Ewald sum corrections in simulations of ion and dipole solvation and electron transfer

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Periodic boundary conditions and Ewald sums used in standard simulation protocols require finite-size corrections when the total charge of the simulated system is nonzero. Corrections for ion solvation were introduced by Hummer, Pratt, and Garcia and refined by Hünenberger and McCammon. The later approach is extended here to derive finite-size correction for the Stokes shift and reorganization energy applied to electron-transfer reactions. The same correction term, scaling inversely with the box size, adds to the reorganization energy from the energy-gap variance, but is subtracted from the reorganization energy calculated from the Stokes shift. Finite-size corrections thus widen the gap between these two quantities which were recently found to diverge for protein electron transfer. Corrections to the free energy of dipole solvation and the variance of the electric field scale as m^2/L^3 with the solute dipole m and the box size L.

I. INTRODUCTION

Simulation of electrostatic interactions requires corrections for artifacts introduced by periodic boundary conditions in combination with Ewald sums.[1,2] Corrections become particularly significant for simulations of infinite-dilution ionic solvation when the total charge of the simulation cell is non-zero.[3–6] There are two corrections involved. The first correction is the self free energy of interaction of an ionic charge in the simulation cell with its periodic replicas and the neutralizing background charge in each replica cell. The neutralizing background charge is imposed by the requirement of periodicity of the electrostatic potential $\phi(\mathbf{r})$, which implies that the electric field should vanish at the boundary of the simulation cell. This condition is obtained from the Poisson equation

$$\int_V d\mathbf{r}\nabla^2\phi = -\oint_{S_L} d\mathbf{S}_L\cdot\mathbf{E} = -4\pi\int_V d\mathbf{r}\tilde{\rho} = 0. \quad (1)$$

Here, the electric field $\mathbf{E}=-\nabla\phi$ vanishes on the surface S_L of the simulation box and the charge density $\bar{\rho}$ is composed of that of the ion ρ and of the compensating uniform background charge

$$\tilde{\rho} = q\left[\rho - L^{-3}\right]. \quad (2)$$

A cubic simulation cell with the side length L is adopted here.

The replica charges and the background charge are introduced instantaneously when the ionic charge is altered (in analogy with solvation by electronic polarization). The corresponding contribution to the electrostatic energy of an ion comes in the form of free energy of charging[3,7]

$$u_{\rm el} = q\phi_s + \tfrac{1}{2}q^2\xi. \quad (3)$$

Here, $\xi = -2.837298/L$ is the Wigner potential of the lattice of replicas of the central cell surrounded by a conducting sphere[2] ("tin-foil" boundary conditions) and ϕ_s is the electrostatic potential of the solvent in the central simulation cell

$$\phi_s = \sum_{i=1}^{N}\sum_{\alpha} q_{i\alpha}\psi(\mathbf{r}_{i\alpha}). \quad (4)$$

Further, $q_{i\alpha}$ are partial atomic charges of N solvent molecules with coordinates $\mathbf{r}_{i\alpha}$. The Ewald potential is given as a sum of the real-space and reciprocal-space terms[1,8]

$$\psi(\mathbf{r}) = \frac{\mathrm{erfc}(\kappa r)}{r} + \frac{4\pi}{L^3}\sum_{\mathbf{k}\neq 0}\frac{1}{k^2}e^{-k^2/(4\kappa^2)+i\mathbf{k}\cdot\mathbf{r}} - \frac{\pi}{L^3\kappa^2}, \quad (5)$$

where $\mathrm{erfc}(x)$ is the complementary error function and the last term is chosen to make the Ewald potential integrate to zero over the cell volume[2,4]

$$\int_V d\mathbf{r}\psi = 0. \quad (6)$$

The decay parameter κ in Eq. (5) is typically chosen to be sufficiently large to eliminate the need to perform lattice sums in real space, $\mathbf{k}$ is the lattice vector in reciprocal space.

Because of the instantaneous character of solvation by replica charges, the second term in Eq. (3) needs to be added to the instantaneous electrostatic energy of the ion calculated along the simulation trajectory. When the simulated configurations are used to calculate thermodynamic free energies of solvation, the need for a second type of correction appears.

Solvation of an ion in a polar liquid occurs through the interaction of the ionic charge with the medium polarization induced by it. For a periodic system, it can be viewed as the interaction of the ion with the polarization density in the primary cell plus the interactions with dipole moments in the replica cells. However, those are zero by symmetry, and a lattice of cubic cells undersolvates compared to an infinite system.[6] To account for this fact, Hummer, Pratt, and Garcia[9] suggested to estimate the difference in the solvation free energies between the infinite system and the lattice of cell replicas from

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dielectric theories. Their result for the difference of solvation free energies in the the dielectric cube and in the infinite dielectric becomes

$$F_L^q - F_\infty^q = -\tfrac{1}{2}q^2\left(1-\epsilon^{-1}\right)\zeta(R,L). \tag{7}$$

In this equation,

$$F_\infty^q = -\frac{q^2}{2R}(1-\epsilon^{-1}) \tag{8}$$

refers to the Born solvation free energy in the infinite system and F_L^q is the solvation energy of the ion placed at the center of the dielectric cube. Their numerical calculations[9] produced

$$\zeta(R,L) = \xi + \frac{\Omega}{2RL^3}, \tag{9}$$

where the expansion terms in R/L of the order higher than $(R/L)^2$ have been omitted; $\Omega = (4\pi/3)R^3$ is the ion volume.

