Mean ionic activity coefficients in aqueous NaCl solutions from molecular dynamics simulations

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The mean ionic activity coefficients of aqueous NaCl solutions of varying concentrations at 298.15 K and 1 bar have been obtained from molecular dynamics simulations by gradually turning on the interactions of an ion pair inserted into the solution. Several common non-polarizable water and ion models have been used in the simulations. Gibbs-Duhem equation calculations of the thermodynamic activity of water are used to confirm the thermodynamic consistency of the mean ionic activity coefficients. While the majority of model combinations predict the correct trends in mean ionic activity coefficients, they overestimate their values at high salt concentrations. The solubility predictions also suffer from inaccuracies, with all models underpredicting the experimental values, some by large factors. These results point to the need for further ion and water model development.

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I. INTRODUCTION

Aqueous electrolyte solutions play an important role in industrial and biological applications, and the study of geothermal brines. Thermodynamic descriptions of aqueous electrolytes typically rely on the Debye-Hückel limiting law or empirical models (e.g., the extended Debye-Hückel equation and the Pitzer model). The Debye-Hückel limiting law is exact in the limit of low electrolyte concentration but fails at higher concentrations. The empirical models rely on parameters fitted to experimental results. In order to overcome the limitations of phenomenological descriptions, there is significant interest in developing methods and models to predict accurately the properties of aqueous electrolyte solutions via molecular simulations.

One previous approach for molecular-based calculations of activity coefficients is the use of implicit-solvent models, avoiding sampling issues associated with explicit water. Lenart et al. proposed implicit-solvent models for the mean ionic activity coefficients of NaCl, LiCl, and KCl aqueous solutions. Short-range hydration interactions were added to the model to describe solvent-separated ion pairs, and a distance-dependent dielectric permittivity was used. Non-Coulombic interactions were described by the Huggins-Mayer potential, with parameters obtained by Pettitt and Rossky from the data of Tosi and Fumi for salt crystals. The model produced good agreement with experiment but provides little transferability to higher temperatures. Gavryushov and Linse measured the potential of mean force acting between cation–cation, cation–Cl–, and Cl–Cl– ion pairs surrounded by SPC/E water where the cation was Li+, Na+, K+, Mg2+, Ca2+, Sr2+, and Ba2+, using molecular dynamics simulations with a spherical cavity approach. The effective potentials constructed with the PMF were used in Monte Carlo simulations with implicit water to calculate mean ionic activity coefficients for concentrations 0.1–1 M. The simulations for NaCl provide accurate predictions compared with experiment, while simulations for KF capture the correct qualitative trends. Gavryushov and Linse found that simulations involving salts with alkaline earth metals correctly predict the mean ionic activity coefficients at 0.1 M but observed significant deviations at higher salt concentrations. These deviations were attributed to the effect of salt concentration on the permittivity and the polarization deficiency arising from the ordering of water molecules in the ion hydration shells.

Ferrario et al. demonstrated that it is possible to calculate the chemical potential of salt in an aqueous electrolyte solution with the Kirkwood generalized thermodynamic integration using an explicit-water model and Ewald summation to account for the long-ranged nature of the Coulombic interactions. The chemical potential of the salt in solution was estimated from adding a single cation and anion to the system. The chemical potential of the salt crystal was calculated with the Einstein crystal method of Frenkel and Ladd. The solubility of KF in SPC/E water was determined using ion-water interactions of Smith and Dang (SD) and ion-ion interactions of the Born-Huggins-Mayer type with Tosi-Fumi (TF) parameters. A solubility of 26 M (moles of solute per liter of solution) for KF at a temperature of 320 K and pressure of 1 bar was obtained from the simulations, while the experimentally determined solubility is 17 M.

Sanz and Vega determined the solubility of KF and NaCl with the model used by Ferrario et al. via thermodynamic integration from a Lennard-Jones (LJ) reference system with a known free energy. The simulations were performed in the canonical (NVT) ensemble using densities determined in previous isothermal-isobaric (NPT) runs. The chemical potential was determined from a quadratic function fitted to the free energy versus ion concentration data. The calculated solubility of KF in water at 320 K and 1 bar was 24 ± 3 M. The calculated solubility of NaCl in water at 298 K and 1 bar was 4.8 ± 0.7 M.

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or $m = 5.4 \pm 0.8$ mol/kg. The experimental solubility is $m = 6.144$ mol/kg.\textsuperscript{13}

Paluch et al.\textsuperscript{30,31} used a self-adaptive Wang-Landau transition-matrix Monte Carlo method in the expanded isothermal-isobaric ensemble to predict the solubility of NaCl in SPC/E water using the ion-water interactions of SD\textsuperscript{27} and the ion-ion interactions of the Born-Huggins-Mayer type with TF parameters.\textsuperscript{19,21,22,28} The predicted solubility of 8.08 mol/kg differed significantly from the value of Sanz and Vega\textsuperscript{29} (5.4 \pm 0.8 mol/kg) due to disagreements in both the solution and crystal chemical potentials.

Arboles et al.\textsuperscript{32} calculated the solubility of NaCl using SPC/E water along with the Joung-Cheatham (JC)\textsuperscript{33} model for both the ion-ion and ion-water interactions, SD\textsuperscript{27} water-ion interactions and TF\textsuperscript{19,21,22,28} ion-ion interactions, and the SD\textsuperscript{27} model for both ion-water and ion-ion interactions. This study used an improved version of the methodology of Sanz and Vega.\textsuperscript{29} Arboles et al.\textsuperscript{32} lengthened both the NPT and NVT simulations, increased the number of $\lambda$-states used to calculate the free energy from 11 to 21, and incorporated a partial molar volume contribution to the calculation of the chemical potential. The solubilities for SPC/E water with the SD, TF, and JC ion models were obtained as $m = 0.9 \pm 0.4$, $4.3 \pm 0.3$, and $4.8 \pm 0.3$ mol/kg, respectively.

