Experimental studies on ion-water clusters have provided insights into the microscopic aspects of hydration phenomena. One common view is that extending those experimental studies to larger cluster sizes would give the single ion absolute hydration free energies not obtainable by classical thermodynamic methods. This issue is reanalyzed in the context of recent computations and molecular theories on ion hydration, particularly considering the hydration of H\textsuperscript{+}, Li\textsuperscript{+}, Na\textsuperscript{+}, and HO\textsuperscript{−} ions and the hydration of neutral ion pairs. The hydration free energies of neutral pairs computed here are in good agreement with experimental results, whereas the calculated absolute hydration free energies, and the excess chemical potentials, deviate consistently from some recently tabulated hydration free energies based on ion-water cluster data. We show how the single ion absolute hydration free energies are not separated from the potential of the phase in recent analyses of ion-water cluster data, even in the limit of large cluster sizes. We conclude that naive calculations on ion-water clusters ought to agree with results obtained from experimental studies of ion-water clusters because both values include the contribution, somewhat extraneous to the local environment of the ion, from the potential of the phase.

I. INTRODUCTION

The interactions between the ions and inner shell water molecules are much stronger than thermal energies and typically display chemical complexities even in the simplest cases \cite{1, 2}. Computational chemistry and the theories of solutions are approaching the stage that calculations on the free energies of ions in water must be taken seriously. Despite this progress, there is still a non-trivial level of confusion about what is to be learned from experimental comparisons, particularly with comparisons developed from current experimental studies of ion-water clusters. This paper attempts to provide guidance on these issues by presenting a thermodynamic reconsideration of conclusions drawn from ion-water cluster experiments, and results of recent molecular calculations.

Computational results are presented for aqueous ions H\textsuperscript{+}, Li\textsuperscript{+}, Na\textsuperscript{+}, and HO\textsuperscript{−} which participate in a myriad of biological processes \cite{3}. These are common ions in aqueous phase chemistry, and this is especially true for H\textsuperscript{+} and HO\textsuperscript{−}. These species also play a significant role in current problems such as the speciation of beryllium metal in the environment \cite{4} or in the lungs. Understanding beryllium speciation, and the development of beryllium toxicity, is of substantial technological interest, and would benefit from a molecular understanding of ion hydration phenomena.

Absolute hydration free energies, or equivalently single ion activities, that we wish to clarify are not measurable by purely thermodynamic means \cite{5, 6}: correct single ion activities will contain fundamental extra-thermodynamical information and hence their usefulness in thermodynamical analysis might be questioned. Extra-thermodynamical, single ion activities, however, are not unknowable (see \cite{7} and \cite{8}). Furthermore, that knowledge would clarify the molecular understanding of ion hydration, and permit a compact, tabulated consensus of molecularly valid, experimental thermodynamic information.

The existing tables, for example \cite{9, 10, 11}, should naturally be consistent in describing hydration free energies for neutral combinations of ions, since those combinations are thermodynamically measurable. But the alignment of those tables depends on extra-thermodynamical information. An accurate determination of the properly defined single ion activity for any ion represented in those tables would be sufficient to align those tables. It has been pointed out recently \cite{12} that in favorable cases the inaccuracies of computed single ion hydration free energies could probably be made less than the misalignments in current tables of single ion hydration free energies. The present paper pursues this possibility further.

Because simulated extra-thermodynamical information is available from molecular simulations, it is possible to compute solely the work of coupling the ion with the solvent in its locality, i.e., the absolute hydration free energies of the ion separated from the contribution from the potential of the phase (section II). Simulation results, however, critically depend on parameterized molecular models and on the treatment of electrostatic interactions. Moreover, for many ions, particularly H\textsuperscript{+} and HO\textsuperscript{−}, the interactions with water are not easily described by conventional force-fields. This problem is circumvented by the quasi-chemical theory of solutions, within which the excess chemical potential of the solute is partitioned into an inner-sphere contribution, accounting for the chemistry in the inner shell, and an outer-sphere contribution. This latter contribution describes the interaction of the inner-sphere quasi-component with the rest of the fluid and can usually be well described by simple force-field models or dielectric continuum models. This quasi-chemical approach has been used before to treat ions, such as, H\textsuperscript{+} \cite{12}, Li\textsuperscript{+} \cite{13}, Na\textsuperscript{+} \cite{14}, and HO\textsuperscript{−} \cite{15}. Chemical reactions in solution, such as speciation of Fe\textsuperscript{3+} \cite{16} and Be\textsuperscript{2+} \cite{17},
are also well described.

