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The Hydration Free Energy of Aqueous Na^+ and Cl^- at High Temperatures Predicted by ab Initio/Classical Free Energy Perturbation: 973 K with 0.535 g/cm^3 and 573 K with 0.725 g/cm^3

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The ab initio/classical free energy perturbation (ABC-FEP) method combines the free energy calculated from a classical simulation of an approximate model with the free energy of perturbing the approximate interactions to ab initio interaction energies. This method was used to calculate the hydration free energies of Na^+ and Cl^- at two high temperature state points (973 K with 0.535 g/cm^3 and 573 K with 0.725 g/cm^3). At 573 K with 0.725 g/cm^3 our result for the sum of free energies for the two ions, $\Delta_h^m G = -657$ kJ/mol, is in good agreement (4 kJ/mol) with the well-known experimental value. The ab initio result at 973 K with 0.535 g/cm^3 is $\Delta_h^m G = -538$ kJ/mol, in good agreement (7 kJ/mol) with semiempirical extrapolations from low-temperature experimental results. The accuracy of the ab initio methods and estimates of the sampling error indicate that this result is more reliable than previous predictions using either molecular dynamics simulations or empirically parametrized equations of state. Analysis of the results showed that Lennard-Jones plus charge models for ion−water interactions are not as accurate as models with exponents less than 6 and 12, because of short-range multibody interactions. Even the best smaller-exponent models for Na^+(aq) do not accurately reproduce the ab initio energies, but the best model for Cl^-(aq) is reasonably accurate. The short-range multibody interactions are not negligible and effective model parameters depend on density and temperature. The multibody interactions are particularly strong for Na^+(aq) so that even if an accurate effective pairwise model can be found for one temperature, it will not be accurate at other temperatures. Fortunately, the ABC-FEP method allows accurate prediction of free energies including multibody effects that are neglected in the approximate models.

1. Introduction

Studies of aqueous NaCl at high temperatures and pressures have attracted considerable interest because of their importance in industrial and natural chemical processes such as solid deposition,[1] metal corrosion in steam cycles,[2] solvent extraction[3] and hydrothermal ore formation.[4] Calorimetric measurements[5,6] are available up to about 673 K. Electrical conductance,[7] X-ray diffraction, neutron diffraction,[8] and phase equilibria are available at higher temperatures. Except for the conductance measurements, the experimental results are often prone to large error for very dilute solutions due to limitations of technique. Even with all of this effort there are large regions of the phase diagram where no measurements exist, so that predictive methods are essential.

A wide variety of semiempirical predictive methods for high-temperature aqueous solutions have been developed. These models have been based on the Born model,[9] the compressible continuum model;[10−12] stepwise association models with Born terms,[13,14] Langmuir adsorption models with Born terms,[15] hard sphere plus charge models,[16] and direct correlation function integral models.[17−19] The accuracy of these predictive models is very hard to assess. It was our hope that the present calculations would be accurate enough to indicate which of the semiempirical models are the most accurate and/or allow development of more accurate models.

Molecular dynamics (MD) and Monte Carlo (MC) simulations have played a major role in developing a detailed molecular level picture of aqueous ions at extreme conditions, because they offer a direct route from intermolecular forces to macroscopic properties. Three kinds of models of the potential energies can be used for these simulations: (1) analytic functions of the nuclear coordinates fit to experimental measurements or quantum calculations, e.g., Lennard-Jones plus charge models, (2) semiempirical quantum models, and (3) ab initio quantum models (DFT, MP2, etc). The problem with analytic models is that they are difficult to develop, their accuracy is not easily assessed, and they often include multibody interactions only in an average way. For example, there are many different models for water−water interactions (such as SPC,[20] TIP4P,[21] TIP4P−FQ[22]), and for sodium−water interactions,[23−27] yet it is not clear which of these models gives the best description for water or Na^+ in aqueous solutions even at ambient conditions. Even with these limitations, analytic models have yielded by far the most extensive information about high temperature aqueous solutions. Many different authors have used approximate models to explore the structure and energies of aqueous ions under supercritical conditions. Because of the approximate models used, only qualitative or semiquantitative conclusions could be drawn, and the accuracy of any predictions of real aqueous solution properties cannot be assessed (for some recent contributions see ref 28). Free energies of hydration of approximate models of ions under supercritical conditions have been calculated by

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TABLE 1: Model Potential Parameters for Cl^-−H_2O and Na^+−H_2O Interactions (See Eqs 1 and 2)

model	a	b	A_{XO} (kJ·mol^{-1}·A^a)	B_{XO} (kJ·mol^{-1}·A^b)	A_{XH} (kJ·mol^{-1}·A^a)	B_{XH} (kJ·mol^{-1}·A^b)	$q_{H,O}$[a]
Preliminary Models							
Cl^-(I)	12	6	26844000.42	9086.31			FQ
Cl^-(II)	9	6	669636.27	22010.82	2319.16		FQ
Na^+(I)	12	6	394707.84	1049.92			FQ
Na^+(II)	6	4	7341.56	719.97	1627.21	258.78	FQ
Na^+(III)	8	4	30917.97	878.85	295.95		FQ
Optimized Models							
Cl^-(6,9,FQ)	9	6	631109.46	14304.46	1192.37		FQ
Cl^-(6,12,FQ)	12	6	14334115.88	1947.18			FQ
Cl^-(6,12,TIP4P)	12	6	26844000.42	9086.31			TIP4P
Na^+(4,8,FQ)	8	4	34116.63	975.92	355.45		FQ
Na^+(6,12,FQ)	12	6	349368.28	733.31			FQ
Na^+(6,12,TIP4P)	12	6	774018.52	2964.03			TIP4P

[a] $q(Na^+) = +1.0$ and $q(Cl^-) = -1.0$; FQ indicates that the charges on O and H are determined by the fluctuating charge model for water, with the polarization due to the solute and other water molecules. TIP4P indicates that the charges are fixed at the TIP4P values ($q_O = -1.28$, $q_H = 0.64$) for purposes of calculating solute−solvent interactions.

Balbuena et al.[29] and by Fernandez-Prini,[30] but the water densities of the calculations are too low to be compared with the present results. Semiempirical quantum models and ab initio quantum models also have limitations. Semiempirical methods are not yet accurate enough for our purposes. In principle, one might use ab initio molecular dynamics, and analogous calculations have been done for some systems.[31] However, it is infeasible to do the configurational sampling required for accurate predictions of solvation free energies with these methods due to their computational cost. Moreover, these methods have been limited to using density functional theory, which (in its present implementations) is inadequate for solvation energies, since it does not accurately predict dispersion interactions. Methods that combine quantum models for some interactions with analytic functions of nuclear coordinates for other less important interactions (QM/MM models) are being developed and show promise.

Wood et al.[32] have recently proposed a hybrid technique (ABC-FEP), which allows calculation of the free energy of a QM/MM hybrid model without the computer-intensive simulation of the model. The hybrid model consists of ab initio solute−solvent interactions for a cluster of *n* water molecules and approximate analytic models for all other interactions. The method uses the free energy from a classical simulation with an approximate model for all interaction energies as a starting point. Free energy perturbation theory is then used to determine the effect of changing the approximate solute−solvent interactions to ab initio interactions. This method shows whether the analytic model is a good representation of the system (allowing refinement of the analytic model if necessary) and predicts solvation properties of any substance with essentially the accuracy of the quantum method used. The ABC-FEP method has been tested by calculating the hydration free energy of water at ambient conditions (298.15 K with density 1 g/cm^3),[33] supercritical water states (973 K with density 0.6 g/cm^3)[33] and at extreme conditions (2344 K with density 1 g/cm^3 and 2000 K with density 1.8 g/cm^3).[34] In this paper, we apply the ABC-FEP method to the prediction of the free energy of hydration of two ions (Cl^- and Na^+) at two state points (973 K with density 0.535 g/cm^3 and 573 K with density 0.725 g/cm^3). The 573 K state point is the highest temperature point where an accurate experimental value is available; at the 973 K state point there is an accurate experimental association constant that we intend to predict in future work. Both points are far enough from the critical point of water that large correlation lengths are not a problem for our simulations. We did not do 298 K calculations because the available approximate ion−water interaction models are not accurate enough. Our results are compared with other methods, and we assess the ability of some simple model potentials to reproduce the ABC-FEP results.