Arboles et al.\textsuperscript{32} also calculated solubility by performing direct coexistence calculations between a salt crystal and solution using a slab geometry. This procedure resulted in a solubility of $1.9 \pm 0.4$ mol/kg and $5.5 \pm 0.4$ mol/kg for the SPC/E water model combined with the SD and JC ion models, respectively. The differences between the solubility values predicted by the free energy and direct calculation methods were attributed, potentially, to insufficient run time in the direct calculations and finite size effects in the free energy calculations. Kobayashi et al.\textsuperscript{34} performed similar direct coexistence calculations using the SPC/E water and the JC ion models to obtain a solubility of 8.07 mol/kg for a system initialized with 256 NaCl ion pairs for the crystal and 1208 water molecules and 190 NaCl ion pairs for the solution and a solubility of 6.20 mol/kg for a system initialized with 500 NaCl ion pairs for the crystal and 2000 water molecules and 320 NaCl ion pairs for the solution.

Smith and coworkers in a series of papers\textsuperscript{35–37} developed the osmotic ensemble Monte Carlo simulation method for calculating the chemical potential of salts in solution. The third paper in the series\textsuperscript{37} calculated the solubility of several salts in water using the generalized reaction field (GRF) method for the treatment of the long-ranged Coulombic interactions. The solubility was determined by equating the calculated chemical potential of the salt in solution with the experimentally determined chemical potential of the salt crystal, resulting in values of $m = 4.74 \pm 0.15$ and $5.41 \pm 0.20$ mol/kg for the solubility of NaCl at 298.15 K and 1 bar for the JC\textsuperscript{13} ion model with SPC/E\textsuperscript{34} and TIP4Pew\textsuperscript{38} water, respectively. In a subsequent study,\textsuperscript{39} the osmotic ensemble Monte Carlo simulation method was used to obtain the solubilities predicted by various ion models with SPC/E water. The Ewald summation method was used to account for the long-ranged Coulombic interactions, and the solubility calculations were performed by obtaining the solid chemical potential via simulation using the same electrolyte force fields in the solid and solution phases. This approach for obtaining the solubility is also used in the current paper. The best model for solubility was found by Smith and coworkers\textsuperscript{30} to be the JC ion model, $m = 3.64$ mol/kg at 298.15 K and 1 bar, while the SD model provides a poor prediction for solubility, $m = 0.61$ mol/kg.

The mean ionic activity coefficient quantifies the deviation of the salt chemical potential from Henry’s law (ideal solution) behavior. The chemical potentials of salt $\mu_{\text{NaCl}}$ and water $\mu_{\text{H}_2\text{O}}$ are expressed in terms of the mean ionic coefficient $\gamma$ and thermodynamic activity $a$ as

$$\beta \mu_{\text{NaCl}} = \beta \mu_{\text{NaCl}}^0 + 2 \ln m + 2 \ln \gamma,$$

$$\beta \mu_{\text{H}_2\text{O}} = \beta \mu_{\text{H}_2\text{O}}^0 + \ln a,$$

where $\mu_{\text{NaCl}}^0$ is the Henry’s law standard chemical potential of the salt, $\mu_{\text{H}_2\text{O}}^0$ is the chemical potential of pure water, $\beta = 1/k_BT$ is the inverse thermal energy, $m$ is the concentration of salt in terms of moles of solute per kg of solvent, $T$ is temperature in K, and $k_B$ is the Boltzmann constant.

There have been few prior simulation studies of mean ionic activity coefficients for explicit-water systems, despite their importance and relative abundance of experimental measurements. The main reason for this is that calculation of activity coefficients involves obtaining the chemical potential of a salt at a specific concentration and estimating the corresponding chemical potential at infinite dilution, both to high precision. The first reported simulation study of a salt in explicit water was that of Sanz and Vega,\textsuperscript{29} who determined approximate values for the mean ionic activity coefficient of NaCl in SPC/E\textsuperscript{24} water at “standard conditions” of 298 K and 1 bar, using the SD\textsuperscript{27} model for the water-ion interactions, and TF\textsuperscript{19,21,22,28} for ion-ion interactions. Joung and Cheatham\textsuperscript{40} calculated the mean ionic activity coefficient of NaCl and KF using the combination of the TIP3P\textsuperscript{41} water model and JC\textsuperscript{33} ion parameters. To avoid the difficulties with estimating the chemical potential of salt at infinite dilution, $\mu_{\text{NaCl}}^0$ was determined by assuming that the mean ionic activity coefficients at the lowest concentration simulation runs, $m = 0.038$ mol/kg, match the experimental value of $k_BT \ln \gamma = -0.1$ kcal/mol. More recently, Moučka et al.\textsuperscript{42} calculated the mean ionic activity coefficient using the SPC/E\textsuperscript{24} water model with the JC\textsuperscript{33} ion model at 298.15 K and 1 bar. Moučka et al.\textsuperscript{42} expressed the mean ionic activity coefficient as

$$\beta \mu_{\text{NaCl}} = \beta \mu_{\text{NaCl}}^0 + 2 \ln m + 2 \ln \gamma + 2 \ln(10) \left( -\frac{A\sqrt{m}}{1 + B\sqrt{m}} + bm + Cm^2 + Dm^3 \right),$$

where $A = -0.5108$ and $B = 1.4995$ and $b$, $C$, and $D$ are parameters fitted to the simulation data. The value of $A$ was chosen so that the Debye–Hückel limiting behavior in real water is recovered at $m \to 0$. Since this constant depends on the relative permittivity of the solvent, $\kappa$, using a value appropriate for real water introduces some inconsistency; different water models have values of $\kappa$ that deviate, sometimes significantly, from the experimental value ($\kappa = 78$ at 298 K). Equation (3)
was then fitted to the simulated values of $\mu_{\text{NaCl}}$ for the whole range of $m$, to obtain estimates for $\mu_{\text{NaCl}}^\dagger$ and parameters $b$, $C$, and $D$.