In this article we bring together our earlier observations on the hydration of monovalent ions in conjunction with classical force-field based estimates of outer-sphere contributions. The results so obtained for neutral ion pairs are in good accord with experiments, but our single ion values differ consistently from current tabulations based on cluster-ion hydration experiments.

Our plan for this report is as follows: First, we define our problem and establish the notation we will use. We then discuss the experimental studies leading to current estimates of absolute hydration free energies of the ions. After that, we present the quasi-chemical theory and our computational results. Finally, we return to analyze the experimental cluster-ion hydration results in this context. In the last section we identify conclusions of this work.

II. ABSOLUTE HYDRATION FREE ENERGIES OF IONS IN WATER

We will consider the chemical potentials of ionic solutes in liquid water and we cast these chemical potentials in the form

\[ \mu_{M^+}(w) = e\phi(w) + RT \ln \left[ \rho_{M^+}(w) \Lambda_{M^+}^{-3} \right] + \Phi_{M^+}(w). \]  

(1)

This treats an ionic solute \( M^+ \) suggested to be a metal ion of charge \( e \), but the notation here will be extended naturally to anions \( X^- \). The qualifier \( (w) \) in Eq. (1) indicates the macroscopic phase to which this chemical potential, or another quantity there, applies. Thus, \( \rho_{M^+}(w) \) is the number density of \( M^+ \) in a liquid water phase. (Though we will be particularly interested in the case of liquid water as a solvent, other cases must be permitted also in the typical thermodynamic analysis.) The quantity \( \phi(w) \) is the electrostatic potential of the \( w \) phase. This may be introduced on the basis of the principle that a mean electric field must be zero through interior regions of a macroscopic conductor at equilibrium, and we will use the language that \( \phi(w) \) is the potential of the phase. Only differences in these potentials between phases will be involved, however, in our analysis. The quantity \( \Lambda_{M^+} \) is the thermal deBroglie wavelength for the species \( M^+ \), a known function of the internal characteristics of an \( M^+ \) ion, and of the temperature \( T \), but with no dependences of further thermodynamic relevance. (The standard state adopted by Eq. (1) is sometimes referred to as the Ben-Naim standard state.)

Finally, \( \Phi_{M^+}(w) \) is the object of the present study. It depends on temperature, pressure, and composition of the system. In the limit of vanishing solute concentration we will call it the absolute hydration free energy of \( M^+ \). We are principally interested in standard temperature and pressure conditions. As Eq. (1) is formulated, \( \Phi_{M^+}(w) \) depends on the energetic interactions of solution constituents, i.e., the solvent and dissolved species, with \( M^+ \) ions, and would vanish if those interactions were to vanish. That is also the case for the contribution \( e\phi(w) \).

The separation imposed by Eq. (1) is clear on the basis of our mechanical understanding of electrostatics. But from a thermodynamical view it is a nonoperational separation [17].

As a gauge of molecular structure and energetics of the solution in the neighborhood of an \( M^+ \) ion, \( \Phi_{M^+}(w) \) is worthy of interest. In contrast, \( \phi(w) \) reflects distribution of charge on the surface of the system, and is of less intrinsic interest because it is not sensitive exclusively to the local condition of an ion of interest. The goal is to separate \( \Phi_{M^+}(w) \) from thermodynamic combinations such as \( \Phi_{M^+}(w) + \Phi_{X^-}(w) \), to which the potentials of the phases don’t contribute, and to separate \( \Phi_{M^+}(w) \) from \( e\phi(w) \).

Our notation here is deficient in one respect. For equilibrium of two conducting phases containing ionic solutes at low concentration, the potential difference \( \Delta\phi = \phi(\gamma) - \phi(\eta) \) across the phase boundary is not simply a property of the pair of solvents in contact with one another [8, 18]. (Note that many materials can be considered conductors for sufficiently long times.) From a formal point of view of macroscopic thermodynamics, this follows from the requirement that the bulk compositions of a macroscopic conductor be electrically neutral. More physically, the ions make a Donnan-like contribution to the difference between the electrostatic compositions of the phases to achieve neutral bulk compositions. This potential difference does not progressively vanish as the concentration of the ionic solutes decreases, so it is not operationally avoidable by confining attention to low electrolyte concentrations. The difference \( \Delta\phi \) whatever its source, does not contribute to the thermodynamic combinations \( \Phi_{M^+}(w) + \Phi_{X^-}(w) \). Therefore an accurate evaluation of \( \Phi_{M^+}(w) \) on any basis would avoid consideration of \( \Delta\phi \) altogether.

