

Structural arrangement and dynamics of the hydrated Mg^{2+} : An ab initio QM/MM molecular dynamics simulation

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Received 28 March 2005

Available online 8 June 2005

Abstract

The structural arrangement and dynamics of solvated Mg^{2+} in dilute aqueous solution have been studied by ab initio QM/MM molecular dynamics simulation, in which the whole first and most of the second hydration shell of the ion were treated at Hartree–Fock level using LANL2DZ basis sets. Besides the most stable $\text{Mg}^{2+}(\text{H}_2\text{O})_6$ species, intermediates such as $\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$, where at least one water molecule temporarily moves into the inter-shell region but remains H-bonded to inner-shell water, as well as transition complexes of the $\text{Mg}^{2+}(\text{H}_2\text{O})_6(\text{H}_2\text{O})$ type, exist in aqueous solution. The dynamics of solvate and surrounding water molecules are discussed in connection to the ‘structure-forming’ ability of Mg^{2+} .

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1. Introduction

Characteristics of ions solvated in aqueous electrolyte solutions have been a topic of special interest since such detailed knowledge is essential for understanding the role of these ions in chemical and biological processes [1]. Both theoretical and experimental methods have been successfully employed to provide such data [2–4]. In conjunction with experiments, computer simulations allow a direct exploration of microscopic behavior of electrolyte solutions, especially for elucidating of some specific properties difficult to measure experimentally.

For ions in aqueous solution, the inclusion of many-body effects is compulsory for obtaining a correct description of the ion–water interactions, since polarization and charge transfer usually cause strong cooperative effects. With respect to this point, a combined ab initio QM/MM molecular dynamics technique has been proven to be an elegant method to include all necessary

many-body interactions in simulations, and thus has been successfully applied to various solvated ions [4–14]. Such QM/MM simulations also provide a good theoretical basis for the interpretation of experimental data. For example, the QM/MM simulations of Na^+ and K^+ in aqueous solution have provided a clear evidence for the background of the experimentally observed transition from ‘structure-making’ to ‘structure-breaking’ behavior from Na^+ to K^+ [6,13]. Another example is the femto- and picosecond dynamics of the Jahn–Teller effect of hydrated Cu^{2+} and Ti^{3+} , which are only revealed by the quantum mechanical treatment of the solvated ion, and to a full extent only after including two complete hydration shells [9,10].

In the present work, a QM/MM molecular dynamics simulation was extended from a previous study [7], in order to obtain a more detailed interpretation of the structural arrangement and the dynamics of Mg^{2+} hydrate in aqueous solution. For the structure it is known, both through experiment and theoretical approaches, that Mg^{2+} prefers to coordinate six water molecules in an octahedral arrangement [2,7,15,16]. However, the

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dynamical details of water molecules surrounding the ion are less clear since the scattering lengths of different magnesium isotopes are too similar to make full use of neutron diffraction with isotopic substitution (NDIS) [17]. Interestingly, the blackbody infrared radiative dissociation (BIRD) experiments [18] have suggested that there exist two isomeric forms of hexahydrated Mg^{2+} in the gas phase, namely $\text{Mg}^{2+}(\text{H}_2\text{O})_6$ at low temperatures and $\text{Mg}^{2+}(\text{H}_2\text{O})_4(\text{H}_2\text{O})_2$ at high temperatures. Thus, it became of particular interest to investigate the structural arrangement and dynamics of this hydrated ion complex in aqueous solution, since such details are of great importance according to the role this ion plays in biological systems [19,20].

