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Max F. Döpke, Othonas A. Moultos, and Remco Hartkamp[a)]

AFFILIATIONS

Process & Energy Department, Delft University of Technology, Leeghwaterstraat 39, 2628 CB Delft, The Netherlands

[a)]**Electronic mail:** r.m.hartkamp@tudelft.nl

ABSTRACT

Countless molecular dynamics studies have relied on available ion and water force field parameters to model aqueous electrolyte solutions. The TIP4P/2005 model has proven itself to be among the best rigid water force fields, whereas many of the most successful ion parameters were optimized in combination with SPC/E, TIP3P, or TIP4P/Ew water. Many researchers have combined these ions with TIP4P/2005, hoping to leverage the strengths of both parameter sets. To assess if this widely used approach is justified and to provide a guide in selecting ion parameters, we investigated the transferability of various commonly used monovalent and multivalent ion parameters to the TIP4P/2005 water model. The transferability is evaluated in terms of ion hydration free energy, hydration radius, coordination number, and self-diffusion coefficient at infinite dilution. For selected ion parameters, we also investigated density, ion pairing, chemical potential, and mean ionic activity coefficients at finite concentrations. We found that not all ions are equally transferable to TIP4P/2005 without compromising their performance. In particular, ions optimized for TIP3P water were found to be poorly transferable to TIP4P/2005, whereas ions optimized for TIP4P/Ew water provided nearly perfect transferability. The latter ions also showed good overall agreement with experimental values. The one exception is that no combination of ion parameters and water model considered here was found to accurately reproduce experimental self-diffusion coefficients. Additionally, we found that cations optimized for SPC/E and TIP3P water displayed consistent underpredictions in the hydration free energy, whereas anions consistently overpredicted the hydration free energy.

I. INTRODUCTION

Aqueous electrolyte solutions have been studied extensively using Molecular Dynamics (MD), for applications ranging from water desalination to osmotic power harvesting.[1–3] These simulations rely strongly on the selection of force field parameters. To simulate an aqueous electrolyte, one needs a force field to describe the interactions between water molecules, at least one to describe the interactions between ions, and a combination rule or parameters to describe interactions between water and ions. In principle, any set of water and ion parameters could be combined, but this is not guaranteed to produce physically meaningful results. Ion parameters are optimized in combination with a specific water model and for certain physical properties, which are not necessarily conserved with a different water model. This paper focuses on the transferability of ion parameters between water models, leaving the combination rules aside. However, the reader should be aware that many shortcomings in ionic systems have also been attributed to combination rules.[4,5] A variety of force fields optimized to reproduce different properties of water exist. These water models range from polarizable to rigid force fields, each with their own benefits and disadvantages. Our focus will be on rigid water force fields, since these are most commonly used to represent water in aqueous electrolyte solutions.

Some of the most common rigid water force fields are the SPC/E,[6,7] TIP3P,[8] TIP4P/Ew,[9] and TIP4P/2005[10] water models. The

TIP4P/2005 model has emerged as one of the best all-around models.[10–12] Despite this, many of the widely used ion parameters are optimized with TIP3P[8] or TIP4P/Ew,[9] since these water models are used in the Assisted Model Building with Energy Refinement (AMBER)[13] and Chemistry at Harvard Macromolecular Mechanics (CHARMM)[14] force fields. Even when ion parameters optimized in combination with TIP4P/2005 are available, ions optimized with other water models might represent some physical properties more accurately, depending also on the optimization criteria of the parameter set. As a result, many studies[15–37] used ion parameters optimized for other water models in combination with TIP4P/2005, hoping to leverage the strengths of both the ion and water parameter sets.

One of the first studies combining ions and the TIP4P/2005 water model was performed by Alejandre *et al.*[15] In this study, crystal formation in water was studied using 8 NaCl force field models combined with SPC/E, SPC/Fw,[38] TIP4P/2005, and SPC/Fh[15] water models. Despite not using ion parameters optimized for TIP4P/2005, it was found that cluster formation was best predicted by the TIP4P/2005 water model and by a water model introduced in the same study (SPC/Fh[15]). Two years later, Pérez and Rubio[18] studied droplet nucleation of a supersaturated vapor using the TIP4P/2005 water model combined with Optimized Potentials for Liquid Simulations (OPLS)[39] ion parameters. While transferability to TIP4P/2005 water was not directly studied, the authors noted that the ion parameters would require reparameterization. Shortly after, Moučka *et al.*[19] used the Joung and Cheatham[40] (JC) TIP4P/Ew-optimized ion parameters combined with TIP4P/2005. The choice was justified by finding good agreement of the predicted and experimental chemical potential of NaCl. In the following years, a variety of studies have followed suit, combining the JC TIP4P/Ew-optimized ion parameters (JCTIP4PEw) or other ion parameters with the TIP4P/2005 water model.[20–37]

Following the increased use of TIP4P/2005 and demand of ion parameters specifically optimized for TIP4P/2005, the Vega group started working on obtaining parameters for NaCl in terms of solubility.[41,42] The final parameters are presented in the study of Benavides *et al.*[43] Recently, additional ion parameters were published,[44] for Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-, and SO_4^{2-}. However, their performance considering hydration free energies relies on a scaling parameter in order to account for the reduced charges, as will be shown in Sec. III. Furthermore, modeling of many applications such as waste water treatment, nuclear waste disposal, or heavy metal removal requires modeling of, for example, RbCl, $SrCl_2$, or $LaCl_3$. Higher valency ions remain rare in the literature and also cannot be combined easily with the Benavides *et al.*[43] and Zeron *et al.*[44] ions due to the use of $\pm 0.85e$ and $\pm 1.7e$ as partial charges for monovalent and divalent ions, respectively. This choice of partial charges, known as Electronic Charge Correction (ECC), was argued to be necessary in a nonpolarizable model to account for the electronic contribution to the dielectric constant.[45,46] ECC has received increased attention in recent years[24,29,47–49] but remains unusual for most ion force fields.

Because of the large body of studies combining various ion parameters with the TIP4P/2005 water model, we aim at providing a comprehensive transferability study of the most commonly used ion parameters in combination with TIP4P/2005 water in terms of solvation properties. This study can serve as a baseline for safely combining ion parameters with the TIP4P/2005 water model in cases where no suitable ion parameters are available. It will be shown here that, in some situations, even though parameters optimized combined with TIP4P/2005 are available, mixing force fields may yield better performance in terms of specific properties of interest.

We focus on the hydration free energy (ΔG_{solv}), ion-oxygen distance (r_{IO}), and coordination number (CN) of the first hydration shell, ion self-diffusion coefficient ($D_{i,self}$), chemical potential (μ), and mean ionic activity coefficients (γ), of which ΔG_{solv} and r_{IO} are commonly fitted in the parameterization procedure of ions in water. For many parameterization studies, ΔG_{solv} is used as the first step in the optimization,[39,40,50–55] with r_{IO} generally being provided as an independent check of quality and validity of the parameters. For example, Smith and Dang[51] optimized Na^+ and Cl^- ions for SPC/E water by fitting to experimental gas-phase binding energies of small ion-water clusters and to solvation energies, ΔG_{solv}, of ionic solutions. r_{IO} was provided as an independent check to match the experimental data. The parameters of Smith and Dang have been used frequently, and the corresponding ion properties have been evaluated in combination with a multitude of water models, from the prediction of mean ionic activity coefficients to thermodynamic transport properties.[56–58] Joung and Cheatham[40] (JC) performed a thorough optimization by first mapping ΔG_{solv} for a range of Lennard-Jones (LJ) length σ and energy ϵ parameters, assuming a unitary partial charge. Second, they computed the lattice constant and energy of salt crystals by varying σ across the LJ parameter space, while keeping ΔG_{solv} constant. Finally, quantum mechanical simulations were used to tune r_{IO} of various ion-water structures. Mamatkulov *et al.*[53,54] followed a similar strategy for divalent cations, first mapping ΔG_{solv} for a σ-ϵ parameter space, but as a second step, they fitted the mean ionic activity coefficients using Kirkwood-Buff theory. The radii of the first hydration shell were computed with the final parameters and shown to be in good agreement with experimental results. The JC and Mamatkulov ions have gained popularity in MD studies, and many properties have also been investigated for these ions.[25,41,42,56] Trivalent and quadrivalent cations were parameterized by Liu and Patey,[30] who fitted ion parameters to experimental ΔG_{solv} and r_{IO} values. However, for these highly charged ions, it was found that the standard 12-6 LJ potential could not simultaneously reproduce both properties accurately. Therefore, a 12-6-4 LJ potential was introduced, with which both ΔG_{solv} and r_{IO} could be reproduced reasonably well. Because this 12-6-4 LJ potential is not implemented in common MD packages, Nikitin and Del Frate recently optimized monovalent and multivalent ion parameters using the standard 12-6 LJ potential and ECC.[49] However, these ions were optimized in combination with the TIP3P water model and were shown to be poorly transferable to the TIP4P/Ew water model. Finally, Benavides *et al.*[43] and very recently Zeron *et al.*[44] produced the only ion parameters known to us specifically optimized for the TIP4P/2005 water model. Benavides *et al.* adjusted Na^+ and Cl^- LJ parameters and charges to reproduce electrolyte properties at finite concentrations, such as the solubility and mean ionic activity coefficients, whereas Zeron *et al.* optimized Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-, and SO_4^{2-} parameters in terms of solution densities and structural properties at multiple finite ion concentrations.