Thermodynamic considerations will involve differences in these free energies and differences \( \Delta\phi \) in the electrostatic potentials. If a dilute gas is considered to be the coexisting conducting phase, it is instinctive to assign the potential of that phase to be zero. No other considerations need be affected by this choice. It is then convenient to take \( \phi(w) \), for example, to be the potential relative to a dilute gas phase.

III. ANALYSES BASED UPON ION-WATER CLUSTER DATA

Discussions of the difficulty of obtaining the absolute hydration free energy \( \Phi_{M^+}(w) \) often begin with the observation that thermodynamic processes for bulk phases involve manipulation of neutral combinations of material. It is natural, therefore, to consider adding a single ion to a sub-macroscopic amount of solvent, for example

\[ M^+ + (H_2O)_n \rightarrow M(H_2O)_n^+ \]  

(2)
for \( n \) not too large. This leads to the consideration of ion-water cluster experiments as a potential source of information on \( \Gamma_{M+}(w) \). Coo [14] helpfully reviews that work. These experimental methods permit determination of a standard contribution to the chemical potential of the cluster on the right side of Eq. 4 in a dilute gas, for cluster sizes typically including \( n=4, 5, 6 \). It is helpful to keep in mind that these quantities can be targets of molecular simulation [20, 21] as well.

We collect several relevant points about these quantities. A first point is that the standard chemical potential of such a cluster includes contributions from the kinetic motion of the ion over the interior of the cluster. For mesoscopic clusters, this contribution may be awkward because the volume of the cluster accessible to the ion can be ambiguous. An extreme example of this ambiguity is the phenomenon, now well appreciated [22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33], that some ions might be localized on the surfaces of small water clusters. Fortunately, the cluster sizes studied in ion-water cluster experiments considered here are so small that even the surface vs. interior question doesn’t appear to be a significant problem.

A second basic point is that neither the experiment nor the typical simulation calculations further separate \( \Delta \mu_{M+}(w) \equiv e\phi + \Gamma_{M+}(w) \) into an absolute hydration free energy and a contribution from the potential of the phase. This is natural because both of these contributions derive from intermolecular interactions, and in the case of simulations it would take a special separate calculation to evaluate the potential of the phase separately.

Our third basic point about the separation Eq. 1 is that the difficulties in separating the various contributions to the interaction contribution to the chemical potential Eq. 1 from physical data are not trivially simpler for a particular \( n \). Though the contribution \( e\phi \) is expected to depend on \( n \), it will typically vanish neither for small nor for large values of \( n \).

Returning to the experimental analysis, we note that the conventional hydration free energies of ions are referenced to the case for \( H^+ \) in compiling the conventional ion hydration free energies. The evidence presented [14, 34] suggests that this procedure is successful to an interesting degree, and remarkably so for small values of \( n \). In view of those results and the analysis from Eq. 5 we conclude that the values obtained have not separated the absolute hydration free energy \( \Gamma_{M+}(w) \) from the potential of the phase in \( \Delta \mu_{H^+}(w) \).

In concluding this section, we return to consider the Donnan-like contribution to \( \Delta \phi \) that was noted above [8, 15]. This electrostatic contribution has its source in sorting of ions of different charges within the ion correlation length of an interface. Though the source of this contribution is the ions distributed in interfacial regions, this contribution typically achieves a non-zero value in the limit of vanishing ionic contributions. This contribution is present in the macroscopic description Eq. 1. But because the ion-water cluster experiments considered here treat clusters with only one ion that Donnan-like ionic effect isn’t present in those experimental data.

### IV. QUASI-CHEMICAL THEORY

In the quasi-chemical theory [35], the region around the solute of interest is partitioned into inner and outer shell domains. A variational check of this partition exists, if desired [13]. Here we treat the inner shell, where chemical effects are important, quantum mechanically. The outer shell contributions have been assessed using both a dielectric continuum model and classical molecular dynamics simulations.