Hünenberger and McCammon reviewed this problem[6] and mostly confirmed the results of Hummer et al,[5] but they found that the $(R/L)^2$ correction term (second term in Eq. (9)) does not require the factor of $1/2$. More specifically the $\zeta(R,L)$ function in Eq. (7) becomes[6,10]

$$\bar{\zeta}(R,L) = \xi + \frac{\Omega}{RL^3} - \frac{\Omega^2}{5RL^6}. \tag{10}$$

Simulations with periodic systems extend far beyond the problem of calculating the free energy of ion solvation and involve many applications of electrostatics.[8] Among those are simulations of electron-transfer reactions[11,12] and applications to spectroscopy when one often needs to calculate the electric field in addition to the electrostatic potential[13,14] to address solvatochromism.[15] Another significant area is dielectric phenomena where finite-size corrections are very essential.[16,17]

The main parameter of interest in simulations of electron-transfer reactions is the statistics of the energy gap between the donor and acceptor states of the transferred electron.[18,19] The electrostatic component of the energy gap often dominates and is typically the main focus of simulations of charge-transfer reactions.[20] Ayala and Sprik[21] reviewed corrections for the reorganization energy of electron transfer by applying the formalisms due to Hummer et al[5] and Hünenberger and McCammon[6] to the classical Marcus model[22] in which this parameter can be calculated either from the variance of energy-gap fluctuations or from the difference in the mean values of the energy gap (Stokes shift). However, they also noticed that the Marcus description breaks down for some molecular systems[23,24] and the free energy barrier cannot be described by a single reorganization energy. This difficulty gains in significance for protein electron transfer[25] for which the reorganization energy obtained from the energy gap variance often significantly exceeds that from the Stokes shift. Separate corrections for the Stokes-shift and variance reorganization energies are required and those are introduced here through the cumulant expansion considered by Hummer and co-workers.[3] They are briefly reviewed below.

Finally, simulations[26,27] and experimental measurements[14,28,29] of electric fields in proteins and molecular assemblies is a quickly developing area of research. Given that proteins possess high dipole moments of hundreds of Debye units,[30,31] finite-size corrections in the calculation of the field statistics and solvation energies might be required. Corrections to the dipole solvation energy and electric field variance are derived here based on the algorithm proposed by Hünenberger and McCammon.[6]

II. ION SOLVATION

The discussion of ion solvation and corrections required to calculate the electron-transfer activation barrier starts with a brief review of the Hünenberger and McCammon[6] algorithm. One needs to solve the Poisson equation $\nabla^2\phi = -4\pi\tilde{\rho}$ for the charge-neutralized charge density $\tilde{\rho}$ in Eq. (2). The solution for the electrostatic potential ϕ of the ion is sought as a sum of the Ewald potential (Eq. (5)) and a general homogeneous solution of the Laplace equation given as an expansion in spherical harmonics. The electrostatic potential inside the ion is ϕ_1 and within the dielectric cubic cell with the dielectric constant ϵ is ϕ_2

$$\begin{aligned} \phi_1 &= q\psi + \psi_1, \\ \phi_2 &= (q/\epsilon)\psi + \psi_2, \end{aligned} \tag{11}$$

where $\nabla^2\psi_i = 0$, $i = 1, 2$. One writes[32]

$$\begin{aligned} \psi_1(\mathbf{r}) &= \sqrt{4\pi}\sum_{n,m} a_{nm} r^n Y_{mn}(\hat{\mathbf{r}}), \\ \psi_2(\mathbf{r}) &= \sqrt{4\pi}\sum_{n,m}\left[b_{nm}r^n + \frac{c_{nm}}{r^{n+1}}\right] Y_{mn}(\hat{\mathbf{r}}), \end{aligned} \tag{12}$$

where $Y_{nm}(\hat{\mathbf{r}})$ are spherical harmonics of the unit vector $\hat{\mathbf{r}} = \mathbf{r}/r$. Given that $\nabla^2\psi_2 = 0$ and the electric field vanishes on the sides of the cube, one finds from the Gauss theorem that the average of ψ_2 over the surface of the solute S_Ω must vanish as well

$$\oint_{S_\Omega} d\mathbf{S}\cdot\nabla\psi_2 = 0. \tag{13}$$

This implies $c_{00} = 0$ in Eq. (12). From this result, one finds that only coefficients a_{00} and b_{00} are required to calculate the solvation free energy by the dielectric cube. Specifically, one calculates

$$F_L^q = \tfrac{1}{2}\int_V d\mathbf{r}\tilde{\rho}\left[\phi - q\psi\right], \tag{14}$$

where the term in square brackets represents the electrostatic potential of the dielectric medium. This formula

reduces[6] to the expression in terms of the surface and volume integrals of the Ewald potential

$$F_L^q = -\frac{q^2}{2}\left(1-\epsilon^{-1}\right)\left[\left(1-\frac{\Omega}{L^3}\right)B(R)+C(R)\right], \quad (15)$$

where the main function to determine is the surface integral of the Ewald potential (Eq. (5)) over the surface of the ion S_Ω

$$B(R) = S_\Omega^{-1}\oint_{S_\Omega} dS\psi. \quad (16)$$

The second term in the brackets in Eq. (15) is the integral of the Ewald potential over the volume of the solute, which can be represented in terms of the function $B(r)$

$$C(R) = \frac{1}{L^3}\int_\Omega d\mathbf{r}\psi = \frac{4\pi}{L^3}\int_0^R drr^2 B(r). \quad (17)$$

