Effects of the translational and rotational degrees of freedom on the hydration of simple solutes

Tomaž Mohorič, Barbara Hribar-Lee, and Vojko Vlachy^{a)}

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, SI-1000 Ljubljana, Slovenia

(Received 28 February 2014; accepted 25 April 2014; published online 14 May 2014)

Molecular dynamics simulations with separate thermostats for rotational and translational motion were used to study the effect of these degrees of freedom on the structure of water around model solutes. To describe water molecules we used the SPC/E model. The simplest solute studied here, the hydrophobe, was represented as a Lennard-Jones particle. Since direct interaction between the hydrophobe and water molecules has no angular dependence the influence of the increase of the rotational temperature on the solvation of a hydrophobe is only indirect. In the next step the central solute was assumed to be charged with either a positive or a negative charge to mimic an ion in water. Hence, depending on the charge of the ion, the neighboring water molecules assumed different angular distributions. The principal conclusions of this work are: (i) an increase of the translational temperature always decreases the height of the first peak in the solute-water radial distribution function; (ii) an increase of the rotational temperature yields an increase in the first peak in the solute-water radial distribution function for hydrophobes and cations; (iii) in contrast to this, the solvation peak decreases around ions with sufficiently large negative charge; and (iv) an increase of the rotational temperature affects cations in an opposite way to anions. For this reason complex molecules with a small net charge may not be very sensitive to variation of the rotational temperature. © 2014 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4875280>]

I. INTRODUCTION

Correlation between solutes in water (see, for example, Ref. 1) is determined not only by their direct interaction, but also by the ability of water to hydrate the solutes.^{2,3} Hydration of hydrophobic and ionic solutes is therefore an important topic in electrochemistry, geochemistry, and especially biology,^{4–6} where it is not uncommon for protein structures to be stabilized by the charges held together by bridging water molecules. The problem is not trivial, even at infinite dilution with respect to the solute where subtle competition between solute-water and water-water interactions exists. This and similar problems have recently been studied in molecular dynamics simulations by detailed force-field modeling,^{7–19} as also by the integral equation technique.²⁰

Temperature is considered to be the most important thermodynamic parameter and the ability of water to solvate a solute depends on it. An interesting question is how the fundamental degrees of freedom, such as translation and rotation contribute to hydration. A biologically important situation arises when water molecules are irradiated with microwaves of appropriate frequency to excite their rotational motion.

The interaction of microwaves with water has been studied using the non-equilibrium molecular dynamics simulation,²¹ where electric field was modelled explicitly. It has been shown that microwaves induce heating by excitation of rotational motion in water molecules. Excess rotational kinetic energy is then transferred to translational degrees of freedom. In the present work in a spirit of Ref. 22 a direct in-

teraction of microwaves with solvent is replaced by a model system in which the rotational degree of freedom is having different temperature than the translational motion. Such a non-equilibrium picture, where different degrees of freedom can have different temperatures, has already been successfully used in explaining experimental phenomena, such as increased chemical reaction rates and altered polar solvent boiling points.^{23,24} Studies of the influence of microwave irradiation on the hydration of various solutes might have practical implications for biology. It has been reported that microwave irradiation enhances the folding and unfolding kinetics of globular proteins,^{25–27} as well as protein aggregation through alteration of the protein conformation.²⁸ Several studies suggest that microwaves induce structural rearrangements of proteins not related to the temperature.^{29,30} In organic synthesis the thermal and non-thermal microwave effects are still being debated.^{31,32}

The idea of studying the effects of individual degrees of freedom is appealing for many reasons. An important previous contribution was made by Bren and Janežič.²² These authors used molecular dynamics in conjunction with the Split Integration Symplectic Method to decouple individual degrees of freedom of water molecules and connect them with the relevant thermostats. The main conclusion of their work is that increase of the rotational temperature, T_R , affects the hydration of cations in a non-monotonous way, while on the other hand, the solvation of a hydrophobe is slightly increased. Solvation of anions and the effect of the ion charge density have not yet been examined.