The organization of this paper is as follows. Section 2 describes the methods used in the classical simulations for aqueous Na^+ and Cl^-. In section 3, we present a summary of the ABC-FEP method and the methods used to calculate ab initio interaction energies. Section 4 discusses the ABC-FEP predictions for the hydration free energies of the ions and section 5 compares these results with those of other methods. In section 6, the abilities of some simple model potentials to predict hydration free energies are assessed and we conclude with a summary in section 7.

2. Molecular Dynamics Simulations with Approximate Models

The molecular dynamics simulations with our approximate models were performed using the DL-POLY MD package[35] with some modifications to include the fluctuating charge TIP4P−FQ water model.[22] The TIP4P−FQ model is polarizable but has a rigid geometry. The hydrogen and oxygen charges were constrained ($0.3 < q_H/e < 1.0$ and $-2.0 < q_O/e < 0$) to prevent them from going toward infinity, which otherwise occurs occasionally in high-temperature simulations. The model potentials used for the ion−water interactions had the form

$$U_{X,O} = \frac{A_{XO}}{r_{XO}^a} - \frac{B_{XO}}{r_{XO}^b} + \frac{q_X q_O}{r_{XO}} \tag{1}$$

$$U_{X,H} = \frac{A_{XH}}{r_{XH}^a} - \frac{B_{XH}}{r_{XH}^b} + \frac{q_X q_H}{r_{XH}} \tag{2}$$

where the interaction parameters *A*, *B*, *q*, *a*, and *b* for different approximate models are listed in Table 1. The ion (Cl^- or Na^+) was held fixed at the center of a cubic box containing 200 TIP4P−FQ water molecules. To save equilibration time, simulations were first run from random initial configurations in the *NVT* ensemble at fixed density. The simulation was continued in the *NPT* ensemble with the pressure adjusted to give the desired density. A hydrogen mass of 8 g/mol was used to improve the simulation efficiency by allowing an increased time step.[36] Periodic boundary conditions were employed and the long-range columbic interactions were treated using the Ewald Sum technique with conducting boundary. A continuum correction for the difference between the free energy of the

Ewald Sum calculation and the ion at infinite dilution was applied.[37] Examination of pressure, temperature and energy auto correlation functions indicated that independent configurations could be obtained at both state points by sampling at 0.4 ps intervals for Cl^- while 1 ps intervals were necessary for Na^+.

3. Methodology

3.1 Brief Summary of ABC−FEP Method. A detailed discussion of the ABC-FEP method has been given[32] and will not be repeated here. The main idea is that the hydration free energy of solute (X) in solvent (S) is calculated as the sum of the hydration free energy of an approximate model ($\Delta G[\bullet \rightarrow A]$) plus the free energy of transforming the approximate solute−solvent interactions to quantum (i.e., ab initio) interactions ($\Delta G[A \rightarrow Q]$),

$$\Delta G = \Delta G[\bullet \rightarrow A] + \Delta G[A \rightarrow Q] \quad (3)$$

The hydration free energies of the approximate model, $\Delta G[\bullet \rightarrow A]$, were obtained using thermodynamic integration. The calculations are done in two steps, first growing a point mass into an uncharged particle and then charging the particle. The reverse process was also calculated to check that the hysteresis was small and verify that our equilibration time was sufficient. The Ben-Naim and Marcus[38] definition of hydration was used (solute concentration is the same in the gas phase and in solution). The conversion to the usual standard states of ideal gas ($p^\theta = 1$ bar) and solution ($m^\theta = 1$ mol/kg), $\Delta_h^m G$, is given by

$$\Delta_h^m G = \Delta G + RT \ln[RTm^\theta \rho^0/p^\theta] \quad (4)$$

where ρ^0 is the pure solvent density.

The free energy of perturbing the approximate solute−solvent interaction energies to the ab initio interaction energies, $\Delta G[A \rightarrow Q]$, was calculated by free energy perturbation using N_{conf} independent configurations chosen from the classical simulations,

$$\Delta G[A \rightarrow Q] = -RT \ln \langle \exp[-(U_{XS}^Q - U_{XS}^A)/RT] \rangle_A \quad (5)$$

Here, U_{XS}^A and U_{XS}^Q indicate the approximate and quantum solute−solvent interaction energies, respectively. The brackets with subscript A indicate an average over configurations generated in a classical simulation with the approximate potential. $\Delta G[A \rightarrow Q]$ is the key to the ABC-FEP method. The calculated free energy would be exact if an infinite number of configurations were used in eq 5. In previous work, we found that if the approximate solute model is reasonably accurate, then 50−100 configurations are enough to obtain an accurate free energy. Such a small sample of configurations is sufficient in our present calculations because the FEP term (eq 5) contributes less than 4% of the total free energy, so a 10% uncertainty in this term contributes less than 0.4% to the uncertainty in ΔG. Our criteria for an accurate approximate model are that the bootstrap error estimate[39] of $\Delta G[A \rightarrow Q]$ is small (<1.5 kJ/mol), and the peak in the distribution of $\exp[-\Delta U/kT]$ is well sampled. The bootstrap technique is a reasonably accurate way of estimating the standard deviation of a distribution by using many random choices (with duplication in the data set) of N_{conf} configurations from the sample of N_{conf} independent configurations selected from a simulation. In each of these random choices, some configurations are duplicated and others are not included. This method assesses the probable error due to picking only a single set of N_{conf} configurations. If these criteria for an accurate model are not satisfied, more configurations must be included in the average, or the approximate model must be reparametrized to obtain a better sample.

Our goal in this work is to achieve predictions with essentially the accuracy of the ab initio method (~4 kJ/mol). Thus, we have required sampling errors (as estimated with the bootstrap method) in the ABC-FEP calculations to be less than 1.5 kJ/mol and thermodynamic integration errors to be less than 2.6 kJ/mol.

3.2 Ab Initio Calculations of the Interaction Energy. To evaluate $\Delta G[A \rightarrow Q]$, the difference between the ab initio and approximate solute−solvent interaction energies, $\Delta U = U_{XS}^Q - U_{XS}^A$, are required at each of the sampled configurations. To reduce the cost of calculating U_{XS}^Q, we calculated ΔU only for the interaction of the solute with the nearest n water molecules (in most results reported here, $n = 60$). This assumes that the approximate model is accurate enough for the more distant water molecules. We further approximate the interaction energies of the solute with the nearest n solvent molecules as a sum of n pairwise interaction energies and the multibody interaction energy of solute with the nearest m solvent molecules:

$$U_{XS} = U_{XS,n}[\text{pair}] + U_{XS,m}[\text{multi}] \quad (6)$$

Here, the pairwise interaction energy, $U_{XS,n}[\text{pair}]$, is the sum of all n solute (X)−solvent (S_i) pair interaction energies, $U_{XS,n}[\text{pair}] = \sum_{i=1}^{n} u_{X,S_i}$. The multibody interaction energy, $U_{XS,m}[\text{multi}]$, is the difference between the pairwise and total interaction energies of a cluster with m solvent molecules, $U_{XS,m}[\text{multi}] = U_{XS,m} - U_{XS,m}[\text{pair}]$. The full interaction energy for this cluster, $U_{XS,m}$, is obtained from the total energy of the cluster by subtracting the energies of isolated X and of the cluster with the solute particle removed (keeping the solvent molecules in exactly the same positions). The advantage of this approach is that it allows substantial savings in computational effort for a given level of accuracy. We find that the multibody interactions can be calculated with m much less than n and that less demanding ab initio methods can be used to calculate the multibody interactions. Of course, when m and n are large enough, $\Delta U = U_{XS}^Q - U_{XS}^A$ does not change with increasing n or m. We note that in order to avoid surface free energy effects in the outer shell of water molecules, the choice of water molecules included in the cluster is based on distances from the solute to a point equidistant from the three atoms in the water molecules.[40]

We have explored several ab initio methods for calculating pairwise and multibody interaction energies. For pairwise interactions, these include second and fourth order Møller−Plesset perturbation theory (MP2 and MP4) and a local MP2 method (LMP2). The accuracy of the predictions is expected to increase as one goes from LMP2 to MP2 to MP4. Earlier work[33] has shown that density functional methods do not predict accurate enough pairwise interaction energies, but that they are useful for predicting multibody interactions. In this work, we have compared B3LYP hybrid density functional theory (DFT) calculations to MP2 calculations of the multibody interaction energies. We have explored the accuracy of these different approaches for both Na^+ and Cl^-. All ab initio calculations were done with Gaussian 98,[41] except for the local MP2 (LMP2) calculations which were done with Jaguar 3.5.[42]