In the present study, mean ionic activity coefficients of aqueous NaCl solutions are obtained for a number of common fixed-charge (non-polarizable) water and ion model combinations at 298.15 K and 1 bar. Chemical potentials are obtained from the free energy changes, resulting from adding an anion and cation pair (or water molecule) to the system. These free energy changes are obtained using Bennett’s acceptance ratio method. Unlike in prior studies, the Henry’s law standard state chemical potential for the salt, $\mu_{\text{NaCl}}^\dagger$, is determined from runs at low salt concentration so that the calculated mean ionic activity coefficients match the Debye-Hückel limiting behavior consistent with the specific water model in use.

The structure of this paper is as follows. In Sec. II, we define the molecular models studied in this work. Section III describes the methods for calculation of the chemical potentials of salt and water in solution and for converting the salt chemical potentials into mean ionic activity coefficients. We also describe the bootstrapping algorithm used to obtain the statistical uncertainty in the chemical potentials. The mean ionic activity coefficients are compared to experiments in Sec. IV, where we also present calculations for the thermodynamic activity of water used to verify Gibbs-Duhem consistency. Conclusions are presented in Sec. V.

II. MOLECULAR MODELS

We used the SPC/E water model in combination with the Smith and Dang and Joung and Cheatham ion models (abbreviated as SPC/E+SD, SPC/E+JC, respectively) and the TIP4Pew water model combined with the Joung-Cheatham ion model (TIP4Pew+JC). These water and ion models contain LJ and Coulombic interactions. The LJ part is

$$u_{ij,\text{LJ}} = 4\epsilon_{ij} \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{6},$$

where $r_{ij}$ is the distance between sites $i$ and $j$. The cross-interaction parameters for the well depth $\epsilon_{ij}$ and size $\sigma_{ij}$ are computed from the Lorentz-Berthelot combining rules

$$\epsilon_{ij} = \sqrt{\epsilon_i \epsilon_j}; \quad \sigma_{ij} = \frac{\sigma_i + \sigma_j}{2},$$

where $\epsilon_i$ and $\sigma_i$ are the LJ well-depth and size of particle $i$. The electrostatic interactions for all models are given by

$$u_{ij,\text{Coul}} = \frac{q_i q_j}{4\pi \varepsilon_0 \kappa(r_{ij})},$$

where $q_i$ is the charge of site $i$ and $\kappa_0$ is the dielectric permittivity of free space.

The SPC/E+SD model was also combined with the Born-Huggins-Mayer-Toxi-Fumi (TF) model to obtain the SPC/E+SD+TF model combination, for which the ion-water interactions are obtained from Eq. (5) using the SD and SPC/E parameters, and the interactions between ions are based on the TF model with parameters $A_{ij}$, $\rho_{ij}$, $B_{ij}$, and $C_{ij}$. The TF parameters are used in a potential equation of the form

$$u_{ij,\text{TF}} = A_{ij} \exp\left(-\frac{B_{ij}}{\rho_{ij}^\alpha} \frac{C_{ij}}{r_{ij}^\beta} \right).$$

We also used the exponential-6 water model (Exp-6), combined with the TF parameters for the ions (termed “Exp-6+TF”). The Exp-6 water potential has the form

$$u_{ij,\text{Exp-6}} = \frac{\epsilon}{1 - \frac{6}{a}} \exp\left(\alpha\left[1 - \frac{r_{ij}}{r_m}\right]^6\right),$$

where $\epsilon$ and $\alpha$ are Exp-6 parameters and $r_m$ is the location of the minimum in the potential. The parameters of the Exp-6 water can be easily converted to $A_{ij}$, $\rho_{ij}$, and $B_{ij}$ parameters as seen in the TF potential. They can subsequently be combined with the TF ion parameters according to

$$A_{ij} = \sqrt{A_i A_j}, \quad \rho_{ij} = \frac{\rho_i + \rho_j}{2},$$

$$C_{ij} = \sqrt{C_i C_j}, \quad D_{ij} = \sqrt{D_i D_j}.$$

Values of the potential parameters used in the present study are given in tables in the supplementary material that accompanies the online version of this article.

III. SIMULATION METHODS

The chemical potential of the salt, $\mu_{\text{NaCl}}$, as a function of temperature $T$, pressure $P$, number of water molecules $N_w$, number of Na$^+$ ions $N_{\text{Na}^+}$, and number of Cl$^-$ ions $N_{\text{Cl}^-}$ was estimated from the change in Gibbs free energy $G$ of adding an anion-cation ion pair

$$\mu_{\text{NaCl}}(T,P,N_w,N_{\text{Na}^+},N_{\text{Cl}^-}) = G(T,P,N_w,N_{\text{Na}^+},N_{\text{Cl}^-};\lambda = 1,\phi = 1) - G(T,P,N_w,N_{\text{Na}^+}-1,N_{\text{Cl}^-}-1;\lambda = 1,\phi = 1).$$

The Gibbs free energy is expressed in terms of the isothermal-isobaric (NPT) partition function $\Xi$ as

$$\beta G(T,P,N_w,N_{\text{Na}^+},N_{\text{Cl}^-};\lambda,\phi) = -\ln \Xi(T,P,N_w,N_{\text{Na}^+},N_{\text{Cl}^-};\lambda,\phi).$$