In this work, we took ion parameters from the studies of Smith and Dang,[51] Joung and Cheatham,[40] Mamatkulov *et al.*,[53] Li *et al.*,[55] Benavides *et al.*,[43] and Zeron *et al.*[44] and calculated ΔG_{solv}, r_{IO}, CN, and $D_{i,self}$ at infinite dilution (no ion-ion interactions are considered) and standard atmospheric conditions combined with the TIP4P/2005 water model. We also computed the density, ion pairing, chemical potential, and mean ionic activity coefficients for selected ion parameters to assess their performance at finite concentrations. These properties are often neglected during parameter optimization. An exception to this are the studies of Benavides *et al.*[43] and Zeron *et al.*,[44] which considered these properties during their parameter optimization, obtaining good agreement with experiments. We verified our simulation approach by reproducing the results obtained from these ion parameters with the water model that they were originally optimized for. Additionally, some of the properties calculated here, such as the CN and $D_{i,self}$, have not been published previously for many ion parameters. As such, our results provide an extensive overview and analysis that will assist in the selection of ion parameters for the TIP4P/2005 water model by providing a clear overview of their performance and transferability. It will be shown that TIP4P/Ew optimized ion parameters can be used safely combined with the TIP4P/2005 water model, benefiting from the ability of TIP4P/2005 to accurately represent water properties.

The remainder of this paper is organized as follows: The methodology is described in Sec. II, the results are presented in Sec. III, and the conclusions are provided in Sec. IV.

II. METHODS

The systems simulated can be divided into two types: (1) infinite dilution systems with a single solvated ion and (2) finite concentration simulations with a finite number of ion pairs.

In the infinite dilution systems, a single ion was placed in a cubic periodic box containing 523 water molecules. Each system was energy minimized using the conjugate gradient method, followed by an initialization phase in the NPT ensemble at 1 atm and 298 K to eliminate overlaps between molecules. During the initialization, the time step was increased in consecutive runs of 10 000 steps from *dt* = 0.001 fs to 0.01, 0.1, 0.2, 0.5, until reaching a time step of 1 fs, which was used in all subsequent simulations. The systems were then equilibrated in the NPT ensemble, for 100 ps in the case of infinite dilution systems and 500 ps in the case of finite concentration systems.

Two types of production simulations were performed: (1) the thermodynamic integration cycle from which the hydration free energy (ΔG_{solv}) was obtained and (2) a bulk simulation from which the density, ion pairing, Radial Distribution Functions (RDFs), and self-diffusion coefficient were obtained.

All simulations were performed with the LAMMPS simulation package[59] using the Nosé-Hoover thermostat and barostat where appropriate, with coupling constants of 100 *dt* and 1000 *dt*, respectively.[60,61] A cutoff of 10 Å was used for Lennard-Jones and Coulombic interactions, and long range electrostatic interactions were computed with the particle-particle particle-mesh (PPPM) method with a relative precision of 10^{-6}. In all simulations, the Lorentz-Berthelot mixing rules were used, except for the simulations including the Benavides *et al.*[43] or Zeron *et al.*[44] ions, for which cross-species interactions were given explicitly.

A. Hydration free energy computation

The hydration free energy was obtained using a two-stage thermodynamic integration method.[62] In the first stage (*annihilation*), the charge of the ion was slowly neutralized in water, followed by the second stage (*decoupling*) in which the van der Waals interactions were slowly removed. For the annihilation phase, 6 integration windows from 1 to 0 with equal spacing were used, and for the decoupling phase, unequal spacing with λ_i = 1.0, 0.8, 0.6, 0.5, 0.4, 0.35, 0.3, 0.25, 0.2, 0.15, 0.1, 0.05, and 0.0 was used. This number and spacing of integration windows was found to be sufficient for accurate results, as shown in Fig. 1, which shows that identical results for ΔG are obtained for the annihilation with 12 and 6 λ_i states and for the decoupling with 26 and 13 λ_i states. Each integration window was equilibrated for 100 ps, followed by a 500 ps production run in the NPT ensemble. Furthermore, for the decoupling phase, a soft core potential[63] was used to avoid singularities,

$$U = \lambda^n 4\epsilon \left\{ \frac{1}{\left[\alpha_{LJ}(1-\lambda)^2 + \left(\frac{r}{\sigma}\right)^6\right]^2} - \frac{1}{\alpha_{LJ}(1-\lambda)^2 + \left(\frac{r}{\sigma}\right)^6} \right\}, \tag{1}$$

where $n = 1$ and $\alpha_{LJ} = 0.5$ are fitting constants chosen to produce the smallest variance in the results.[64–67]

For each integration window, $\langle \partial U/\partial\lambda \rangle_{\lambda_i}$ was calculated using the perturbation method,[68]

$$\frac{\partial U(\lambda_i)}{\partial\lambda} = \left\langle \frac{U(\lambda_i+\delta) - U(\lambda_i)}{\delta} \right\rangle_{\lambda_i}, \tag{2}$$

with a perturbation of $\delta = 0.002$. This method calculates the Gibbs free energy at λ_i and $\lambda_i + \delta$ without changing the particle positions. The obtained λ_i states were fitted with a cubic spline, and finally, ΔG_{solv} was obtained by integrating over the spline,

$$\Delta G_{solv} = \sum_k \left\langle \frac{\partial U}{\partial\lambda} \right\rangle_{\lambda_k}. \tag{3}$$

Path independence was verified by reversing the annihilation and decoupling phases to go from $\lambda = 0$ to $\lambda = 1$.

Some studies[52,53,69] have suggested that finite system size effects need to be considered, adding Eq. (S5) (shown in the supplementary material) to ΔG_{solv}. In simulation boxes with 66, 523, and

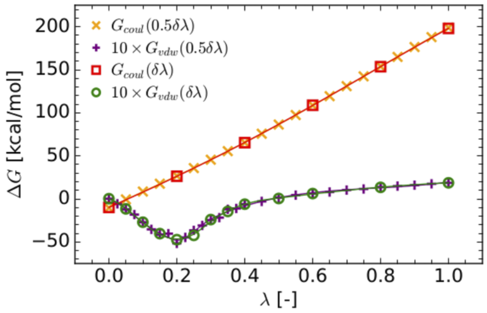

FIG. 1. Lambda states used in this study.

4179 SPC/E water molecules (12.5, 25, and 50 Å box side lengths) and a single Smith and Dang Na^+ ion, we have shown the finite size effect to be negligible. Without finite size-corrections, hydration energies of 88.3, 87.5, and 87.5 kcal/mol were obtained, whereas with the correction, 90.8, 88, and 87.7 kcal/mol were obtained, respectively. The correction appears to overcorrect for the finite system size effects, and we did not apply this correction.

Uncertainty quantification was performed for the Joung and Cheatham SPC/E optimized Na^+ ion in SPC/E water from 5 independent simulations with different starting conditions. Hydration free energy values were found to be almost identical for the independent simulations [$\Delta G = (89.1, 89.1, 89.1, 89.0, 89.0)$]. Therefore, we did not run independent simulations for other combinations for computational efficiency.

B. Ion-oxygen distance and coordination number computation

r_{IO} and CN were obtained from 4 independent 2 ns simulations with a single solvated ion in the NVT ensemble. The simulations were started as described previously, followed by 100 ps equilibration before every production run.

The RDF was sampled every 1 fs up to a distance of 10 Å with 2000 bins. The radii of the first hydration shell, r_{IO}, were obtained by identifying the location of the first peak of the RDF. The CN of the first hydration shell was computed by integrating over the RDF up to the first minimum following that peak.

Finite size independence of the RDF was verified for simulations with 66, 523, and 4179 SPC/E water molecules (12.5, 25, and 50 Å box side lengths) and a single Smith and Dang Na^+ ion. The obtained r_{IO} and CN were, respectively, 2.36, 2.37, and 2.36 Å and 5.7, 5.7, and 5.8.

C. Self-diffusion coefficient computation

The self-diffusion coefficient was obtained from 4 independent simulations with a single solvated ion. The simulations were started as described previously, followed by 100 ps equilibration and 2 ns production runs in the NVT ensemble. During the production runs, the Mean Squared Displacement (MSD) was sampled, from which the self-diffusion coefficient was obtained as follows:[70]

$$D_{i,sim} = \lim_{t\to\infty} \frac{1}{6tN_i}\left\langle \sum_{j=1}^{N_i} \left(r_{j,i}(t) - r_{j,i}(0)\right)^2 \right\rangle, \tag{4}$$

where t indicates the time, N_i indicates the number of atoms of the species i, and $r_{j,i}$ indicates the position of the j-th atom of the species i. The MSD was sampled every 1 ps using the On-the-Fly Calculation of Transport Properties (OCTP) LAMMPS plugin from Jamali *et al.*,[71] which calculates the MSD on the fly using the order $-n$ algorithm.[72] The self-diffusion coefficient then follows from the linear regime in a log-log plot, as shown in Fig. S2 in the supplementary material and Eq. (4).

