Activity coefficients of aqueous electrolytes from implicit-water molecular dynamics simulations

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ABSTRACT

We obtain activity coefficients in NaCl and KCl solutions from implicit-water molecular dynamics simulations, at 298.15 K and 1 bar, using two distinct approaches. In the first approach, we consider ions in a continuum with constant relative permittivity (ε_r) equal to that of pure water; in the other approach, we take into account the concentration-dependence of ε_r , as obtained from explicit-water simulations. Individual ion activity coefficients (IIACs) are calculated using gradual insertion of single ions with uniform neutralizing backgrounds to ensure electroneutrality. Mean ionic activity coefficients (MIACs) obtained from the corresponding IIACs in simulations with constant ε_r show reasonable agreement with experimental data for both salts. Surprisingly, large systematic negative deviations are observed for both IIACs and MIACs in simulations with concentration-dependent ε_r . Our results suggest that the absence of hydration structure in implicitwater simulations cannot be compensated by correcting for the concentration-dependence of the relative permittivity ε_r . Moreover, even in simulations with constant ε_r for which the calculated MIACs are reasonable, the relative positioning of IIACs of anions and cations is incorrect for NaCl. We conclude that there are severe inherent limitations associated with implicit-water simulations in providing accurate activities of aqueous electrolytes, a finding with direct relevance to the development of electrolyte theories and to the use and interpretation of implicit-solvent simulations.

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INTRODUCTION

Aqueous electrolyte solutions are widely present in many industrial,^{1,2} environmental,^{3,4} and biological applications.^{5,6} Parallel to the experimental measurements, numerous theoretical and modeling frameworks have been developed to study the liquid structure of these complex solutions on a molecular scale and predict their various thermophysical and transport properties, as reviewed extensively in the literature.^{7–11} Mean ionic activity coefficients (MIACs) are properties of significant interest in studying aqueous electrolytes as these quantities determine deviations from ideal solutions. While the Debye–Hückel (DH) limiting law provides an exact expression for MIACs at infinite dilution, deviations become significant at concentrations above 0.1 mol salt/kg H₂O.⁹ Various extensions of the DH theory have been presented to expand its applicability to higher concentrations by introducing empirical parameters. These "phenomenological" models express MIACs as combinations of several contributions of different physical origins and predict the MIACs for uni- and multi-valent electrolyte solutions.¹²⁻¹⁸ Although these models have been broadly adopted by the process industry, there are inherent drawbacks associated with some of them including but not limited to the lack of reliable extrapolations beyond the range of available experimental data. Furthermore, decomposing certain properties into several distinct contributions may not be trivial nor may this decomposition necessarily be physically justified.

Molecular simulations are alternative approaches that have been used to obtain predictions of thermodynamic and transport properties of aqueous electrolyte solutions. Molecular simulations connect macroscopic thermodynamic properties such as MIACs to the microstructure of a system using proper molecular models that describe the intra- and inter-molecular interactions, together with well-established statistical mechanical theories. Comprehensive reviews of such studies are available.^{7–9} Molecular simulations of aqueous systems are carried out either in the explicit or implicit solvent. In the former, water molecules are explicitly introduced to simulation boxes, while in the latter, molecules of interest are placed in a dielectric continuum. One advantage of explicit-water simulations is that the relative permittivity (ε_r) is an outcome and not an input, and thus, one does not need to take into consideration the concentration-dependence of ε_r . Furthermore, due to the presence of water molecules, hydration of ionic species is inherently accounted for, and as such, no further hypotheses are required. Implicit-water simulations, on the other hand, are computationally much less demanding and do not carry the sampling issues associated with the explicit-water simulations.

It is well-established—both experimentally and theoretically that the relative permittivity in aqueous electrolytes decreases with salt concentration.¹⁹⁻²⁵ Despite this, in many implicit-water simulations, the relative permittivity is considered to be independent of salt concentration for simplicity. One such example is the work of Young and Panagiotopoulos²⁶ where the MIACs of aqueous NaCl were calculated with implicit molecular dynamics (MD) while keeping the ε_r constant at 73, which is the value previously calculated²⁷ for the extended simple point charge (SPC/E)²⁸ model of water. Predictions of MIACs were shown to be satisfactory when compared to experimental data²⁹ and results from explicit-water simulations.²⁶ This is rather surprising, as the relative permittivity near the experimental solubility limit is significantly smaller than that of pure water.²⁰ Hence, this question arises as to why, for example, considering such a high ε_r value around the experimental solubility limit would result in reasonable MIACs. Furthermore, one might wonder whether the results would improve further if concentration-dependence of ε_r were taken into account. We address this question in the present work.

To further provide insight into the performance of implicitwater simulations and compare them to their explicit-water counterpart, it is useful to examine the behavior of individual ions separately rather than the combined value that is represented by the MIAC. It has been shown previously in a study of phenomenological models¹⁸ that correct values for MIACs do not necessary translate to meaningful individual ion activity coefficients (IIACs). We have recently developed³⁰ a framework to obtain IIACs in aqueous electrolyte solutions from explicit-water molecular simulations. Furthermore, various experimental data reported for IIACs from different researchers,^{31–44} a brief history of controversies associated with these data, as well as prior molecular simulation works with a focus on calculating IIACs were reviewed.³⁰ Most of prior studies utilized implicit-water simulations, and only a few of them used the explicitwater approach to calculate the activity coefficients or hydration free energies of individual ions.

