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PAPER

Effective solvent mediated potentials of Na^+ and Cl^- ions in aqueous solution: temperature dependence

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The effective solvent-mediated potentials for Na^+ and Cl^- ions in aqueous solution were calculated in a wide range of temperatures from 0 to 100 °C. The potentials have been determined using the inverse Monte Carlo approach, from the ion–ion radial distribution functions computed in 50 ns molecular dynamics simulations of ions and explicit water molecules. We further separated the effective potentials into a short-range part and an electrostatic long-range part represented by a coulombic potential with some dielectric permittivity. We adjusted the value of the dielectric permittivity to provide the fastest possible decay of the short-range potentials at larger distances. The obtained temperature dependence of the dielectric permittivity follows well the experimental data. We show also that the largest part of the temperature dependence of the effective potentials can be attributed to the temperature-dependent dielectric permittivity.

1. Introduction

Multiscale modeling techniques aiming at consistent, hierarchical development of molecular models from the atomistic level to the mesoscale have received increasing attention during the last decade. This interest originates in the understanding that it is impossible to model many important phenomena in biophysics and soft matter at the atomistic level due to the large size of these systems, as well as due to too long time needed for them to equilibrate. An evident way to attain progress in addressing the mesoscale problem is to use coarse-grained and/or implicit solvent models, which contain only important, principal features of the studied system while unimportant ones (local details of the molecular structure, solvent) are disregarded. A practical way to build such models was suggested in paper,¹ where the Inverse Monte Carlo (IMC) method was introduced allowing us to reconstruct coarse-grained interaction potentials from radial distribution functions determined in atomistic simulations. Related approaches, appeared recently and addressing the same problem, are iterative Boltzmann inversion,^{2,3} the force matching approach,⁴ use of integral equations based on the hypernetted chain^{5,6} or the Yvon–Born–Green theory.⁷ During the last decades, these methods were applied for computations of effective solvent-mediated potentials for various systems: ion solutions,^{8,9} ion–DNA interactions,¹⁰ various molecular liquids,^{7,11,12} coarse-grained lipid models,^{13–15} and polymers.^{3,6}

A principal problem with effective coarse-grained potentials derived from atomistic simulations is that they, by the way of

their definition, are dependent on thermodynamics conditions, such as temperature and concentration of different components.^{6,16,17} In some cases this dependence may be weak or of no importance, but in principle, thermodynamical transferability of the effective potentials should be controlled in each specific case. In this paper we investigate temperature dependence of the effective solvent mediated potentials between ions in aqueous solution.

Ion solutions, and specifically Na^+ – Cl^- aqueous solution, have been extensively studied during the last decades.^{9,18–24} This interest is motivated by the great importance of ions and their solutions in many areas of biophysics and physical chemistry. One of the simple models of ionic solutions, often used in investigation of polyelectrolytes including biological macromolecules, is the primitive electrolyte model^{25–28} describing solvent as a continuum medium and the ions as hard spheres interacting by potential $\frac{q_i q_j}{4\pi\epsilon_0 \epsilon r}$ (where q_i and q_j are ion charges, r is the interionic distance, ϵ_0 is the vacuum dielectric permittivity and ϵ is the relative permittivity of the solvent). Clearly, this expression is a rather rough approximation on short distances between the ions when the intermediate solvent cannot be considered as a continuum due to its molecular structure. Also, specific short-range features of ion–ion interactions, including van der Waals forces, are not taken into account within the primitive model.

Solvent-mediated interionic effective potentials, taking into account the molecular structure of the solvent and specific short-range interactions, can be built from atomistic molecular dynamics simulations as it was done in a number of previous studies.^{1,5,8,29} Hess *et al.*⁹ investigated concentration dependence of NaCl ion–ion effective potentials constructed from atomistic simulations. It was shown that the main part of this

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dependence can be attributed to the change of the effective dielectric permittivity, which decreases with the ion concentration, affecting the long-range behaviour of the effective potentials. Taking into account concentration-dependence of the dielectric permittivity, osmotic coefficients of ions can be reproduced in a wide concentration range.^{9,21} Nevertheless the temperature dependence of the ion–ion effective potential and the corresponding effective dielectric permittivity has not been studied yet. In this work we address this problem and calculate the effective potentials for Na⁺ and Cl[−] ions in aqueous solution for a wide range of temperatures from 0 to 100 °C. Furthermore, we show that computation of the effective potentials provide an alternative route to determine static dielectric permittivity in molecular liquids which may further contribute to our general understanding of dielectric properties of various solutions.