For the diffusion coefficient, a finite-size correction was found to be necessary. For simulation boxes with 66, 523, and 4179 SPC/E water molecules (12.5, 25, and 50 Å box side lengths) and a single Smith and Dang Na^+ ion, diffusion coefficients of 0.9, 1.1, and 1.4×10^{-9} m^2/s were obtained without finite-size correction. In order to account for the finite size effects, the correction of Yeh and Hummer[73] is applied,

$$D_{i,self} = D_{i,sim} + \frac{\xi k_B T}{6\pi\eta L}, \tag{5}$$

where k_B is the Boltzmann constant, L is the side length of the simulation box, η is the viscosity, and T is the temperature. ξ is the Wigner constant given as 2.837 297 for cubic simulation boxes with periodic boundary conditions. Applying the finite-size correction, the diffusion coefficients changed to 1.6, 1.5, and 1.6×10^{-9} m^2/s, respectively.

D. Mean ionic activity coefficients

Mean ionic activity coefficients, henceforth referred to as activity coefficients, were obtained from the solvation energies at various molalities following the approach presented by Mester and Panagiotopoulos.[57] In short, the activity coefficient γ as a function of molality m can be expressed in terms of the chemical potential μ as

$$\begin{aligned}\mu &= \mu^\dagger + 2k_BT\ln m + 2k_BT\ln\gamma\\ &= \mu^\dagger + 2k_BT\ln m + 2k_BT\ln 10\left(-\frac{A\sqrt{m}}{1+B\sqrt{m}} + bm + Cm^2 + Dm^3\right),\end{aligned} \tag{6}$$

where B, b, C, and D are fitting parameters and A is given by

$$A = \frac{1.824\times 10^6}{(\kappa T)^{3/2}}, \tag{7}$$

with κ being the dielectric permittivity of the respective water model and T being the temperature. $\mu^\dagger$ is Henry's law standard chemical potential, which we obtained by combining the Debye-Hückel limiting law activity coefficient [see Eq. (S12)] with the chemical potential obtained from a simulation at $m = 0.05$ kg/mol. μ is the chemical potential, composed of the ideal gas contribution μ_{ig} and the contribution from the interactions of the ion pair μ_{ex} as

$$\mu = \mu_{ig} + \mu_{ex}, \tag{8}$$

with

$$\mu_{ig} = \mu_0^{cation} + \mu_0^{anion} + 2k_BT\ln\frac{k_BTN_{ion-pairs}}{N_AP\langle V\rangle} \tag{9}$$

and

$$\mu_{ex} = \Delta G_{solv}. \tag{10}$$

The standard chemical potentials μ_0 are obtained from the NIST-JANAF thermochemical tables.[74] N_A is Avogadro's number. The solvation energies ΔG_{solv} of an ion pair at multiple molalities were obtained following the approach described in Subsection II A with some modifications. For better resolution, the λ steps were increased and spaced uniformly from 0 to 1 in steps of 0.05 for annihilation and decoupling. Furthermore, each integration window was extended to 300 ps equilibration and 1500 ps production. The numbers of water molecules and ion pairs of each simulation performed for the chemical potential and activity coefficients along with the results are provided in Tables SII–SIV.

III. RESULTS

Simulations for a variety of ion parameters[40,43,44,51,53,55] and water models were performed to test the transferability of ion parameters optimized for SPC/E,[6] TIP3P,[8] and TIP4P/Ew[9] water models to the TIP4P/2005[10] water model in terms of the hydration free energy, radius, and coordination number of the first hydration shell and self-diffusion coefficient at infinite dilution. The results are displayed throughout Figs. 2–6, which show ΔG_{solv}, r_{IO}, CN, and $D_{i,self}$ obtained from the simulations and experimental results where available. For selected ion parameters, finite concentration properties were also evaluated, as shown throughout Figs. 8–10. For convenience, the data are also tabulated in the supplementary material. In the main body of this paper, we only discuss in detail the first hydration shell, whereas Figs. S3–S7 in the supplementary material show r_{IO} and CN of the second hydration shell. The naming convention of the references henceforth will be as follows: SD for the Smith and Dang ion parameters,[51] JC for the Joung and Cheatham parameters,[40] and the remaining ion parameters from Mamatkulov,[53] Li,[55] Benavides,[43] and Zeron[44] will be referred to by their full names. For the trivalent and quadrivalent ions from Li, we consider only the parameters derived for the 12-6 LJ potential, with LiHFE referring to the ion parameters optimized for ΔG_{solv} and LiIOD referring to the ion parameters optimized for r_{IO}. Verification of our simulation and analysis procedure is presented in the supplementary material. In general, good reproducibility was found, and instances where we could not reproduce the results in very good agreement are discussed in detail throughout the discussion below.

A. Hydration free energy

1. Monovalent ions

Figures 2(a) and 3(a) show ΔG_{solv} of monovalent ions in SPC/E, TIP3P, TIP4P/Ew, and TIP4P/2005 water. We will discuss the results in a chronological order of publication, starting with the SD ions, followed by the JC ions, and concluding with the Benavides and Zeron ions.

The SD Na^+ and Cl^- ϵ and σ parameters were originally tuned to reproduce the gas-phase binding energy and liquid phase hydration energy of NaCl together with the SPC/E water model.[51] After parameterization, ΔG_{solv} = 182 ± 3 kcal/mol was reported, which is close to the experimental value of 188 kcal/mol from Friedman and Krishnan.[77] We attempted to reproduce this result by adding $\Delta G_{solv}^{Na^+} + \Delta G_{solv}^{Cl^-}$ from two separate infinite dilution simulations, obtaining 175.5 kcal/mol. The discrepancy may arise due to the method used to compute ΔG_{solv}. Smith and Dang[51] calculated the total potential energy of the system and subtracted the energy of the water molecules, while we used thermodynamic integration for single ions in water. Despite this, 175.5 kcal/mol is actually in better agreement with more recent experimental results,[75] which report ΔG_{solv}^{NaCl} = 177.7 kcal/mol. The single ion ΔG_{solv} for the SD Na^+ and Cl^- ions is 87.5 and 88.3 kcal/mol when in SPC/E water and 85.1 and 90.4 kcal/mol when in TIP4P/2005 water, as shown in Figs. 2(a) and 3(a). These values compare well to the experimental results of Marcus[76] (87.2 and 81.3 kcal/mol) and Schmid[75] (88.7 and 89.1 kcal/mol, for Na^+ and Cl^-, respectively). As a result, the SD ion parameters display good agreement with experimental results in terms of hydration free energy with both water models, SPC/E and TIP4P/2005.

Joung and Cheatham performed a comprehensive optimization of monovalent ion-parameters for three water models, SPC/E, TIP3P, and TIP4P/Ew. For each combination, the JC ion parameters performed well in terms of ΔG_{solv} compared to the experimental results (errors below ±1%) provided by Schmid *et al.*,[75] as shown in Figs. 2(a) and 3(a). In terms of transferability to TIP4P/2005, the TIP4P/Ew optimized ion parameters (JCTIP4PEw) perform best, providing nearly identical results between the 2 water models. Differences between using either water model and the experimental

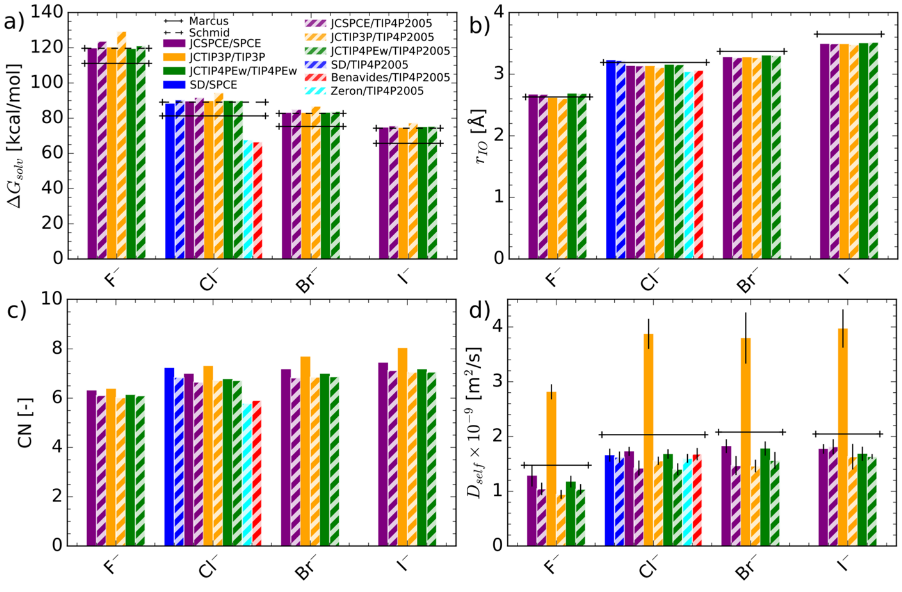

FIG. 2. Transferability of monovalent anion parameters in terms of ΔG_{solv} (a), r_{IO} (b), CN (c), and $D_{i,self}$ (d). 95% uncertainty is shown only for $D_{i,self}$, and other uncertainties were negligible and are therefore not shown. Experimental ΔG_{solv} values are obtained from Schmid[75] and Marcus.[76] All other experimental results are obtained from Marcus.[76]