The partition function is

$$\Xi(T,P,N_w,N_{\text{Na}^+},N_{\text{Cl}^-};\lambda,\phi) = \frac{N_{\text{Na}^+}! N_{\text{Cl}^-}!}{N_{\text{Na}^+}^{N_{\text{Na}^+}} N_{\text{Cl}^-}^{N_{\text{Cl}^-}} N_w^{N_w}} \times \int dV e^{-\beta U - \beta X(\lambda) - \beta Y(\phi)} d\mathbf{r}^{N_w} d\mathbf{r}^{N_{\text{Na}^+}} d\mathbf{r}^{N_{\text{Cl}^-}} d\mathbf{r}^{N_{\text{Na}^+}} d\mathbf{r}^{N_{\text{Cl}^-}},$$

where $U(r^{N_w}, r^{N_{\text{Na}^+}-1}, r^{N_{\text{Cl}^-}})$ is the potential of the $N_{\text{Na}^+}$, $N_{\text{Cl}^-}$, and $N_w$ molecule systems, $z_k$ is the internal partition function of species $k$, and $\Lambda$ is the thermal De Broglie wavelength. The van der Waals (LJ, TF, or Exp-6) potential of the added cation-anion pair (indicated by indices $i$ and $j$, respectively) is given by

$$X(r^{N_{\text{Na}^+}}, r^{N_{\text{Cl}^-}}, \lambda) = \lambda \sum_{k \neq i} u_{ki,ij}(r_{kj}) + \lambda \sum_{k \neq j} u_{kj,ij}(r_{ki}),$$

and the Coulombic potential of the added cation-anion pair is given by

$$\lambda \sum_{k \neq i} u_{ki,ij}(r_{kj}) + \lambda \sum_{k \neq j} u_{kj,ij}(r_{ki}).$$
that the scaling of the Coulombic interactions presented in Eq. (14) is equivalent to scaling the charges of the added cation-anion pair by \( \phi \).

Using
\[
\frac{z_k}{\Lambda_k^2} = \beta \mu_0^0 \exp(-\beta \mu_0^0)
\]
along with Eqs. (10)–(12), we obtain

\[
\beta \mu_{\text{NaCl}} = \beta \mu_{\text{NaCl}}^{ig} + \beta \mu_{\text{Cl}^-}^{ig}
\]

\[
\beta \mu_{\text{NaCl}}^{ig} = \beta \mu_{\text{Na}}^{ig} + \beta \mu_{\text{Cl}^-}^{ig} + 2 \ln \left( \frac{N_{\text{NaCl}}}{\beta \rho(V)} \right)
\]

\[
\beta \mu_{\text{NaCl}}^{ex} = -\frac{\int dV e^{-\beta PV} \int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} \exp(-\beta X(0,1) - \beta Y(\phi=1))}{\int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} e^{-\beta U}}.
\]

Applying BAR to Eq. (18) directly is impractical. At \( \lambda = 0 \) and \( \phi = 0 \), the particles can get close together, leading to large fluctuations in the potential of state \( \lambda = 1 \) and \( \phi = 1 \) in the \( \lambda = 0 \) and \( \phi = 0 \) ensemble. We used several strategies for avoiding this problem. We define arrays of scaling parameters \( \lambda = [0,\ldots,1] \) and \( \phi = [0,\ldots,1] \) and calculate the free energy change between neighboring states. The van der Waals parameter \( \lambda \) is increased to unity before any attempt is made to increase the Coulombic parameter \( \phi \) from zero. This early introduction of core-repulsion prevents large fluctuations in the potentials used to calculate the Coulombic part of the free energy. We also introduce soft-core potentials to remove the divergence of the LJ interactions at \( r_{ij} \to 0 \). The soft-core potentials are obtained by replacing \( r_{ij} \) in the LJ potential given by Eq. (4) with \( r_{ij}^{soft} \), which is given by

\[
r_{ij}^{soft} = \left( \theta \sigma_{ij}^0 (1-\lambda) + r_{ij}^0 \right)^{1/6},
\]

where \( \theta = 0.5 \) is a parameter of the equation. Since the soft-core interactions are identical to the original LJ potentials at \( \lambda = 0 \) and \( \lambda = 1 \), the soft-core potentials produce the correct free energy estimation over this range. The nonphysical portions of the TF and Exp-6 potentials are removed with \( u_{ij,TF}(r_{ij} < r_{max}) = u_{ij,TF}(r_{max}) \) and \( u_{ij,Exp-6}(r_{ij} < r_{max}) = u_{ij,Exp-6}(r_{max}) \) where \( r_{max} \) is the distance between particles that produces the maximum in the potential.

Following this procedure, the excess chemical potential is expressed as a sum between states as

\[
\mu_{\text{ex}}^{Cl^-} = \sum_k \mu_{\text{vdW}}^{\text{Cl}^-} + \sum_l \mu_{\text{Cl}^-}^{\text{vdW}} + \mu_{\text{Cl}^-}^{\text{pot}}
\]

\[
\beta \mu_{\text{vdW}}^{\text{Cl}^-} = -\frac{\int dV e^{-\beta PV} \int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} \exp(-\beta X_{(0,1)} + \beta Y_{(\phi=1)})}{\int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} e^{-\beta U}}.
\]

\[
\beta \mu_{\text{Cl}^-}^{\text{vdW}} = -\frac{\int dV e^{-\beta PV} \int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} \exp(-\beta X_{(1-\phi)} + \beta Y_{(\phi=1)})}{\int d\mathbf{r}^{N_{\text{Na}}^+} d\mathbf{r}^{N_{\text{Cl}^-}^+} d\mathbf{r}^{N_{w}^+} e^{-\beta U}}.
\]
Using BAR, the incremental excess chemical potential $\mu_{\text{NaCl}}^{\text{vdW}}$ for the van der Waals portion is obtained from

$$\frac{n_k}{n_{k+1}} = \frac{\langle f (\beta X(\lambda_k) - \beta X(\lambda_{k+1}) + C) \rangle_{k+1}}{\langle f (\beta X(\lambda_k) - \beta X(\lambda_k) - C) \rangle_k},$$

where $n_k$ is the number of statistically independent samples at state $k$ and $f(x) = 1/(1 + e^x)$. The number of statistically independent samples was estimated according to Chodera et al.\textsuperscript{52}

The excess chemical potential of water $\mu_{\text{H}_2\text{O}}^{ex}$ was calculated similarly to $\mu_{\text{NaCl}}^{\text{vdW}}$ by estimating the free energy change of increasing the potential of a single water molecule from that of an ideal gas molecule to its full interaction. The only difference from the salt chemical potential calculations is that the Coulombic potential of the added charge centers follows the linear scaling of the van der Waals potential in Eq. (13).