2. Models and methods

2.1 Explicit water molecular dynamics simulations

Atomistic molecular dynamics (MD) simulations of 20 Na⁺Cl[−] ion pairs dissolved in 1000 water molecules (which correspond to ion concentration ≈ 1.0 M) have been performed in the range of temperatures from 0 to 100 °C. Water was presented by the flexible simple point charge (SPC-F) model by Toukan and Rahman.³⁰ For the ion–ion and ion–water interactions, Smith–Dang parameters were used:³¹ $\sigma_{\text{Na}} = 2.35$ Å, $\epsilon_{\text{Na}} = 0.544$ kJ mol^{−1}, $\sigma_{\text{Cl}} = 4.4$ Å, $\epsilon_{\text{Cl}} = 0.42$ kJ mol^{−1}, together with the Lorentz–Berthelot rules for cross-interactions. The system was put into a cubic periodic box, and long range electrostatic interactions were treated by the Ewald method.³² The equations of motion were integrated by the constant-temperature–constant-pressure molecular dynamics algorithm,³³ with Nose–Hoover relaxation parameters for 50 fs for the thermal bath and for 1 ps for the volume fluctuations. The double time step algorithm by Tuckerman *et al.*,³⁴ with a short time step of 0.25 fs for intramolecular and short-range interactions (within 5 Å distance) and a long time step of 2.5 fs for longer range interactions (between 5 Å and 12 Å cutoff), has been implemented. Eleven temperature points were chosen between 273 K and 373 K with a step of 10 K, and the pressure was set to 1 bar for all of them. For each temperature, 50 ns MD simulation was performed and the first 5 ns was treated as equilibration. Configurations were saved in the trajectories each 1 ps, and they were used for subsequent calculation of NaNa, NaCl, and ClCl radial distribution functions. The MD simulations were performed by the MDynaMix software package.³⁵

2.2 Calculation of effective ion–ion potentials by the inverse Monte Carlo method

The method of reconstruction of effective pair potentials from the corresponding RDFs, using an iterative inverse Monte Carlo procedure, was published elsewhere.¹ The inverse simulations were carried out in the NVT ensemble conditions, using the same number of ions and average periodic cell size as in the corresponding atomistic MD simulations, but without explicit water molecules. Thus possible size effects on the

RDFs should be essentially avoided. Potential of the mean force $U(r) = -kT\ln(g(r))$ was taken as the starting trial potential, and then was refined in about 20 IMC iterations, allowing to reach a complete convergence between newly generated RDF and the reference ones. Each iteration consisted of 5×10^7 Monte Carlo steps of which first 1×10^7 steps were considered as equilibration. The long range part of the electrostatic interaction, outside the cut-off distance (which was set to half of the box length), was treated using the Ewald summation method for coulombic potential with dielectric permittivity defined initially as for pure water at ambient temperature ($\epsilon = 80$), and then optimized according to the procedure described below.

2.3 Effective pair potential decomposition and computation of effective dielectric permittivity

By analogue with previous studies,^{1,5,9} we used decomposition of the effective potential into a short-range part and a long-range electrostatic part, the latter being defined by the macroscopic dielectric permittivity:

$$U_{\text{eff}}^{ij}(r) = U_{\text{sr}}^{ij}(r) + \frac{q_i q_j}{4\pi\epsilon_0 \epsilon r} \quad (1)$$

The potential $U_{\text{eff}}^{ij}(r)$ is the one coming from the IMC procedure, thus choice of dielectric permittivity ϵ defines the short range part $U_{\text{sr}}^{ij}(r)$. The second part of this decomposition is supposed to account for all long-range interactions, that is why improper choice of ϵ value will produce a certain long-range contribution in $U_{\text{sr}}^{ij}(r)$. Since dielectric permittivity depends on temperature, the initial guess $\epsilon = 80.0$ (which had been proven to be a good choice for the SPC-F water model at $T = 298$ K),⁸ may not be optimal for other temperatures. By a proper choice of ϵ , the long range component of $U_{\text{sr}}^{ij}(r)$ can be minimized. A complicating circumstance is that, in the case of ion solution, the long-range parts of all three potentials, namely Na–Na, Na–Cl and Cl–Cl, should be minimized by varying the same value of ϵ . We used the following procedure to obtain values of the dielectric permittivity providing fastest decay of all three short-range potentials with distance. First, we introduce numerical criteria of a short range potential deviation from zero at large distances:

$$W(U_{\text{sr}}^{ij}(r)) = \int_{r_1}^{r_2} |r^2 U_{\text{sr}}^{ij}(r)| dr \quad (2)$$

where r^2 factor implies a higher weight of larger distances, r_1 and r_2 are the lower and upper boundaries of the range of distances defining the long-range part (the r_2 value is taken as the cut-off of RDF and tabulated effective potential, which is also equal to half of the box size). The absolute value in eqn (2) is used in order to deal with oscillations of the short range part of the potential, which are typical for effective ion–ion potentials.^{5,8}

Taking in mind eqn (1), we can write for the short-range part of the potential:

$$W(U_{\text{sr}}^{ij}(r)) = \int_{r_1}^{r_2} \left| r^2 \left(U_{\text{eff}}^{ij}(r) - \frac{q_i q_j}{4\pi\epsilon_0 \epsilon r} \right) \right| dr \quad (3)$$

Assume that we define the long-range coulombic potential using another value of permittivity ϵ^* . This, according to (1), introduces a new short-range potential as:

$$U_{\text{sr}}^{ij} = U_{\text{sr}}^{ij}(r) + \frac{q_i q_j}{4\pi\epsilon_0 r} \left(\frac{1}{\epsilon} - \frac{1}{\epsilon^*} \right) \quad (4)$$

Now we shall find the optimal ϵ^* , which produces the fastest decay of all three short range potentials according to criteria defined by eqn (2). We minimize the sum:

$$W(U_{\text{sr}}^{\star\text{NaNa}}(r)) + W(U_{\text{sr}}^{\star\text{NaCl}}(r)) + W(U_{\text{sr}}^{\star\text{ClCl}}(r)) \quad (5)$$

by varying ϵ^* . The optimized value of ϵ^* can be considered as effective dielectric permittivity corresponding to the given thermodynamic conditions (temperature, concentration). We need to remember however that the value of the effective dielectric permittivity may affect the IMC procedure itself through Ewald treatment of the long-range part of the effective potential (outside the cutoff distance). We therefore rerun the IMC simulation with the new corrected value of ϵ . After 3–4 such iterations ϵ^* values stop to change and reach convergence. They are considered as final optimized values of the dielectric permittivity.

3. Results and discussion

3.1 Atomistic MD simulation results

Previous simulations of NaCl ion solution described by the model used in this work have been carried out at temperature 298 K.^{5,8,36} In order to test briefly the applicability of this model at other than ambient temperature, we compare the density obtained in our NPT-MD simulations with the experimental one.³⁷ The results are presented in Fig. 1. Unfortunately we found density data for 1 M NaCl solution only in a rather narrow temperature interval, that is why we plot also pure water data for the whole temperature range. Direct comparison of the MD simulation results with experimental temperature dependence of the density of Na^+Cl^- solution and pure water shows quite reasonable agreement.

Fig. 1 Temperature dependence of the density of Na^+Cl^- aqueous solution. Green squares—explicit water MD simulations (this work), red circles—experimental data for Na^+Cl^- aqueous solution,³⁷ blue triangles—experimental data for pure water.³⁹

Fig. 2 Radial distribution functions for Na^+Na^+ , Na^+Cl^- and Cl^-Cl^- ion pairs for different temperatures. Arrows show direction of the temperature growth in the same order as in the legend.

The computed $\rho(T)$ dependence shows the same trend as pure water in the 20–100 °C temperature range, but does not show nearly temperature-independent behavior in the range 0–10 °C. This is a known deficiency of the SPC water model, which is unable to reproduce the water density maximum at 4 °C.³⁸ Anyway, the overall agreement with experimental data can be considered as an argument for reliability of the explicit solvent MD simulations.

Ion–ion radial distribution functions obtained in MD simulations are displayed in Fig. 2. They all show strong dependence on the temperature. The curves for all 3 ion–ion pairs are clearly ordered from lower to higher temperature within each oscillation of the RDFs. The general trend is that the first peak of RDF between likewise ions is decreasing at higher temperatures, while the first peak of NaCl RDF is increasing, showing higher tendency to form ion pairs at higher temperatures.