It is clear from Eqs. (15)-(17) that the only function that needs to be calculated is

$$B(R) = \frac{\mathrm{erfc}(\kappa R)}{R} + \frac{4\pi}{L^3}\sum_{\mathbf{k}\neq 0} k^{-2}e^{-k^2/(4\kappa^2)}j_0(kR) - \frac{\pi}{L^3\kappa^2}, \quad (18)$$

where $j_0(x)$ is the zeroth-order spherical Bessel function. One can use the definition of the Wigner potential[1,2]

$$\xi = \lim_{r\to 0}\left[\psi(r) - r^{-1}\right] \quad (19)$$

to rewrite Eq. (18) as

$$B(R) = \xi + \frac{\mathrm{erfc}(\kappa R)}{R} + \frac{2\kappa}{\sqrt{\pi}} + S, \quad (20)$$

where Eq. (5) was used to arrive at the correction term

$$S = \frac{4\pi}{L^3}\sum_{\mathbf{k}\neq 0} k^{-2}e^{-k^2/(4\kappa^2)}\left(j_0(kR)-1\right) \quad (21)$$

The term $j_0(kR)-1$ in Eq. (21) vanishes at $k\to 0$ thus eliminating the small lattice vectors from the sum. It therefore can be evaluated by switching to a continuous integration over the wavevectors (subscript ∞) with the result

$$S_\infty = \frac{\mathrm{erf}(\kappa R)}{R} - \frac{2\kappa}{\sqrt{\pi}}, \quad (22)$$

where $\mathrm{erf}(x) = 1-\mathrm{erfc}(x)$ is the error function. One therefore finds

$$B(R) = \xi + \frac{1}{R}, \quad (23)$$

which recovers Eq. (7) with $\zeta(R,L)$ according to Eq. (9). This approximate evaluation of the lattice sum leads to the result reported by Hummer et al[5] while omitting the corrections of the order $(R/L)^5$.

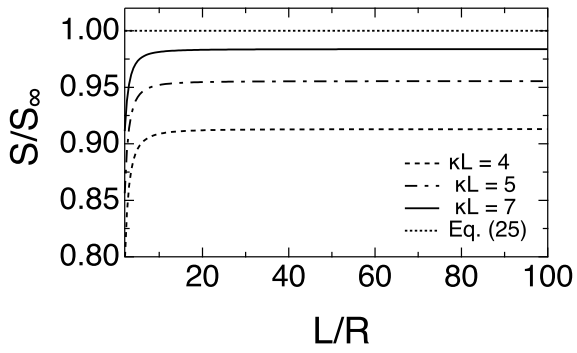

Figure 1. S/S_∞ from Eqs. (21) and (22) at the values of κL indicated in the plot. The sum S in Eq. (21) is calculated numerically. Replacing S_∞ with $\bar{S}_\infty$ according to Eq. (25) leads a nearly exact agreement with the numerical summation as shown by the dotted line referring to $\kappa L = 7.0$.

The calculations of Hünenberger and McCammon[6] have resulted in a different expression for $B(R)$

$$\bar{B}(R) = \xi + \frac{1}{R} + \frac{\Omega}{2RL^3}. \quad (24)$$

and

$$\bar{S}_\infty = \frac{\mathrm{erf}(\kappa R)}{R} - \frac{2\kappa}{\sqrt{\pi}} + \frac{\Omega}{2RL^3}. \quad (25)$$

At $R\to 0$, all expressions tend to the limit proposed by Figueirido et al.[33]

Equations (10) and (25) are superior in accuracy to Eqs. (9) and (22) when compared to direct numerical summation in Eq. (21) (Fig. 1). This improvement can be achieved by eliminating the second-order term from the small-k expansion of $j_0(kR)$ in Eq. (21) when switching to the continuous $k-$integral

$$S = S' - \frac{\Omega}{2RL^3}\sum_{\mathbf{k}\neq 0} e^{-k^2/(4\kappa^2)}, \quad (26)$$

where by applying the continuum k-integral one gets

$$S' = \frac{2}{\pi}\int_0^\infty dke^{-k^2/(4\kappa^2)}\left[j_0(kR) - 1 + \tfrac{1}{6}(kR)^2\right]. \quad (27)$$

By using the identity for the theta function[34]

$$\sum_{m=-\infty}^{\infty} e^{-m^2x} = (\pi/x)^{1/2}\sum_{m=-\infty}^{\infty} e^{-m^2\pi^2x^{-1}} \quad (28)$$

one arrives at

$$S = S_\infty + \frac{\Omega}{2RL^3}\left[1+\left(\frac{\kappa L}{\sqrt{\pi}}\right)^3\left(1-\theta_3(e^{-(\kappa L)^2})^3\right)\right], \quad (29)$$

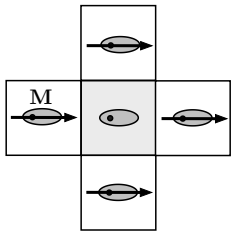

Figure 2. Schematic representation of dipole moments of replica cells produced by non-spherical solutes with asymmetric charge distribution (denoted with an off-center dot). The central cell is shaded.

where S_∞ is from Eq. (22) and $\theta_3(z) = \sum_n z^{n^2}$ is Jacobi's theta function.[34] The second term in the square brackets can be dropped at $\kappa L \gg 1$ and one arrives at $S = \bar{S}_\infty$ supplied by Hünenberger and McCammon.[6] This result agrees well with numerically evaluated lattice sum S (Fig. 1). It is obvious that one can consistently produce terms of higher order in R/L by eliminating higher-order expansion terms of $j_0(kR)$ when switching to the continuous k-integral. This extension is not practically significant since the term quadratic in R/L is the only one that matters for most simulations. The same note applies to the fact that Eq. (15) neglects[6] solvation by the corners of the simulation cell at $r > L/2$ since those are insignificant for simulation boxes currently employed in molecular dynamics simulations. These effects can be evaluated at the expense of including more expansion terms in Eq. (12).