3.2.1. Calculation of Cl^-−H_2O Interactions. Our initial calculations of pairwise interaction energies for Cl^- were done with the relatively inexpensive LMP2 method (using a pVTZ++ basis). This was compared to more accurate MP2 and MP4 calculations (both using the 6-311++G(3df,3pd) basis). Figure

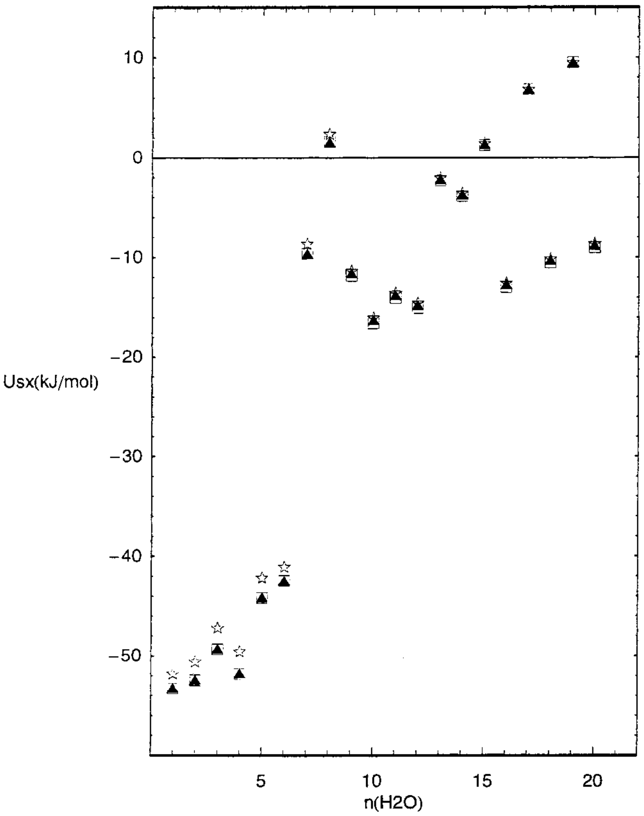

Figure 1. Ab initio pair interaction energies of Cl^- and H_2O for the nearest 20 water molecues in a single configuration at 973 K with density of 0.535 g/cm^3: LMP2/cc-pVTZ++ (☆); MP2/6-311++G-(3df,3pd) (△); MP4/6-311++G(3df,3pd) (□).

1 shows a comparison of the pairwise interaction energies for Cl^- with the nearest 20 water molecules in a single configuration, as calculated with these three ab initio methods (the configuration was taken from a simulation with $Cl^-{-}H_2O$ model II at 973 K and 0.535 g/cm^3, as described in more detail below). As is particularly clear for the nearest six water molecules, the LMP2 method is systematically more positive than the MP2 and MP4 methods; these latter two are in good agreement with each other for all pairs. The same trend was found consistently in calculations on three separate configurations: the average difference between LMP2 and MP2 calculations of the sum of pairwise interaction energies for the first 20 water molecules is 15.3 kJ/mol; the corresponding difference between MP2 and MP4 is only 0.7 kJ/mol. We have also found that the difference in pairwise interaction energies among all three methods is very small when $n > 20$. Thus, for the calculations described in section 4, we used MP2 energies for the pair interactions with the nearest 30 water molecules and LMP2 energies when $n > 30$. This substantially reduces the computing time and introduces very little error. We demonstrate below that multibody interactions can be calculated effectively for this system with a cluster of five water molecules. We have compared the multibody interaction energies ($m = 5$) as calculated with B3LYP (using the aug-cc-pVDZ basis set) to those from MP2 (using the 6-311++G(3df,3pd) basis set) for three configurations and find that the average difference is 1.5 kJ/mol. We conclude that B3LYP/aug-cc-pVDZ can give reasonably accurate multibody interaction energies, and we have used this method since it has a much lower computational cost than MP2.

3.2.2. Calculation of $Na^+{-}H_2O$ Interactions. For Na^+, the ab initio pairwise energies for the ABC-FEP calculations in section 4 were done at the MP2/6-311++G(3df,3pd) level. As a check on this method we compared the pairwise interaction energies with the first 20 water molecules in three configurations to the corresponding energies at the MP4/6-311++G(3df,3pd) level (the configurations were taken from a simulation with $Na^+{-}H_2O$ model II at 973 K and 0.535 g/cm^3, as described in more detail below). The average difference between the sum of pairwise energies was only 0.8 kJ/mol for the first 20 water molecules, indicating that the MP2 energies are accurate enough. The multibody interaction energies were calculated with B3LYP/6-311++G(3df,3pd). As shown below, the bulk of the multibody interactions for this system can be calculated in a cluster of six solvent molecules. We compared the B3LYP multibody interaction energy ($m = 6$) to that at the MP2/6-311++G-(3df,3pd) level for three configurations. The average difference for the multibody interactions was 2.5 kJ/mol. Since the MP2 calculations have a higher computational cost than B3LYP, with only a small difference in energy, we use B3LYP to obtain the multibody interaction energy.

3.2.3. BSSE Corrections. The pairwise ab initio energies reported in this article were corrected for basis set superposition error (BSSE) using the counterpoise method.[43] In our previous paper,[33] in which water was the solute as well as the solvent, BSSE values were found to be very similar in different configurations, so a single correction was calculated by averaging over only five configurations and then applied to all configurations. In the present work, we found the BSSE corrections for Cl^- and Na^+ were relatively large. The BSSE correction was found to be largest for the nearest 10 water molecules, so we calculated BSSE corrections explicitly for the first 10 water molecules of every configuration. For the sum of the pairwise interactions with more distal water molecules, we have used the average BSSE correction calculated for five configurations. Bootstrap error estimates showed that this limited sampling of the outer water BSSE only increases the uncertainty by about 0.5 kJ/mol. In addition, we checked the BSSE for multibody interaction energies with five configurations. These corrections to $U_{XS,m}$[multi] are very small because the BSSE corrections to the total cluster energy ($U_{XS,m}$) and to the sum of m pair interactions ($U_{XS,m}$[pair]) essentially cancel each other. This difference was calculated for five configurations and varied from 0.4 to 1.0 kJ/mol, so no BSSE corrections were made for the multibody interactions.

3.3. Stochastic Model of Interactions with Distal Solvent Molecules. In calculating the pairwise interaction energies in a cluster of n molecules, we find that the outermost water molecules (those beyond the nearest thirty) contribute very little to ΔU, and that this contribution is uncorrelated with the total value of ΔU. This allows another efficient approximation if we separate the solute−solvent interactions into contributions from “inner” water molecules and “outer” molecules. The inner molecules are taken to be the thirty molecules closest to the solute; their pairwise interactions with the solvent are calculated explicitly as described in the last section. For the outer molecules, which are the next n-30 nearest molecules, we explicitly calculate pairwise interaction energies only for a subset of N_{out} configurations. This subset represents the distribution of contributions to ΔU from the outer set of water molecules. Rather than explicitly calculating the interactions with outer water molecules in every configuration, we sample this distribution by randomly selecting a value from among the N_{out} values that have been calculated. This procedure amounts to a stochastic approximation to this contribution to ΔU from the outer waters. Since we have only a finite sample available as an approximation to the full distribution, we have used the following bootstrap