The inner shell reactions pertinent to the hydration of \( X^\pm (=H^+, Li^+, Na^+, HO^-) \) are

\[
X^\pm + nH_2O \Leftrightarrow X \cdot [H_2O]^n_{\pm}
\]

Based on earlier work, the inner shell hydration numbers are \( n = (2, 4, 3, 4) \) for \( H^+ [12], Li^+ [11], Na^+ [13], \) and \( HO^- [14] \), respectively. The free energy change for these reactions were calculated using the Gaussian suite of programs [38]. The \( X \cdot [H_2O]^n_{\pm} \) clusters (and \( H_2O \)) were geometry optimized in the gas phase using the B3LYP hybrid density functional [37] and the 6-31+G(d,p) basis set. Frequency calculations confirmed a true minimum, and the zero point energies were computed at the same level of theory. Single point energies were calculated using the 6-311+G(2d,p) basis set.

**Dielectric continuum model:** For estimating the outer shell electrostatic contribution, the ChelpG method [38] was used to obtain partial atomic charges. The non-electrostatic contributions are expected to make negligible contributions to the hydration free energy and are not considered further. Then with the radii set developed by Stefanovich et al. [39], surface tessera were generated [40], and the hydration free energies of the clusters were calculated using a dielectric continuum model [41]. With this information and the binding free energies for the chemical reactions, a primitive quasi-chemical approximation...
to the excess chemical potential of \(X^\pm\) (aq) in water is:

\[
\beta \mu_{X^\pm} \approx -\ln \left( K_n \rho_{H_2O} n \right)
\]

where \(K_n = K_n^{(0)} \exp \left[ -\beta \left( \mu_{X(H_2O)}^{(0)}(w) - n \mu_{H_2O}(w) \right) \right] \).

\(K_n^{(0)}\) is the equilibrium constant for the reaction in an ideal gas state, with \(n\) of Eq. 4 the hydration number of the most stable inner shell cluster, and \(\beta = 1/\text{KB}T\). The density factor \(\rho_{H_2O}\) appearing in eq. 4 reflects the actual density of liquid water and its effect is accounted for by including a replacement contribution of \(-nk_B T \ln(1354)\). A detailed statement on standard states and this replacement contribution can be found in Grabowski et al.\[12\]. Relevant energies are collected in TABLE I. For the

\[
\begin{array}{cccccc}
\text{Energy} (\text{a.u.}) & \text{Thermal corrections (a.u.)} & \mu_{ex}^e_s \\
\hline
\text{H}_2\text{O} & -76.45951 & 0.00298 & -7.7 & -6.6 & -6.5 \\
\text{H}^+ & 0 & 0 & -0.01 & -0.01 & -0.01 \\
\text{H}[\text{H}_2\text{O}]_2^+ & -153.24860 & 0.03253 & -77.5 & -66.0 & -64.5 \\
\text{H}^+ & -153.24860 & 0.03253 & -77.5 & -66.0 & -64.5 \\
\text{H}[\text{H}_2\text{O}]_3^+ & -305.32036 & 0.04705 & -72.7 & -85.2 & -87.6 \\
\text{Li}^+ & -305.32036 & 0.04705 & -72.7 & -85.2 & -87.6 \\
\text{Li}[\text{H}_2\text{O}]_4^+ & -468.05512 & 0.05095 & -62.0 & -51.5 & -49.8 \\
\text{Na}^+ & -468.05512 & 0.05095 & -62.0 & -51.5 & -49.8 \\
\text{Na}[\text{H}_2\text{O}]_4^+ & -468.05512 & 0.05095 & -62.0 & -51.5 & -49.8 \\
\end{array}
\]

TABLE I: Electronic energy (a.u.), thermal corrections (a.u.) to the free energy, and electrostatic contributions to the excess chemical potential (kcal/mole) using dielectric continuum (DC) approximation and molecular dynamics (with TIP3P and SPC/E water models). The statistical uncertainties in the molecular dynamics values are of the order of 1.5 kcal/mole (Fig. 1). The partial charges are obtained at B3LYP/6-311+G(2d,p).

dielectric continuum calculations, an observation volume of radius 1.9 Å and 2.3 Å was centered on the Li\(^+\) and Na\(^+\) ions, respectively. For H\(^+\) and HO\(^-\) these radii were 1.172 Å and 1.56 Å respectively. The calculated values change only modestly to increases in these values.