The present work differs from the previous study²² in several aspects and it goes a step further. In particular we

^{a)} Author to whom correspondence should be addressed. Email: vojko.vlachy@fkkt.uni-lj.si

aimed to examine the differences in hydration of cations and anions caused by variation of the rotational and translational temperatures. In order to explore the solvation properties of model water around model solutes, we applied molecular dynamics (MD) simulations, where the rotational and translational motions were coupled to separate thermostats. We used a rigid model of water (SPC/E);³³ the effect of vibrational temperature variations was, namely, found to be small.²² Different prototype solutes were studied; hydrophobes, positively and negatively charged ions, all at different values of the translational and rotational temperatures. The focus of this study was on the structure of water around these solutes. For this purpose we calculated the pair-distribution functions between solutes and water, as well as the orientational distributions of water molecules in the first solvation layer. In view of the different response of cations and anions on increase of the rotational temperature, we were interested how these differences arise as a consequence of the gradual transformation of a hydrophobe into an ion. For this purpose we performed MD simulations for “ions” with fractional charge and analyzed the microscopic distributions of water around such solutes. The simulations provide a step toward better understanding of aqueous solvation. The paper is organized as follows: after the Introduction we describe the model and simulation method used. The theoretical part is followed by the discussion and a brief summary of the main results at the end.

II. MODEL AND SIMULATION DETAILS

The molecular dynamics simulations were performed in the canonical (N, V, T) ensemble, which consisted of 256 SPC/E water molecules and a fixed solute in the middle of the simulation box. The number density of water molecules corresponds to 1.0 g/cm^3 , and the time step used was 1.0 fs . The MD systems were initially prepared by short Monte Carlo runs (just to avoid particle overlap at the start of MD runs), which were followed by 100 ps long MD equilibration runs and 4900 ps long MD production runs, during which the statistics were collected.

The translational motion of a single water molecule i was described by its center-of-mass position $\mathbf{r}_i$, velocity $\mathbf{v}_i$, and the force $\mathbf{f}_i$ acting on it. Similarly the rotational motion of a single water molecule i was described by its orientation (using quaternion representation) $\mathbf{q}_i$, angular velocity $\boldsymbol{\omega}_i$, and torque $\boldsymbol{\tau}_i$. While the acceleration of the center-of-mass follows immediately from the force acting on it, the angular acceleration must be computed from Euler’s equations of motion for rigid bodies. We employed the standard Verlet algorithm to integrate the equations of motion.³⁴ To hold T_R and T_T fixed at their respective values we employed a simple velocity rescaling scheme. Use of the Berendsen thermostat was found to be less convenient, because for a coupling constant τ_B longer than the time step, it was not possible to keep the temperatures constant (due to the heat flow from higher to lower temperature).

We studied the solvation of several prototype solutes. We started with the Lennard-Jones (LJ) particle representing a hydrophobe. The ions were modeled as LJ particles of the same size as the hydrophobe, with positive or negative charges at

TABLE I. Parameters of the SPC/E water model.

σ_{WW} [$\text{\AA}$]	3.169
ϵ_{WW} [J/mol]	650.2
r_{OH} [$\text{\AA}$]	1.0
α_{HOH} [$^\circ$]	109.4
q_{H}	+0.4238
q_{O}	−0.8476