For the salt chemical potential calculations using the SPC/E+SD, SPC/E+JC, and TIP4Pew+JC model combinations, the scaling parameters used in the calculations were $\lambda = [0,0.1,...,1]$ and $\phi = [0,0.05,...,1]$. At each point of the simulation, the system was run with a potential consistent with its scaling parameters. The GROMACS\textsuperscript{53} open-source molecular dynamics package, version 4.6.5 (available for download from gromacs.org), was used in the calculations. We equilibrated for 2 ns and used a 20 ns production period in the NPT ensemble using the velocity-Verlet integration method with time steps of 2 fs, the Nose-Hoover thermostat\textsuperscript{54,55} with time constant 1 ps, and the Martyna-Tuckerman-Tobias-Klein (MTTK) barostat\textsuperscript{56} with time constant 2 ps. The cut-off radii for the LJ and Coulomb potentials were 0.9 nm, the cut-off radius for the neighbor list 1.15 nm, and the neighbor list was updated every 10 steps. The potentials were shifted at the inner cut-off radius. Our simulation boxes contained 500 water molecules except for concentrations $m = 0.01$ and 0.06 m, which contained 5000 and 10000 water molecules, respectively. For selected points, system-size effects were tested by running significantly larger systems (5000 instead of 500 water molecules). Results for the larger systems agreed within statistical uncertainties with those of the standard size. We used the particle-mesh Ewald summation\textsuperscript{57,58} to account for the long-ranged nature of the Coulombic interactions. We set the Fourier spacing to 0.1 nm, the relative strength of the Ewald-shifted direct potential at the cut-off to $1 \times 10^{-6}$, and the order of the interpolating function to 6.

The calculations involving the TF potential were run for a total of 12 ns with equilibration period of 2 ns. The scaling parameters for model combinations involving the TF ion model were $\lambda = [0,0.005,0.01,0.02,0.04,...,0.1,0.2,...,1]$ and $\phi = [0,0.05,...,1]$. The run parameters were the same as for the SPC/E+SD, SPC/E+JC, and TIP4Pew+JC model combinations described above except that the potential and neighbor list cut-off distances were both set to 1.0 nm and the neighbor list was updated at every step.

Calculations of the water chemical potential also have run parameters similar to the SPC/E+SD, SPC/E+JC, and TIP4Pew+JC model combinations. The differences are that the production runs for these systems were 100 ns long, the thermostat and barostat time constants were set to 5 ps, and the scaling parameters were $\lambda = [0,0.1,...,1]$ and $\phi = [0,0.1,...,0.5,0.55,...,1]$. For water chemical potential simulations, the water molecules were constrained with the SHAKE algorithm\textsuperscript{50} using a relative tolerance of 0.00005. The SETTLE algorithm\textsuperscript{50} was used to constrain the water molecules in the salt chemical potential calculations.

The chemical potential of the salt is expressed in terms of the mean ionic activity coefficient $\gamma$ according to Eq. (1). In order to use Eq. (1) to determine $\gamma$ from our simulated values of $\mu_{\text{NaCl}}$, we first need to obtain the Henry’s law standard state chemical potential $\mu_{\text{NaCl}}^l$. Generally, this requires calculating the chemical potential of salt in the infinite dilution limit. Since this is not realistic in molecular simulations, we calculated the chemical potential for the lowest concentration system, $m = 0.01$ mol/kg, that we could reasonably simulate. At this low concentration, the activity coefficient is close to that predicted by the Debye-Hückel limiting law. We set $\mu_{\text{NaCl}}^l$ so that our calculated $\gamma$ matched the Debye-Hückel prediction for the corresponding system. The value of the mean ionic activity coefficient predicted by the Debye-Hückel limiting law depends on the dielectric permittivity $\kappa$ of the solvent, which was obtained from simulations of pure water using

$$\kappa = 1 + \frac{\beta((M^2 - \langle M^2 \rangle) \langle M^2 \rangle)}{3 \kappa_0 V},$$

where $M = [M_x,M_y,M_z]$ is the total dipole moment. We equilibrated the systems of 5000 water molecules for 2 ns and used 10 ns production periods in the NPT ensemble. Configurations for the calculation of dipole moments were saved every 0.1 ps.

From the values of excess chemical potential of water $\mu_{\text{H}_2\text{O}}^{ex}$ we can obtain the thermodynamic activity as

$$a = \frac{f}{f^*},$$

where $f$ is the fugacity of water in solution at molality $m$ and $f^*$ is the fugacity of pure liquid water. Both quantities can be determined from

$$f = \frac{N_w}{\beta(V)} \exp \left( \beta \mu_{\text{H}_2\text{O}}^{ex} \right),$$

where $\langle V \rangle$ is the ensemble average volume in the $(T,P,N_{\text{H}_2\text{O}},N_{\text{NaCl}}=1,\phi = 1)$ ensemble. The chemical potential of pure liquid water $\mu_{\text{H}_2\text{O}}^0$ is determined according to

$$\beta \mu_{\text{H}_2\text{O}}^0 = \beta \mu_{\text{H}_2\text{O}} + \ln \left( \frac{f^*}{1 \text{ bar}} \right),$$

where $\beta \mu_{\text{H}_2\text{O}}^0 = -228.582$ kJ/mol is the standard state free energy of formation of water in the gas phase taken from the NIST-JANAF thermochemical tables.\textsuperscript{51} The chemical potential for water in salt solutions is subsequently constructed from Eq. (2).
The statistical uncertainties in the free energy differences between states were obtained through the derivation of the BAR method given by Eqs. (23)–(26) (see Ref. 43). The uncertainties for \( \mu_{\text{NaCl}}^{\text{Na}} \) and \( \mu_{\text{NaCl}}^{\text{Cl}} \) do not add independently due to both sharing the \( k + 1 \) data series. This is also the case for the Coulombic chemical potentials. We circumvented this problem by estimating the statistical uncertainty via bootstrapping \(^{56,61}\). For each value of \( \lambda \) and \( \phi \), we randomly selected \( n \) values with replacements from each set of \( n \) uncorrelated samples constructed from our simulation data according to Ref. 52 and calculated the chemical potential \( \mu_{\text{NaCl}} \). We repeated this procedure 200 times and obtained the standard deviation of the \( \mu_{\text{NaCl}} \) estimates to compute the statistical uncertainties.