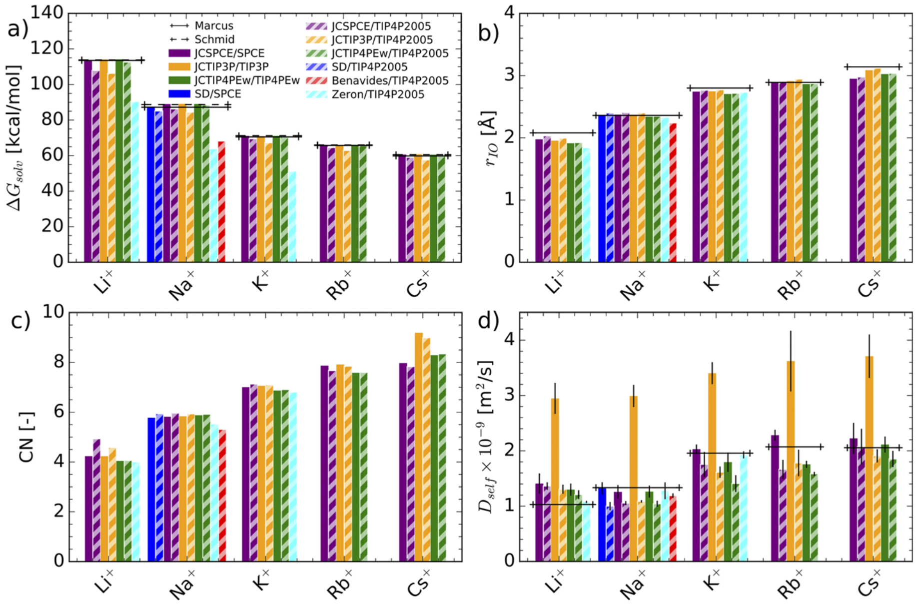

FIG. 3. Transferability of monovalent cation parameters in terms of ΔG_{solv} (a), r_{IO} (b), CN (c), and $D_{i,self}$ (d). 95% uncertainty is shown only for $D_{i,\mathbf{self}}$, and other uncertainties were negligible and are therefore not shown. Experimental ΔG_{solv} values are obtained from Schmid[75] and Marcus.[76] All other experimental results are obtained from Marcus.[76]

results of Schmid[75] were found to be below ±1% for all ions. The SPC/E and TIP3P optimized ion parameters (JCSPCE and JCTIP3P) display an increase in ΔG_{solv} prediction for anions and a decrease for cations when in TIP4P/2005 water. In TIP4P/2005 water, the SPC/E optimized ions display errors below ±5% between predicted and experimental ΔG_{solv}, while for TIP3P optimized ions, errors up to ±8% are obtained. Due to the consistent overprediction of anion ΔG_{solv} and underprediction of cation ΔG_{solv}, the errors in ion pair ΔG_{solv} obtained from the SPC/E and TIP3P optimized ions only range between ±1 and ±3% for SPC/E and TIP3P optimized ions, respectively.

Benavides *et al.*[43] optimized NaCl ion parameters for a number of properties, including solubility and activity coefficients. While this model performs very well over a range of concentrations and temperatures (often not considered in other parameterization studies), ΔG_{solv} is significantly underpredicted, as shown in Figs. 2(a) and 3(a). In the original publication,[43] the hydration energy was not reported, but instead the lattice energy was reported to be considerably underpredicted with 145 kcal/mol, compared to 188.6 kcal/mol obtained in experiments. This underprediction was argued to originate from the charge scaling of the ions from 1 to 0.85. Also indeed, scaling ΔG_{solv} by $1/0.85^2$, as was done for the lattice energy

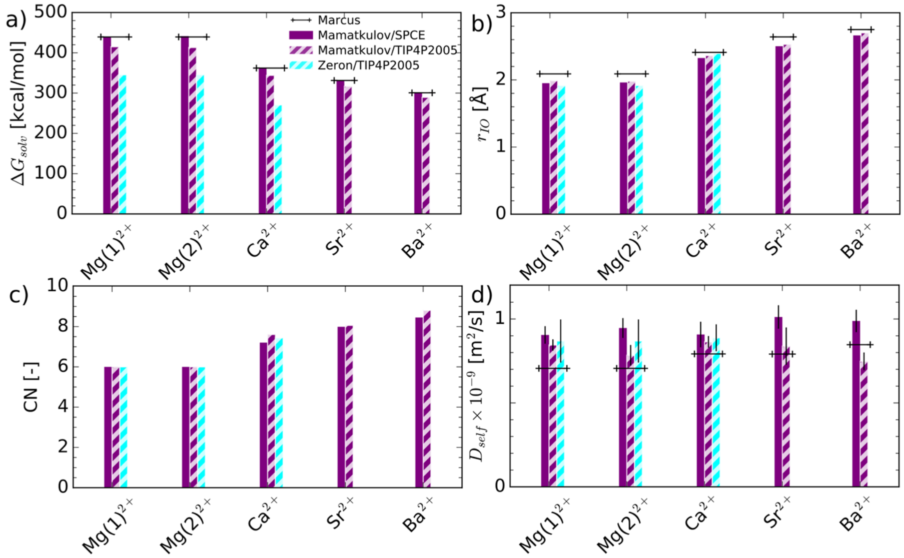

FIG. 4. Transferability of divalent cation parameters in terms of ΔG_{solv} (a), r_{IO} (b), CN (c), and $D_{i,self}$ (d). 95% uncertainty is shown only for $D_{i,\mathbf{self}}$, and other uncertainties were negligible and are therefore not shown. All experimental results are obtained from Marcus.[76]

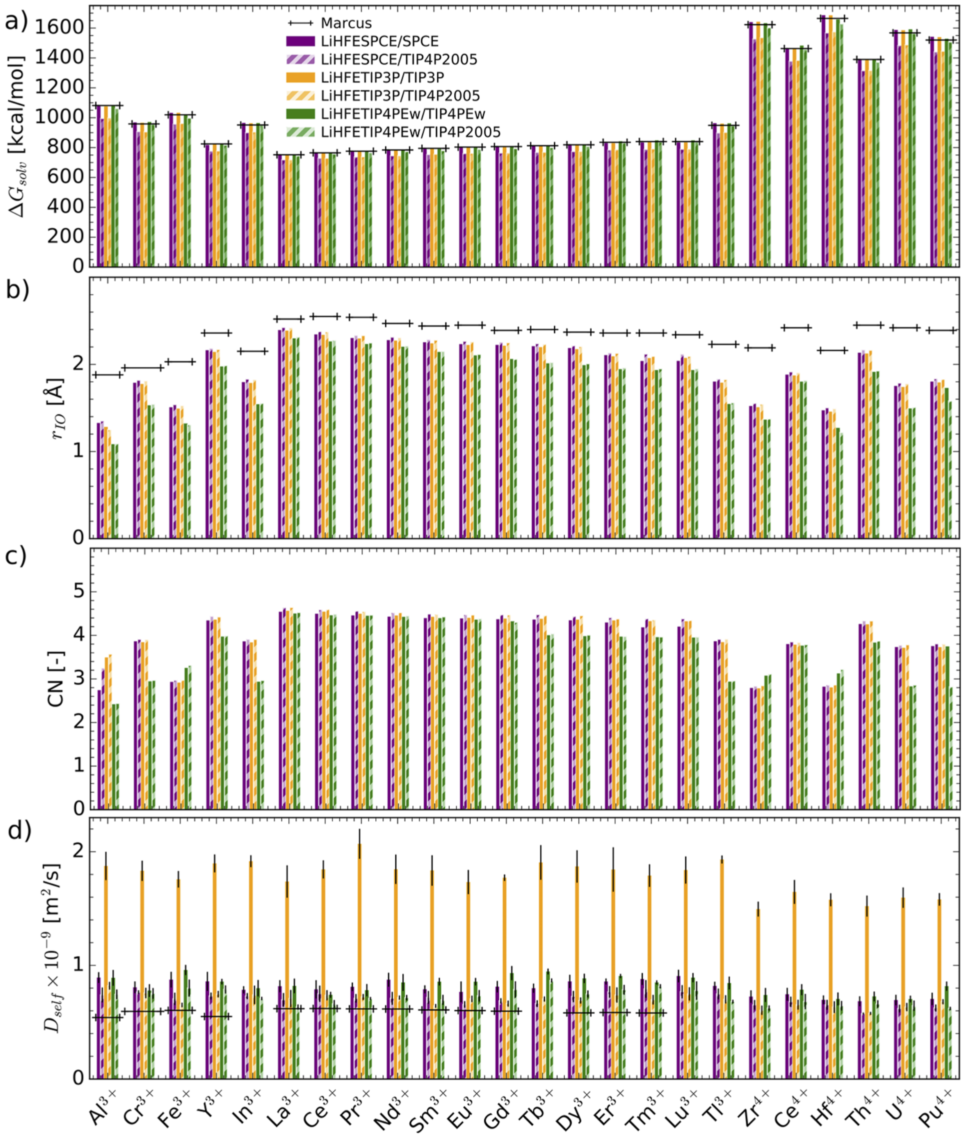

FIG. 5. Transferability of tri- and quadrivalent cation parameters in terms of ΔG_{solv} (a), r_{IO} (b), CN (c), and $D_{i,self}$ (d). 95% uncertainty is shown only for $D_{i,\mathbf{self}}$, and other uncertainties were negligible and are therefore not shown. All experimental results are obtained from Marcus.[76]