the centers. The values of the LJ parameters examined here were $\sigma_{\text{SS}} = 3.0 \text{ \AA}$, while the well-depth was equal for all solutes and had the value of the SPC/E water model, that is $\epsilon_{\text{SS}} = 650.2 \text{ kJ/mol}$. The parameters of the SPC/E water model are collected in Table I. In addition we performed a complete set of calculations for $\sigma_{\text{SS}} = 2.0$ and $4.0 \text{ \AA}$, but these results did not provide additional insights, so they are not shown here. The solute-water LJ parameters were obtained as $\sigma_{\text{WS}} = \frac{1}{2}(\sigma_{\text{SS}} + \sigma_{\text{WW}})$ and $\epsilon_{\text{WS}} = (\epsilon_{\text{WW}}\epsilon_{\text{SS}})^{\frac{1}{2}}$. In the part of the study where we gradually charged the hydrophobe, the fractional charges on the solutes were ± 0.125 , ± 0.25 , ± 0.50 , ± 0.75 , and ± 1 . For the reference case, representing a polar solute, we examined the solvation of the SPC/E water molecule. The results were presented in such a way that for one set of degrees of freedom the temperature was fixed at 300 K , while the temperature for the second set of degrees of freedom assumed values of 300 , 500 , 600 , and 700 K , respectively. For the sake of clarity the radial distribution functions and the angular distribution functions for 600 K , which fall between the results for 500 K and 700 K , are not shown.

III. RESULTS AND DISCUSSION

The simulation results are presented in the form of the solute-water oxygen radial distribution functions (RDFs, g_{SO}), the angular distribution functions (ADFs, $p(\theta)$) for the OH bond lying in the first shell of the solute, and the average solute-water interaction energy E^{SW} , which is split into the Lennard-Jones $E_{\text{LJ}}^{\text{SW}}$ and electrostatic E_{c}^{SW} parts. The radius of the first hydration shell is defined as the distance to the first minimum in g_{SO} . The angle θ in the angular distribution function is defined as the angle between the OH bond and the vector from the water oxygen to the solute.

A. Solvation of hydrophobes

The hydrophobe-water pair interaction, which is of the Lennard-Jones type, is rotationally invariant. Therefore an increase of T_R (faster rotational motion of water molecules) influences the hydrophobe-water interaction only indirectly; i.e., by affecting the interaction among neighboring water molecules. Rapidly rotating water molecules are expected to be less likely to form hydrogen-bonds with other water molecules. Figure 1(a) indicates that an increase of T_R causes a modest increase in the height of the first peak of g_{SO} . Weaker interactions among the water molecules increase their ability to solvate the solute.

While an increase of T_R affects the rotational motion of water molecules, a higher T_T increases their translational kinetic energy. Faster translational motion decreases

FIG. 1. The hydrophobe-water RDF for $\sigma_{SS} = 3 \text{ Å}$ at (a) different T_R (at fixed $T_T = 300 \text{ K}$) and (b) different T_T (at fixed $T_R = 300 \text{ K}$). Different colors correspond to different temperatures: 300 K (blue), 500 K (magenta), and 700 K (orange). Arrows indicate the direction of the changes of RDFs with temperature increase.

correlations among the particles; Figure 1(b) shows that the first peak of g_{SO} decreases. Additionally the water molecules with higher kinetic energies are more likely to penetrate the solute, shifting g_{SO} slightly to the left. Accordingly, we observe an increase of the E_{LJ}^{SW} term (Figure 2, green line) with increase of the translational temperature.

As the direct hydrophobe-water interaction is rotationally invariant, we do not expect the ADF to be highly structured (structure occurs only due to the water-water correlation). Figures 3(a) and 3(b) show that the ADFs have broad peaks at $\theta \sim 60^\circ$ and $\theta \sim 180^\circ$ indicating water's tendency to conserve hydrogen-bonds. Increasing T_R makes the angular distribution less structured, but the effect is small.

B. Solvation of cations

By charging the solute from the previous example (hydrophobe) with one positive charge ($z = +1$) we introduce orientationally dependent solute-water interactions. Now an increase of T_R directly affects the water-water as well as the ion-water interactions. Figure 4(a) shows that the first peak in the cation-water distribution function g_{SO} increases with

FIG. 2. The average hydrophobe-water interaction energy as a function of T_R at $T_T = 300 \text{ K}$ (red) and as a function of T_T at $T_R = 300 \text{ K}$ (green) for a hydrophobe of size $\sigma_{SS} = 3 \text{ Å}$.