TABLE 2: Convergence of Average Energies and Free Energies with Respect to the Number of Water Molecules in Cluster Calculations of Pair (*n*) and Multibody (*m*) Interactions (All Energies Reported in Units of kJ/mol)

n	m	N_{conf}	N_{out}	$\langle \Delta U(\text{pair}) \rangle$	$\langle \Delta U(\text{multi}) \rangle$	$\langle \Delta U(\text{total}) \rangle$	$\Delta G(\text{A}\rightarrow\text{Q})$
				Cl^- at 973 K with 0.535 g/cm^3 (Cl^-−H_2O Model II)			
60	5	50	30	−9.0(5.1)[b]	−1.0(6.1)[b]	−10.0(6.4)[b]	−12.9(1.3)[c]
40	5	50		−8.3(4.9)	−1.0(6.1)	−9.3(6.2)	−12.5(1.4)
60[a]	10	50		−9.0(5.1)	2.0(8.8)	−7.0(8.0)	−10.9(1.2)
40	10	50		−8.3(4.9)	2.0(8.8)	−6.3(7.9)	−10.5(1.3)
60	15	25		−9.5(5.4)	3.2(9.8)	−6.2(8.4)	−10.1(2.0)
40	15	25		−8.8(5.3)	3.2(9.8)	−5.5(8.3)	−9.7(2.0)
				Cl^- at 573 K with 0.725 g/cm^3 (Cl^-−H_2O Model II)			
60[a]	5	80	50	−0.9(5.1)	−3.2(6.4)	−4.1(6.5)	−8.9(1.0)
40	5	80		0.4(4.9)	−3.2(6.4)	−2.8(6.5)	−7.8(1.3)
60	10	40		−0.2(3.9)	−4.4(8.6)	−4.7(8.2)	−11.2(2.2)
40	10	40		1.2(3.8)	−4.4(8.6)	−3.2(8.3)	−10.7(2.5)
				Na^+ at 973 K with 0.535 g/cm^3 (Na^+−H_2O Model II)			
60	6	100	60	−38.5(17.4)	31.3(10.0)	−7.2(11.3)	−14.1(1.4)
40	6	100		−40.6(17.5)	31.3(10.0)	−9.3(11.3)	−16.9(1.5)
60[a]	9	100		−38.5(17.4)	38.4(13.0)	−0.1(10.4)	−6.2(1.3)
40	9	100		−40.6(17.5)	38.4(13.0)	−2.2(10.4)	−9.0(1.3)
60	12	40		−38.0(17.9)	40.6(14.2)	2.6(12.4)	−8.1(2.5)
40	12	40		−37.1(17.9)	40.6(14.2)	3.5(12.7)	−10.9(2.6)
				Na^+ at 573 K with 0.725 g/cm^3 (Na^+−H_2O Model III)			
60	6	30	60	−40.4(16.6)	40.8(9.0)	0.4(13.7)	−14.4(2.9)
40	6	30		−43.5(16.2)	40.8(9.0)	−3.3(13.6)	−11.2(3.1)
60	9	40		−41.9(16.8)	48.9(12.9)	6.9(11.5)	−8.1(1.9)
40	9	40		−44.9(16.4)	48.9(12.9)	4.0(11.5)	−10.2(2.1)
60[a]	12	100		−41.7(18.1)	51.7(16.6)	10.0(10.7)	−1.0(1.4)
40	12	100		−43.5(18.0)	51.7(16.6)	6.22(10.5)	−3.6(1.5)

[a] This calculation was chosen as the most accurate and used in our final calculations. [b] Figures in parentheses are the standard deviation of the values of ΔU. [c] In the case of $\Delta G(\text{A}\rightarrow\text{Q})$ the figure in parentheses is the uncertainty due to limited sampling. Bootstrap resampling was used to estimate this error (the error in the ab initio method is not included).

TABLE 3: Predicted Hydration Free Energies from the ABC-FEP Method for Cl^- and Na^+ at 973 K with Density of 0.535 g/cm^3 and 573 K with Density of 0.725 g/cm^3

system	$\Delta G[\bullet\rightarrow\text{A}]$ (kJ/mol)	pair (n)	multi (m)	N_{conf}	$\Delta G[\text{A}\rightarrow\text{Q}]$ (kJ/mol)	ΔG (kJ/mol)	$\Delta_h^m G^a$ (kJ/mol)
Cl^-, 973 K	−283.5(2.1)[b]	60	10	50	−10.9 (1.2)[c]	−294	−264(5)[d]
Cl^-, 573 K	−338.7(2.4)	60	5	80	−8.9 (1.0)	−347	−330(5)
Na^+, 973 K	−298.7(2.6)	60	9	100	−6.2 (1.3)	−305	−274(5)
Na^+, 573 K	−343.6(1.9)	60	12	100	−1.0 (1.4)	−345	−328(5)

[a] The conversion of ΔG to $\Delta_h^m G$ is based on eq 4. [b] Figures in parentheses are the estimated 67% confidence limits. [c] In the case of $\Delta G(\text{A}\rightarrow\text{Q})$ the figure in parentheses is the uncertainty due to limited sampling as estimated by bootstrap resampling (the uncertainty in the ab initio method is not included). [d] This error estimate includes an estimated uncertainty in the ab initio method of 4 kJ/mol.

Monte Carlo resampling method to estimate the error due to this limited outer water molecule sampling. We have N_{conf} values of ΔU_{in} (the pairwise interaction energy with the first 30 waters), and N_{out} values of ΔU_{out} (the pairwise interaction energy with the outer $n - 30$ waters). We generate a sample of N_{conf} energies as follows. For each of the $N_{conf} - N_{out}$ values of $\Delta U_{XS,in}$ for which we do not know ΔU_{out}, we choose one of the N_{out} values at random. We then sum the energies to get the total energy for each configuration, and calculate ΔG using eq 5. This is one estimate of ΔG. We repeat this procedure 100 times. The average of these estimates is our best estimate of ΔG and is reported in Tables 2 and 3; the standard deviation is an estimate of the error due to our limited sample of ΔU_{out}, but does not account for other sources of sampling error.

To estimate the total error due to our limited sampling of both ΔU_{in} and ΔU_{out}, we used a modified bootstrap method. This involved picking at random a value of ΔU_{in} from the N_{conf} values. If ΔU_{out} is known it is added to ΔU_{in} to get ΔU. If ΔU_{out} is not known, a random value of ΔU_{out} is picked and added to ΔU_{in} to get ΔU. This procedure is repeated N_{conf} times with each random choice of ΔU_{in} coming from the whole list of N_{conf} values. Note that duplicate values are used for both ΔU_{in} and ΔU_{out}. Finally, ΔG is calculated from this sample of N_{conf} values for ΔU. This calculation of ΔG is repeated 100 times. The standard deviation of the resulting ΔG's is the bootstrap estimate of the error due to limited sampling of both ΔU_{in} and ΔU_{out}. This error estimate is given in Tables 2 and 3.

4. Predicted Hydration Free Energy with the ABC−FEP Method

4.1. Cl^- at 973 K with 0.535 g/cm^3. To simulate Cl^- at 973 K with a density of 0.535 g/cm^3, we began with a Lennard-Jones plus charge model, model I (see Table 1 for model parameters). Fifty independent configurations for ABC-FEP calculations were generated from simulations with model I. We calculated LMP2 pair-wise interaction energies for clusters up to $n = 60$, and DFT multibody interaction energies with $m = 5$. The results showed that the solute (Cl^-)−solvent interaction energies for model I were far from the ab initio energies. A histogram showed that $\exp[-\Delta U/kT]$ was not well sampled by the configurations used, and the bootstrap error estimate (4.2 kJ/mol) was large. To get an accurate hydration free energy, we derived an improved model II by adjusting the model parameters to fit the total interaction energies of the 50 configurations, as calculated with LMP2 pairwise interaction energies up to $n = 60$ plus DFT multibody interaction energies

