrm{erf}(\alpha r)/r$, especially for a small α, is almost constant in the range (see the discussion in Sec. IV E and Fig. 7); viz., $u(r) - 1/r \sim -\mathrm{erf}(\alpha r)/r \sim -\lim_{r\to 0}\mathrm{erf}(\alpha r)/r = -2\alpha/\sqrt{\pi}$. This fact, again using Eq. (31), leads to the desired compensation.

2. Truncation mode

For issue (b), the AC mode was used in the current ZD simulations. However, many simulations treating molecular systems utilize the GC mode. Namely, all atom–atom interactions in any two molecules should be on or off, according to a certain "marker" being inside or outside the cutoff sphere, respectively. Such a marker is usually chosen to be a certain center of the molecule[76] (e.g., the center of mass,[63,66] the center of geometry,[77,78] or possibly, the center of absolute charges), a certain atom (e.g., oxygen in a water molecule[65] and C_α in a residue of protein[79]), or a certain distance (e.g., a minimal atomic distance between the two molecules[30,79]). There are several variations: smoothed on-off is also possible,[14] and a certainly defined (neutrally charged) atom group is usually used, instead of a whole molecule itself (in particular, for a large molecule).

The reasons why the GC has been frequently used are as follows: (1) [Chemical] it would be chemically natural, since a force-field is usually developed on molecule–molecule (not atom–atom) interactions; (2) [Energetic] to avoid a large amount of energy fluctuations near the cutoff distance when one encounters the straight atom-based cutoff for two molecules, particularly in case where the strength in an individual atom–atom interaction is significantly large, as compared with that in the molecular–molecular interaction;[14,79] this fluctuation is physically unnatural and causes instabilities in MD simulations; (3) [Screening] if both molecules are neutral, then the leading term of the molecular interaction can be described by the dipole–dipole interaction [$\sim(r_\mathrm{MM})^{-3}$], whose enhanced screening or damping feature, as compared with the charge–charge interactions, is conformed to justify the interaction truncation.

However, when we use the idea in the current ZD summation method, we can balance the above three requirements with the AC mode. Namely, (1) the interaction naturally vanishes smoothly at the cutoff length, so the truncation even in the AC mode is not unnatural. This smoothly zero-damping (vanishing) feature also enables us to avoid the large energy fluctuations described above in (2); in fact, this can be confirmed by the AC mode utilizing a certain smoothing procedure, e.g., the force-switching technique.[14] For (3), in the ZD summation method, the damping (screening) factor is already involved, and the neutrality of the charges along with the dipoles is taken into account, not by individual molecules but by a set of molecules in the cutoff sphere, and is reflected by the energy formula itself.

We would like to draw attention to the artifacts of the GC mode itself. As clearly discussed by Baumketner,[76] a dipole layer on the truncation sphere of each atom i, artificially created by the GC in the following mechanism, results in an energy error: (i) a water molecule with the "center" that is near and *inside* the cutoff sphere interacts with i, even if the hydrogen atoms are outside the sphere, whereas (ii) a molecule with the center that is near and *outside* the sphere does not interact with i, even if the hydrogen atoms are inside the sphere;[80] these interaction unbalances break the compensation of charges near the truncation surface,[81] so that the outward dipoles across the surface generate the layer. Although an atomic force error may be well canceled if the layer is spherically symmetric, the energy error remains in *any* cutoff length; moreover, such symmetry is easily disrupted in a heterogeneous system.[76] The artifact in the Kirkwood factor of a water system using the GC was also reported previously,[12,13,63–65] as stated in Sec. IV C, and was lessened by the AC mode[82] when utilizing either the potential deformation (via the force-switching[13] or more effectively via the shifting[12,13]) or a truncated octahedron cell (space-filling polyhedron that is more spherical than a cube).[17] As for the other systems, the artifact in the explicitly solvated peptide conformation in the GC mode truncation was obtained,[78] and physically reasonable behaviors were confirmed in the AC mode with a force-shifting method.[83] Also note that the cutoff center should be consistently chosen. For instance, instead of the standard choice of the center, i.e., the "marker" that is defined in an identical manner for every molecule, if we choose just a single atom as the center, then there should be inconsistency such that the interaction from i to j is counted, but the interaction from j to i is not counted.