The statistical uncertainty of the dielectric constants \( \kappa \) was obtained by applying the rules of error propagation to the estimated uncertainties of \( M_1 \), \( M_2 \), and \( M_3 \) and \( M_4 \), which are calculated from taking the standard deviations of the averages over 1 ns blocks. Since we fix the mean ionic activity coefficient to be equal to the value predicted by Debye-Hückel theory at \( m = 0.01 \text{ mol/kg} \), \( \ln \gamma \) has the propagated uncertainty of \( \kappa \) at this concentration. The resulting Henry’s law standard chemical potential \( \mu_{\text{NaCl}} \) contains the uncertainties of both \( \kappa \) and \( \mu_{\text{NaCl}} \) at \( m = 0.01 \text{ mol/kg} \). Subsequently, we propagate both the uncertainties in \( \mu_{\text{NaCl}} \) and \( \mu_{\text{NaCl}} \) for the appropriate concentrations to the rest of the \( \ln \gamma \) values. The uncertainties of water activities \( \ln a \) are obtained by propagating the uncertainties of the excess chemical potentials \( \mu_{\text{H}_2\text{O}}^{\text{ex}} \) both for the pure water and the solution at the concentration of interest. The activity of pure water is unity by definition, and thus, this value does not have an uncertainty associated with it. The uncertainties of \( \mu_{\text{H}_2\text{O}}^{\text{ex}} \) both for pure water and at the salt concentration of interest are also propagated to the chemical potentials of water in solution, \( \mu_{\text{H}_2\text{O}} \).

IV. RESULTS AND DISCUSSION

We obtained the densities for all model combinations as functions of the salt molarity \( m \) (mol NaCl/kg water) at 298.15 K and 1 bar. Numerical values of system volumes for all the simulations performed (from which the densities can be easily computed) are listed in the supplementary material.\(^{50}\) Figure 1 shows comparisons of the model densities to experimental values.\(^{62}\) The SPC/E- and TIP4P-based model combinations accurately predict the densities at low salt concentrations, but the predictions deteriorate at higher concentrations. More specifically, the SPC/E+SD and SPC/E+SD+TF model combinations underestimate densities at high concentrations while SPC/E+JC and TIP4Pew+JC model combinations overestimate them. The Exp-6+TF model combination overestimates the densities at low salt concentrations and underestimates the density at high concentrations. These results are consistent with previous studies.\(^{29,32,37}\)

Table I shows the chemical potentials of salt in solution \( \mu_{\text{NaCl}} \) and water \( \mu_{\text{H}_2\text{O}} \) predicted by the SPC/E+JC model as a function of molarity \( m \) both from our study and the equations fitted in the study of Moučka \textit{et al.}\(^{42}\) The standard molar chemical potentials \( \mu_{\text{NaCl}}^0 = 574.317 \text{ kJ/mol} \), \( \mu_{\text{Cl}^-}^0 = -240.167 \text{ kJ/mol} \), and \( \mu_{\text{H}_2\text{O}}^0 = -228.582 \text{ kJ/mol} \) were used to obtain \( \mu_{\text{NaCl}} \) and \( \mu_{\text{H}_2\text{O}} \), are taken from the NIST-JANAF thermochemical tables.\(^{51}\) These values do not affect the mean ionic activity coefficients, osmotic coefficients, and solubility results obtained in the simulations but were chosen to facilitate a direct comparison between our data and the chemical potential results of Moučka \textit{et al.}\(^{42}\) The raw simulation data used to construct \( \mu_{\text{NaCl}} \) and \( \mu_{\text{H}_2\text{O}} \) are located in Tables IV and X of the supplementary material.\(^{50}\) The chemical potentials for the other model combinations can be constructed from the data in Tables V to VIII of the supplementary material.\(^{50}\)

By comparing our results to the values predicted by the fitted equation of Moučka \textit{et al.},\(^{42}\) we see that there is excellent agreement between the two studies, often well within the 68.3% confidence level of our study. It is harder to verify the agreement at low concentrations (<0.56 mol/kg) due to the fact that the simulations of Moučka \textit{et al.}\(^{42}\) return a concentration \( m \) for a given value of \( \mu_{\text{NaCl}} \) and even a small uncertainty in \( m \) at low concentrations is equivalent to a large uncertainty.

![Figure 1](image-url)  
**Figure 1.** Density \( \rho \) versus molarity \( m \) of NaCl aqueous electrolyte solutions at 298.15 K and 1 bar. Statistical uncertainties (at the 68.3% confidence level) are less than 0.0005 g/cm\(^3\). Experimental values are taken from Rogers and Pitzer\(^{62}\) and are fitted to a cubic polynomial.

<table>
<thead>
<tr>
<th>( m ) (mol/kg)</th>
<th>( \mu_{\text{NaCl}} ) (kJ/mol)</th>
<th>( \mu_{\text{H}_2\text{O}} ) (kJ/mol)</th>
</tr>
</thead>
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<tr>
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</table>

**TABLE I.** The chemical potentials of salt in solution \( \mu_{\text{NaCl}} \) and water \( \mu_{\text{H}_2\text{O}} \) for the SPC/E+JC model as a function of molarity \( m \) from the present work and from Eqs. 14 and 15 in Ref. 42. Numbers in parentheses indicate statistical uncertainties at the 68.3% confidence level for the corresponding quantity, in units of the last decimal point listed. For example, \(-414.6(2)\) means \(-414.6 \pm 0.2\).
in $\mu_{\text{NaCl}}$. We likewise conclude that there is good agreement approximately within the combined uncertainties between the two studies for the values of $\mu_{\text{H}_2\text{O}}$ for both pure water and NaCl solutions. Most of the differences in the concentration dependent chemical potentials are attributable to the difference in the pure water chemical potential between the two studies, suggesting excellent agreement in terms of ln $a$.