**Classical molecular dynamics:** The electrostatic contribution to the hydration (excess) free energy is given by

\[
\Psi = \int_0^q \langle \psi \rangle_\lambda d\lambda,
\]

where \(\lambda\) is the coupling parameter which switches the solute charge from 0 to q. \(\langle \psi \rangle_\lambda\) is the ensemble-averaged potential on the ion at a particular charge state, \(\lambda\). Gauss-Legendre quadratures \[12\] provide a facile route to estimate this integral. In particular, treating \(\langle \psi \rangle_\lambda\) as a third degree polynomial, the following two-point formula

\[
\Psi \approx \frac{q}{2} (\langle \psi \rangle_{\lambda_+} + \langle \psi \rangle_{\lambda_-})
\]

where \(\lambda_{\pm} = q/(1/2 \pm 1/\sqrt{12})\), is exact to \(4^{th}\) order in perturbation theory \[12\]. Trial calculations using a purely linear response approximation (\(2^{nd}\) order in perturbation theory) deviate modestly from the above approximation, and hence for greater realism we employed the above form. For clarity the above expressions pertain to an atomic ion, but are easily generalized to complex ions with distributed charges.

Since the solute is largely buried within the first shell water molecules, there is no need for developing accurate parameters for those. This is true for the cations. For HO\(^-\), the hydroxyl hydrogen is largely free \[14\]. But the charge on this hydrogen is small, being about half the charge of the hydrogen atoms in the classical water models \[14\]. Based on these observations, the van der Waals parameters for Li\(^+\) and Na\(^+\) were obtained from \[13\] and \[14\], respectively. The H and O atoms in the cluster were assigned the same van der Waals parameters as those in classical water model, of which both TIP3P \[45, 46\] and SPC/E \[47\] were used. The charge distribution on these clusters were the ChelpG charges. The clusters were simulated in simulation cells of different sizes to estimate ion finite-size effects, and included 32, 64, 216 and 306 water molecules in addition to the cluster of interest.

The simulations were all performed with the NAMD \[48\] code which uses the particle mesh Ewald method to treat long range electrostatic interactions. For each λ, the simulation consisted of 200 ps of equilibration with velocity scaling every 250 fs, followed by another 200 ps of equilibration with velocity scaling every 1 fs. The water geometry was constrained using SHAKE. The cluster was held fixed. For the 32 and 64 water molecule boxes, a production run of 375 ps was conducted. For the 216 and 306 water molecule boxes, the production run lasted 150 ps. Frames were stored every 5 fs. Then using programs developed in-house, the Ewald potential at the solute charge sites were calculated, and statistical uncertainties were estimated by block-averaging in block sizes of 7.5 ps, corresponding roughly to the dielectric relaxation of pure water \[49\]. Then the free energy was assembled.

Electrostatic finite size corrections were applied as described in Hummer et al.\[21\]. As in Hummer et al.\[21\], the real-space screening factor was \(\eta = 5.6/L\), where \(L\) is the box length. A cutoff of \(k^2 \leq 38(2\pi/L)^2\) was applied in Fourier space, resulting in \(2 \times 510\) \(k\) vectors. A cutoff of \(L/2\) was applied for the real-space electrostatic interactions.

To check the accuracy of our code, we simulated some earlier results for ion hydration, including the charging free energy of imidazolium \[21\]. Hummers et al.\[21\] studied imidazolium charging using Monte Carlo techniques in boxes ranging from 16 water molecules to 512 water molecules. In the 16, 64, and 512 water molecule boxes, they find that the average interaction energy at full charge is \(-119.7 \pm 0.24\) kcal/mole, \(-113.3 \pm 0.36\) kcal/mole, and \(-110.3 \pm 0.4\) kcal/mole, respectively. We find \(-118.9 \pm 1.6\) kcal/mole, \(-113.6 \pm 1.3\) kcal/mole,
and \(-111.3 \pm 2.2\) kcal/mole, respectively. Given the different methodologies this agreement is good.

Figure 1 shows that for the clusters under consideration, ion finite size effects are quite modest. The values in table I using the TIP3P water model are obtained from fig. 1. The least square line fits are weighted by the statistical error. Since the ion finite size effect is small, the TIP3P and SPC/E values (TABLE I) were all obtained with the box of 306 water molecules.