Including the self-energy due to the Wigner potential, the electrostatic free energy of an ion $F_{\rm el}$ corrected for finite-size effects becomes[6]

$$F_{\rm el} = F_L + \tfrac{1}{2} q^2 \zeta_{\rm solv}, \tag{30}$$

where F_L is the free energy calculated from simulations in the periodically replicated simulation box and

$$\zeta_{\rm solv} = \epsilon^{-1}\xi - \left(1-\epsilon^{-1}\right)\left[\frac{\Omega}{RL^3} - \frac{\Omega^2}{5RL^6}\right]. \tag{31}$$

As expected, the correction term is overall negative, consistent with the expectation that periodic systems undersolvate the charge. For highly polar systems with $\epsilon \gg 1$, the second term in this equation, $\propto R^2/L^3$, gains in prominence.

Before proceeding to applying the formalism to electron-transfer reactions, it is useful to summarize the assumptions made in the analysis. In addition to neglecting the corner effects mentioned above, the formalism does not specify an algorithm of dealing with nonspherical particles. All the issues pertinent to specifying an effective radius of the spherical cavity representing a nonspherical solute apply here. In addition, when solutes or their charge distributions are non-spherical, the argument that the dipole moments of the replica cells are zero by symmetry does not apply anymore. The replica cells carry dipole moments and calculating the solvation energy by the dielectric in the central simulation cell is generally not sufficient (Fig. 2). This complication does not apply to the cubic simulation cell since, from Lorentz argument,[35] a cubic lattice of dipoles makes zero electric field at a tagged lattice node (see below). However, deviations from the cubic symmetry should produce additional corrections not accounted for here. Multipolar expansion can be applied when the charge distribution of the solute deviates from the spherical symmetry of a spherical ion. The leading correction term due to the solute dipole m is considered below in the discussion of the electric field produced by the solvent at the solute. Solutes lacking inversion symmetry require a correction term $\propto qm\Omega/(R^2L^3)$ to the free energy of ion solvation. This correction can be of the same order of magnitude as the leading term in Eq. (31).

III. ELECTRON TRANSFER

Solvation thermodynamics considered here can also be used to derive finite-size corrections for activation parameters of electron-transfer reactions. We will follow the arguments presented by Hummer et al[3] in viewing the solvation problem in terms of the cumulant perturbation expansion. To simplify the argument, we consider a nonpolarizable solvent with a single redox site to which the charge $\Delta q = q_f - q_i$ is transferred in a half reaction to alter the solute charge from q_i to q_f. The main problem of interest is the electrostatic component of the energy gap[18] (cf. to Eq. (3))

$$\Delta E = \Delta q \phi_s + \tfrac{1}{2}(q_f^2 - q_i^2)\xi. \tag{32}$$

The free energy of solvating the charge Δq in the Gaussian approximation becomes[3]

$$F^{\Delta q} = \langle \Delta E \rangle_L + \frac{\beta}{2}\langle(\delta\Delta E)^2\rangle_L - \tfrac{1}{2}(q_f^2 - q_i^2)(1-\epsilon^{-1})\bar{\zeta}, \tag{33}$$

where $\delta\Delta E = \Delta q \delta\phi_s$, $\delta\phi_s = \phi_s - \langle\phi_s\rangle_L$ and the angular brackets $\langle \dots \rangle_L$ specify averages over configurations taken from simulations. By applying the identity $q_f^2 - q_i^2 = \Delta q(2q_i + \Delta q)$, one can separate the correction terms into the ones linear in Δq, which apply to the first moment of ΔE, and the terms quadratic in Δq applying to the second moment. The second cumulant of the energy gap is associated with the reorganization energy of electron transfer

$$\lambda = \tfrac{1}{2}\beta\langle(\delta\Delta E)^2\rangle. \tag{34}$$

This definition corresponds to the curvature at the minimum in the picture of crossing parabolas (Fig. 3).

By collecting the corresponding terms, one obtains

$$\langle \Delta E \rangle = \langle \Delta E \rangle_L + \tfrac{1}{2}(q_f^2 - q_i^2)\xi - \Delta q q_i (1-\epsilon^{-1})\bar{\zeta} \tag{35}$$

and

$$\lambda = \lambda_L - \tfrac{1}{2}(\Delta q)^2(1-\epsilon^{-1})\bar{\zeta}. \tag{36}$$

The physical meaning of Eq. (35) is straightforward: the average vertical transition energy $\langle\Delta E\rangle_L$ is corrected by two contributions: the instantaneous solvation by the replica charges (similar to the free energy of solvation by electronic polarization) and a constant electrostatic potential by the nuclear degrees of freedom $-q_i(1-\epsilon^{-1})\bar{\zeta}$ which does not change for a vertical transition. This electrostatic potential disappears at $\epsilon \to 1$.

The correction to the free energy of reorganizing the nuclei (electron-transfer reorganization energy λ[22]) comes solely from the nuclear degrees of freedom and disappears at $\epsilon \to 1$. Equation (36) is equivalent to the one previously derived by Ayala and Sprik.[21] When the solvent is viewed as polarizable with the high-frequency dielectric constant ϵ_∞, the Born solvation factor $1-\epsilon^{-1}$ is often replaced with the Pekar factor $\epsilon_\infty^{-1}-\epsilon^{-1}$, but the polarizability corrections can become involved when a more careful treatment of electronic polarization is introduced[36] or when the solvent is treated on the microscopic scale.[37]

The derivation by Ayala and Sprik[21] follows the standard arguments of the Marcus theory. These arguments invoke[38] the linear response approximation when one obtains $\langle\Delta E\rangle = -\beta\langle(\delta\Delta E)^2\rangle$ resulting in the solvation energy equal to $-\beta\langle(\delta\Delta E)^2\rangle/2$. This final expression is in fact used in the Marcus theory, which interprets the reorganization energy as the negative of the free energy of solvation of the difference charge distribution (after electron transfer minus before electron transfer) by the nuclear degrees of freedom of the solvent.[39] Since this result is used as the definition of the reorganization energy in Eq. (34), the present derivation is equivalent to the one given by Ayala and Sprik.