Implicit-water molecular simulations of electrolytes have mostly been carried out by considering variations of primitive model together with Monte Carlo (MC) simulations. In the primitive model, ionic species are considered as charged hard spheres with either the same sizes (restricted primitive model) or different sizes (unrestricted primitive model or UPM) and are placed in a dielectric continuum with either constant or concentration-dependent relative permittivity ε_r . Svensson and Woodward⁴⁵ calculated chemical potentials and activity coefficients of single ions using MC with the restricted primitive model for several 1:1, 2:1, and 2:2 aqueous solutions. In their work, relative permittivity was kept constant at that of pure water over the concentration range studied. Lund et al.46 later followed their approach to calculate IIACs in sea water, although they treated the ionic radii as adjustable parameters fitted to the activity coefficients data. Sloth and Sørensen⁴⁷⁻⁴⁹ used MC with constant relative permittivity to calculate IIACs, with both restricted and unrestricted primitive models. Lamperski⁵⁰ also considered these two models in the calculation of IIACs using grand canonical MC (GCMC), an approach that was later improved by Malasics and Boda.⁵¹ Valiskó and Boda⁵² accounted for the concentration-dependence of ε_r in their calculations of IIACs by fitting a polynomial function to experimental data.⁵³ They expressed the total excess chemical potential as a combination of two contributions: ion-ion and ion-water interactions. The ion-ion part was calculated using GCMC with the unrestricted primitive model and the ion-water part was obtained from Born's treatment of solvation.⁵⁴ Finally, Abbas and Ahlberg⁵⁵ utilized MC with the unrestricted primitive model to calculate IIACs of several aqueous solutions by taking into account the concentration-dependence of ε_r as a polynomial fitted to experiments.⁵³ They treated the radii of cations as adjustable parameters to indirectly account for ion hydrations, while the crystallographic values were used for the radii of anions.

In the present study, we use our previously developed thermodynamic framework³⁰ for the calculation of IIACs in explicitwater simulations to investigate the applicability and reliability of such calculations in implicit-water simulations. Conducting such a comparison between implicit- and explicit-water simulations helps us analyze the trade-off between rapid computations from implicit simulations and the physical relevance and accuracy of the results thus obtained. Two electrolytes, namely, NaCl and KCl, are selected as their results from explicit-water simulations are readily available.³⁰ The implicit-water simulations at each salt concentration are carried out by placing the ionic species in an empty box comprising a dielectric continuum in lieu of water molecules. For such a continuum, both a constant ε_r equal to that of pure SPC/E²⁸ water and a concentration-dependent ϵ_r are considered. ϵ_r at each concentration is calculated from total dipole moment fluctuations obtained from our previous explicit-water simulations.³⁰ The IIACs are computed from chemical potentials that are obtained using the gradual single ion insertion method. Such an insertion is carried out by first placing a "ghost" single ion into solution and then slowly turning on, in succession, the Lennard-Jones (LJ) and Coulombic interactions between the added particle and the rest of solution constituents. The results are extrapolated to infinite system size to eliminate any possible artifacts attributed to the added neutralizing background in Ewald electrostatics in non-neutral systems

The remainder of this article is organized as follows: In the section titled "*Methods*," we present the model parameters used for the ionic species as well as the pertinent thermodynamic relations for the calculation of IIACs and ε_r . In the section titled "*Results and Discussion*," we discuss the simulation results and take a deeper look at the aqueous solutions on a molecular level to compare implicit-vs explicit-water molecular dynamics simulations. The section will then be followed by "*Conclusions*." The supplementary material contains additional tables and graphs to further support our results and conclusions.

METHODS

We performed implicit-water simulations for two alkali halide salts, namely, NaCl and KCl, to calculate the IIACs at 298.15 K and 1 bar. Table S1 in the supplementary material lists the force field parameters for ions ((Joung and Cheatham or JC⁵⁶) used in our implicit-water simulations, together with model parameters for SPC/E water²⁸ employed in the calculation of ϵ_r from explicit-water simulations. Simulations were performed at several concentrations up to the solubility limits in the ranges (0.005-5.3) and (0.005-4.3) M for NaCl and KCl, respectively, where M denotes mol salt/L. These concentrations are equivalent to those previously considered in our explicit-water simulations;³⁰ this correspondence allows us to use the relative permittivity obtained from explicit-water simulations at each concentration to compute the electrostatic forces in our implicit-water calculations. Conversion between the molarity and molality units of the implicitand explicit-water simulations was carried out using the computed explicit-water solution densities (ρ).³⁰ Figure S1 in the supplementary material illustrates simulation results for ρ vs concentrations in molality for both NaCl and KCl, along with the experimental data. Densities were calculated by performing simulations with 5500 SPC/E²⁸ water molecules.