in Ref. 43, yields $\Delta G_{solv}^{Na^+} = 94.4$ kcal/mol, $\Delta G_{solv}^{Cl^-} = 92.0$ kcal/mol, and $\Delta G_{solv}^{NaCl} = 186.4$ kcal/mol, which is close to the experimental results from Marcus[76] and Schmid *et al.*[75] (188.6 and 177.7 kcal/mol, respectively). The Zeron[44] ions suffer from the same charge scaling effect as the Benavides ions, underpredicting ΔG_{solv} without scaling and obtaining errors of 10%, −1%, −1%, and 5% with scaling for Li^+, Na^+, K^+, and Cl^-, respectively. In Sec. SII in the supplementary material, it is shown that scaling by $1/0.85^2$ is analogous to the approach of calculating ΔG_{el} as proposed by Leontyev and Stuchebrukhov.[45,46]

Concluding the discussion on the monovalent ions, the TIP4P/Ew optimized ion parameters from Joung and Cheatham are found to perform best with the TIP4P/2005 water model in terms of hydration free energy without scaling. When considering the charge scaling, the Benavides and Zeron ions also perform reasonably well. We hypothesize that the TIP4P/Ew optimized ions perform best due to this model also being a 4 point model. In 4 point models, the ionic charge of the water oxygen atom is displaced by a length M ($M = 0.125$ Å in the case of TIP4P/Ew and $M = 1.546$ Å in the case of TIP4P/2005). Consequently, when transferring ions from SPC/E and TIP3P water models to the TIP4P/2005 water model, the perceived distance r_{ij} in the Coulombic contribution toward the solvation energy increases by 0.1546 Å between cation and water oxygen, reducing $\Delta G_{solv}^{\text{cation}}$, while that between the anion and water oxygen decreases by 0.1546 Å, increasing $\Delta G_{solv}^{\text{anion}}$. When transferring ion parameters optimized for the TIP4P/Ew water model to TIP4P/2005, the change in perceived r_{ij} is only 0.0296 Å (0.1546 Å–0.125 Å), with limited impact on ΔG_{solv}.

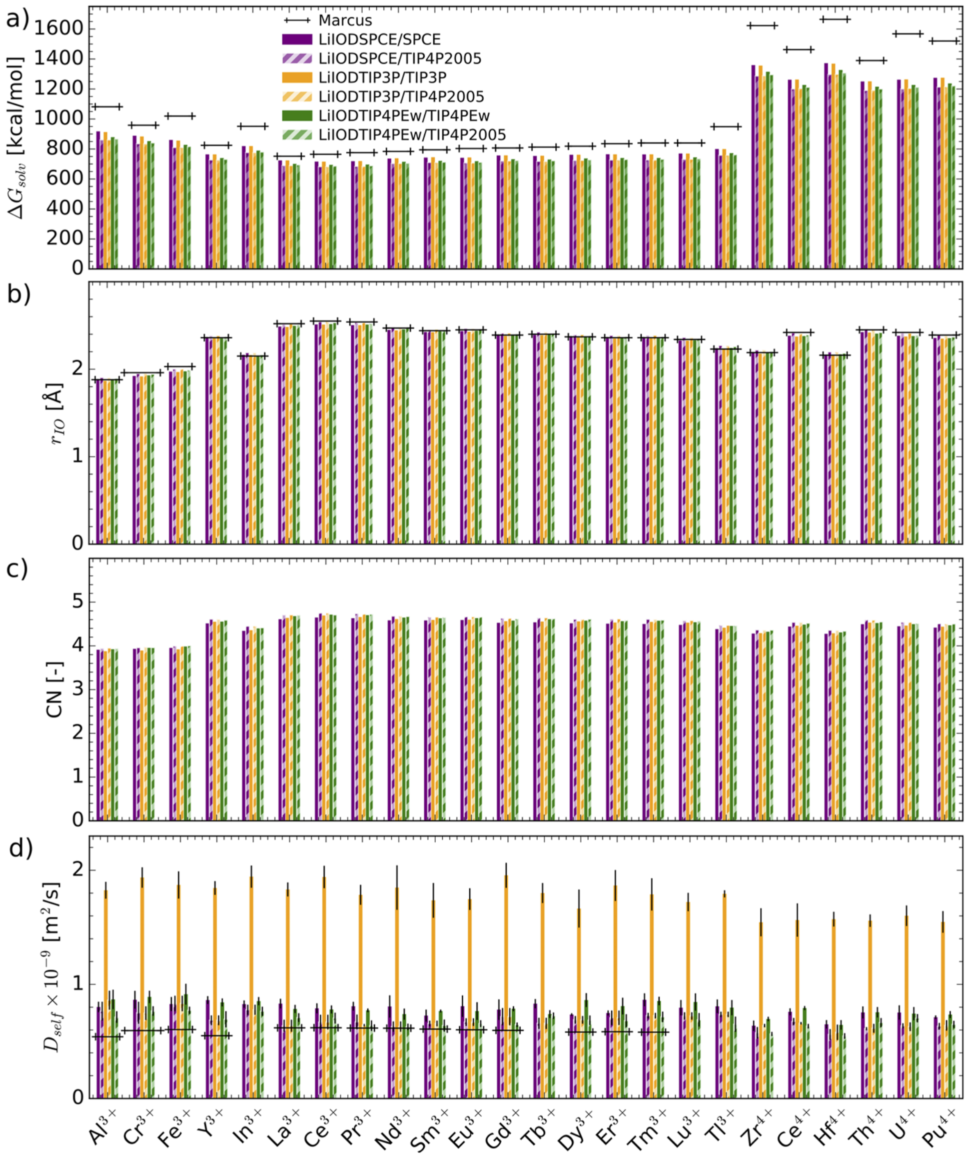

FIG. 6. Transferability of tri- and quadrivalent cation parameters in terms of ΔG_{solv} (a), r_{IO} (b), CN (c), and $D_{i,self}$ (d). 95% uncertainty is shown only for $D_{i,\mathbf{self}}$, and other uncertainties were negligible and are therefore not shown. All experimental results are obtained from Marcus.[76]

2. Divalent ions

Figure 4(a) shows the computed ΔG_{solv} for divalent cations. The values for the Mamatkulov ions depicted in this figure differ from those reported in the original publication[54] due to corrections applied to the data, as detailed in Sec. SI in the supplementary material. Mamatkulov *et al.*[53] computed the single ion ΔG_{solv} and corrected it to match ion pair ΔG_{solv} of a divalent cation together with 2 Cl^- anions. Furthermore, the authors included a finite system size correction, which we have shown to overcorrect the results. We reversed these changes to retrieve the single ion hydration energy without finite system size correction.

In SPC/E water, nearly identical results are found for the Mamatkulov ions between the predicted and experimental values. In TIP4P/2005 water, a consistent underprediction in the cation ΔG_{solv} is found, ranging between −4% and −6% compared to both, the results in SPC/E water and the experimental results. This underprediction can be found to be growing as the hydration energy increases, −4% for Ba^{2+} and Sr^{2+}, −5% for Ca^{2+}, and −6% for Mg^{2+}. This behavior is consistent with the results found for monovalent cations optimized for SPC/E water.

The Zeron[44] ions underpredict the solvation energy by −21% in the case of Mg^{2+} and −25% in the case of Ca^{2+}. For monovalent ions, it was argued that this underprediction can be partially related to the charge scaling, multiplying ΔG_{solv} by $1/0.85^2$. Applying the same logic to the divalent ions, overpredictions of the experimental results of 8.8% and 3.4% were found, respectively.

In conclusion, the Mamatkulov ions perform reasonably well without scaling, while the choice between Mamatkulov and Zeron ions for Mg^{2+} and Ca^{2+} would be based on the desired target properties.

3. Tri- and quadrivalent ions

The hydration free energy obtained from the Li[55] parameters optimized for ΔG_{solv} (LiHFE) and r_{IO} (LiIOD) is given in Figs. 5(a) and 6(a), respectively. From these figures, it appears that the parameters optimized to fit the experimental hydration energy result in very good agreement between predicted and experimental ΔG_{solv} (±1%). On the contrary, the parameters optimized to reproduce the experimental r_{IO} result in a consistent underprediction of ΔG_{solv} between −6% and −20%. Despite this, the correct ordering in terms of ΔG_{solv} emerges, for example, $\Delta G_{solv}^{\mathrm{La}^{3+}} < \Delta G_{solv}^{\mathrm{Ce}^{3+}} < \ldots < \Delta G_{solv}^{\mathrm{Hf}^{4+}}$. The only irregularities in terms of the order are between ions for which the experimental ΔG_{solv} is within 10 kcal/mol of each other.