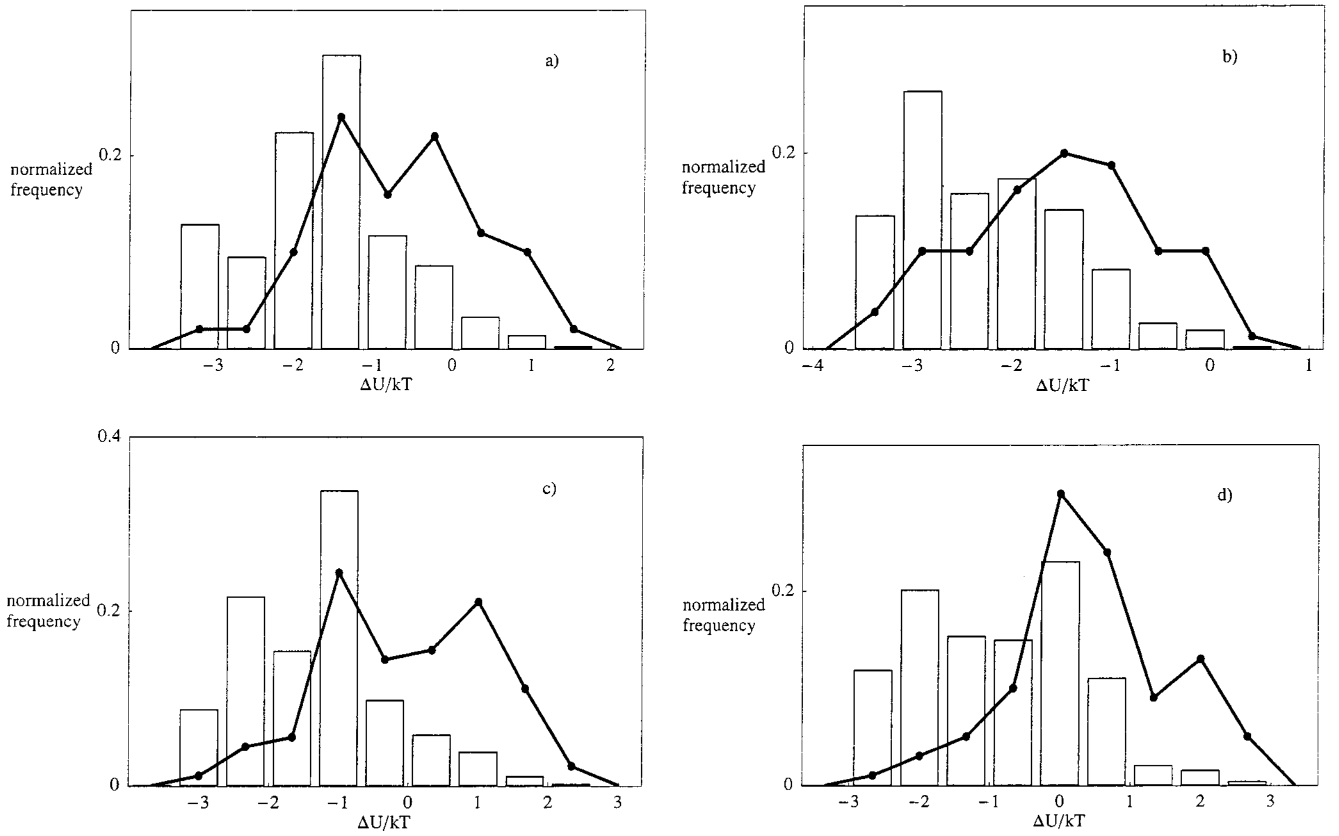

Figure 2. Normalized $\Delta U/kT$ distributions: (a) Cl^- at 973 K with 0.535 g/cm^3; (b) Cl^- at 573 K with 0.725 g/cm^3; (c) Na^+ at 973 K with 0.535 g/cm^3; (d) Na^+ at 573 K with 0.725 g/cm^3. Solid line: $\Delta U/kT$ distribution (N_{bin}/N_{conf}). Histogram: exponentially weighted distribution of $\Delta U/kT$ ($\Sigma_{i=1}^{N_{bin}} \exp[-\Delta U_i/kT]/\Sigma_{j=1}^{N_{conf}} \exp[-\Delta U_j/kT]$), where N_{bin} is the number of configurations in a bin and N_{conf} is the total number of configurations used for the FEP.

with $m = 5$. The parameters obtained for model II are listed in Table 1. Although model II was derived from LMP2 energies (which are not adequate for calculating interaction energies), the preferred configurations for LMP2 and MP2 are close enough that this model achieved good sampling of configurations.

Model II was used in a simulation to find the free energy of charging a point mass to the full approximate model II, and then to obtain 50 new independent configurations for the ABC-FEP calculation. As described above, pairwise solute−solvent interaction energies for the 30 water molecules nearest to the solute were calculated with MP2, while LMP2 was used for the next 30 water molecules. The calculated results are shown in Table 2. We note that the pairwise interaction energy contributions to ΔU for $n = 40$ and $n = 60$ differ by only 0.7 kJ/mol. We have used $n = 60$ in our calculations, which appears to ensure satisfactory convergence. The multibody interaction energies (calculated with DFT) for $m = 5$ and $m = 10$ differ by 3.0 kJ/mol (using 50 configurations in each case), while calculations with $m = 10$ and $m = 15$ (using only 25 configurations in the latter case) differ by only 1.4 kJ/mol. We have used the results with $m = 10$ in our final calculations. While a larger cluster would recover slightly more of the multibody interaction energy, the added computational cost (which scales roughly as m^3) limits the number of configurations that may be sampled. If we compare the data in Table 2 for $m = 10$ ($N_{conf} = 50$) and $m = 15$ ($N_{conf} = 25$), the difference in total ΔU (−7.0 versus −6.2 kJ/mol) is achieved at a cost of larger sampling error (1.4 versus 2.0 kJ/mol). Since the difference in sampling errors is comparable to the cluster size errors, any effort to improve the calculation of multibody energies must balance the need to include more configurations against the need for larger clusters.

Figure 2a shows that the peak of $\exp[-\Delta U/kT]$ for model II is well sampled, and the bootstrap error estimate is small (1.2 kJ/mol). Thus, model II is adequate to achieve small errors in the ABC-FEP calculation with 50 configurations. Table 3 reports the free energy of charging a point mass to the full, approximate model II solute, and the difference in free energy between the approximate and ab initio energies calculated with ABC-FEP (eq 5). Estimates of the sampling error are also included. Our final predictions of $\Delta_h^m G$ (eqs 3 and 4) are given with a confidence interval that includes a 4 kJ/mol estimate of uncertainty in the accuracy of ab initio methods, in addition to the FEP sampling and the thermodynamic integration uncertainties.

4.2. Cl^- at 573 K with 0.725 g/cm^3. We have used the $Cl^-−H_2O$ model II, developed from the calculations above, to calculate the free energy of Cl^- at 573 K with a density of 0.725 g/cm^3. Since this model is an effective pairwise potential, developed to reproduce the free energy at a different state point where different configurations may dominate, it was not certain that the same model will be effective in these new calculations. We chose 80 independent configurations from simulations with model II and calculated ab initio pairwise interaction energies and multibody interaction energies as described above. Table 2 shows that ΔU is well converged (with respect to cluster size) for the $Cl^-−H_2O$ pair interaction energies when clusters of $n = 60$ water molecules are used. The average contributions to ΔU from multibody interaction energies with $m = 10$ and $m = 5$ differ by only 1.4 kJ/mol (using 40 configurations), so we used the $m = 5$ results with 80 configurations rather than $m =$

10 with 40 configurations. Again, this reduces the sampling error, while neglecting a small portion of the multibody interactions.

The resulting free energy predictions are reported in Table 3. The bootstrap error estimate of $\Delta_h^m G$ (1.0 kJ/mol) is small and the peak in the histogram of $\exp[-\Delta U/kT]$ is reasonably well sampled (Figure 2b). We conclude that $Cl^- - H_2O$ model II, as developed to predict free energies at 973 K with a density of 0.535 g/cm^3, is also adequate for ABC-FEP calculations at 573 K with a density of 0.725 g/cm^3.

4.3. Na^+ at 973 K with 0.535 g/cm^3. A review of the literature shows that there are many $Na^+ - H_2O$ interaction models with very different parameters. In our calculations, we started with $Na^+ - H_2O$ model I, a Lennard-Jones 6−12 plus charge model (parameters in Table 1). We picked 30 configurations generated from a simulation with model I and calculated MP2 pair-wise interaction energies ($n = 40$) and DFT multibody interaction energies ($m = 6$). These calculations showed that $\exp[-\Delta U/kT]$ was not well sampled, and the bootstrap error estimate (6.2 kJ/mol) was large. This indicates that model I is inaccurate relative to the ab initio energies for the dominant configurations at this state point. To develop an improved model, the model parameters were modified to fit the total ab initio interaction energies for the 30 configurations. Parameters for the resulting model II are reported in Table 1. Note that the exponents a and b in eqs 1 and 2 have been reduced to 4 and 6 (from the traditional LJ values of 6 and 12, respectively).

Model II was used in a simulation and 100 new independent configurations were selected. The contribution of pairwise interaction energies to ΔU with $n = 40$ and $n = 60$ differ by only 2.1 kJ/mol, so again, MP2 calculations with $n = 60$ were judged sufficient for the pairwise interactions (Table 2). DFT calculations of the multibody interactions were done with $m = 6$ (100 configurations), $m = 9$ (100 configurations), and $m = 12$ (40 configurations). Table 2 shows that the contributions of multibody interactions to ΔU differ by 7.1 kJ/mol between $m = 6$ and $m = 9$, but they differ by only 1.8 kJ/mol between $m = 9$ and $m = 12$ (using 40 configurations). We have used calculations of 100 configurations with $m = 9$ for our final results.