![Figure 1: Electrostatic contribution to the excess chemical potential of the clusters using the TIP3P water model. L is the box size and from left to right, the boxes contain 306, 216, 64, and 32 water molecules, respectively. The box volume is adjusted to give a density of 1 gm/cc including the water molecules part of the cluster. The ions are given a partial specific volume of zero (0), but this choice is more for convenience and a more appropriate negative value would not change the results substantially.](image)

V. RESULTS

The hydration free energies obtained with the three different calculations of the outer-sphere contributions are given in TABLE III. The agreement between our absolute hydration free energies and Coe and coworkers'\(^{12, 50}\) values is poor for the molecular dynamics results, and fairs only somewhat better for the dielectric continuum results. The computed hydration free energies for neutral ion pairs, however, are in markedly improved agreement with the experimentally suggested values table III, particularly for the molecular dynamics values which are in error by about 2-3 kcal/mole compared to the dielectric continuum predictions which err by 8-11 kcal/mole.

\(\text{pK}_w\) of water: A further test of the pair hydration free energy for \(H^+\) and \(HO^-\) is to compute the \(\text{pK}_w\), a quantity of immense interest in solution chemistry, especially protein biochemistry.

Earlier, Haymet and coworkers\(^{51}\), Guissani and coworkers\(^{52}\) and Tawa and Pratt\(^{53}\) considered the ionization of water. Tawa and Pratt\(^{53}\) went further, describing this ionization at different thermodynamic states. These are important works, but are not \textit{ab initio} descriptions of dissociation.

The reaction under consideration is the ionization of water (in water solvent):

\[
H_2O \rightleftharpoons H^+ + HO^- \tag{7}
\]

The equilibrium constant for the reaction can be written as

\[
K_w = \frac{q_{H+}q_{HO^-}}{q_{HOH}} \left(\frac{\rho}{\rho_o}\right)
\]

Here \(\rho_o=1\) M is the reference concentration for \(H^+\) and \(HO^-\). \(\rho=55\) M is the reference concentration of water. \(q_i = q_i^{\text{ab initio}}\langle\exp^{-\beta\Delta U}\rangle_o\) is the partition function. \(q_i^{\text{ab initio}}\) is the ideal gas partition function, and \(\langle\exp^{-\beta\Delta U}\rangle_o\) is the Widom factor. \(\Delta U\) is the interaction energy of the solute with the solvent\(^{54}\). \(-RT\ln\langle\exp^{-\beta\Delta U}\rangle_o\) is precisely the excess chemical potential obtained above using the quasi-chemical approach.

For the ionization reaction in gas phase, the free energy change is computed (using TABLE II) to be 384.4 kcal/mole, which compares favorably with 384.1 kcal/mole estimated experimentally\(^{55, 56}\). The

| DC | TIP3P | SPC/E | Expt |
|----|-------|-------|------|
| H⁺ | -254.6 | -245.3 | -244.0 | -265.9 |
| Li⁺ | -120.5 | -115.1 | -112.7 | -128.4 |
| Na⁺ | -96.1 | -90.0 | -88.7 | -103.2 |
| HO⁻ | -105.3 | -121.1 | -123.8 | -104.9 |

| DC | TIP3P | SPC/E | Expt |
|----|-------|-------|------|
| HOH | -359.9 | -366.4 | -367.8 | -370.7 |
| LiOH | -225.8 | -236.2 | -236.5 | -233.3 |
| NaOH | -201.4 | -211.1 | -212.5 | -208.1 |

TABLE III: Solvation free energy of neutral ion pairs (kcal/mole). The solutes are transferred from 1 M (ideal gas) to 1 M (ideally diluted solute). Experimental numbers are from table II above. † For water, based on the experimental gas phase free energy of dissociation (384.1 kcal/mole), the known \(\text{pK}_w\) of water (15.7) and the known hydration free energy of water (−6.3 kcal/mole), we calculate a value of −366.6 kcal/mole for the HOH pair. Klots\(^{54}\) quotes a value of −368 kcal/mole for this quantity.
calculated pK_a’s are 21.1, 15.6 and 14.5, respectively, for the outer-sphere contributions using dielectric continuum, TIP3P water, and SPC/E water. The agreement between the molecular dynamics results and the experimental value of 15.7 is excellent.

VI. DISCUSSION

From a molecular standpoint, the quantity of most interest is \(\bar{\mu}_X\), the absolute hydration free energy. This absolute quantity is understood to be relative to the average potential of the phase, or equivalently to the value of that potential of the phase being taken as zero.