The reorganization energy in terms of the second cumulant of the energy gap (Eq. (34)) is not the only possible definition of this parameter. An alternative route within the picture of crossing parabolas is through the Stokes shift[24,40,41]

$$\lambda^{\mathrm{St}} = \tfrac{1}{2}\left|\langle\Delta E\rangle_i - \langle\Delta E\rangle_f\right|, \tag{37}$$

where the averages $\langle\Delta E\rangle_a$, $a = \mathrm{i},\mathrm{f}$ are taken in the initial and final states of the redox complex. The vertical transition energies $\langle\Delta E\rangle_a$, $a = \mathrm{i},\mathrm{f}$ represent charge-transfer absorption ($a = i$) and emission ($a = f$) energies when the final state is sufficiently lifted in energy such that the return electron transfer is in the inverted electron-transfer region and both optical transitions can be observed. The difference of transition energies is the Stokes shift between absorption and emission, whence the name[24] for the reorganization energy λ^{St}. The average energy $\langle\Delta E\rangle_f$ becomes negative in the normal electron-transfer region (Fig. 3). This is related to Warshel's definition of the energy-gap reaction coordinate[18] for electron transfer, which gives $\Delta E(\Gamma) = E_f(\Gamma) - E_i(\Gamma)$ as the difference of energies in the final and initial states at a given instantaneous nuclear configuration Γ. The index i, f in the average $\langle\ldots\rangle_a$ applies to the state over which the statistical average is performed while keeping

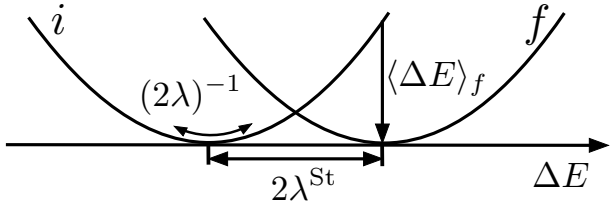

Figure 3. Picture of crossing parabolas with curvatures $(2\lambda)^{-1}$ and separation between the minima $2\lambda^{\mathrm{St}}$. $\langle\Delta E\rangle_f$ marks the average energy of the vertical transition in the final state, which is negative in the normal region of electron transfer and positive when backward electron transfer is in the inverted region (corresponding to the emission energy). "i" and "f" mark the electron-transfer initial and final states. Displayed is the configuration with zero reaction free energy.

the same definition of the reaction coordinate ΔE in both states. Applying this rule to Eq. (35) leads to the following result

$$\langle\Delta E\rangle_a = \langle\Delta E\rangle_{aL} + \tfrac{1}{2}(q_f^2 - q_i^2)\xi - \Delta q q_a(1-\epsilon^{-1})\bar{\zeta}, \tag{38}$$

where the "instantaneous" solvation term by the background charge is the same for both vertical energy gaps, similarly to the analogous result for the instantaneous solvation by electronic medium polarization.

Subtracting the energies $\langle\Delta E\rangle_a$ according to Eq. (37) leads to the following expression for the Stokes-shift reorganization energy

$$\lambda^{\mathrm{St}} = \lambda_L^{\mathrm{St}} + \tfrac{1}{2}(\Delta q)^2(1-\epsilon^{-1})\bar{\zeta}. \tag{39}$$

Importantly, the finite-size correction for this parameter becomes equal in magnitude but opposite in sign to that for λ defined from the second cumulant of the energy gap according to Eq. (34).

Two average vertical transition energies can also be used to arrive at the reaction free energy (electrostatic component)[21,24,41] for which one obtains

$$\Delta F_{\mathrm{el}} = \tfrac{1}{2}\left(\langle\Delta E\rangle_i + \langle\Delta E\rangle_f\right) = \Delta F_L + \tfrac{1}{2}(q_f^2 - q_i^2)\zeta_{\mathrm{solv}}. \tag{40}$$

As anticipated, and consistent with the preceding discussion, the parameter ζ_{solv} from Eqs. (30) and (31) provides correction to the equilibrium free energy.

The main result of this derivation is that the finite-size correction enhances λ but reduces λ^{St}. A number of recent simulations of protein electron transfer[25] have shown $\lambda_L^{\mathrm{St}} < \lambda_L$. Applying finite-size corrections must broaden this gap. For the sake of an estimate, our recent simulations of protein azurin[42] used the cubic simulation box with side length $L = 104$ Å and the protein volume $\Omega = 12508$ Å^3 and $R \simeq 14.4$ Å. With these parameters and $\epsilon \simeq 97$ for TIP3P water, one arrives at the correction term in Eq. (36) equal to $\simeq 0.19$ eV, which is about 10% of $\lambda_L \simeq 1.65$ eV, in accord with similar corrections reported by Ayala and Sprik.[21] Applying corrections of opposite signs in Eqs. (36) and (39) adds a gap of 0.38 eV to the difference between λ and λ^{St}.