Two approaches were considered for the implicit-water simulations: first, a dielectric continuum with a constant ε_r equal to that of pure SPC/E²⁸ water over the entire concentration range studied and second, a concentration-dependent ε_r . For the first approach, ε_r was set to 73, as calculated previously.²⁷ In the second approach, a different value of ε_r at each concentration, obtained from explicit-water simulations, was used. The electrostatic potential between ionic species *i* and *j* (U_{ij}^{Coul}) with charges q_i and q_j (with the distance r_{ij}) in a dielectric continuum with relative permittivity ε_r can be expressed as

$$U_{ij}^{\text{Coul}} = \frac{q_i q_j}{4\pi\varepsilon_0 \varepsilon_r r_{ij}},\tag{1}$$

where ε_0 is the permittivity of vacuum. In explicit-water calculations, ε_r is set to 1, and the actual permittivity can be calculated from total dipole moment fluctuations during the simulations as described later in the paragraph. By contrast, in implicit-water simulations, ε_r is required as an input to account for the screening of ionic charges in the absence of explicit water molecules. Accordingly, to perform such simulations, the ionic species were placed in an empty box that comprised a dielectric continuum with relative permittivity calculated from explicit-water simulations.³⁰ Relative permittivity in a pure dipolar environment can be calculated using the total dipole moments fluctuations^{25,27} according to linear response theory⁵⁷ as

$$\varepsilon_{\rm r} = 1 + \frac{\langle \mathbf{M}^2 \rangle - \langle \mathbf{M} \rangle^2}{3V k_B T \varepsilon_0},$$
 (2)

where $\mathbf{M} = [M_x, M_y, M_z]$ denotes the total dipole moment, *V* is volume, k_B is the Boltzmann constant, and *T* is temperature. The angle brackets denote time averages. In electrolyte solutions, the presence of ionic species makes it rather challenging to compute relative permittivity as only the frequency-dependent dielectric susceptibility will be measurable.²⁵ At the limit of low frequencies, however, one can obtain an estimate of the "static dielectric

constant" using Eq. (2), with two simplifying considerations: one by ignoring the ion contributions to the summation over all dipole moments in the supercell and the other by neglecting the kinetic cross terms.²⁵ Similar calculations have been previously carried out in the literature to show the decrement of relative permittivity of aqueous electrolytes with increasing salt concentrations, including the study of Fuentes-Azcatl and Barbosa⁵⁸ in their development of a new force field for sodium chloride. More elaborate discussions on calculation of relative permittivity are available in the literature.^{25,59,60}

We used trajectories from our previous database from explicitwater molecular dynamics simulations.³⁰ At each salt concentration, the first 2 ns of the runs were discarded, and M_x, M_y , and M_z were calculated using the *dipole* module in GROMACS. After discarding another 3 ns of trajectories as "initial noise," the average and standard errors gave the value and associated uncertainty for the relative permittivity, respectively. Calculations were repeated for several system sizes and extrapolated linearly against the inverse box length (1/L) to infinite system size. The specifics of system sizes considered are presented in Tables S2-S20 in the supplementary material of our previous study.³⁰ Instrumental weighting $(1/\sigma_i^2)$ was used to determine the uncertainty of the extrapolated ε_r , where σ_i is the standard error for each simulation data. The associated uncertainties of the intercept of fitted lines at the infinite system size are reported within 68.3% confidence interval. We may add that Eq. (2) is the "biased estimator" version due to the $\langle M \rangle^2$ term, as discussed elaborately in the study of Kolafa and Viererblová.⁶¹ However, as these authors mention, the effect of this term would approach zero in the thermodynamic limit. Since our final results for ε_r are extrapolated to infinite system size, the use of Eq. (2) instead of the unbiased version without the $\langle M \rangle^2$ term would not create significant discrepancy in the final values and associated standard errors. We confirmed that by recalculating ε_r for a select concentration, as an example, without the $\langle M \rangle^2$ term, and no significant differences were observed for the final values of the relative permittivity and the associated uncertainty.

IIACs are obtained from the Henry's law expression for the chemical potential at finite concentrations,

$$\mu_i = \mu_i^{\mathsf{T}} + RT \ln m_i \gamma_i, \tag{3}$$

where μ_i^{\dagger} is the Henry's law standard chemical potential using molality concentration units and m_i is the concentration of single ion *i* in molality (mol salt/1000 kg H₂O), equal to that of monovalent salt. Even though in this equation the unit for concentration is molality and the corresponding activity coefficients are referred to as "molality-based activity coefficients," we convert the unit for concentration to *M* as introduced earlier. This is to be consistent with the "constant-volume" nature of the canonical ensemble used in implicit simulations. Equations (4) and (5) are used for conversion of concentrations from *m* to *M* as well as to obtain the number of ion pairs (N_{salt}) in the implicit-water simulations corresponding to given molalities, solution densities (ρ_s), and simulation box lengths (*L*),

$$M = \frac{m\rho_s}{mM_{w,\text{salt}} + 1000},\tag{4}$$

where $M_{w,\text{salt}}$ is the molecular weight of the salt. At low concentrations at which the reference state chemical potential is determined, the two units (molality vs molarity) are essentially the same as the density of the solution is very close to that of pure water.