FIG. 3. The angular distribution function for a water OH bond lying within a hydrophobe first shell ($\sigma_{SS} = 3 \text{ Å}$) at (a) different T_R (with $T_T = 300 \text{ K}$) and (b) different T_T (with $T_R = 300 \text{ K}$). The color codes are as for Figure 1. Arrows indicate the direction of the changes of ADFs with temperature increase. The most probable water orientation in solute's hydration shell is shown schematically.

increase of T_R . This suggests that cation hydration becomes somewhat stronger.

An increase of T_T causes a considerable decrease of the ion-solvent and solvent-solvent correlations due to the faster translational motion. Figure 4(b) shows that the first peak in the cation-water g_{SO} decreases and moves slightly to the left; water molecules with higher translational kinetic energy may penetrate the solute.

Data presented in Figures 5(a) and 5(b) (red lines) show that the average cation-water electrostatic interaction energy, E_C^{SW} , decreases, while the Lennard-Jones contribution E_{LJ}^{SW} increases with increase of the rotational temperature. This indicates again that water better solvates a cation at higher T_R . Notice that at the highest T_R studied here (700 K), E_C^{SW} starts to increase (Figure 5(b)). This is to be expected the cation-water interaction depends on the orientation of water molecules and the faster rotational motion of water eventually weakens this interaction too. This is illustrated in the behavior of the RDF as seen in Figure S1 of the supplementary material,³⁵ where the first peak starts to decrease as T_R

FIG. 4. The cation-water RDF for a cation $\sigma_{SS} = 3 \text{ Å}$, $z = +1$ at (a) different T_R (with $T_T = 300 \text{ K}$) and (b) for different T_T (at $T_R = 300 \text{ K}$). The color codes are as for Figure 1. Arrows indicate the direction of the changes of RDFs with temperature increase.

FIG. 5. The average cation-water (a) Lennard-Jones and (b) Coulomb interaction energy as a function of T_R at $T_T = 300$ K (red) and T_T at $T_R = 300$ K (green) for a cation $\sigma_{SS} = 3$ Å, $z = +1$.

increases from 900 to 1500 K. The influence of T_T is shown in Figures 5(a) and 5(b) (green lines). Because the main contribution to E_{LJ}^{SW} comes from repulsion ($E_{LJ}^{SW} > 0$), the decrease of the first peak in g_{SO} causes the decrease in E_{LJ}^{SW} . Accordingly E_C^{SW} increases.

The angular distribution function for the water OH bond within the cation first shell is presented in Figures 6(a) and 6(b). All the ADFs exhibit broad peaks at $\sim 109^\circ$, indicating some preference for this orientation. Higher values of T_R do not affect the angular distributions significantly; it seems that higher T_R values primarily affect the water-water interaction by disrupting hydrogen bonds in water. As we already noticed, the decrease in strength of the solvent-solvent interaction increases the solvent's ability to solvate the solute. The effect of an increase of the translational temperature is documented on Figure 6(b).

C. Solvation of anions

Figure 7(a) presents the effect of T_R on the anion-water radial distribution function. Here an increase of T_R is followed

FIG. 6. The angular distribution function for a water OH bond lying within a cation first shell for a cation $\sigma_{SS} = 3$ Å, $z = +1$ at (a) different T_R (with $T_T = 300$ K) and (b) different T_T (with $T_R = 300$ K). The color codes are as for Figure 1. Arrows indicate the direction of changes of ADFs with temperature increase. The most probable water orientation in solute's hydration shell is shown schematically.

FIG. 7. The anion-water RDF for an anion $\sigma_{SS} = 3$ Å, $z = -1$ at (a) different T_R (with $T_T = 300$ K) and (b) different T_T (with $T_R = 300$ K). The color codes are as for Figure 1. Arrows indicate the direction of the changes of RDFs with temperature increase.

by a decrease in the height of the first peak, indicating somewhat weaker solvation. This result is in contrast to the behavior of the cation studied in Sec. III B. Higher T_T , due to the faster translational motion of water molecules, Figure 7(b), diminishes the anion-water and water-water correlations.