Considering both the background of the motivation of the GC mode and the artifacts themselves, we are not forced to use the GC mode. As well as the truncation method itself, the truncation mode and the harmonization of the bonding interaction should be suitable for an effective estimation of the electrostatic interaction. To reveal an artifact hidden in the default setting or in an *ad hoc* combination of relevant techniques, it would be better to pay more attention to such elemental and general techniques, although they seem to be trivial matters.

If we dare to use the GC mode in the ZD summation method (cf. the GC protocol described in Sec. IV E), we encounter an increase of the pair-potential function value beyond the cutoff length. Of course, such an artificial feature can be removed if we simply redefine $u(r) = u(r_c)$ for $r > r_c$. However, the artifact of the GC mode itself is intrinsic, and as demonstrated above, we recommend the AC mode in the ZD summation method. We have actually used the AC mode for the current ZD method in all of the simulations, and the results were far better than those of the conventional AC method, and better than those of the conventional "RESA cutoff" GC method, which nevertheless can lessen the artifact (as stated in remark[80]) intrinsic to the GC mode (we thus chose the "RESA cutoff" for the comparison study) and consider the charge neutrality.

3. *Assignment of parameter value*

For issue (c), we have found the parameter dependencies to be clear, along with the observation that $\alpha = 0$ is recommended in a realistic cutoff distance region. In contrast to the ZC scheme, this feature is favorable because we can be free from the choice of the optimal parameter value, as noted in Sec. IV A 1 c.

The ZD summation method with $\alpha = 0$ is closely related to other methods, such as the RF and PA methods, as stated previously.[24] This fact may give the reason why $\alpha = 0$ is effective, since these methods have provided lots of reasonable simulation results, as investigated in Refs. 17, 50, 82, 84–86 for the RF method and Refs. 68, 69, 87–90 for the PA method, respectively. However, note that although they give similar formulas to Eq. (16) in the ZD summation method, they are not identical and in fact their physical interpretations are totally different from that of the ZD scheme. The specific features of these two methods are represented by their individual requirements. In fact, the RF method requires a pre-assigned dielectric constant outside the truncation sphere, $\varepsilon_{\mathrm{RF}}$, which is often different from the resultant value. The PA method requires a particular cutoff distance, $r_{\mathrm{m}} \equiv (3/4\pi)^{1/3}L \doteqdot 0.62L$, which would become long enough because L is the MD cell length.

It should be noted that the best parameter is not necessarily $\alpha = 0$, and in general it depends on the system of our target. In fact, as investigated in the NaCl ion system,[24] the damping effect via $\alpha > 0$ is still effective in a practical cutoff distance for the liquid states, and it is more effective for the crystal state. In other words, the crossing of the energy error curves for individual α values occurs at a small r_c for the water system, a medium r_c for the NaCl liquid system, and a large r_c for the NaCl crystal system. Since fast convergence enhances fast crossing, these results can be interpreted such that the system with more randomness or the system involving more mobile particles experiences faster convergence.

We consider how this interpretation can be supported. First, recall the reasons, explained in Sec. IV A 1, for the accuracy improvement according to the enlargement of the cutoff length: (a) the replacement by the ZD summation, Eq. (1), makes a better approximation for a larger r_c, and (b) the excess energy approximation is better for a larger r_c. More randomness or more mobility would enhance the construction of a *favorable* neutralized subset in an easier manner; specifically, they must provide a more flexible combination so as to construct a neutralized subset that is larger (or an excess subset that is smaller) relative to the cutoff sphere. Since this feature provided by randomness or mobility would especially enhance (b) above in the following mechanisms, the fast convergence follows. The estimation of the excess energy is more accurate if the displacement vector becomes small [see the last term in Eq. (6)], which can be attained in the case where (A) there are fewer non-zero components of the vector, and (B) the value of each non-zero component is small. The number of the non-zero component grows according to the increase in the surface-area, as increasing r_c in general; but the randomness or mobility can moderate the growth of the number, viz., they provide an advantage in view of (A). On the other hand, as r_c increases, the chance of choosing a large (relative to the sphere) neutralized subset becomes large, and in other words, the chance to keep (B) grows; and the randomness or mobility can enhance this chance. These are the possible mechanisms for the enhancement of (b) above. Regarding the convergence speed, the dependence of the Fourier-part approximation [Eq. (7)] on the system configuration should also be an important factor.