The picture of crossing parabolas[22] anticipates that a Gaussian bath coupled to a quantum subsystem makes the distribution of energy gap a Gaussian function with the maximum depending on the electron-transfer state (i, f). The application of the Gibbsian statistics and the linear-response approximation leads to a specific connection between the width of the Gaussian distribution (Eq. (34)) and the separation between the distribution maxima (Eq. (37)) in terms of a single reorganization energy $\lambda = \lambda^{\rm St}$. When sampling is incomplete (nonergoidic), the direct correspondence between the difference of two first distribution moments ($\lambda^{\rm St}$) and the second cumulant (λ) is broken[43] and two separate reorganization energies are required.[25] However, the Gaussian statistics of energy gap is often preserved through the central-limit theorem given that many particles affect the energy state of the electron by electrostatic interactions. When two parabolas characterized by $\lambda^{\rm St} < \lambda$ are allowed to cross (Fig. 3), the Marcus expression for the activation barrier $\Delta F^\dagger$ is preserved

$$\Delta F^\dagger = \frac{(\lambda^r \pm \Delta F_0)^2}{4\lambda^r}, \tag{41}$$

but with an effective[25] (reaction, subscript "r") reorganization energy

$$\lambda^r = (\lambda^{\rm St})^2/\lambda. \tag{42}$$

In Eq. (41), + and − refer to the forward, $i \to f$, and backward, $f \to i$, reactions, respectively and ΔF_0 is the reaction free energy.[22] In contrast to the standard description combining full Gibbsian sampling with linear response, the condition $\lambda^{\rm St} < \lambda$ of incomplete sampling allows low activation barriers facilitating efficient charge transfer in biology's energy chains.[44] According to the derivation presented here, finite-size corrections widen the gap between $\lambda_L^{\rm St}$ and λ_L found from statistics of ΔE in a finite-size simulation box.

IV. DIPOLE SOLVATION AND ELECTROSTATIC FIELD

Lorentz was first to establish that the field on a tagged dipole in a dipolar lattice is zero.[35] Dipole lattice calculations[45] support this result for a finite lattice of dipoles within a spherical cutoff (the dipole lattice sum is piecewise convergent at $\mathbf{k} = 0$ for an infinite lattice). The lattice of simulation cell replicas (Fig. 2) surrounded by a conducting sphere is typically adopted in simulation protocols and one does not need to worry about calculating the electrostatic energy of the solute dipole with its images in cell replicas. For correcting the solvation free energy of a dipole and the electric field moments, one only needs to account for solvation corrections.

The solute at the center of the cubic cell now carries the charge q and dipole m, which we assume to be aligned with the z-axis of the laboratory frame. The general solution for the electrostatic potential becomes

$$\begin{aligned} \phi_1 &= q\psi - m\partial_z\psi + \psi_1, \\ \phi_2 &= (q/\epsilon)\psi - \chi_c m\partial_z\psi + \psi_2, \end{aligned} \tag{43}$$

where $\chi_c m$ is the dipole moment screened by the surface charge at the dividing surface of the dielectric and specified by the cavity field susceptibility $\chi_c = 3/(2\epsilon + 1)$.[46] The solutions of the homogeneous Laplace equation ψ_1 and ψ_2 are given by Eq. (12).

Repeating calculations for the ion solvation free energy in Eq. (15), one obtains

$$F_L^q - F_\infty^q = -\tfrac{1}{2}q^2\left(1 - \epsilon^{-1}\right)\bar{\zeta}(R, L) + \frac{3qmf}{2R}\frac{\Omega}{L^3}D(R), \tag{44}$$

where

$$f = \frac{2(\epsilon - 1)}{2\epsilon + 1} \tag{45}$$

is the reaction-field polarity function[35] and

$$D(R) = S_\Omega^{-1}\oint_{S_\Omega} dS\hat{n}_z\psi. \tag{46}$$

Here, $\hat{n}_z = \hat{\mathbf{n}}\cdot\hat{\mathbf{z}}$ is the projection of the normal $\hat{\mathbf{n}}$ at the surface S_Ω on the z-axis. It is clear that $D(R) = 0$ for a lattice allowing inversion symmetry and the presence of a dipole does not affect charge solvation. However, there is a nonvanishing correction to ion solvation due to solute's dipole for solutes with more complex geometry. Similarly to the leading term in Eq. (31), this correction term scales as $\Omega/(RL^3) \times (m/R)$ assuming that $D(R) \sim 1/R$.

The solvation free energy for the dipole reads

$$F_L^m = \tfrac{1}{2}\int_V d\mathbf{r}\rho_m\partial_z\left(\phi - q\psi + m\partial_z\psi\right), \tag{47}$$

where $\rho_m = m\delta(\mathbf{r})$ is the dipolar density. From this equation and the expansion in Eq. (12), one obtains

$$F_L^m = \frac{\sqrt{3}}{2}ma_{10}. \tag{48}$$

The electrostatic potential ϕ satisfies the following boundary conditions at the surface of the solute

$$\begin{aligned} \phi_1\big|_R &= \phi_2\big|_R, \\ \partial_r\phi_1\big|_R &= \epsilon\partial_r\phi_2\big|_R. \end{aligned} \tag{49}$$

Assuming $b_{nm} = 0$ for $n > 0$ in Eq. (12), these boundary conditions lead to the following relations for the expansion coefficients a_{01} and c_{01}

$$\begin{aligned} \frac{c_{10}}{R^3} - a_{10} &= -\frac{\sqrt{3}mf}{R}E(R), \\ \frac{2\epsilon c_{10}}{R^3} + a_{10} &= -\frac{\sqrt{3}mf}{2}F(R), \end{aligned} \tag{50}$$

where

$$E(R) = S_\Omega^{-1} \oint_{S_\Omega} dS \hat{n}_z^2 \partial_r \psi,$$
$$F(R) = S_\Omega^{-1} \oint_{S_\Omega} dS \hat{n}_z^2 \partial_r^2 \psi. \quad (51)$$