The data presented in Figures 8(a) and 8(b) (red lines), showing that the Lennard-Jones part of the energy E_{LJ}^{SW} decreases (the repulsive interaction becomes less important when the anion has fewer surrounding water molecules) and the E_C^{SW} term increases, are consistent with the behavior of g_{SO} . The effect of T_T is shown by the green lines.

As can be seen from Figure 9(a) the probability distribution of finding an OH bond pointing toward the anion ($\theta \sim 0^\circ$), which is energetically by far the most favorable configuration, is very narrow and decreases substantially (compare with Figure 6(a)) with increase of T_R . Note that the peak is much higher than that belonging to the cation. This is perhaps the most important difference compared with the hydration of a cation. When water molecules hydrate an anion the OH bonds tend, for optimal effect, to point practically directly to the anion. Because the corresponding angular distribution is very narrow, such an optimal orientation is increasingly more

FIG. 8. The average anion-water (a) Lennard-Jones and (b) Coulomb interaction energy as a function of T_R at $T_T = 300$ K (red) and T_T at $T_R = 300$ K (green) for an anion $\sigma_{SS} = 3$ Å, $z = -1$.

FIG. 9. The angular distribution function for a water OH bond lying within an anion first shell for an anion $\sigma_{SS} = 3$ Å, $z = -1$ at (a) different T_R (with $T_T = 300$ K) and (b) different T_T (with $T_R = 300$ K). The color codes are as for Figure 1. Arrows indicate the direction of the changes of ADFs with temperature increase. The most probable water orientation in solute's hydration shell is shown schematically.

difficult to achieve as the rotational temperature increases. It is worth noting, Figure 9(b), that the ADF with the peak at $\theta \sim 0^\circ$ remains practically unchanged with increase of T_T .

D. From hydrophobes to ions

From the results presented so far we see that anions respond to an increase of the rotational temperature differently from cations and hydrophobes. In order to understand better how these differences arise, we performed a study in which we gradually charged the hydrophobe to the final charge $z = +1$ forming a cation, or in the second case to $z = -1$ forming an anion. The intermediate (partial) charges were $z = \pm 0.125, \pm 0.25, \pm 0.50$, and ± 0.75 . In what follows we present the evolution of the distribution functions with increase of T_R ; the corresponding results for T_T are less interesting and accordingly shown in Figure S2 of the supplementary material.³⁵

1. Solvation of cations with fractional charges

From Figure 10 we see that all the cation-water RDFs follow the same trend: the height of the first peak increases with increase of T_R . The behavior of cations and hydrophobes indicates that in these examples an increase of T_R weakens the water-water interaction more than the solute-water interaction, in such a way increasing water's ability to solvate the cation. The angular distributions shown in Figure 11 are relatively uniform in comparison to the ADFs for anions (compare the scales), and do not change dramatically with increase of T_R . The two equivalent peaks at around 60° and 180° merge into one at 109° for a higher charge density of the cation ($z = +0.75$).

2. Solvation of anions with fractional charges

Charging the hydrophobe with a negative charge results in nonmonotonous behaviour of the height of the first peak of g_{SO} with respect to T_R (Figure 12). For anions with small

FIG. 10. The cation-water RDF for cations $\sigma_{SS} = 3$ Å with various charges at different T_R (with $T_T = 300$ K). RDFs for different cation charges are vertically shifted for better clarity; from top to bottom: $z = +0.75$ (solid line), $+0.50$ (long dashed), $+0.25$ (short dashed), and $+0.125$ (dotted). The color codes are as for Figure 1. Arrows indicate the direction of the changes of RDFs with temperature increase.

negative charges (i.e., for $z = -0.125$ and -0.25), the first peak in g_{SO} increases only slightly. However, for anions with $z = -0.50$ and -0.75 , the height of the first peak in g_{SO} decreases with increase of T_R .