In the Ewald summation method there is no interface, and the mean potential in the cell is zero. Thus, use of Ewald potential to compute charging free energies naturally conforms to computation of the absolute hydration free energy.

In a cluster, however, the reference potential is not zero. Simulations of the vapor-water interface by Sokhan and Tildesley\(^\text{[53]}\) suggests that the potential in bulk SPC/E water is -12.7 kcal/mole-e relative to the vapor value of 0 (zero). Adding this value to our SPC/E estimate we obtain -256.7 kcal/mole for the hydration free energy of the proton in the presence of the potential of the phase. This greatly improves the agreement with the value of the value of -265.9 kcal/mole obtained by Coe and coworkers\(^\text{[19, 50, 59]}\) and -264.3 kcal/mole obtained by Klots\(^\text{[34]}\). Consistent with this but probably more significantly, the consensus results of TABLE II suggest a value that is negative and somewhat greater than 10 kcal/mole-e in magnitude.

A classic alternative to the ion-cluster experimental studies for obtaining the absolute hydration free energies of ions is the tetr phenyl arsonium tetr phenyl borate (TATB) hypothesis\(^\text{[60]}\). The molecular intuition is that these oppositely charged ions have the same non-ionic interactions with any solvent molecules. If it were precisely true that the absolute hydration free energy of these two solutes were precisely the same, then the Donnan-like effects discussed above would imply \(\Delta\Phi = 0\) at equilibrium of this salt between two coexisting fluids. If true, this would be a satisfactory solution of the present problem. But because the values obtained that way would not include a contribution from the potential of the phase, those values would be different from values extracted from the ion-cluster studies analyzed here. The computational testing of that TATB hypothesis has lead to energetic uncertainties of nearly the same size as the energetic contributions of issue here\(^\text{[60]}\). Therefore, the TATB hypothesis must be currently viewed as not satisfactorily proven. One important consideration is the following: because of the particular electrical asymmetry of water molecules, positively and negatively charged ions with exactly the same non-ionic interactions with water molecules will not have the same absolute hydration free energies. It is commonly observed in simulation that anions are better hydrated than cations of the same non-ionic interactions\(^\text{[9, 61, 62]}\); an intuitive view of that phenomenon is that water molecule hydrogen atoms, carrying some positive charge, are able to approach anionic solutes closely and this is different for the corresponding cationic solutes.

Our computed hydration free energy estimates, especially for ion pairs, is in good agreement with experiments. This agreement should not obscure the approximations made in applying a rigorous theory to practical calculations. These calculations might be improved in several respects. For example, in calculating the excess free energy of the cluster and the water ligand, we neglected packing effects and dispersion interactions. The tacit assumption in the analysis is that in composing \(K_n\) (eq. 4), errors in the cluster and the \(n\) water ligands balance out. For ionic species this appears to be a good assumption, but it does fail for hydration of non-polar solutes\(^\text{[65]}\). We foresee refining these aspects of the calculation in future studies.

The neglect of packing contributions is probably more easily remedied; see the discussion\(^\text{[2]}\). Packing contributions are expected to be only a few percent of the chemical and electrostatic effects included already. But those packing contributions are expected to be positive. Those contributions would probably improve the agreement for LiOH and NaOH in TABLE III. On the other hand, several additional effects of comparable size would have to be included at the same time. For example, the effects of anharmonicity on the thermal motion of the clusters is a comparable worry.

VII. CONCLUSIONS

We find that the absolute hydration free energy, \(\bar{\mu}_{H^+}(w)\), is somewhat smaller than the acknowledged -251 to -264 kcal/mole span of numbers. The present analysis suggests that the more negative of these values include the potential of the phase, a contribution distinct from the absolute hydration free energy.

Calculations on ion-water clusters can be compared properly with experiments on ion-water clusters. Those results and comparisons can test the adequacy of such calculations. But they don’t exclusively test the description of hydration of the ion; part of those results derives from the surface structure of the cluster and that contribution does not vanish for large clusters.

This study reinforces the idea that strenuous calculation of the absolute hydration free energy, \(\bar{\mu}_{M^+}(w)\), for a favorable case such as M=Li could probably reduce the computational errors to less than the present experimental uncertainties. This would permit a more precise alignment of available tables of single ion absolute hydration free energies.
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