Recently, we have developed a methodology³⁰ to calculate IIACs in explicit-water solutions based on a "gradual single ion insertion" approach. In this approach, a single ion is inserted into solution from an ideal gas state, and the free energy change along this path—also known as excess chemical potential (μ^{Ex})—is calculated using the thermodynamic integration approach previously used by Panagiotopoulos and co-workers.^{26,27,30,62,63} μ^{Ex} is then added to the chemical potential at the initial ideal gas state (μ^{IG}) resulting in the total chemical potential (μ_i),

$$\mu_i = \mu^{\rm IG} + \mu^{\rm Ex}.$$
 (6)

The ideal gas state chemical potential can be expressed as

$$\mu_i^{\rm IG} = RT \, \ln \frac{N_i \Lambda_i^3}{V},\tag{7}$$

where N_i is the number of ions obtained as the midpoint value before and after ion insertion. For example, the final number for Na⁺ (Cl⁻) after the insertion of a single Na⁺ (Cl⁻) into a solution with ten "salt molecules" is reported to be 10.5. Furthermore, since such insertions are accompanied by neutralizing backgrounds, the number of ion pairs (salt molecules) is also reported as the midpoint before and after insertion. When combining the contributions of the added Na⁺ and Cl⁻ to the solution, the final number of ion pairs is also reported to be 10.5 in the above example. Λ_i is the de Broglie wavelength, and V is total volume of the system. μ_i^{Ex} , on the other hand, is obtained from the Helmholtz free energy difference as

$$\mu_i^{\rm Ex} = \frac{\partial F}{\partial N} \approx \frac{\Delta F}{\Delta N}.$$
(8)

The insertion of single ions is carried out slowly as described in previous studies.^{26,27,3} 0,62,63 As such, a "ghost" particle—without any interactions with other solution species-was randomly inserted into the simulation box. The Lennard-Jones (LJ) and Coulombic (Coul) interactions were then gradually-and in succession-turned on between the inserted particle and the rest of solution constituents by utilizing coupling parameters (λ for LJ and ϕ for Coul). The formalisms of LJ and Coul interactions as functions of the coupling parameters are presented by Young and Panagiotopoulos.²⁶ Eleven windows were considered, equally spaced in the range [0, 1], for both LJ and Coul coupling parameters. Note that a soft-core shifted potential was applied when the LJ interactions were turned on (in the absence of electrostatic interactions) to avoid discontinuity. In each window, the free energy difference was calculated using Bennet's acceptance ratio (BAR).^{27,64} The total excess chemical potential was then calculated from the summation of the LJ ($\mu_{i,k}^{\dot{\mathrm{ex}},\mathrm{LJ}}$) and Coul ($\mu_{i,k}^{\text{ex,Coul}}$) contributions as

$$\mu_i^{\text{Ex}} = \sum_k \mu_{i,k}^{\text{Ex,LJ}} + \sum_k \mu_{i,k}^{\text{Ex,Coul}}.$$
(9)

Statistical uncertainties were obtained from block averaging over the final NVT production runs after discarding the first 2 ns of trajectories for equilibration. The mean and standard errors over several uncorrelated blocks were taken as the final values and associated uncertainties, respectively. The uncorrelated blocks were determined through autocorrelation function for potential⁶⁵ energies.

In the present study, we refrain from adding extra discussion related to the Galvani portion of the individual ion chemical potentials and its effects on (electro-)chemical potentials, since the current manuscript focuses on the deficiency of the implicit-water simulations and comparison to their explicit-water counterpart. The readers are referred to an earlier study of Zhang *et al.*⁶⁶ wherein such effects, attributed to the potential jump at the water/air interface while transferring a single ion into solution, were discussed more elaborately.

The simulation technique was adapted from earlier articles of Mester and Panagiotopoulos^{27,62} wherein chemical potentials at finite concentrations were calculated from pair insertions. The difference between the two methodologies is that adding a single ion into solution will lead to a non-neutral system. The extra charge is, however, countered with a static neutralizing background charge (with an opposite sign) when employing Ewald electrostatics under periodic boundary conditions. The added background would not alter the solution structure, though it will create artifacts attributed to perturbations to the Hamiltonian of the system. We circumvented this problem in our previous study³⁰ by performing several simulations with increasing system sizes and extrapolated the results to the thermodynamic limit, thus eliminating these artifacts. More details are presented in previous studies^{26,30,63} on linear extrapolation vs the inverse box length (1/L) to infinite system size. The uncertainties of the extrapolated results-as explained previously-were calculated using instrumental weighting. We report 68.3% confidence interval as the uncertainty associated with the intercept of the fitted line.

To calculate the standard state chemical potential (μ_i^{\dagger}) , the simulation results at the lowest concentration, i.e., 0.005 M, were forced to pass along the Debye–Hückel limiting slope. Equation (3) can be rearranged as follows:

$$\mu_i^{\dagger} = \mu_i - RT \ln m_i + ART \sqrt{m_i}, \tag{10}$$

where the ln γ_i is replaced with $-A\sqrt{m_i}$ in the limit of high infinite dilution. A is the Debye–Hückel parameter expressed as

$$A = \frac{q_e^3 \sqrt{2N_{\rm A}\rho_s}}{8\pi(\varepsilon_r \varepsilon_0 k_{\rm B}T)^{3/2}},\tag{11}$$

where N_A is the Avogadro's number. ε_r was selected as 73, the value calculated²⁷ for the SPC/E²⁸ water. We used the same approach in our previous study³⁰ with explicit-water simulations to which we referred to the method as *enforcing the Debye–Hückel Slope* (DS).