E. Stabilities

Total energy conservation in the NEV MD simulation, or, in general, the conservation of the invariant function[91,92] of the equations of motion given the statistical mechanics ensemble, is important to conduct an accurate and stable simulation. Figure 6 shows the total-energy trajectories of the NEV simulations on the water system, provided by the ZD summation method. Considering the fact that the SHAKE algorithm was used to maintain the rigidity of the molecular shape and that the straight cutoff of 12 Å was used for the vdW interactions, the energy conservation is sufficient in the tolerance for an ordinary simulation. The splitting of the trajectory with $\alpha = 0$ and that with $\alpha = 0.1$ is due to the error of the electrostatic potential energy and the initial splitting in the numerical

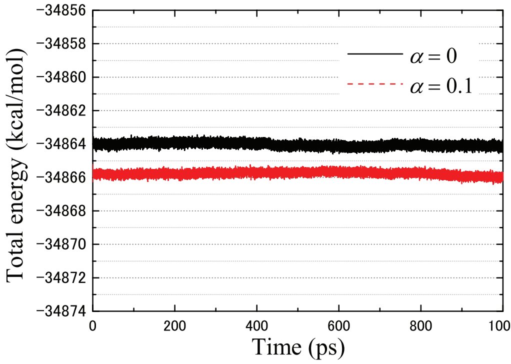

FIG. 6. Total-energy trajectory of the NEV MD simulation for the water system, using the velocity-Verlet integrator with a 1 fs timestep. The electrostatic energy was calculated by the ZD summation method, with the cutoff length $r_c = 12$ Å and the damping factor $\alpha = 0$ or 0.1 Å^{-1}.

integration yielded from the initial condition difference (individual atomic velocities).

We recommend the AC mode cutoff, and in fact, we used it in the NEV simulations. Alternatively, in practice, we can choose the conventional procedure utilizing the GC mode to make the interaction table with less computational cost than that in the AC mode, along with a certain buffer length to set a (pre)cutoff distance. Then, in the actual pair-list loop implemented for estimating Eqs. (19) and (20), the AC-mode cutoff with the originally intended cutoff length, r_c, can be used.

We note the second term in the energy formula, Eq. (19), which is not contained in the study of the pure atomic system discussed in Ref. 24. The atomic distance r_{ij} in this bonding term oscillates quickly in general, inferring the requirement for special care to numerically integrate the equations of motion. Fortunately, however, we are free from such special handling, since the variation of the function $-\mathrm{erf}(\alpha r)/r + br^2$ is actually small in the range of the bonding interactions. In fact, for $\mathrm{erf}(\alpha r)/r$, it appears to be clear; for br^2 notice that the constant b [Eq. (21)] is strictly monotonic decreasing with respect to both α and r_c, and is very small in many cases, e.g., $b = 1/2r_c^3$ even if $\alpha = 0$; see Fig. 7.

In addition to the favorable property for this term, the good results in the current method are basically supported by the employment of the following issues: an atom-based cutoff, a smooth potential function, and a simple pairwise form. The first two issues are useful not only to diminish the artifact in the cutoff procedure as demonstrated, but also to conduct the stable MD simulation. The last issue seems to be trivial, but should be reconsidered since the method using a non-pairwise form often causes a side effect. For example, although the fast multipole method[93] used in the tree-based approaches is very efficient to approximate the function value at a very long distance, it suffers from a lack of good energy conservation, in general.[94–96] The other example is seen in the PME method used in the grid-based approaches.[97] In contrast, the approach with the above three issues also ensures the conservation of the total momentum (the center of mass) of the system. This is yielded by the vanishment of the total force, and in fact it was almost zero (in the double precision accuracy) via the ZD summation method.