The angular distributions in Figures 13(a) and 13(b) reveal a difference in the solvation of weakly ($z = -0.125, -0.25$) and strongly charged ($z = -0.5, -0.75$) anions. The ADFs for more highly charged anions (Figure 13(a)) resemble those for the fully charged $z = -1$ anion (Figure 9(a)) with a strong peak at $\theta \sim 0^\circ$, and are very sensitive to variation in rotational temperature. On the other hand, the ADFs for weakly charged anions are much more uniform (Figure 13(b)), looking much like the corresponding distributions for hydrophobes (Figure 3(a)). In this case an increase of T_R does not affect aqueous solvation significantly.

E. Solvation of water molecules

To estimate the solvation of polar molecules we simply fix a water molecule in the center of the MD cell. Figure 14(a)

FIG. 11. The angular distribution function for a water OH bond lying within an anion first shell for anions $\sigma_{SS} = 3$ Å and various charges at different T_R (with $T_T = 300$ K). Functions for different anion charges are vertically shifted for better clarity; from top to bottom: $z = +0.75$ (solid line), $+0.50$ (long dashed), $+0.25$ (short dashed), and $+0.125$ (dotted). The color codes are as for Figure 1.

FIG. 12. The anion-water RDF for anions $\sigma_{SS} = 3$ Å with various charges at different T_R (with $T_T = 300$ K). RDFs for different anion charges are vertically shifted for better clarity; from top to bottom: $z = -0.75$ (solid line), -0.50 (long dashed), -0.25 (short dashed), and -0.125 (dotted). The color codes are as for Figure 1. Arrows indicate the direction of the changes of RDFs with temperature increase.

shows that an increase of T_R causes little change in the height of the first peak, while the second peak diminishes. This behavior can be explained by looking at g_{SO} for the anionic and cationic parts of the SPC/E molecule separately in Figures 14(b) and 14(c), respectively. We define the cationic and anionic parts of the solute in the following way. An SPC/E molecule is fixed with its oxygen at the center of the cubic box ($x = y = z = 0$) and its symmetry axis pointing along the z -axis. To obtain g_{SO} for the cationic part, we count only distances to the molecules in that half of the box ($z < 0$), which includes the solute's hydrogens. Conversely, we use the other half of the box for the anionic g_{SO} .

The first peak around the anionic part of the fixed water molecule decreases as would be expected for the solvation of anions, while it increases in the case of solvation of the cationic part (the same behavior as for solvation of simple cations). The combined effect, however, causes almost no change in g_{SO} . As observed in all the cases studied so far, an

FIG. 13. The angular distribution function for a water OH bond lying within an anion first shell for anions $\sigma_{SS} = 3$ Å and various charges at different T_R (with $T_T = 300$ K). Functions for different anion charges are vertically shifted for better clarity; from top to bottom in (a) $z = -0.75$ (solid line), -0.50 (long dashed) and in (b) $z = -0.25$ (short dashed) and -0.125 (dotted). The color codes are as for Figure 1.

FIG. 14. The fixed water-water RDFs at different T_R . (a) total RDF. (b) RDF around the anionic part of fixed water. (c) RDF around the cationic part of fixed water. For details of the definitions of cationic/anionic parts of fixed water molecules, please see Sec. III E. The color codes are as for Figure 1. Arrows indicate the direction of the changes of RDFs with temperature increase.

increase of T_T decreases the first peak (see Figure S3 in the supplementary material³⁵).

IV. CONCLUSIONS

In this work we examined how the fundamental degrees of freedom, such as translation and rotation, affect the hydration of model solutes. To obtain the numerical results we employed molecular dynamics simulations with separate thermostats for rotational and translational motion. To describe a water molecule we used the SPC/E model. The model solutes studied here were the hydrophobe, pictured as a Lennard-Jones particle, and the cation and anion, which differ from the hydrophobe only by charge. For simplicity, and to better understand the difference between the solvation of different species, the sizes of the cation and anion were assumed to be equal. We studied the model hydrophobe and ions at several values of the translational and rotational temperature. In addition to the fully charged, also the partially charged ions were investigated.