The accuracy of RDF calculations is very important for producing reliable effective potentials. Our previous studies⁵ have shown that reliable estimation of ion–ion RDFs, and especially the height of the first peak of RDFs, requires simulations on at least 10 ns time scale. To be on a safe side, we carried out 50 ns simulations for each temperature point, and performed a test on whether such trajectories are long enough for producing stable radial distribution functions. In Fig. 3 we displayed RDF calculated during the first 20 nanoseconds of the trajectory after finishing the equilibration period, another RDF calculated during the following 25 ns of the same trajectory, and the RDF averaged over the whole trajectory. There are no major deviations in the curves, and difference of the curves does not exceed a few percent. This indicates that the 5 ns period was enough for equilibration and following 45 ns of simulation provides reasonable amount of data to produce smooth and stable RDF. The same kind of behavior was observed for all other temperatures and ion pairs.

3.2 Inverse Monte Carlo results

The computed ion–ion RDFs were passed to the inverse Monte Carlo procedure, where 20 iterations were performed for each temperature point. The value of the regularization parameter defining the factor for potential correction in the IMC procedure

Fig. 3 RDFs stability test: red line— Cl^- — Cl^- pair integrated over 5 to 25 ns, black line— Cl^- — Cl^- pair integrated over 25 to 50 ns, green line— Cl^- — Cl^- pair integrated over the whole trajectory. Purple line— Na^+ — Na^+ pair integrated over 5 to 25 ns, blue line— Na^+ — Na^+ pair integrated over 25 to 50 ns, orange line— Na^+ — Na^+ pair integrated over the whole trajectory. The data correspond to temperature 323 K.

was kept equal to 0.5, thereby a reasonable convergence level of RDFs was provided. An example illustrating convergence of the IMC procedure for the case $T = 323$ K is shown in Fig. 4. The orange dotted line showing RDF computed using the starting trial potential of mean force does not show good agreement with the reference RDF. After five IMC iterations (light blue line) RDFs become much closer to the reference and after five more iterations (green, dark blue, red lines) the results are stable and coincide with the reference RDF within uncertainty of the latter. In all other cases the IMC procedure reached reasonable convergence after 10–15 iterations.

The short-range parts of the effective potentials, defined by eqn (1) with effective dielectric permittivity $\epsilon = 80$ and computed for different temperatures, are displayed in Fig. 5. The potentials show noticeable temperature dependence, they

Fig. 4 Convergence of the Inverse Monte Carlo procedure for the 323 K temperature point. Solid black line—reference RDF, orange line—RDF after 1 IMC iteration, light blue dots—after 5 IMC iterations, dash-dot-dot green line—after 10 iterations, short blue dashes—after 15 iterations, dashed red line—after 20 iterations.

Fig. 5 Effective short range ion-ion potentials for different temperatures, corresponding to dielectric permittivity $\epsilon = 80.0$. Arrows show direction of the temperature growth in the same order as in the legend.

are ordered on the plot exactly as the temperature. Noteworthy, the curves with highest temperature are highest in the case of NaNa and ClCl ion pairs, while it is lowest in the case of NaCl pair, and they keep this arrangement through the whole range of distances. This is a clear indication that such effective potentials contain some long-range coulombic contribution, which in fact should be prescribed to the long-range part by choosing a proper value of the dielectric permittivity. Also, analysis of the curves obtained at other temperatures shows that coulombic parts of the potentials are either over- or underestimated depending on the temperature.

3.3 Effective potentials with temperature-dependent dielectric permittivity

In order to provide an adequate decomposition of the effective potential into short-range and long-range (coulombic) parts and to extract the effective dielectric permittivity, we used the procedure described in Section 2.3, minimizing the tails of the short range parts of the effective potentials in the range of distances 10–15.5 Å, where the higher boundary was limited by a half of the cell size. The corrected short-range effective potentials for different temperatures are shown in Fig. 6, and values of the effective dielectric constant at different temperatures are shown in Fig. 7.

Fig. 6 Effective short range ion-ion potentials for the whole temperature range. Dielectric permittivity has been optimized in order to provide the fastest decay of the short-range part.

Fig. 7 Dielectric permittivity of $\text{Na}^+\text{--Cl}^-$ water solution at 1 M concentration. Green triangles—values calculated in the present work from the long-range behavior of the effective potentials; blue circles—values calculated from the dipole fluctuations (eqn (6)); purple dash line—experimental data for pure water; orange points—experimental values referring to 1 M NaCl water solution; yellow line—wide range extrapolation of the experimental data. The experimental data were taken from Peyman *et al.*⁴⁰

As it can be seen from Fig. 6, effective short range potentials calculated with corrected dielectric permittivity do not show strong temperature dependence. They also become practically equal to zero at distances larger than 10 Å. Though certain difference between the curves can be noted, it is substantially less than it was in the case of uncorrected potentials in Fig. 5. Moreover, the curves in Fig. 6, while showing some trends indicated by arrows in the figure, do not follow the same order as the temperature, which indicates that a large part of the difference between them is from statistical uncertainty.