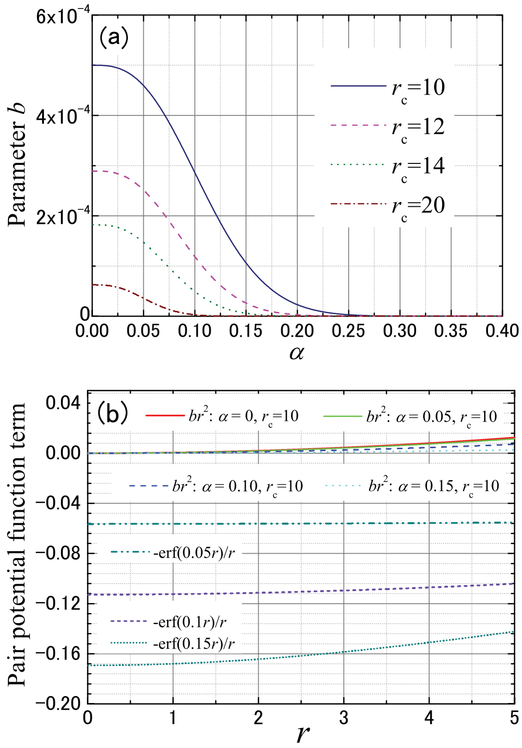

FIG. 7. The bonding term in the energy formula, Eq. (19), in the ZD summation method applied to a molecular system is represented: (a) Dependence of the constant b [Eq. (21)] on the damping parameter α, as well as on the cutoff length r_c; (b) Curves for $\mathrm{erf}(\alpha r)/r$ and br^2 for several values of α. A slow increase in br^2 ($r_c = 10$ Å) in the distance range of the bonding interaction is seen, which will be further emphasized for larger r_c due to the feature of b, as observed in (a).

F. Computational timing

In general, the real part of the PME method with short cutoff length requires a shorter computational timing than that of the ZD summation method. However, the difference becomes very small with increasing the number of parallel processors. This is shown by the computational timing of the ZD summation in a practical cutoff range[98] (supplementary material) for the current TIP3P water system, in comparison with that of the conventional real part of the PME method. The ZD summation method with $\alpha = 0$ has an advantage of a rapid computation of the Coulombic potentials and forces without calculating the complementary error functions, which always appear in the real part of the PME method. The results indicate that the computational timing required by the ZD summation method with a long r_c value could become comparable to that by the PME method including the Fourier part.

V. CONCLUSION

Some practitioner might think that the truncation method generally yields too many artifacts, and thus would exclude it when choosing a method for evaluating the electrostatic interactions. In this work, we showed that such an evaluation does not necessarily hold via the application of the currently developed ZD summation method to a molecular system. Here, we stated that, as well as the pair potential functional form itself, suitable treatments of the following issues are important: bonding-interaction removal, truncation-mode choice, and parameter-value assignment. For a fair judgment of the method, we should consider these issues at the same time.

Specifically, for the first issue, under the current neutralization principle, we presented a simple removal and discussed a manner for harmonizing the electrostatic and bonding interactions. We also provided a rough estimation of the electrostatic energy, giving rise to the compensation of the bonding interaction and the self energy terms.

For the second issue, reviewing the GC mode to recognize both the expected attainments and the unexpected artifacts, we argued that the AC mode coupled with the current ZD summation method can realize such attainments. The atom-based cutoff and the realization of neutrality can be individually or partly attained by the conventional methods. For example, the GC mode of the pure Coulombic function can attain the charge neutrality, and the ZC method coupled with the atom-based cutoff can attain the neutrality of charges, but not the neutrality of dipoles. These concepts can be concurrent in the ZD summation method, and the effects have been confirmed through the numerical comparisons with these conventional methods.