Figure 2c shows that the peak of $\exp[-\Delta U/kT]$ for model II is well sampled and the bootstrap error estimate (1.3 kJ/mol) is small, indicating that model II for the $Na^+ - H_2O$ interactions can reproduce the ab initio energies accurately enough to obtain a reliable perturbation free energy from 100 configurations. The final values of free energies and their confidence intervals are shown in Table 3.

4.4. Na^+ at 573 K with 0.725 g/cm^3. We attempted to predict the free energy of Na^+ at 573 K with 0.725 g/cm^3 by using $Na^+ - H_2O$ model II as derived in the last section. We chose 40 independent configurations from simulations with model II and calculated the ab initio interaction energies with the same methods as at 973 K with 0.535 g/cm^3. Results for clusters with $n = 40$ and $m = 9$ showed that most of the peaks in the histogram of $\exp[-\Delta U/kT]$ were not well sampled, and the bootstrap error estimate was slightly larger than we would like (2.0 kJ/mol). Thus, while model II is adequate for free energies at 973 K with 0.535 g/cm^3, it is not sufficiently accurate at 573 K with 0.725 g/cm^3. An improved $Na^+ - H_2O$ model III was derived by fitting to the ab initio energies calculated for the 40 configurations from simulations with model II. The parameters are given in Table 1. Note again that this is not a typical 6-12 potential.

TABLE 4: Comparison of Hydration Free Energies with Various Prediction Methods

	$\Delta_h^m G(Na^+) + \Delta_h^m G(Cl^-)$ (kJ/mol)	
prediction methods[a]	$T = 973$ K, $\rho = 0.535$ g/cm^3	$T = 573$ K, $\rho = 0.725$ g/cm^3
ab initio	−538 (7)[b]	−657 (7)[b]
Archer		−661
SUPCRT92	−545	−663
Tanger-Pitzer	−545	−662
SOW	−544	−663
Born[R298=1.845A]	−581	−683
Born[R573=1.901A]	−560	
CC[R298=1.813A]	−573	−675
CC[R573=1.853A]	−559	

[a] See text for discussion of the predictive methods. The prediction of Archer is from an equation fitting all of the experimental results up to 573 K so it is essentially an experimental value. [b] Estimated 67% confidence limits.

Model III was used in a simulation and 100 new independent configurations were obtained. Table 2 shows that the pairwise energy contributions to ΔU are again nearly converged at $n = 60$. Multibody interaction energies were calculated with $m = 6$ (40 configurations), $m = 9$ (40 configurations) and $m = 12$ (100 configurations). Table 2 shows that the contributions to ΔU for $m = 6$ and $m = 9$ differ by 8.1 kJ/mol, but the difference between $m = 9$ and $m = 12$ is only to 2.8 kJ/mol (using 40 configurations). In this case, we used $m = 12$ and $n = 60$ for our final calculations.

The calculated results show that the bootstrap error estimate is small (1.4 kJ/mol), and most of the peaks in the histogram of the exponential distribution were sampled (Figure 2d). Table 3 gives the calculated free energy of charging a point mass to the full approximate model III solute, the perturbation free energies and the final predicted $\Delta_h^m G$.

5. Comparison to Other Predictions

Table 4 gives a comparison of the present predictions for the sum of $\Delta_h^m G$ for Na^+(aq) and Cl^-(aq) with predictions by other methods. Free energies of hydration for individual ions are not compared because the “experimental” values for the individual ions are not as accurate as the values for the sum. Reasonably accurate individual ion hydration values are only available at 298.15 K. Note that this is a stringent test of the ABC-FEP method, where calculations of the individual ions are done independently and no cancellation of errors due to sampling or the ab initio methods is expected by adding the results. In other words, the ABC-FEP calculations must be accurate for both ions in order for the sum to agree with experiment. Furthermore, by not comparing individual ions we avoid the surface free energy problem. The surface of a large drop of water has a surface dipole moment which contributes equal and opposite free energy increments to cations and anions inside the drop. This surface free energy increment has not been measured accurately[44] and our calculations use an Ewald Sum technique, which produces a zero surface dipole moment.[40,44,45]

At 573 K with 0.725 g/cm^3, we have a very accurate experimental value for $\Delta_h^m G[Na^+(aq)+Cl^-(aq)]$ of −661 kJ/mol[46] and this is in excellent agreement with the present results of −657 ± 7 kJ/mol. The estimates of the revised HKF model (SUPCRT 92)[9] and of Tanger and Pitzer[13] are also very reliable because they are fit to experimental data near this temperature and density. The accuracy of the present estimate is all the more remarkable because it is essentially determined by the accuracy of our ab initio method.

At 973 K with 0.535 g/cm^3 there are no direct experimental measurements and the predictive methods at this high temperature are of unknown accuracy because they are semiempirical extrapolations. We believe that our present ABC-FEP estimate is the most reliable available so we will use it as a standard for comparing other predictions.

We have found only three predictions of the free energies of hydration of ions at temperatures above 650 K and densities above 0.5 g/cm^3. Table 4 allows a comparison of these three methods with our present results. The SUPCRT92 prediction,[9] based on the revised HKF model,[48] is in excellent agreement with our calculation at 973 K (-545 versus -538 kJ/mol). The predictions of Tanger and Pitzer[13] are almost the same as the SUPCRT92 prediction at 973 K. This may not be a completely independent prediction at this density because the parameters of this model were adjusted to fit the hydration free energies of Tanger and Helgeson[47] at higher densities.

Sedlbauer et al.[17] have developed a model (SOW) for predicting the free energies of hydration of electrolytes and nonelectrolytes based on an empirical representation of the temperature and density dependence of $\bar{V}_2°/\kappa RT$. The equations for ions were parametrized with experimental data that was limited to temperatures less than 673 K. The accuracy of the extrapolation to higher temperatures is unknown. The prediction of the SOW equation at 573 K is expected to be accurate, and is in excellent agreement with the present work (-661 versus -663 kJ/mol). The prediction at 973 K is also in good agreement (-538 versus -544 kJ/mol).

Agreement at 973 K and 0.535 g/cm^3 is very good among all three predictive schemes. However, it is not clear whether this agreement will hold up at lower densities and near the critical point of water.

As an additional exercise we compared the above sophisticated predictive schemes with two very simple continuum model predictions: (1) the Born equation and (2) the compressible continuum (CC) model. Both models include the appropriate standard state term and a continuum cavity term (for details of these models see Wood et al.[12]). These models have one adjustable parameter, the radius of the hard sphere ion. To make predictions, this radius was determined by fitting to experimental data at a reference temperature (both 298.15 and 573 K have been used). Predictions were then made at higher temperatures. The results in Table 4 show that neither model is very accurate, though the CC model is marginally better.

Other predictive methods are not included in our comparison because they were parametrized only at lower densities,[14] require simulated structural information,[15] or require complex parametrization using low-temperature data.[16]

6. Optimized Approximate Models

Ideally, we would like to develop approximate model potentials that accurately reproduce all of the properties of a given ion in water, regardless of temperature and density. Toward this end we have explored the important features of model potentials for these ions, by developing newly optimized potentials based on the results described above. These potentials all have the general form of eqs 1 and 2, but are of three types (see optimized models in Table 1). In the first type, exponents *a* and *b* in eqs 1 and 2 are set to the values found in the models that work best at 573 K and 0.725 g/cm^3 (i.e., $Cl^-{-}H_2O$ model II, with exponents 6 and 9, and $Na^+{-}H_2O$ model III, with exponents 4 and 8). Previous ab initio calculations indicate that short-range multibody forces result in "softer" potentials (*a* and *b* less than the traditional 6 and 12) at high densities[34,48,49] and this has again been seen in developing the models used for ABC-FEP. The charge on the ion is fixed, but the charges within each water molecule are determined by the TIP4P−FQ model. Because of the fluctuating charges in the water model, the ion−water interactions are not pairwise additive. These first two models for Cl^- and Na^+ are denoted (6,9,FQ) and (4,8,FQ), respectively. In the second set of models, the exponents *a* and *b* are set to the traditional Lennard-Jones values of 6 and 12, again with fluctuating charges in the water model, and are denoted as (6,12,FQ). In the final model, the exponents are set to 6 and 12, and the ions interact with the water through a fixed charge, given by the TIP4P model (without fluctuating charges). These pairwise additive models are denoted (6,12,TIP4P). Values of the remaining parameters in each model (Table 1) are set to fit our total ab initio interaction energies in the configurations from the $Cl^-{-}H_2O$ model II or $Na^+{-}H_2O$ model III simulations at 573 K and 0.725 g/cm^3, for which ab initio energies were calculated in the ABC-FEP calculations.