In terms of transferability, the same conclusions as for the JC ions are drawn. The TIP4P/Ew ion parameters transfer best to the TIP4P/2005 water model, with nearly identical results (reduction of up to −2% in ΔG_{solv}), and the TIP3P ion parameters have the worst transferability. Similarly as for monovalent and divalent cations, tri- and quadrivalent cations optimized for SPC/E or TIP3P water consistently underpredict ΔG_{solv} when combined with TIP4P/2005. The LiHFE ions display a reduction in ΔG_{solv} between −5% and −8%, while a reduction of −5% to −6% is obtained for the LiIOD ions.

B. Ion-oxygen distance and coordination number

1. Monovalent ions

The radii of the first hydration shell for monovalent ions are provided in Figs. 2(b) and 3(b). In these figures, it is observed that the SD ions combined with SPC/E water provide excellent agreement with the experimental results from Marcus[76] for r_{IO}. Overpredictions are found to be 0.3% for Na^+ and 1.5% for Cl^-. When using the same parameters with TIP4P/2005, the agreement remains very good, with errors of 2% and 1%, respectively. The respective CN of the first hydration shell is provided in Figs. 2(c) and 3(c). For the SD ions, we find that the CN for Na^+ increases from 5.77(1) to 5.94(1) when in TIP4P/2005 water, while for Cl^-, it decreases from 7.23(9) to 6.84(3). These results are within experimental measurement errors found in the literature,[78,79] which place the coordination number of Na^+ between 5 and 6 water molecules and of Cl^- at approximately 6 water molecules.

The JC ions provide good agreement with the experimental results for r_{IO} in SPC/E, TIP3P, TIP4P/Ew, and TIP4P/2005 water, with errors up to ±8%. In terms of transferability of the parameters optimized for the SPC/E and TIP3P water models to the TIP4P/2005 water model, we found that the r_{IO} predictions for cations are consistently increased between 1% and 3% for SPC/E optimized cations and between 1% and 2% for TIP3P optimized cations. For TIP4P/Ew optimized cation parameters, on the contrary, almost identical r_{IO} is obtained with both the TIP4P/Ew and TIP4P/2005 water models. All anion parameters showed nearly identical results, with the maximum observed difference being 0.04 Å, considerably below the change in r_{ij} discussed above between 3-site and 4-site water models.

In terms of the CN, larger differences between ion parameters and water models can be observed. For example, for Cs^+, differences between JCSPCE/SPCE, JCTIP3P/TIP3P, and JCTIP4PEw/TIP4PEw combinations are already significant, ranging between CN = 7.97(17) and CN = 9.19(31). This large range also persists when combining the JC ion parameters with the TIP4P/2005 water model. For the JCSPCE Cs^+ ion in TIP4P/2005 water, CN = 7.83(7) is found, while for the JCTIP3P Cs^+ ion in TIP4P/2005 water, CN = 8.99(27) is found. For other JC ions, the range of predicted CNs with SPC/E, TIP3P, and TIP4P/2005 is smaller. Transferability to TIP4P/2005 water shows that the difference in the predicted CN between the combinations JC⟨water model⟩/⟨water model⟩-JC⟨water model⟩/TIP4P2005 is smallest for the TIP4P/Ew optimized ions.

The Benavides ions are found to underpredict the radii of the first hydration shell by −5% and −3% for Na^+ and Cl^-, respectively, and the Zeron ions by −11.5%, −1.2%, −2.5%, and −4.7% for Li^+, Na^+, K^+, and Cl^- ions, respectively. These values are in good agreement with those reported in their publications[43,44] at different molalities (see Table SV). The respective CNs are 5.31(2), 5.91(5), 4.00(0), 5.53(1), 6.81(8), and 5.79(4).

In conclusion, we recommend the TIP4P/Ew optimized ion parameters (JCTIP4PEw) and the Benavides and Zeron ion parameters when using TIP4P/2005 water in terms of r_{IO} and CN. Furthermore, the SD ions are found to provide remarkable agreement with experimental results when combined with the TIP4P/2005 model.

2. Divalent ions

Figures 4(b) and 4(c) show r_{IO} and CN found from our simulations with divalent cations. It is observed that the Mamatkulov ion parameters underpredict the radii of the first hydration shell, by −3% to −7% when combined with the SPC/E water model, but only by −2% to −6% when combined with the TIP4P/2005 water model. This increase in r_{IO} for cations is consistent with the results found for monovalent JCSPCE cations [see Fig. 3(b)]. Consequently, the combination of Mamatkulov ion parameters with TIP4P/2005 water shows better agreement in terms of r_{IO} with experimental results than that with SPC/E water. Along with the increase in r_{IO} when using TIP4P/2005 water, the CN also increases for some cations. For Ca^{2+}, Sr^{2+}, and Ba^{2+}, the CN is increased from 7.21(2) to 7.61(3), from 7.99(1) to 8.06(1), and from 8.45(3) to 8.81(4), respectively, while the CN for Mg^{2+} is identical at 6 for both water models. These values are within the experimental ranges reported by Neilson and Enderby,[78] 6.5–10 for Ca^{2+}, 8 for Sr^{2+}, and 6 for Mg^{2+}.

The Zeron ions predict r_{IO} of 1.92(0) Å for Mg^{2+} and 2.39(0) Å for Ca^{2+}, resulting in underpredictions of −8% and −1%, respectively. This is in agreement with the values reported by Zeron *et al.*[44] of 1.92 Å and 2.38 Å at molalities of 5 mol/kg and 6 mol/kg, respectively. The respective CNs are 6 and 7.44, respectively.

In conclusion, both ion parameter sets perform similarly well when combined with the TIP4P/2005 water model in terms of r_{IO} and CN.

3. Tri- and quadrivalent ions

r_{IO} for the LiHFE and LiIOD parameter sets combined with SPC/E, TIP3P, TIP4P/Ew, and TIP4P/2005 water is provided in Figs. 5(b) and 6(b). We find that parameters fitted by Li to predict r_{IO} (LiIOD) result in very good agreement between experimental and predicted r_{IO}. On the contrary, ion parameters optimized to reproduce ΔG_{solv} (LiHFE) show poor agreement in terms of ion-oxygen distance.

Comparing the RDFs obtained with the LiHFE and LiIOD parameters, it becomes clear that optimizing for ΔG_{solv} can provide, what appears to be, completely unrealistic predictions. This is shown in Fig. 7 for the Fe^{3+} ion. The results obtained with the LiIOD and LiHFE parameters show different first peak locations, and subsequently, also the location of the second peak is misaligned. Consequently, the water layering surrounding the Fe^{3+} ion is likely not predicted correctly when using the LiHFE parameters. This behavior is most pronounced for the smallest ions, as can be observed in Figs. 5(b), 5(c), 6(b), and 6(c) for r_{IO} and CN. Figures S6(a), S6(b), S7(a), and S7(b) in the supplementary material show how the misalignment in r_{IO} and CN strongly affects also the second hydration shell. Because of these results, we disregard the LiHFE parameters and only discuss in detail the transferability to TIP4P/2005 water of the LiIOD parameters in terms of r_{IO} and CN.

r_{IO} and CN predicted when combining the LiIOD cations with TIP4P/2005 follow the same trend as observed for monovalent and divalent cations. For SPC/E and TIP3P optimized cations, r_{IO} and CN are increased when combined with TIP4P/2005 water, while for TIP4P/Ew optimized cations, nearly identical results are found. Comparing r_{IO} obtained with TIP4P/2005 water with experimental results, errors of, on average, 1.4%, 1.6%, and 0.6% are found for the LiIODSPCE, LiIODTIP3P, and LiIODTIP4PEw ion parameters, respectively.

Concluding, ion parameters optimized for TIP4P/Ew water were found to transfer best to TIP4P/2005 in terms of r_{IO} and CN.

C. Ion self-diffusion coefficient

Very few parameterization studies optimize force fields to reproduce experimental ion self-diffusion coefficients. In fact, the self-diffusion coefficients of many ion parameters have not previously been reported, and those that have been reported may deviate substantially from experimental measurements. An exception are the studies from Benavides *et al.*[43] and Zeron *et al.*,[44] who computed self-diffusion coefficients at various molalities and compared them to experimental results. In this paper, we compute the self-diffusion coefficients at infinite dilution, meaning that no concentration effects nor ion-ion interactions are considered, and standard atmospheric conditions, and compare them to experimental values from Marcus[76] in Figs. 2(d)–6(d).

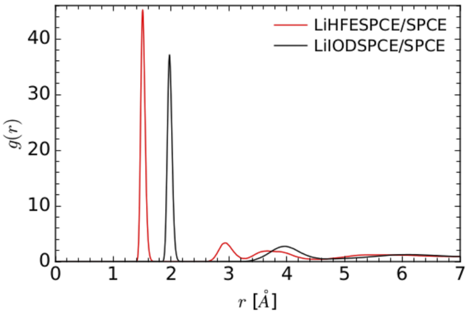

FIG. 7. RDF for the LiHFE and LiIOD Fe^{3+} ion.