Figure 2 shows the natural logarithm of the mean ionic activity coefficient, ln $\gamma$, as a function of the square root of the molality $m^{1/2}$ for the model combinations examined in this work and compares them to experimental values from Ref. 13. Statistical uncertainties for ln $\gamma$ are between 0.04 and 0.07 (68.3% confidence interval). Numerical values of the activity coefficients and individual statistical uncertainties are listed in the supplementary material. Curves in Figure 2 are obtained by fitting the mean ionic activity coefficient data to a functional form of ln $\gamma$ given by Eq. (3). B, b, C, and D in Eq. (3) are fit parameters. According to Debye-Hückel theory, $A$ is given by

$$ A = \frac{1.824 \times 10^6}{(kT)^{3/2}}. \tag{31} $$

We used our calculated values for the dielectric permittivities $\kappa$ for each individual water model in the calculation of $A$. These values were $\kappa = 73 \pm 2$ for the SPC/E model, $\kappa = 65 \pm 2$ for the TIP4Pew model, and $\kappa = 61 \pm 1$ for the Exp-6. The values of $\kappa$ are in good agreement with prior studies on SPC/E, TIP4Pew, and Exp-6.

All model combinations underestimate the experimentally measured activity coefficients at low concentrations, as expected based on the fact that their dielectric permittivities are lower than the value $\kappa = 78$ of real water. All models except Exp-6+TF overestimate the activity coefficients at salt concentrations higher than approximately $m = 1$ mol/kg. The SPC/E+SD model comes closest to the experimental data overall. The Exp-6+TF model combination severely underestimates the activity coefficients at all concentrations. To allow for a reasonable scale, most of the Exp-6+TF results are not portrayed in Fig. 2; they are listed in the supplementary material.

Figure 3 shows the mean ionic activity coefficients at low values of $m$, to illustrate the effects of the different dielectric permittivities of the models. Our results follow the Debye-Hückel limiting behavior for the corresponding water model, by construction. The underestimation of the activity coefficient at low salt concentrations can be attributed to two factors. The first is the underestimate of the dielectric constant by the water models that has already been mentioned. The second reason is a possible deviation of $\gamma$ at $m = 0.01$ mol/kg predicted by the Debye-Hückel equation from the corresponding experimental value.

There is good agreement between results of the present study and prior calculations of Moučka et al. for the mean ionic activity coefficients of the SPC/E+JC model combination (see Fig. 4). Most of the difference between the values of ln $\gamma$ in the two studies is attributable to a small difference in the values of the Henry’s law standard chemical state potentials $\mu_{\text{NaCl}}$ for our study, $-391.6 \pm 0.2$ kJ/mol and for Moučka et al., $-391.278$ kJ/mol. The agreement with the early results of Sanz and Vega for the SPC/E+SD+TF model combination, however, is poor. At low salt concentrations, Sanz and Vega obtained $\gamma$ from a fitting equation with one fitting parameter. The fitting equation is consistent with the limiting behavior of real water and salt rather than the SPC/E+SD+TF model combination. At high salt concentrations, $\gamma$ is solved from the simulation results of $\mu_{\text{NaCl}}$ using a fitted value of $\mu_{\text{NaCl}}^\diamond$. The deviation in the results at high salt concentrations is probably due to underestimation in Ref. 29 of the values of $\mu_{\text{NaCl}}$. This problem was addressed in a later paper, but the mean ionic activity coefficient calculation was not repeated.
The mean ionic activity coefficient can be converted to the thermodynamic activity of water via the Gibbs-Duhem equation

\[ \frac{\partial \ln a}{\partial \ln m} = \frac{2mM_w}{\gamma} \left( -m + m \ln \gamma + \int_0^m \ln \gamma(m') dm' \right) \tag{32} \]

so that

\[ \ln a = 2mM_w \left( -m + m \ln \gamma + \int_0^m \ln \gamma(m') dm' \right), \tag{33} \]

where \( M_w \) is the molecular weight of water. The fitted equation for salt activity coefficient taken from Eq. (3) can be integrated according to Eq. (33) to obtain the thermodynamic activity. This is compared with our simulated \( \ln a \) values in Fig. 5. The statistical uncertainty of the simulation results is ±0.02. Water activities obtained via the Gibbs-Duhem equation from the computed salt activity coefficients agree with the direct simulation results for the water chemical potentials within their statistical uncertainties, confirming the thermodynamic consistency of the calculations.

Finally, we calculated the solubilities of NaCl in water by finding the molality \( m \) at which the chemical potential of the salt in solution equals the chemical potential of the solid crystal. The values of the solid chemical potential we used are from earlier simulation studies, in particular, \(-391.62 \text{ kJ/mol}\) for the TIP4Pew parametrization of JC, \(-384.37 \text{ kJ/mol}\) for the SPC/E parametrization of JC, \(-384.28 \text{ kJ/mol}\) for SD, and \(-371.888 \text{ kJ/mol}\) for TF. The intersection is determined by fitting Eq. (3) to the chemical potential of salt in solution simulation data using the previously calculated values for \( A \) and \( \mu_{\text{NaCl}} \) and solving for the value of \( m \) where the chemical potentials are equal. The experimental solubility of NaCl in water at 298.15 K and 1 bar is \( m = 6.144 \text{ mol/kg} \). Figure 6 shows that the SPC/E+JC and SPC/E+SD+TF provide the best estimation of solubility compared to experiment at 3.59 ± 0.04 and 3.57 ± 0.05 mol/kg, respectively, a little over half of the experimental value. The SPC/E+SD and Exp-6+TF model combinations are the most deficient in predicting the solubility, resulting in values of 0.61 ± 0.01 and 0.088 ± 0.002 mol/kg—underestimations by factors of 10 and 70, respectively. The TIP4Pew+JC model predicts an intermediate solubility of 1.43 ± 0.03 mol/kg. The statistical uncertainties of the solubility results were obtained by repeating the solubility calculations for chemical potentials obtained from bootstrapping for all values of \( m \).