We can summarize the most important conclusions as follows: (i) For the Lennard-Jones hydrophobe, an increase of T_R causes an increase in the first peak of g_{SO} . (ii) For cations of the size of the hydrophobe an increase of T_R causes an increase of the first peak of g_{SO} . (iii) The situation is different for anions. Here an increase of T_R is followed by a decrease in the first peak of g_{SO} . (iv) The trend of a decrease of correlations with increase of the translational temperature, T_T , can be noticed for all the examples studied here.

It is very likely that for molecules with a net charge zero, i.e., molecules having an equal number of positive and negative charges, the overall effect of an increase of rotational

temperature will be marginal. This is actually reflected in the results for solvation of the “water” molecule, as an example of a polar molecule. The actual situation, however, may be slightly more complicated. As revealed in the section entitled “From hydrophobes to ions” it is not the value of the charge which is important, but rather the charge density of the ion or part of the molecule. Notice that the behavior exhibited by anions depends on their charge density. A higher T_R causes slightly better solvation of less charged anions and weaker solvation of more highly charged anions.

Due to their narrow angular distribution peaking at $\theta \sim 0^\circ$, anions are more sensitive to T_R variations. The shape of the first peak of the angular distribution depends on the charge density of the ion; we expect the effects to be stronger with smaller and/or doubly charged ions. The effects of varying T_R may accordingly be amplified in the case of highly charged macroions. In the present study the focus was on the solvation of a single solute. In a future contribution we wish to examine the effect of water’s rotational and translational temperatures on the potential of mean force between the solute particles.

The simulation results may be influenced by the choice of thermostat. As was shown in the supplementary material of Ref. 22 the time constant of Berendsen thermostat, τ_B , has to be sufficiently small in order to keep the temperatures at desired values. The other choice, Andersen’s thermostat,³⁶ if applied at short time scale, would largely disturb the system’s dynamics. There were no obvious advantages on choosing Nose-Hoover thermostat, which to our knowledge was devised for correct canonical sampling of equilibrium systems. Following the previous work in which Bren and Janežič²² explored the Berendsen thermostat in some detail we used their procedure. The chosen simulation protocol satisfied our main purpose, which was to reveal the role of individual degrees of freedom in hydration of various species. However, as was already pointed out before,²² the use of more advanced thermostats should be explored in future studies.

Finally, we wish to stress that the results may depend on the model of water used in the simulation. This aspect is currently under investigation.

ACKNOWLEDGMENTS

This study was supported by the Slovenian Research Agency (ARRS) fund through the Program 0103–0201, Project J1–4148, Young Researchers Program (T.M.), and by NIH research grant (GM063592).