All ion models considered here overpredict the ion self-diffusion by a factor more than 2 in combination with the TIP3P water model. It has been proposed[54] that this overprediction can be compensated by scaling the ion self-diffusion by $\eta_{\text{water model}}/\eta_{\text{water}}$ (0.321 mPa s for TIP3P water, 0.89 mPa s found experimentally for water at 298 K).[80,81] Indeed, this scaling was found to provide better agreement with experimental results, as shown in Figs. S3(d)–S7(d) in the supplementary material. However, we argue this scaling to be arbitrary. For example, scaling by $D_{\text{water},self}/D_{\text{water model},self}$ also provides better agreement with experimental results ($D_{\text{TIP3P},self}$ = 5.2×10^{-9} m^2/s, $D_{\text{exp},self}$ = 2.3×10^{-9} m^2/s).[82] Yet, both scalings are applied *a posteriori* and do not improve the actual ion diffusion in the simulation. Therefore, we consider the unscaled self-diffusion coefficients from Figs. 2(d)–6(d) for further analysis.

In general, we find that, for all ion/water combinations, the agreement with experiments is reasonable, except for those including TIP3P water. Starting with the SD ions in Figs. 2(d) and 3(d), we find that the diffusion in the SPC/E water model is in good agreement with experiments. The simulated diffusion coefficient of Na^+ is extremely close to its experimental counterpart, with 1.32(11) × 10^{-9} m^2/s predicted from our simulations and 1.33 × 10^{-9} m^2/s obtained from experiments.[76] The diffusion of Cl^- is worse, underpredicting diffusion by −18%. When using the SD cation or anion in combination with the TIP4P/2005 water model, it is found that the Cl^- diffusion does not change (within uncertainty), while the Na^+ diffusion is reduced to 1.00(7) × 10^{-9} m^2/s, corresponding to an underprediction of −8% compared to experiments. The Benavides Na^+ ion in TIP4P/2005 water shows better agreement with the experimental value, predicting 1.19(4) × 10^{-9} m^2/s, and the predicted Cl^- self-diffusion is similar to that found with the SD Cl^- ion (1.68(11) × 10^{-9} m^2/s). These values yield underpredictions of −11% and −17%, respectively. The Zeron cations show the best agreement, with self-diffusivities within ±4.5% of the experimental values, while the Cl^- anion D_{self} is underpredicted by 21%.

The predicted self-diffusion coefficients for the JC Na^+ ion are 1.26(12) × 10^{-9} m^2/s and 1.06(4) × 10^{-9} m^2/s for the SPC/E optimized ions in SPC/E and TIP4P/2005, respectively, and 1.26(11) × 10^{-9} m^2/s and 1.04(5) × 10^{-9} m^2/s for the TIP4P/Ew optimized ions in TIP4P/Ew and TIP4P/2005, respectively. Hence, combining the JCSPCE or JCTIP4PEw Na^+ ion with TIP4P/2005 results in both cases, in a poorer agreement with experimental ion self-diffusion coefficients. The self-diffusion prediction of the JC Cl^- ion deteriorates from −15% (optimized for and combined with SPC/E) and −16% (optimized for and combined with TIP4P/Ew) to −28% and −31% when combined with TIP4P/2005, respectively. This reduction in self-diffusion coefficient prediction in TIP4P/2005 is similarly observed for all other JC ions. The final diffusivities considering both the JCSPCE and JCTIP4PEw ions present errors of +17% to +32% for Li^+, −20% to −28% for Na^+, K^+, and Rb^+, −10% to +1% for

Cs^+, and ≈ −30% for the anions. Thus, while the JCTIP4PEw parameters provide nearly identical predictions of ΔG_{solv}, r_{IO}, and CN when combined with TIP4P/Ew or TIP4P/2005, the self-diffusion is consistently worse with the latter water model. This finding does not extend to the JCTIP3P parameters. These parameters showed a much too high diffusion when combined with TIP3P, while combining these ion parameters with TIP4P/2005 yielded self-diffusion coefficients of comparable performance to other ion parameters combined with TIP4P/2005.

For divalent, trivalent, and quadrivalent ions, similar trends are observed in Figs. 4(d) and 6(d). These results strongly suggest that the self-diffusion coefficients at infinite dilution are more sensitive to the water model than to small differences in the ion parameters. The sensitivity toward the ion parameters is expected to increase at increasing concentration. Nevertheless, it may prove challenging to derive ion parameters that exhibit realistic self-diffusion across a range of concentrations. Finally, based on water diffusion coefficients in aqueous solutions, research has suggested that classical MD simulations may be unable to recover the correct concentration dependence.[20] In light of these facts, selecting ion parameters based on their infinite dilution self-diffusion is trivial and by no means guarantees realistic diffusion at finite concentrations.

D. Density and ion pairing

For selected ion models, the effects of finite concentrations were investigated. Figures 8 and 9 display the density and ion pairing of the electrolytes at increasing concentration for the JCTIP4PEw, Mamatkulov, and Zeron ion parameters. The JCTIP4PEw and Mamatkulov ions are found to provide reasonable agreement between experimental and simulated densities, while the Zeron ions provide excellent agreement.

In terms of ion pairing, which is evaluated by counting the number of Contact Ion Pairs (CIPs) between cations and anions, it is found that the JCTIP4PEw and Mamatkulov ions predict more pairing than the Zeron ions. This is most pronounced for LiCl in Fig. 8 and for $MgCl_2$ and $CaCl_2$ in Fig. 9. For NaCl and KCl, the JCTIP4PEw ions are found to only predict slightly higher ion pairing than the Zeron ions. While experimental data of ion pairing are scarce, the commonly observed ion precipitation or aggregation in MD simulation is often deemed nonphysical.[24,43,44,83–86] Therefore, we believe that the Zeron ions display overall more realistic ion pairing at finite concentrations. The reduction in ion pairing for the Zeron ions is mainly attributed to the scaling of the charges, from 1 to 0.85, which considers the electronic screening of the medium as explained elsewhere.[45,46] Using the scaled charges, it has also been possible to considerably improve predictions on the solubility limits of electrolytes.[43]

In conclusion, scaling the charges as proposed by Leontyev and Stuchebrukhov,[45,46] and used by Zeron *et al.*,[44] appears to provide the best results in terms of density and ion pairing at finite concentrations.

E. Chemical potential and mean ionic activity coefficient

The chemical potential and mean ionic activity coefficients, named hereafter only activity coefficients, for the TIP4P/Ew optimized NaCl ions from Joung and Cheatham and the Benavides NaCl ions were computed at various molalities. The standard chemical potentials $\mu_0^{Na^+}$ = 137.265 kcal/mol and $\mu_0^{Cl^-}$ = −57.401 kcal/mol needed to solve Eq. (9) were taken from the NIST-JANAF thermochemical tables.[74] The upper part of Fig. 10 shows the chemical potential against molality, which in the case of the Benavides NaCl is shifted by −44.1 kcal/mol to match the experimental data as reported in Ref. 43. Our results are found to underpredict μ^{NaCl} when compared with previous results from Mester and Panagiotopoulos[57] and Benavides *et al.*[43] For the JCTIP4PEw/TIP4PEw NaCl combination, the underprediction was found to originate from a difference in ΔG_{solv} of ≈0.53 kcal/mol. In fact, shifting the JCTIP4PEw/TIP4PEw

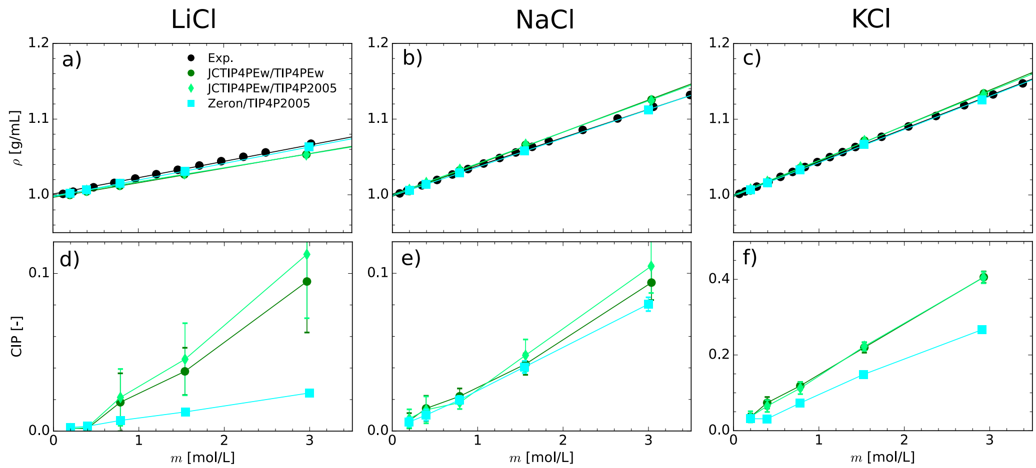

FIG. 8. Density (ρ) [(a)–(c)] and fraction of Contact Ion Pairs (CIPs) [(d)–(f)] vs molarity of the JCTIP4PEw and Zeron LiCl [(a) and (d)], NaCl [(b) and (e)], and KCl [(c) and (f)] ion parameters. Experimental results are taken from Ref. 87. The error bars represent the uncertainty with a 95% confidence interval.