More specifically, the electrostatic energies estimated by the ZD summation method using an MD simulation trajectory were sufficiently accurate in a practical cutoff distance range for the TIP3P water system. They were better than those of the ZC scheme, and far better than those of the conventional atom-based and group-based cutoff truncations. For a static property, we calculated the radial distribution function on NTV MD simulations with the ZD summation method and confirmed its accuracy. The greater impact is in the ability to estimate the dielectric properties accurately, since, as indicated in a number of reports, many conventional cutoff-based methods fail, due to significant artifacts. The attainment by the ZD summation method was confirmed by MD simulations for estimating the dielectric constant and distance-dependent Kirkwood factor. We conducted long-term MD simulations, since the properties were measured by the fluctuations, which require a sufficiently long time to obtain a fine conclusion. We further discussed the compatibility of the large dielectric constant, which is a global property with respect to space and time, and the current monopole and dipole neutralizing assumption, which is a local property. In this sense, the application of the ZD summation method to a water system was challenging.

However, we should mention that there is still room for the refinement of the current scheme, since the comparison with the PME method showed the discrepancies around the cutoff distance in these static and dielectric properties. Although the discrepancies were small, a suitable effort to solve this issue is valuable. We surmised that the discrepancies are related to the smoothness of the pair potential function around the cutoff distance, so a certain smoothing technique would be useful for the solution.

Regarding the third issue, the ZD summation method has two parameters, cutoff length r_c and damping parameter α. Overall, $r_c = 12$ Å or slightly larger is typically sufficient to calculate the energetic, static, and dielectric properties. Such a cutoff length is practical and will be useful for an application to a very large system, using a certain specialized or parallelized computational architecture. Regarding α, small values (e.g., $\alpha \lesssim 0.1$) give superior results, and $\alpha = 0$ is the best, at least in the energy accuracy in a practical cutoff region. This means that the damping factor, which is critical in the ZC methods, viz., the Wolf method and their revisions, is not very important in the ZD summation method in the molecular system we treated. This is a surprising result, considering the fact that the ZD summation method was developed as an idealistic extension of the ZC method. This result was observed from the fact that the crossing of the energy error curves with individual α values occurs at smaller r_c in the ZD summation method, as compared with that in the FSw-Wolf ZC method.

The crossing originates from the balance between the effect of the damping by α and the anti-effect of ignoring the Fourier part, where the former is prominent in small r_c and the latter is prominent in large r_c. The fast crossing is due to the energy accuracy refinement by the ZD summation method against the ZC method, which specifically comes from the improvement in the accuracy of the excess energy for a smaller α. In addition to the theoretical aspect, we discussed the influence of the fast crossing or the fast convergence in the ZD summation method in practical views: (1) positive use of $\alpha = 0$ to speed up the computation without using the complementary error function; (2) freedom from the parameter choice, which is not trivial in the ZC scheme; (3) automatic elimination of the Fourier part via the no-damping procedure, implying that we can reduce the energy error to a desired level without saturation, as when utilizing a larger cutoff length.

Comparing the results of the water system with those of the ionic system, we discussed that the fast convergence in the energy in the water system comes from its randomness or mobility. We surmised that such randomness leads to a large neutralized subset relative to the cutoff sphere, and then enhances the accuracy improvement in the excess energy as the cutoff length increases. We expect that this speculation holds in many biological systems that have fully mobile solvent particles, but more investigations are needed to obtain a universal perspective.

The current ZD summation method can be used in both the Monte-Carlo calculation and the MD simulation. Since an MD simulation requires the numerical integration of the equations of motion, the stability in the simulation is a critical matter. Regarding this, in NEV simulations with the ZD summation method, we confirmed the conservation of the total energy. These results are ensured by the technical issues, such as the atom-based cutoff, a smooth potential function, and a simple pairwise form. The bonding term particular to the application to a molecular system does not require special care in the numerical integration.

This work numerically depicted practical, satisfactory results, regarding the accuracy and stability, from the ZD summation method applied to a molecular system. We believe that this fact, as well as the general discussions on the truncation protocol, also address the potential of the truncation method itself. It also suggests the efficiency of the torus boundary condition, in which the interactions are counted on a three-dimensional torus, although suitable coupling of the energy formula would be needed. Applications to various systems and reconsideration of the boundary conditions will be quite valuable for further understanding and refinement of the scheme. In particular, the application of the ZD summation method to heterogeneous systems is important to validate the potential of the method. We are performing a study on biological systems including a membrane protein and an aqueous DNA solution, and have obtained some positive simulation results, which will be described elsewhere.

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