- ¹J. M. G. Barthel, H. Krienke, and W. Kunz, *Physical Chemistry of Electrolyte Solutions. Modern Aspects*, Topics in Physical Chemistry Vol. 5, edited by H. Baumgärtel, E. U. Franck, and W. Grünbein (Springer, New York, 1998).
- ²Y. Marcus and G. Hefter, *Chem. Rev.* **106**, 4585 (2006).
- ³Y. Marcus, *Chem. Rev.* **109**, 1346 (2009).
- ⁴K. D. Collins, *Biophys. J.* **72**, 65 (1997).
- ⁵K. D. Collins, G. W. Neilson, and J. E. Enderby, *Biophys. Chem.* **128**, 95 (2007).
- ⁶*Specific Ion Effects*, edited by W. Kunz (World Scientific Publishing, Singapore, 2010).
- ⁷Z. Yang and X. Li, *J. Phys. Chem. A* **109**, 3517 (2005).
- ⁸G. Lamoureux and B. Roux, *J. Phys. Chem. B* **110**, 3308 (2006).
- ⁹A. Nag, D. Chakraborty, and A. Chandra, *J. Chem. Sci.* **120**, 71 (2008).
- ¹⁰C. J. Fennell, A. Bizjak, V. Vlachy, and K. A. Dill, *J. Phys. Chem. B* **113**, 6782 (2009).
- ¹¹C. J. Fennell, A. Bizjak, V. Vlachy, K. A. Dill, S. Sarupria, S. Rajamani, and S. Garde, *J. Phys. Chem. B* **113**, 14837 (2009).
- ¹²M. A. Ilhan and E. Spohr, *J. Electroanal. Chem.* **660**, 347 (2011).
- ¹³A. Mirzoev and A. P. Lyubartsev, *Phys. Chem. Chem. Phys.* **13**, 5722 (2011).
- ¹⁴L. Yang, Y. Fan, and Y. Q. Gao, *J. Phys. Chem. B* **115**, 12456 (2011).
- ¹⁵P. Ganguly, P. Schravendijk, B. Hess, and N. F. A. van der Vegt, *J. Phys. Chem. B* **115**, 3734 (2011).
- ¹⁶L. Pegado, O. Marsalek, P. Jungwirth, and E. Wernersson, *Phys. Chem. Chem. Phys.* **14**, 10248 (2012).
- ¹⁷M. W. Lee and M. Meuwly, *Phys. Chem. Chem. Phys.* **15**, 20303 (2013).
- ¹⁸G. Stirnemann, E. Wernersson, P. Jungwirth, and D. Laage, *J. Am. Chem. Soc.* **135**, 11824 (2013).
- ¹⁹D. Laage, G. Stirnemann, F. Sterpone, R. Rey, and J. T. Hynes, *Annu. Rev. Phys. Chem.* **62**, 395 (2011).
- ²⁰Yu. V. Kalyuzhnyi, V. Vlachy, and K. A. Dill, *Phys. Chem. Chem. Phys.* **12**, 6260 (2010).
- ²¹M. Tanaka and M. Sato, *J. Chem. Phys.* **126**, 034509 (2007).
- ²²U. Bren and D. Janežič, *J. Chem. Phys.* **137**, 024108 (2012).
- ²³U. Bren, A. Kržan, and J. Mavri, *J. Phys. Chem. A* **112**, 166 (2008).
- ²⁴M. Bren, D. Janežič, and U. Bren, *J. Phys. Chem. A* **114**, 4197 (2010).
- ²⁵H. Bohr and J. Bohr, *Phys. Rev. E* **61**, 4310 (2000).
- ²⁶H. Bohr and J. Bohr, *Bioelectromagnetics* **21**, 68 (2000).
- ²⁷S. S. R. Chinnadaya, M. Santhosh, and P. Goswami, *J. Biophys. Chem.* **3**, 317 (2012).
- ²⁸D. I. de Pomerai, B. Smith, A. Dawe, K. North, T. Smith, D. B. Archer, I. R. Duce, D. Jones, and E. P. M. Candido, *FEBS Lett.* **543**, 93 (2003).
- ²⁹M. Porcelli, G. Cacciapuoti, S. Fusco, R. Massa, G. d’Ambrosio, C. Bertoldo, M. De Rosa, and V. Zappia, *FEBS Lett.* **402**, 102 (1997).
- ³⁰A. Copt, F. Sakran, O. Popov, R. Ziblat, T. Danieli, M. Golosovsky, and D. Davidov, *Synth. Met.* **155**, 422 (2005).
- ³¹M. A. Herrero, J. M. Kremsner, and C. O. Kappe, *J. Org. Chem.* **73**, 36 (2008).
- ³²L. Perreux and A. Loupy, *Tetrahedron* **57**, 9199 (2001).
- ³³H. J. Berendsen, J. R. Grigera, and T. P. Straatsma, *J. Phys. Chem.* **91**, 6269 (1987).
- ³⁴M. P. Allen and D. J. Tildesley, *Computer Simulation of Liquids* (Clarendon, Oxford, 1987).
- ³⁵See supplementary material at <http://dx.doi.org/10.1063/1.4875280> for additional RDFs.
- ³⁶H. C. Andersen, *J. Chem. Phys.* **72**, 2384 (1980).