It is easy to show that

$$E(R) = \tfrac{1}{3} \partial_r \bar{B}(r)\big|_R, \quad (52)$$

where $\bar{B}(r)$ is given by Eq. (24). One further notices that

$$F(R) + \frac{2}{R} E(R) = S_\Omega^{-1} \oint_{S_\Omega} dS n_z^2 \nabla_r^2 \psi. \quad (53)$$

Assuming $\nabla_r^2 \psi \approx \nabla^2 \psi = -4\pi \left[\delta(\mathbf{r}) - L^{-3}\right]$, one gets

$$c_{10} = -\frac{fm}{2\epsilon + 1} \frac{\sqrt{3}\Omega}{2L^3}. \quad (54)$$

From Eqs. (48) and (50), one finally gets

$$F_L^m = F_\infty^m \left(1 + \frac{\Omega}{L^3} \frac{\epsilon + 2}{2\epsilon + 1}\right), \quad (55)$$

where

$$F_\infty^m = -\frac{m^2}{R^3} \frac{\epsilon - 1}{2\epsilon + 1} \quad (56)$$

is the free energy of dipole solvation in an infinite dielectric. The result of this calculations is that the finite-size correction to the solvation free energy scales as Ω/L^3

$$F_L^m - F_\infty^m = -\tfrac{1}{2} m^2 \chi \quad (57)$$

with

$$\chi = \frac{8\pi}{3L^3} \frac{(\epsilon - 1)(\epsilon + 2)}{(2\epsilon + 1)^2}. \quad (58)$$

The free energy of dipole solvation can be calculated from the perturbation expansion[47] with the result

$$F^m = -\lambda^m = -\tfrac{1}{6} \beta m^2 \langle (\delta \mathbf{E}_s)^2 \rangle_0, \quad (59)$$

where the variance of the solvent field $\mathbf{E}_s$ is calculated at statistical configurations in the absence of the dipole indicated with the "0" subscript. The variance of $\mathbf{E}_s$ is invariant to the presence of the solute multipole in linear response theories and the subscript can be dropped. In analogy with Eq. (34), the variance of the solute-solvent interaction energy is associated with the reorganization energy λ^m for dipole solvation. Given the correction in Eq. (57), one obtains

$$\lambda^m = \lambda_L^m + \tfrac{1}{2} m^2 \chi, \quad (60)$$

where $\lambda_L^m = (\beta m^2/6) \langle (\delta \mathbf{E}_s)^2 \rangle_L$ is the field variance calculated in finite-size computer simulations. The finite-size corrections thus increase the variance of the dipole-liquid interaction energy compared to the result from simulations. Correspondingly, the variance of the electrostatic field gains a temperature-dependent correction

$$\langle (\delta \mathbf{E}_s)^2 \rangle = \langle (\delta \mathbf{E}_s)^2 \rangle_L + 3 k_\mathrm{B} T \chi. \quad (61)$$

Taking the recent simulations of the protein cytochrome c[26] as an example, the average magnitude of the electric field at the iron metal of the active site was found to be $\langle E \rangle \simeq 0.26$ V/Å and the field variance was $\langle (\delta \mathbf{E})^2 \rangle_L \simeq 0.014$ (V/Å)^2. With the simulation box of $L = 100.1$ Å, the last term in Eq. (61) becomes $\approx \pi k_\mathrm{B} T / L^3 \approx 10^{-6}$ (V/Å)^2. With the dipole moment of cytochrome c equal to $\simeq 238$ D,[26] the correction to λ^m in Eq. (60) amounts to 0.055 eV. These corrections are much less significant than corresponding finite-size effects on the electron-transfer reorganization energies for half reactions.

Solvatochromic shift of optical or vibrational spectral lines is often used to quantify microscopic polarity.[48] The shift is caused by an instantaneous change of the chromophore's dipole in the reaction field of the medium nuclei frozen on the time scale of the vertical electronic transition.[15] The reaction field in a given initial configuration of the chromophore $a = \mathrm{i}, \mathrm{f}$ is defined as the derivative of the solvation free energy

$$R_a = -\partial F_a^m / \partial m = R_{La} + m_a \chi. \quad (62)$$

One therefore obtains for the correction of the spectral shift $\Delta E_a = -\Delta m R_a$

$$\Delta E_a = \Delta E_{La} - \Delta m m_a \chi, \quad (63)$$

where χ is from Eq. (58). Half of the Stokes shift provides the Stokes-shift reorganization energy $\lambda^\mathrm{St} = \frac{1}{2} |\Delta E_i - \Delta E_f|$ (Fig. 3) for which one obtains

$$\lambda^\mathrm{St} = \lambda_L^\mathrm{St} + \tfrac{1}{2} \Delta m^2 \chi. \quad (64)$$

In contrast to a half reaction of electron transfer, the correction is the same for λ^m and λ^St. The reason is the absence of the instantaneous solvation energy by the replicas of the solute dipole and no need to account for the interaction of the dipole with either the solute charge or with the neutralizing background. Intramolecular electron-transfer reactions in which the total charge of the simulation cell does not change fall into this category and require relatively small finite-size corrections scaling as $\propto L^{-3}$. The charge-transfer dipole $m = e|\mathbf{r}_A - \mathbf{r}_D|$ formed by centroids of the electron $\mathbf{r}_{A,D}$ at the donor and acceptor sites can be used in Eq. (60) given that $|\mathbf{r}_A - \mathbf{r}_D| \ll L$ in most cases of interest.