For the SPC/E+SD and SPC/E+JC model combinations, our results for solubility are in good agreement with the results of Moučka et al.\(^{30}\) (0.61 mol/kg and 3.64 mol/kg, respectively), within the uncertainty of our data sets. For the SPC/E+SD+TF model combination, we estimate from the plot of Moučka et al.\(^{30}\) using linear interpolation between neighboring data points that the chemical potential of the salt in solution calculated by using the Ewald summation method intersects with the salt crystal chemical potential (\(-371.888 \text{ kJ/mol}\)) at approximately 3.6 mol/kg, which is also within the uncertainty of our result. For TIP4Pew water, we see an agreement between our results and the results of Moučka et al.\(^{37}\) which predicts a solubility of approximately 1.4 mol/kg. This solubility was obtained from the results of Moučka et al.\(^{37}\) by finding the intersection of a curve fitted to the simulated salt chemical potentials with the GRF value of salt crystal chemical potential (\(-393.42 \text{ kJ/mol}\)).

The excellent agreement between our results for the chemical potential for NaCl in solution \( \mu_{\text{NaCl}} \) using the SPC/E+JC model combination (see Table 1) and the work of Moučka et al.\(^{42}\) is the reason for the agreement in the solubilities of the current study and Ref. 39. The agreement between the solubilities for the other model combinations with the studies cited above also strongly suggests an agreement in terms of chemical potentials. The exception to this is the study conducted with the TIP4Pew+JC model combination using the GRF method for computing the potentials in the system. While the chemical potentials do not agree with our study, using the appropriate GRF value for the salt crystal chemical potential results in a prediction of solubility that is consistent with our result. This suggests the validity of using GRF in the study of aqueous electrolyte properties. The salt chemical potentials in solution calculated by Paluch et al.\(^{30}\) for the SPC/E+SD+TF model combination were also compared with our results. The two studies were found to be consistent, but the results of the former study have a high degree of uncertainty (i.e., ±2-4 kJ/mol).

Figure 6 indicates that several of our simulations are at salt concentrations above the solubility limit for the corresponding model. This raises the question whether there could be crystallization that influences the chemical potential values obtained. Figure 7 shows the Na\(^+\)−Cl\(^−\) pair correlation functions, \( g(r) \),
for the different model combinations at the highest concentration studied ($m = 6$ mol/kg). The SPC/E+SD pair correlation function from the present study is consistent with the earlier results of Uchida and Matsuoka. For all cases, there is a sharp peak in $g(r)$ approximately at $r = 0.29$ nm, corresponding to contact ion pairs. The broader hydration peaks present at approximately $r = 0.5$ nm for all models except Exp-6+TF correspond to the presence of solvent-separated ion pairs. The lack of solid-like peaks in the $g(r)$ functions confirms that our simulations correspond to the liquid state. The absence of salt precipitation above the solubility limit is due to the use of a closed NPT ensemble and the use of periodic boundary conditions, for which only homogeneous nucleation is possible. In addition, the simulated system volumes are microscopic, and runs are only a few ns long. Homogeneous nucleation rate is not sufficiently high to lead to solid precipitation.

We note that the solubility for the Exp-6+TF model combination is $m = 0.088 \pm 0.002$ mol/kg, deviating the most of all models studied from the experimental data. The mean ionic activity coefficients also deviate significantly from the experimental values, having qualitatively incorrect behavior. As can be seen in Fig. 7, the pair correlation function for this model is quite different from that of the other models. The solvent-separated peak is essentially absent, and the peak corresponding to the contact ion pair is significantly higher. These observations are consistent with a lower-quality solvent due to a relatively low dielectric constant for this model ($\kappa = 61 \pm 1$). The lack of a clear hydration shell is likely connected with the poor agreement of mean ionic activity coefficients of this model with experimental data.

V. CONCLUSIONS

In this work, we have used molecular dynamics simulations with fractional insertion of ion pairs to obtain the mean ionic activity coefficients of sodium chloride (NaCl) aqueous solutions at standard conditions of 298.15 K and 1 bar, with a variety of common ion and water model combinations. We showed that the SPC/E+JC, SPC/E+TIP4Pew, SPC/E+SD, and SPC/E+SD+TF model combinations capture the behavior of mean ionic activity coefficient qualitatively but overestimate solution non-idealities at high salt concentrations. The Exp-6+TF model combination significantly deviates from experimental data at all finite concentrations.

In addition to the mean ionic activity coefficients, we also obtained the solubility of NaCl in water at 298.15 K and 1 bar for the various model combinations of interest. In these calculations, the chemical potential of the salt crystal obtained for the specific salt models in earlier calculations was set equal to the corresponding value in solution obtained from the present study. The solubility results agree with a series of studies performed by Smith and coworkers because of the good agreement in the salt chemical potential values in solution.

All models underpredict the experimental solubility of NaCl in water, some by large factors. The best predictions for solubility were provided by SPC/E+JC and SPC/E+SD+TF model combinations, but even for these models, the predicted solubility is slightly over half of the experimental value.

Overall, the SPC/E+SD model provides the best predictions for the mean ionic activity coefficients with the simulation prediction being approximately within 20% (0.2 units in ln $\gamma$) from the experimental values. In contrast, however, this model combination provides a poor prediction for the solubility, underestimating it by a factor of approximately ten.

Due to the deficiencies in the various models examined here, we conclude that new models are needed for predicting accurately both solubility and mean ionic activity coefficients for aqueous NaCl solutions. One possibility for this would be to use optimized ion-water cross-interaction parameters with existing non-polarizable water models. Moučka et al. attempted to find such parameters to use with SPC/E water, by incorporating concentration-dependent experimental data for the total ionic chemical potential and the density into the fitting procedure for the ion parameters and applying Lorentz-Berthelot combining rules for the ion-water interaction parameters. However, they did not obtain significant improvement in the values of chemical potential for the salt. An alternative procedure for improving the predictions of solubility and mean ionic activity coefficients may be the use of polarizable water and ion models. Such calculations are the subject of an ongoing work.

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