The statistical uncertainty for ln γ is obtained from propagation of errors from multiple origins. Comprehensive uncertainty analyses and comparisons between explicit and implicit-water simulations have been presented previously.²⁶ Briefly, the uncertainties reported for ln γ contain errors from both the total chemical potential μ and standard state chemical potential (μ^{\dagger}), according to Eq. (3), which could be written as

$$RT\delta \ln \gamma_i = \sqrt{\left(\delta\mu_i\right)^2 + \left(\delta\mu_i^{\dagger}\right)^2}.$$
 (12)

The uncertainty in the former quantity $(\delta \mu_i)$ stems only from the excess chemical potential (μ^{EX}) as the ideal gas contribution is "error free," since simulations are carried out in the canonical ensemble, and hence, the volume is not fluctuating. The uncertainties in μ^{EX} are attributed both to the MD runs and extrapolation to infinite system size as explained earlier. Finally, the uncertainty in μ^{\dagger} contains only errors from the total chemical potential at lowest concentration studies, i.e., 0.005 M, according to Eq. (10), where the parameter A was calculated from Eq. (11). Fluctuations in A due to uncertainties in ε_r and ρ did not have any significant effect on the calculated μ_i^{\dagger} and therefore were not considered in the uncertainty analysis.

We used GROMACS version 2019.6 to perform our implicitwater MD simulations. For each simulation, the ionic species were placed in empty boxes with four different system sizes, two different salts, and two approaches for considering the relative permittivity (ε_r fixed at 73 or concentration-dependent ε_r), the details of which are listed in Tables S2-S43 in the supplementary material. Joung and Cheatham⁵⁶ model parameters were used for the ionic species to be consistent with previous works.^{26,27,30,62} After initial energy minimization using the steepest descent method, production runs were performed in the NVT ensemble using a leap-frog integrator at 298.15 K and 1 bar, and trajectories were collected after discarding the first 2 ns. The duration of runs varied as per the number of particles in the range of 10-20 ns. A Nosé-Hoover thermostat^{67,68} with a coupling constant of 0.1 ps was used, with a 2 fs time step for MD runs. The cutoff for the LJ interactions and the real space portion of electrostatic interactions was 2 nm. Standard long-range corrections were applied where a homogeneous system was considered beyond the cut-off distance with the pair correlation function equal to unity. Particle Mesh Ewald (PME) summations were utilized for electrostatic interactions. A Fourierspace grid of 0.16 nm with a fourth order interpolating function was considered.

RESULTS AND DISCUSSION

Figure 1 illustrates our results for ε_r vs the square root of salt concentration in molality units for NaCl and KCl solutions. Each simulation data point shown is the result of extrapolation to infinite system size. Exceptions are the first two points, i.e., pure SPC/E water²⁸ and solutions at concentration 0.005M, where we consider ε_r to be 73. The linear fits in Fig. 1 are only presented as a guide to the eye; the actual values of ε_r at each concentration were used in the implicit-solvent simulations. The fitted lines were forced to intersect with the y axis at 73 to be consistent with the value of ε_r for pure SPC/E water.²⁸ Comparisons of our simulation results for



FIG. 1. Simulation results for the relative permittivity (ε_r) of explicit-water NaCl (green diamonds) and KCl (purple diamonds) vs \sqrt{m} , where *m* is mol salt/kg H₂O, at 298.15 K and 1 bar. Solid lines represent linear fits forced to intersect with the y axis at $\varepsilon_r = 73$. Error bars and shadings indicate 68.3% confidence interval for the simulation results and the fitted lines, respectively.

 ε_r with those reported in the literature from both experiments and simulations are available in the supplementary material.

For each salt, two sets of implicit-solvent simulations were run, one with ε_r fixed at 73 over the entire concentration range and the other by considering the concentration-dependence of ε_r . For each set and at each salt concentration, a single cation or anion was slowly inserted into solution and the excess chemical potential (μ_i^{Ex}) for ionic species *i* calculated. We considered four system sizes as detailed in Tables S2-S43 in the supplementary material and extrapolated the values to infinite system size. Figure 2 shows the excess chemical potentials vs inverse simulation box length at concentration of 0.005 M as an example of the relevant extrapolations to the thermodynamic limit. The top two panels demonstrate $\mu^{\rm Ex}$ for adding a single Na⁺ and Cl⁻ into corresponding simulation boxes comprising NaCl salts, respectively. Similarly, the bottom two panels show the results for insertion of K⁺ and Cl⁻ into KCl, respectively. Even though implicit-water simulations have been shown to predict the mean ionic activity coefficients of electrolyte solutions somewhat satisfactorily,²⁶ the chemical potentials values are not comparable to those obtained from explicit-solvent calculations. The values for the excess chemical potentials plotted in Fig. 2 are several orders of magnitude smaller than their explicit-water counterparts, presented in our previous study.³⁰ Adding the excess chemical potentials to the ideal gas contributions results in the total chemical potentials (μ) listed in Tables S2–S43 and Fig. S3 in the supplementary material.