Before comparing the predictions of these models, it is useful to identify some of their deficiencies. While the fluctuating charge models attempt to model the many-body electrostatic interactions, this model is not expected to be accurate at short range where polarization of the cation or anion and nonlinear polarization of the water are present. In addition, the van der Waals interactions in eqs 1 and 2 are pairwise additive and will be increasingly inaccurate as the density increases. These inaccuracies derive from the neglect of short-range multibody interactions. This effect can be modeled in an effective two-body potential by reducing the exponents *a* and *b* in eqs 1 and 2, but the optimal exponents will depend on the temperature and density. These considerations suggest that the best approximate model of this form can be accurate only over a limited range of density and temperature.

We have used the free energy perturbation approach to find the difference in free energies at 573 K and 0.725 g/cm^3 between these optimized models and the previously developed $Cl^-{-}H_2O$ model II and $Na^+{-}H_2O$ model III. Note that this compares the predictions of different model potentials; no new ab initio calculations were done. Table 5 reports the differences in free energy and the total hydration free energy for each optimized model, as well as the average value of ΔU_{XS} and its standard deviation. To assess the predictive value of the optimized models at other temperatures and densities, Table 5 also gives calculated values of ΔU_{XS} and $\Delta_h^m G$ at 973 K.

The best effective pairwise additive models for the hydration free energies at 573 K with 0.725 g/cm^3 are the (6,9,FQ) model for Cl^- and the (4,8,FQ) model for Na^+. These two optimized models underestimate our ABC-FEP results for $\Delta_h^m G$ by 2.8 and 4.2 kJ/mol respectively. Applying these models at 973 K with 0.535 g/cm^3 yields even larger underestimates (3.1 and 11.8 kJ/mol; see Table 5). The models with Lennard-Jones (6,12) exponents and fluctuating charge on the water (6,12,FQ) yield even larger underestimates at both temperatures. If these potentials are modified so that the ions see a charge on water that is given by the TIP4P model, (6,12,TIP4P), the result is an even larger underestimate.

Each of the optimized Na^+ models is worse than the corresponding Cl^- model. In fact, the optimized Cl^- model (6,9,FQ) is almost as good as the ABC-FEP calculation at fitting U_{XS} and $\Delta_h^m G$. The average values of ΔU_{XS} are -1.3 and -2.8 kJ/mol at 573 and 973 K, respectively and the standard deviations of the individual ΔU_{XS} from the averages are 2.8 and 3.8 kJ/mol. In contrast, the optimized Na^+ model (4,8,FQ) is not a good model for U_{XS} and $\Delta_h^m G$. The average of ΔU_{XS} is

TABLE 5: Hydration Free Energy of Approximate Models Optimized for Cl$^-$ and Na$^+$ at 573 K and 0.725 g/cm^3 (All Energies in kJ/mol)

Cl$^-$ model[a]	$\langle \Delta U_{XS} \rangle$[b]	ΔG_{XS}[c]	$\Delta_h^m G$[d]	δ[e]	Na$^+$ model[a]	$\langle \Delta U_{XS} \rangle$[b]	ΔG_{XS}[f]	$\Delta_h^m G$[d]	δ[e]	$\Delta_h^m G$(total)
573 K with 0.725 g/cm^3										
6,9,FQ	−1.3(2.8)	−5.1(1.3)	−327	2.8	4,8,FQ	9.0(3.1)	3.2(0.8)	−324	4.2	−651
6,12,FQ	0.6(3.1)	−3.3(1.3)	−325	4.6	6,12,FQ	9.6(5.0)	3.8(1.4)	−323	4.8	−648
6,12,TIP4P	2.5(3.5)	−1.1(2.3)	−323	6.8	6,12,TIP4P	12.1(4.2)	6.4(1.9)	−320	7.4	−643
973 K with 0.535 g/cm^3 [g]										
6,9,FQ	−2.8(3.8)	−7.8(1.9)	−261	3.1	4,8,FQ	14.7(5.1)	5.6(2.2)	−263	11.8	−524[e]
6,12,FQ	0.4(3.5)	−4.7(1.7)	−258	6.2	6,12,FQ	16.2(5.6)	7.3(2.5)	−261	13.5	−519[e]
6,12,TIP4P	3.0(5.4)	−2.1(1.8)	−255	8.8	6,12,TIP4P	18.9(6.3)	9.9(2.8)	−258	16.1	−513[e]

[a] See Table 1 for parameter values. [b] $\langle \Delta U_{XS} \rangle$ is the average difference between the ab initio energies and the model energies with the standard deviation of the differences in parentheses. [c] FEP estimate of the difference in free energy between the optimized model and model II for Cl$^-$ with a bootstrap estimate of uncertainty. [d] Free energy of hydration of the model (1 mol/kg and ideal gas standard state). [e] δ is $\Delta_h^m G$[model] − $\Delta_h^m G$[ABC−FEP] [f] FEP estimate of the difference between the optimized model and model III for Na$^+$ with a bootstrap estimate of uncertainty. [g] The predicted results for 973 K with model fitted at 573 K.

9.0 and 14.7 kJ/mol at 573 and 973 K, respectively (with standard deviations of 3.1 and 5.1 kJ/mol). All of the other models for Cl$^-$ and Na$^+$ have higher standard deviations of ΔU_{XS} than the optimized models, showing the importance of low values of the exponents a and b.

In a preliminary investigation of Na$^+$ and Cl$^-$ at 298.15 K and 1.0 g/cm^3, we did not find an adequate effective pairwise model. The Na$^+$ models were particularly bad. We believe that short-range multibody interactions that increase with decreasing ionic radius are mainly responsible for the failure of these models. It seems likely that it will be much easier to develop effective pairwise additive models for the short range, nonelectrostatic interactions of the larger ions and that these models will be useful over a wider range of densities. In contrast, it should be difficult (if not impossible) to develop accurate models of this type for Li$^+$(aq) and Na$^+$(aq).

7. Conclusions

The ABC-FEP method has proven to be effective in predicting hydration free energies of sodium and chloride ions at two high temperature state points. At 573 K, where accurate experimental data are available, there is excellent agreement with the calculations. This is all the more remarkable because the prediction is completely based on first-principles, with no empirical parameters required (the approximate potentials used are simply a convenient starting point). At 973 K, several approximate methods that extrapolate from experimental data at lower temperatures are in close agreement with the ABC-FEP prediction. These calculations provide the first parameter-free prediction of hydration energies at this higher temperature, and the agreement with other methods serves to validate those methods for use near this phase point. The main sources of error in the ABC-FEP calculation are believed to be in the ab initio methods, although sampling error, cluster size errors, and thermodynamic integration errors also contribute. Our error estimates indicate that the current predictions for hydration free energies of individual ions are accurate to within 5 kJ/mol, but if desired, it is straightforward to reduce the error with more extensive calculations.

Table 3 shows that that the ABC-FEP correction to the free energy is a small part of the total in each case. However, this is because the approximate models have been adjusted to ensure that they agree with ab initio energies. Without the ABC-FEP approach, it would not have been possible to identify the failure of the initial models, or to develop improved models. Indeed, the ABC-FEP method may be regarded as an iterative approach to free energy calculations: in cases where the FEP correction is not accurate, an improved approximate model must be developed. An accurate ABC-FEP correction indicates that this iterative process has converged. Even when the FEP corrections to the approximate model are small, they are by no means negligible, so they must be calculated.

One of the great advantages of the ABC-FEP technique is that it provides a way of assessing the accuracy of approximate models. This has allowed us to develop more useful effective potentials for the simulations. Moreover, we have obtained new insight into the form of interactions that are important at high temperature, finding in particular that the short-range interactions are "softer" than those described by the typical 6,12 potential, and that short-range multibody forces make an important contribution. It also appears that there will be fundamental difficulties in developing general two-body potentials particularly for the smaller alkali metal ions. The ABC-FEP method appears to be a promising aid in developing new effective potentials, as well as correcting for the weaknesses of such potentials.