V. CONCLUSIONS

The method of Hünenberger and McCammon[6] is applied to show how to systematically produce the series

expansion in Ω/L^3 for the solvation energy of an ion in a cubic simulation cell. The approach suggested here eliminates low order terms in the series expansion of the spherical Bessel function when the lattice sum is evaluated as a continuous reciprocal-space integral. The numerical result by Hummer et al[9] is reproduced when the lowest order correction is applied. The refined result by Hünenberger and McCammon follows from the next expansion term. It is shown that the correction term, scaling in the leading order as L^{-1}, comes with opposite signs to the variance of the electrostatic energy and the Stokes shift when applied to the electron-transfer half reaction. The gap between the Stokes-shift and variance reorganization energies is widened by finite-size corrections. The same method is applied to define finite-size corrections to solvation free energy of a dipole and the variance of the electric field. Those scale as m^2/L^3 and are less significant for sufficiently large simulation systems.

ACKNOWLEDGMENTS

This research was supported by the National Science Foundation (CHE-1800243). The author is grateful to the anonymous reviewer for insightful comments.

DATA AVAILABILITY

The data that support the findings of this study are available from the author upon request.

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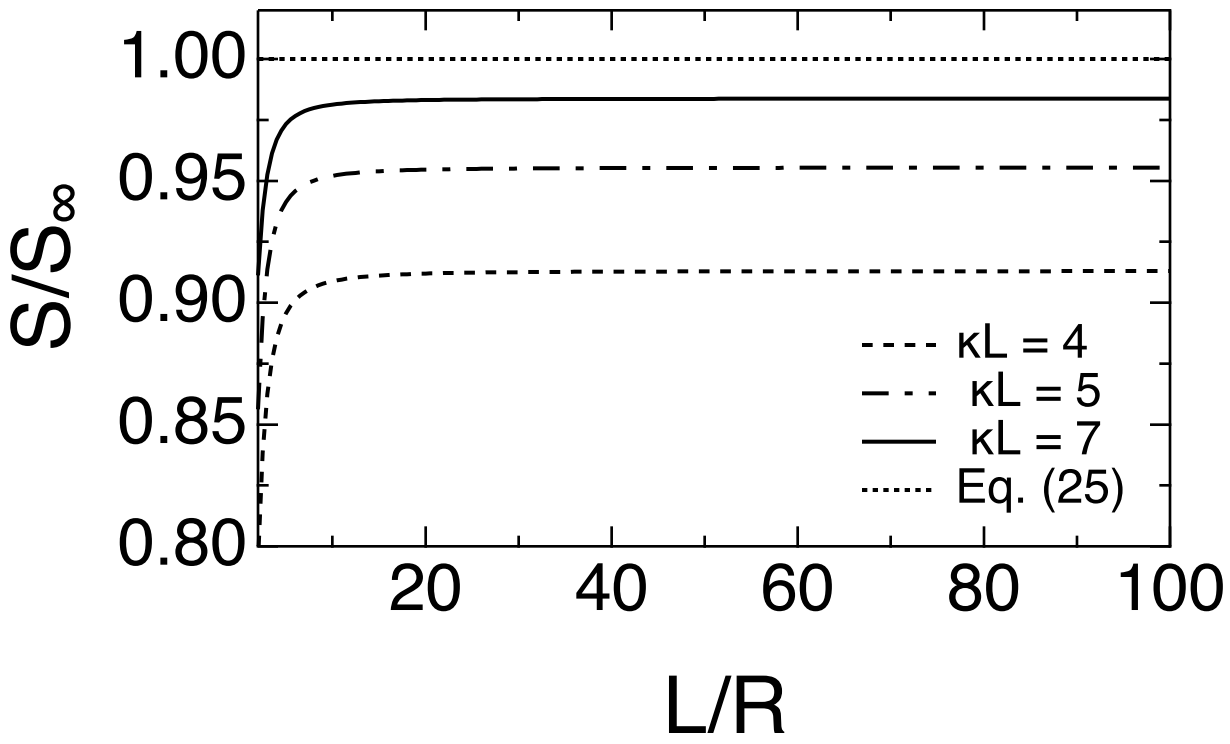
1.00
0.95
0.90
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40
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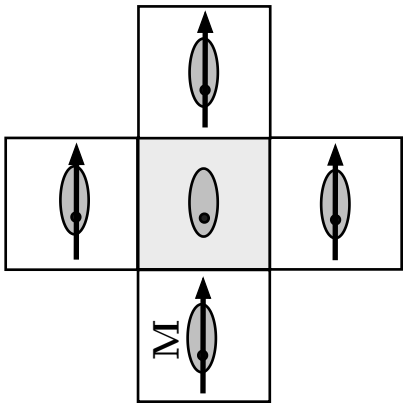
L/R
κL = 4
κL = 5
κL = 7
Eq. (25)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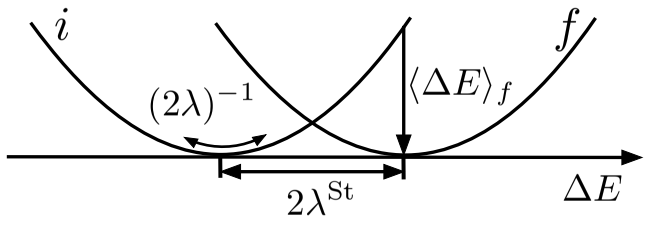
i
f
$(2\lambda)^{-1}$
$\langle \Delta E \rangle_f$
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