Since we have extrapolated all chemical potential values to the thermodynamic limit of infinite simulation box size, it is an interesting question to ask how ionic concentration influences the magnitude of these finite-size effects. For the low concentration of 0.005 M shown in Fig. 2, this dependence is quite strong. Figure 3 shows the slope of the extrapolations (*a*) to infinite system size vs \sqrt{M} for both NaCl and KCl with fixed and concentration-dependent ε_r . At each concentration, the simulation data for *a* are the average between slopes for inserting a single cation and anion into



FIG. 2. Extrapolation of the simulation results for the excess chemical potentials (μ^{ex}) for added Na⁺ (first panel) and Cl⁻ (second panel) into implicit-water NaCl and for added K⁺ (third panel) and Cl⁻ (fourth panel) in implicit-water KCl, at concentration 0.005M, where M is the molarity (mol salt/L). Solid lines represent linear fits and shadings denote 68.3% confidence interval for the fitted lines.

separate simulation boxes. As can be seen from the figure, there is a sharp decline in the slope going from dilute to moderate concentrations before reaching a plateau around 1 M, above which concentration the values of the slope fluctuate around zero. Finite-size effects diminish at higher concentrations, as also seen in previous studies.^{26,30} Furthermore, the magnitude of the a values obtained from insertion of individual ions at low concentrations are almost half the values obtained by Young and Panagiotopoulos²⁶ for pair insertions. The likely cause for this reduced finite-size effect is that the added charge for single-ion insertions is accompanied by a uniform counter charge resulting in zero net added dipole moment, whereas in the pair insertion method, two ions forming a dipole are added to the solution. Figure 4 demonstrates a vs the Debye screening length (κ^{-1}) for NaCl and KCl solutions with fixed ε_r . As it can be seen from the figure, at low salt concentrations where electrostatic forces are the most dominant-and thus the Debye lengths are the highest-the slopes of extrapolations to infinite system size have the largest absolute values. Moving leftward on the x axis (lower κ^{-1} values, corresponding to higher salt concentrations), the absolute values for a become smaller, demonstrating a decline in extrapolation slopes, before fluctuating around zero.



FIG. 3. Simulation results for the average slopes of extrapolation (*a*) to infinite system size for the excess chemical potential of added Na⁺ and Cl⁻ in implicit-water NaCl and K⁺ and Cl⁻ in implicit-water KCl solutions vs \sqrt{M} , where *M* is the molarity (mol salt/L). Black diamonds represent previous simulation results for NaCl with ε_r fixed at 73 from Ref. 26. Filled and open up-pointing triangles denote simulation results from this study for NaCl with fixed and concentration-dependent ε_r , respectively. Filled and open down-pointing triangles denote simulation results for KCl with fixed and concentration-dependent ε_r , respectively.

The standard state chemical potentials for NaCl and KCl were obtained using Eq. (10), as explained earlier. Having calculated both μ_i and μ_i^{\dagger} values, the IIACs and subsequently MIACs can be readily quantified. Figure 5 shows our simulation results for IIACs and MIACs in implicit-water NaCl solution, together with the corresponding experimental data from the literature.^{29,40} Also illustrated in this figure are our previously calculated MIACs and IIACs from explicit-water simulations.³⁰ The top panel shows the MIACs for NaCl, obtained from the contributions of individual ions, using both the constant and concentration-dependent ε_r approaches. The



FIG. 4. Simulation results for the average slopes of extrapolation (a) to infinite system size for the excess chemical potential of added Na⁺ and Cl⁻ in implicit-water NaCl and K⁺ and Cl⁻ in implicit-water KCl solutions vs the Debye screening length (κ^{-1}) in nm. Green and purple stars denote simulation results for NaCl and KCl, respectively, with fixed ε_r .



FIG. 5. Mean ionic activity coefficients (MIACs) (top panel) and individual ion activity coefficients (IIACs) (bottom panel) in implicit-water NaCl solutions vs \sqrt{M} , where *M* is the molarity (mol salt/L), at 298.15 K and 1 bar. Filled and open green triangles denote simulation results for MIACs with ε_r fixed at 73 and concentration-dependent ε_r , respectively. Open red squares denote MIACs from our previous explicit-water simulations.³⁰ Symbols (green plus) and (green circle) denote IIACs of Na⁺ and Cl⁻ in NaCl with $\varepsilon_r = 73$, while (green circles with a plus) and (green circles with a minus) denote IIACs of Na⁺ and Cl⁻ with concentration-dependent ε_r . Symbols (red squares with plus) and (red squares with minus) represent IIACs of Na⁺ and Cl⁻ in NaCl from our previous explicit-water simulations.³⁰ Solid line represents experimental MIACs.²⁹ Dashed (blue) and short dashed (cyan) lines represent experimental data⁴⁰ (fitted to polynomials) for IIACs of Na⁺ and Cl⁻, respectively. Dotted green line represents the Debye–Hückel limiting slope. Statistical uncertainties are smaller than symbol size where error bars are not shown.

MIACs calculated using the constant ε_r compare reasonably with the experimental data²⁹ and those obtained from explicit-water simulations³⁰ using the same force field for ions (JC⁵⁶). On the other hand, MIACs obtained using the concentration-dependent ε_r show negative deviations beyond 1 M, falling precipitously to highly negative values at higher concentrations.