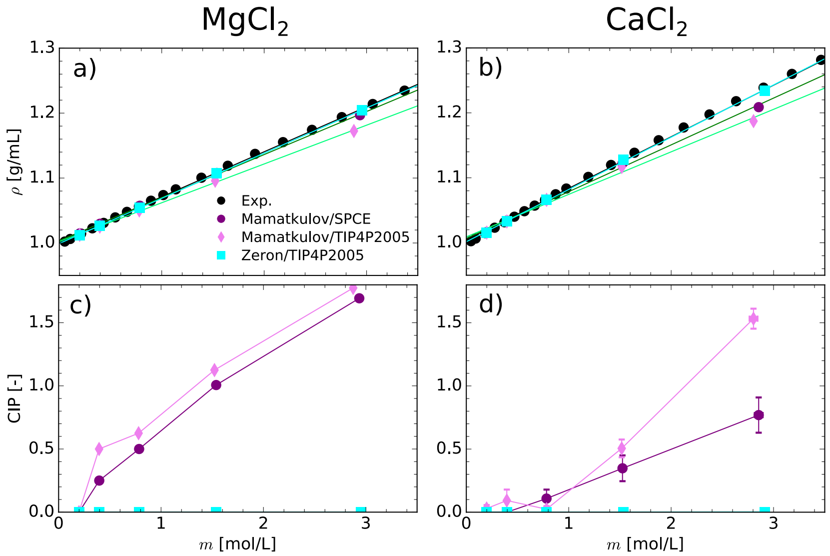

FIG. 9. Density (ρ) [(a) and (b)] and fraction of Contact Ion Pairs (CIPs) [(c) and (d)] vs molarity of the Mamatkulov and Zeron MgCl$_2$ [(a) and (c)] and CaCl$_2$ [(b) and (d)] ion parameters. Experimental results are taken from Ref. 87. The error bars represent the uncertainty with a 95% confidence interval.

NaCl up by 0.53 kcal/mol would provide nearly identical results to those in Ref. 57. The differences between our results and those from Mester and Panagiotopoulos[57] are attributed to the different methods employed to calculate ΔG_{solv}. We used thermodynamic integration, whereas they used the Bennett acceptance ratio method.[88] Benavides *et al.*[43] also used thermodynamic integration, and no shift is necessary to reproduce their results. However, as the molality increases, so does the difference between our and their results of μ. The dashed black lines denote the solid chemical potential obtained with the respective ion parameters, −93.6 kcal/mol and −47.8 kcal/mol, for the JCTIP4PEw and Benavides NaCl, respectively. The molality at which $\mu_{solid} = \mu_{solution}$ is known as the solubility limit. The solubility of the JCTIP4PEw NaCl in TIP4P/Ew and TIP4P/2005 water is found to be, respectively, 1.9 and 2 mol/kg without shift and 1.4 and 1.5 mol/kg with shift. For the Benavides NaCl, we extrapolate the solubility to be 6.75 mol/kg. These values are in reasonable agreement with those from Mester and Panagiotopoulos[57] and Benavides *et al.*[43] of 1.43 and 5.7 mol/kg, respectively.

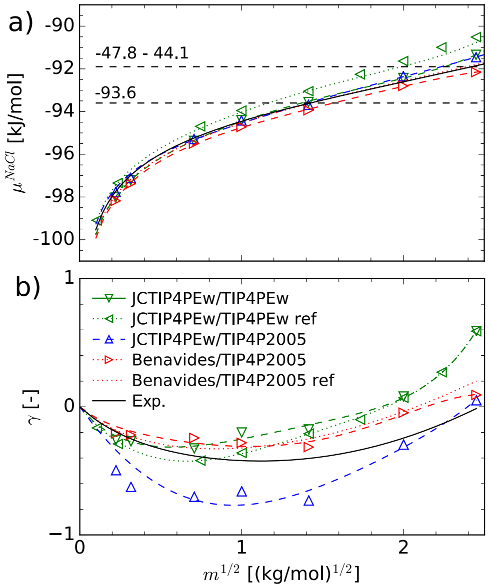

FIG. 10. Chemical potential (a) and activity coefficients (b) against molality for selected NaCl ion parameters and water models. Experimental results were taken from Hamer and Wu.[89] Reference results were taken from Mester and Panagiotopoulos[57] (JCTIP4PEw/TIP4PEw ref) and Benavides *et al.*[43] (Benavides/TIP4P2005 ref).

The logarithm of the activity coefficients, $\ln \gamma$, shown in the lower part of Fig. 10, was obtained by fitting Eq. (6) with the chemical potentials obtained from the simulations. The values of the fitting parameters $\mu^{\dagger}$, A, B, b, C, and D are given in Table SI. $\ln \gamma$ was found to be very sensitive to variations in μ and consequently ΔG_{solv}. As a result, the small differences in μ between our results and those previously reported lead to considerable differences in $\ln \gamma$. A constant shift however, as discussed above, has no influence on $\ln \gamma$. Regardless, the experimental trend can be reproduced fairly well, with all ion-water combinations. Despite this, the JCTIP4PEw NaCl parameters are not transferable in terms of the activity coefficient as indicated by the large difference between the JCTIP4PEw/TIP4PEw and JCTIP4PEw/TIP4P2005 results. The best agreement with the experiments is found for the Benavides NaCl ions.

In conclusion, the Benavides parameters are recommended for the solubility and activity coefficients.

IV. CONCLUSIONS

Transferability of various molecular simulation ion parameters that are frequently used in combination with TIP4P/2005 water was assessed using extensive MD simulations. A single ion was solvated in SPC/E, TIP3P, TIP4P/Ew, and TIP4P/2005 water to study its hydration free energy, ion-oxygen distance, coordination number, and self-diffusion coefficient. The results were compared to available experimental values, and the transferability of ions optimized for other water models to TIP4P/2005 was assessed. Additionally, for selected ions, finite concentration effects were assessed.

The predictions obtained by combining ion parameters with the water model that they were originally optimized with showed good agreement with experimental results in terms of ΔG_{solv}, r_{IO}, and CN. No combination of ion parameters and water model was found to predict accurately the experimental self-diffusion coefficient. It should be noted that no ion parameters were fitted to reproduce this quantity. While it would be possible to optimize force field parameters to reproduce the experimental ion self-diffusion values at infinite dilution, this would be an arbitrary choice and would likely not yield correct self-diffusion coefficients at any other ion concentration. Activity coefficients can serve as a measure to validate the performance of an ion at finite concentrations as has been shown here as well as by Benavides *et al.*[43]

In terms of transferability, it was found that ion parameters optimized for TIP4P/Ew consistently performed best when combined with the TIP4P/2005 water model. The predictions obtained with both water models were not only nearly identical but also in both cases in very good agreement with experimental results. The SPC/E optimized ions were found to transfer reasonably well. A consistent reduction in the cation ΔG_{solv} and increase in the anion ΔG_{solv} were found. This in turn resulted in good ion pair ΔG_{solv} predictions. Similarly, a consistent increase in the cation r_{IO} was found in TIP4P/2005 water, using SPC/E optimized ion parameters. Finally, the TIP3P optimized ion parameters were found to transfer the worst, with the largest differences between both water models and the experimental results when combined with the TIP4P/2005 water model.

For highly charged ions, we found that parameters optimized to reproduce ΔG_{solv} could lead to unrealistic results in terms of r_{IO} and CN. When optimizing highly charged ion parameters in terms of r_{IO}, however, the prediction of hydration free energy was considered to be better in terms of the preserved ΔG_{solv} ordering of ions, $\Delta G^{\mathrm{La}^{3+}} < \Delta G^{\mathrm{Ce}^{3+}} < \cdots < \Delta G^{\mathrm{Hf}^{4+}}$. Given this discovery for the highly charged metal ions, we suspect that an efficient calibration routine for ion parameters should start by reproducing r_{IO}, followed by ΔG_{solv}. In fact, observing the optimization procedure of Joung and Cheatham, this is actually done by selecting σ to fit the lattice constant and energy and adjusting ϵ to match ΔG_{solv}. We expect that whether one fits r_{IO} or lattice constant should provide a similar result.

In conclusion, based on properties at infinite dilution, TIP4P/Ew optimized ions can safely be combined with TIP4P/2005, while for SPC/E optimized ions, at least the change in ΔG_{solv} should be considered when discussing results. We note that these findings may not extend to properties at finite concentrations, as shown in Secs. III D and III E, such that it is advisable to also validate the transferability at finite concentrations. For example, the TIP4P/Ew optimized NaCl parameters from Joung and Cheatham perform very well in the TIP4P/2005 water model at finite concentrations in terms of density and ion pairing, while the LiCl parameters from the same authors perform well in terms of density, but poorly in terms of ion pairing. Ultimately, we encourage parameterization of more ions specifically for TIP4P/2005 in terms of various properties at infinite dilution and finite concentrations. Additionally, for finite concentrations, scaling the ion charges to consider the electronic screening of the medium appears to provide significant improvement in the results compared to unscaled charges.

SUPPLEMENTARY MATERIAL

See the supplementary material for more theoretical background, verification, and additional graphs and tables with extensive data.

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