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References and Notes

(1) Galobardes, J. F.; van Hare, D. R.; Rogers, L. B. *J. Chem. Eng. Data* **1981**, *26*, 363.

(2) Conway, B. E. *Chem. Soc. Rev.* **1992**, 253.

(3) Markovits, G. Y.; Choppin, G. R. *Ion Exchange and Solvent Extraction*; Marcel Dekker: New York, 1973.

(4) Brodholt, J.; Wood, B. J. *Geophys. Res.* **1993**, *98*, 519.

(5) Holmes, H. F.; Mesmer, R. E.; Simonson, J. M.; Mesmerm, R. E.; Archer, D. G.; Wood, R. H. *J. Chem. Thermodyn.* **1987**, *19*, 863.

(6) Quist, A. S.; Marshall, W. L. *J. Phys. Chem.* **1968**, *72*, 684.

(7) Carter, R. W. Ph.D. Thesis, University of Delaware, 1992.

(8) Hewish, N. A.; Neilson, G. W.; Enderby, J. E. *Nature* **1982**, *297*, 138.

(9) Johnson, J. W.; Oelkers, E. H.; Helgeson, H. C. *Comput. Geosci.* **1992**, *18*, 899.

(10) Wood, R. H.; Quist, J. R.; Grolier, J.-P. E. *J. Phys. Chem.* **1981**, *85*, 3944.

(11) Quist, J. R.; Wood, R. H. *J. Phys. Chem.* **1985**, *89*, 380.

(12) Wood, R. H.; Carter, R. W.; Quist, J. R.; Mager, V.; Thompson, P. T.; Boccio, J. R. *J. Chem. Thermodyn.* **1994**, *26*, 225.

(13) Tanger, J. C.; Pitzer, K. S. *J. Phys. Chem*. **1989**, *93*, 4941.

(14) Pitzer, K. S. *J. Phys. Chem*. **1983**, *87*, 1120.

(15) Flanagin, L. W.; Balbuena, P. B.; Johnston, K. P.; Rossky, P. J. *J. Phys. Chem. B* **1997**, *101*, 7998.

(16) Lvov, S. N.; Akinfiev, N. N.; Bandura, A. V.; Sigon, F.; Perboni, G. *Power Plant Chem.* **1999**, *1*, 13.

(17) Sedlbauer, J.; O'Connell, J. P.; Wood, R. H. *Chem. Geol.* **2000**, *163*, 43.

(18) Plyasunov, A. V.; O'Connell, J. P.; Wood, R. H. *Geochim. Cosmochim. Acta* **2000a**, *64*, 495.

(19) Plyasunov, A. V.; O'Connell, J. P.; Wood, R. H.; Shock, E. L. *Geochim. Cosmochim. Acta* **2000b**, *64*, 2779.

(20) Berendsen, H. J. C.; Postma, J. P. M.; van Gunsteren, W. F.; Hermans, J. *Intermolecular Forces*; Reidel: Dordrecht, The Netherlands, 1981.

(21) Jorgenson, W. L.; Chandresekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. L. *J. Chem. Phys*. **1983**, *79*, 926.

(22) Rick, S. W.; Stuart, S. J.; Berne, B. J. *J. Chem. Phys*. **1994**, *101*, 6141.

(23) Chandrasekhar, J.; Spellmeyer, D. C.; Jorgensen, W. L. *J. Am. Chem. Soc*. **1984**, *106*, 903.

(24) Aqvist, J. *J. Phys. Chem*. **1990**, *94*, 8021.

(25) Marrone, T. J.; Merz, K. M., Jr. *J. Am. Chem. Soc*. **1992**, *114*, 7542.

(26) Marrone, T. J.; Merz, K. M., Jr. *J. Phys. Chem*. **1993**, *97*, 6524.

(27) Pettitt, B. M.; Rossky, P. J. *J. Chem. Phys*. **1986**, *84*, 5836.

(28) Balbuena, P. B.; Johnston, K. P.; Rossky, P. J.; Hyun, J.-K. *J. Phys. Chem. B* **1998**, *102*, 3806. Chialvo, A. A.; Cummings, P. T.; Cochran, H. D.; Simonson, J. M.; Mesmer, R. E. *J. Chem. Phys.* **1995**, *103*, 9379. Chialvo, A. A.; Cummings, P. T.; Simonson, J. M.; Mesmer, R. E. *J. Chem. Phys*. **1999**, *110*, 1064. Cui, S. T.; Harris, J. G. *Chem. Eng. Sci*. **1994**, *49*, 2749. Cummings, P. T.; Cochran, H. D.; Simonson, J. M.; Mesmer, R. E.; Karaborni, S. *J. Chem. Phys*. **1991**, *94*, 5606. Gao, J. *J. Phys. Chem*. **1994**, *98*, 6049. Gao, J. *J. Phys. Chem*. **1992**, *96*, 537. Koneshan, S.; Rasaiah, J. C. *J. Chem. Phys*. **2000**, *113*, 8125. Lee, S. H.; Cummings, P. T. *J. Chem. Phys*. **2000**, *112*, 864. Reagan, M. T.; Harris, J. G.; Tester, J. W. *J. Phys. Chem. B* **1999**, *103*, 7935. Wallen, S. L.; Palmer, B. J.; Pfund, D. M.; Fulton, J. L. *J. Phys. Chem. A* **1997**, *101*, 9632.

(29) Balbuena, P. B.; Johnston, K. P.; Rossky, P. J. *J. Phys. Chem*. **1996**, *100*, 2706.

(30) Fernandez-Prini, R. *J. Phys. Chem. B* **1998**, *102*, 257.

(31) For example, Smargiassi, E.; Car, R. *Phys. Rev. B* **1996**, *53*, 9760. Trout, B. L.; Parrinello, M. *Chem. Phys. Lett.* **1998**, *288*, 343.

(32) Wood, R. H.; Yezdimer, E. M.; Sakane, S.; Barriocanal, J. A.; Doren, D. J. *J. Chem. Phys*. **1999**, *110*, 1329.

(33) Sakane, S.; Yezdimer, E. M.; Liu, W.; Barriocanal, J. A.; Doren, D. J.; Wood, R. H. *J. Chem. Phys.* **2000**, *113*, 2583.

(34) Sakane, S.; Liu, W.; Doren, D. J.; Wood, R. H. *Geochim. Cosmochim. Acta* **2001**, *65*, 4067−4075.

(35) *DL_POLY-2.0*; Forester, T. R.; Smith, W. Daresbury Laboratory, Daresbury, England, 1995.

(36) Pomes, R.; McCammon, J. A. *Chem. Phys. Lett*. **1990**, *166*, 425.

(37) Sakane, S.; Ashbaugh, H. S.; Wood, R. H. *J. Phys. Chem. B* **1998**, *102*, 5673.

(38) Ben-Naim, A.; Marcus, Y. *J. Chem. Phys*. **1984**, *81*, 2016.

(39) Efron, B. *The Jackknife, the Bootstrap and Other Resampling Plans*; Society for Applied Mathematics: Philadelphia, PA, 1982.

(40) Ashbaugh, H. S.; Wood, R. H. *J. Chem. Phys*. **1997**, *106*, 8135.

(41) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(42) *Jaguar 3.5*; Schrodinger, Inc.: Potland, OR, 1998.

(43) Boys, S. F.; Bernardi, F. *Mol. Phys*. **1970**, *19*, 553.

(44) Darden, T.; Pearlman, D.; Pedersen, L. G. *J. Chem. Phys*. **1998**, *109*, 10921.

(45) Hummer, G.; Pratt, L. R.; Garcia, A. E. *J. Chem. Phys*. **1997**, *107*, 9275.

(46) Archer, D. G. *J. Phys. Chem. Ref. Data* **1992**, *21*, 793.

(47) Tanger, J. C.; Helgerson, H. C. *Am. J. Sci*. **1988**, *288*, 19.

(48) Periole, X.; Allouche, D.; Daudey, J.-P.; Sanejouand, Y.-H. *J. Phys. Chem. B* **1997**, *101*, 5018

(49) Balbuena, L.; Wang, T. Li.; Derosa, P. A. In *Molecular dynamics: From classical to quantum methods*; Balbuena, P. B., Seminario, J. M., Eds.; Elsevier Science Publishers: Amsterdam, 1999; Chapter 11.