Such significant negative deviations are surprising at first glance. It seems that "correcting" for the concentration-dependence of ε_r makes predictions for the activity coefficients much worse. This seems to suggest that keeping the ε_r fixed at that of pure water over the entire concentration range leads to better results for solution nonideality. However, a closer look at the bottom panel in Fig. 5 reveals that in that case, even though the MIAC results are reasonable, the order of IIACs for Na⁺ and Cl⁻ is reverse, compared to what was observed from explicit-water simulations³⁰ as well as the reported experimental data.⁴⁰ Previously, we have shown that the solvation of the chloride ion is more favorable in water compared to its counterion. Thus, the wrong ordering of IIACs depicted by the implicit-water simulations suggests that the seemingly reasonable agreement between the simulations and experimental data must be the result of a trade-off between two canceling interactions of different origins, namely, ion-ion vs ion-water interactions. Furthermore, we observe that the magnitude of IIACs from implicit-water simulations (with constant ε_r) is much smaller compared to those calculated from explicit-water

simulations and closer to the experimental data. These "closer magnitude," however, is not of physical significance when the positionings of individual activity coefficients are not correct. We have commented on the larger magnitude of IIACs from explicit-water simulations compared to the corresponding experimental data previously.³⁰

To further investigate this, we compared our simulation results for the IIACs of Na⁺ in NaCl with those reported by Valiskó and Boda.⁵² These authors used a combination of Born's treatment of solvation⁵⁴ for ion-water interactions, together with MC simulations with UPM for ion-ion interactions to calculate IIACs, by taking into account the concentration-dependence of relative permittivity. As shown in Fig. 6, the ion-ion portion of simulation results from Valiskó and Boda⁵² demonstrates negative deviations, in great agreement with our results. However, the addition of the opposing "positively deviated" ion-water to ion-ion interactions ultimately results in capturing the correct downward-upward trend of MIACs over the entire concentration range. Therefore, it is apparent that when using a fixed ε_r equal to that of pure water at all concentrations, not accounting for changes in screening of the ions (due to the decrement of ε_r) is somehow compensated with ignoring ion-water interactions. If we correct for only one type of interactions, specifically screening effects, without taking into account the ion-water and ion hydrations, we are inherently-and in a biased way-amplifying the ion-ion interactions. Therefore, one needs to be cautious that the satisfactory MIACs, calculated from implicit simulations with constant ε_r , may not necessarily mean that trends for IIACs are correct. In a more recent study, Abbas and Ahlberg⁵⁵ considered the concentration-dependence of ε_r in the MC simulations of individual ion activity coefficients with the unrestricted primitive model. They obtained reasonable results for the IIACs even though they did not explicitly account for the ion-water interactions, as opposed to the study by Valiskó and Boda.⁵² They, however, treated the cationic radii as adjustable parameters to incorporate indirectly the ion hydration and shortrange interactions with water molecules. This is somewhat similar to



FIG. 6. Simulation results from this study for IIACs of Na⁺ using concentrationdependent ε_r vs \sqrt{M} , where *M* is molarity (mol salt/L), compared with the results from the study of Valiskó and Boda⁵² using a combination of ion–ion (blue dashed line) and ion–water (red dashed line) interactions. Dotted line denotes the Debye–Hückel limiting slope.

a previous study by Chen and Panagiotopoulos⁶⁹ on the calculation of activity coefficients in NaCl + CaCl₂ from implicit-water simulations. In that study, it was shown that implicit-water simulations were able to capture the trend of experimental data when the concentration-dependence of relative permittivity was taken into account. However, they treated the size parameters as adjustable parameters to reproduce pair correlation functions and more importantly the activity coefficients. Fitting the σ parameters to match structural and thermodynamic (e.g., activity coefficients) properties would-unsurprisingly-overcome limitations of implicit-solvent simulations highlighted in the present article. This is, of course, at the cost of rendering the approach more on the correlative side, rather than predictive, since the target properties of interest (activity coefficients) were themselves employed in the force field parameterization, as opposed to the case for JC.56 Therefore, it appears that there are three approaches from which implicit-water simulations perform well in predicting the mean ionic activity coefficients: (1) by introducing adjustable parameters (lack of predictiveness), (2) by adding back the ion-water interactions posteriori (which requires experimental Born radii), or (3) by not taking into account the concentration-dependence of the relative permittivity (at the cost of predicting wrong IIACs).

Finally, Fig. 7 shows the simulation results for MIACs and IIACs in implicit-water KCl solutions, together with the corresponding experimental data from the literature.^{29,40} Our previously calculated IIACs from explicit-water simulations using the same



FIG. 7. Mean ionic activity coefficients (MIACs) (top panel) and individual ion activity coefficients (IIACs) (bottom panel) in implicit-water KCl solutions vs \sqrt{M} , where *M* is the molarity (mol salt/L H₂O), at 298.15 K and 1 bar. Filled and open purple triangles denote simulation results for MIACs with ε_r fixed at 73 and concentrationdependent ε_r , respectively. Open blue squares denote MIACs from our previous explicit-water simulations.³⁰ Symbols (purple plus) and (purple circles) denote IIACs of K⁺ and C⁺ in KCl with ε_r = 73, while (purple circles with plus) and (purple circles with minus) denote IIACs of K⁺ and Cl⁻ with concentration-dependent ε_r . Symbols (blue squares with plus) and (blue squares with minus) represent IIACs of K⁺ and Cl⁻ in KCl from our previous explicit-water simulations,³⁰ respectively. Solid line represents experimental MIACs.²⁰ Dashed (red) and short dashed (cyan) lines represent experimental data⁴⁰ (fitted to polynomials) for IIACs of K⁺ and Cl⁻, respectively. Dotted line represents the Debye–Hückel limiting slope. The symbol size is larger than the uncertainties where error bars are not shown.