Another important result of this analysis is the values of the effective dielectric permittivity obtained for different temperatures, Fig. 7. As expected, dielectric permittivity decreases with temperature. We compare the computed values of the dielectric permittivity with experimental data for pure water⁴⁰ as well as for 1 M NaCl solution (for the latter, experimental data are available only for a limited temperature interval 5–35 °C, and they were complemented by an extrapolation formula from work 40). Finally, we have computed dielectric permittivity directly from atomistic simulations using the following expression for water dipoles fluctuations⁴¹:

$$\varepsilon = 1 + \frac{\langle M^2 \rangle - \langle M \rangle^2}{3\varepsilon_0 V k T} \quad (6)$$

where M is the sum of molecular dipole moments (taken over all water molecules) and V is the volume of the simulation cell. One can see that the two ways of calculation of dielectric permittivity are consistent with each other and are in line with experiment, though direct computations from atomistic MD provide more stable results. Uncertainties of the values of dielectric permittivity defined from the asymptotic behavior of the effective potentials come from the uncertainties in the ion–ion RDFs, as well as from the fitting procedure which is done in the range of distances where oscillations of the effective potentials due to the molecular structure of water

do not disappear completely. Computations of effective potentials in a larger simulation cell may provide more accurate estimation of the dielectric permittivity.

4. Conclusions

We have computed effective solvent-mediated potentials for Na^+ and Cl^- ions in water for the range of temperatures between 0 and 100 °C. Some temperature dependence of the potentials has been observed. We decomposed the potentials into short-range and long-range (coulombic) parts by choosing effective dielectric permittivity ε which provides the fastest decay of the short range part. The ε -corrected short-range potentials turned out to be much less temperature dependent. Taking in mind that a similar effect was previously observed for concentration dependence of ion–ion effective potentials,⁹ we can conclude that thermodynamically non-transferable (that is temperature and concentration dependent) part of the effective NaCl ion–ion potentials consists essentially in the long-range coulombic contribution, which can be described by the concentration- and temperature-dependent dielectric permittivity, while the short-range interaction is essentially invariant with respect to the change of thermodynamical conditions.

Several reservations about the above conclusion should be made. First, our study covers the temperature range for liquid water at normal pressure, and the conclusion about transferability of the short-range part of the effective potentials does not necessarily propagate beyond this range, *e.g.* to the supercritical conditions. Previous molecular dynamics studies of NaCl solution at supercritical conditions^{42,43} have shown that the water structure around ions changes largely when the temperature is raised to a supercritical one, and at such conditions even the short range part of the effective potentials may show considerable change compared to the ambient conditions. Second, the short range potentials are expected to be specific to the kind of solvent, and need to be recalculated for other solvents than water. Third, for large bulky ions, the hydrophobic interactions become more important, which may lead to stronger temperature dependence of the short-range part of effective potentials.

The decomposition of the effective potentials described in the paper may be of importance for further use of the effective ion–ion potentials in different conditions, including their interactions with polyelectrolytes and charged biomacromolecules. One can expect that the short range part of various ion–polyion effective potentials will be specific for different sites of the polyion, but largely not dependent on the temperature and ion concentration. On the other hand, the long-range part of the effective potentials will be determined by the charges of the coarse-grained sites and effective dielectric constant, the latter being dependent on the temperature and ion concentration. Also, decomposition of the effective potential into the coulombic part, which can be treated by a fast Ewald (PME or P3M) summation technique, and short-range part with a short (of the order 10–12 Å) cutoff distance would provide better performance in large scale mesoscopic simulations employing these potentials.

Furthermore, the presented approach represents an alternative way of determination of the dielectric permittivity in molecular

solvents. The dipole fluctuation expression (6) is valid only for rigid molecular models (more rigorously, for point dipoles, which still can be considered as a good approximation for water molecules). Computation of static dielectric permittivity from the long-range asymptotic of effective potentials can be used for higher molecular weight solvents such as alcohols, ionic liquids, etc.

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