force field for ions (IC^{56}) are also illustrated in this figure. We observe a similar behavior for the MIACs of KCl compared to NaCl. As such, using a fixed relative permittivity leads to satisfactory agreement with the experimental data, while systematic negative deviations are seen when considering a concentration-dependent ε_r . However, unlike in NaCl where wrong ordering for IIACs of Na⁺ and Cl⁻ was observed compared to explicit-water simulations³⁰ and experiments,⁴⁰ here the order of IIACs for K⁺ and Cl⁻ is correct. One may interpret that in aqueous salts where ions tend to form hydrations, the implicit-water simulations perform rather poorly in characterizing the behavior of individual ions. On the other hand, in solutions where the ions show strong association, such simulations perform better in predicting the correct orders for IIACs. Previously, we discussed³⁰ these two different tendencies in NaCl and KCl using pair correlation functions. Finally, the larger magnitude for IIACs from explicit-water simulations can also be observed for KCl, consistent with our previous findings, as mentioned earlier in this article and discussed extensively in our previous study.30

CONCLUSIONS

In this study, we compared implicit-water molecular dynamics (MD) simulations with their explicit-water counterparts with respect to their ability to represent activity coefficients in electrolyte solutions. We have recently shown that individual ion activity coefficients (IIACs) in aqueous electrolyte solutions can be obtained from explicit-solvent MD simulations using a "single ion insertion" technique.³⁰ Because of the need to extrapolate to the thermodynamic limit in order to eliminate potential artifacts from neutralizing backgrounds, these simulations are computationally demanding. Therefore, it is compelling to carry out similar implicit-solvent calculations that are much faster and simpler.

We pursued two approaches: the first uses a constant relative permittivity (ε_r) equal to that of pure water, and the second considers the actual concentration-dependent ε_r calculated from our previous explicit-water simulations. Individual ion and mean ionic activity coefficients were calculated for NaCl and KCl solutions. Results for the MIACs of both salts agree well with experimental data when a constant ε_r is used. However, MIACs show strong negative deviations from experimental data when the concentration-dependence of ε_r is taken into account. Therefore, our results demonstrate a rather surprising trend, where using the correct concentrationdependent ε_r values results in incorrect predictions for the MIACs.

Taking a closer look at the behavior of individual ions reveals that the apparent satisfactory predictions of MIACs using implicitwater simulations with constant ε_r may not be physically meaningful. An indicative of that is in NaCl solutions where wrong orders for the IIACs of cations and anions are obtained. The IIACs of Na⁺ are found to be below those of Cl⁻, even though the reverse trend is true according to previous explicit-water simulations and experiments. Hence, it is apparent that the seemingly reasonable results for MIACs with constant ε_r are attributed to two approximations counteracting each other by a happy accident: not accounting for the screening of ions at higher concentrations (by not taking into account the concentration-dependence of ε_r) is somehow offset by not taking into account the short-range interactions due to water molecules as well as the hydration of ions. Furthermore, it is observed that the wrong order for IIACs of Na^+/Cl^- pair is not repeated in KCl where such orders rendered correctly, i.e., IIACs of K⁺ are shown to be below those of Cl⁻. This could be due to "hydration tendency" in NaCl vs "stronger ion association" in KCl. As such, it may be concluded that in salts where there is more tendency for ion hydrations, the implicit-water simulations and thus eliminating the water molecules would result in poor predictions for activity coefficients. On the other hand, in salts with stronger ion association, implicit simulations with constant relative permittivity perform reasonably well for both MIACs and IIACs.

Finally, it is concluded that implicit-water molecular dynamics would fail in predicting MIACs and IIACs-as demonstrated by the strong negative deviations-if the only improvement introduced is taking into account the concentration-dependence of ε_r . That is, unless hydration effects are somehow incorporated in the calculations either by adding ion-water contributions directly using analytical expressions or treating the ionic radii as adjustable parameters, as suggested previously in the literature. On a broader picture, the results indicate that one needs to be extremely cautious when aiming at improving the predictions of activity coefficients in aqueous electrolytes-using either phenomenological models or molecular simulations-when water molecules are not explicitly present in the system. These observations are consistent with previous studies from the literature,¹⁸ where it has been shown that implicit water-based approaches are subject to severe systematic under- or overestimation of activity coefficients when improvements are only made upon an isolated "physical" contribution. In contrast, combinations of several of these contributions-with different physical origins-could potentially produce reasonable predictions of the activity coefficients, although with one caveat: there will always be the possibility of counteracting systematic errors in some of these contributions, hence reaching satisfactory predictions despite the existence of (disguised) physical deficiencies of the methods utilized.

SUPPLEMENTARY MATERIAL

The supplementary material includes figures for solution densities, relative permittivity, and total chemical potentials vs concentration. Furthermore, tables are available for force field parameters used in simulations, as well as numerical values for excess and total chemical potentials at various system sizes, extrapolations to thermodynamic limit, Lennard-Jones and Coulombic contributions, individual and mean ionic activity coefficients, and relative permittivity at different salt concentrations.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors declare no conflicts of interest.

DATA AVAILABILITY

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

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