2. Methods

The QM/MM simulation was performed with the same simulation protocol as reported in the previous work [7]. According to a compromise between the accuracy and computational effort, the QM region with a diameter of 9.0 Å, which includes the complete first and most of the second hydration shell of the ion, was treated at Hartree–Fock level using LANL2DZ basis sets [21,22]. A smoothing function [23] was employed within an interval of 0.2 Å (i.e., between the Mg–O distances of 4.5 and 4.7 Å) to ensure a continuous transition of forces at the boundary between the QM and MM regions. A flexible model, which describes intermolecular [24] and intramolecular [25] interactions, was employed for water. This flexible model allows explicit hydrogen movements, and thus gives access to the water's intramolecular vibrations as well as a smooth transition, when water molecules move from the QM region with its full flexibility to the MM region. The pair potential function for Mg^{2+} – H_2O interactions was obtained from the previous work [7]. The simulation was performed in a canonical ensemble at 298 K with a time step of 0.2 fs. The periodic cubic box, with a box length of 18.19 Å, employed in the simulation contained one ion and 199 water molecules, assuming the experimental density of pure water. Long-range interactions were treated using the reaction-field procedure [26]. The QM/MM simulation was performed for 80000 time steps, using equilibrium configurations from [7], and collecting configuration data every 10th step.

Since the dynamical properties of hydrated ions are rather sensitive to the accuracy of the models used in the simulations, a comparison of the results has been made with others, obtained at similar QM/MM level of accuracy. On the other hand, to accurately describe the influence of Mg^{2+} on the dynamical properties of its surrounding water molecules, the bulk properties discussed in this work have been referenced to the

properties of pure water obtained by a compatible QM/MM simulation [13].

Self-diffusion coefficients (D) of water molecules in the bulk and in the hydration spheres of Mg^{2+} were calculated from the center-of-mass velocity autocorrelation functions (VACFs) using the Green–Kubo relation [27],

$$D = \frac{1}{3} \lim_{t \rightarrow \infty} \int_0^t C_v(t) dt. \quad (1)$$

Power spectra, corresponding to the librational and vibrational motions of water molecules in the bulk and in the hydration shells of Mg^{2+} , were obtained by normal-coordinate analyses [28]. Six scalar quantities Q_2 , Q_1 , Q_3 , R_x , R_y and R_z , were defined to describe the symmetric bending and stretching and asymmetric stretching modes as well as the rotations around the three principal axes of water molecules. Due to the rather constant systematic errors of the Hartree–Fock frequencies, the standard factor of 0.89 [29] was applied to scale all frequencies obtained by the QM/MM simulations.

The rate of reorientation of water molecules in the bulk and in the hydration spheres of the ion was obtained from the reorientational time correlation functions (RTCFs)

$$C_{li}(t) = \langle P_l(\vec{u}_i(0)\vec{u}_i(t)) \rangle, \quad (2)$$

where P_l is the Legendre polynomial of l th order and \vec{u}_i is a unit vector along the three principal axes i defined in a fixed coordinate frame as the rotation above. The correlation functions for $l = 1$ are related to IR lines and for $l = 2$ to Raman line shapes and NMR relaxation [2,30]. Since the RTCFs are usually assumed to decay exponentially, these functions can be fitted to a simple form,

$$C_l(t) = a \exp(-t/\tau_l), \quad (3)$$

where a and τ_l are the fitting parameters, and τ_l is the corresponding relaxation time.

The rates of water exchange processes in the bulk and in the hydration sphere of the ion were evaluated by means of mean residence times (MRT). In this work, all MRT values were calculated using the 'direct' method [12], by the product of the average number of water molecules in the hydration sphere with the duration of the QM/MM simulation, divided by the observed number of exchange events lasting a given time interval t^* . Further dynamical properties, such as the 'lability' of the hydration shell was measured by the number and 'sustainability' of water exchange processes. This allows to determine the number of exchange events which lead to longer-lasting changes in the hydration structure, i.e., by comparing the number of all transitions through a shell boundary (N_{ex}^0), to the number of changes persisting after 0.5 ps ($N_{\text{ex}}^{0.5}$), resulting in a sustainability coefficient,

$$S_{\text{ex}} = N_{\text{ex}}^{0.5} / N_{\text{ex}}^0. \quad (4)$$

Its inverse ($1/S_{\text{ex}}$) accounts how many border-crossing attempts are needed to produce one sustainable change in the hydration structure of the ion [12].

3. Results and discussion

3.1. Structural arrangement of the hydrated Mg^{2+}

Within the total simulation time of 16 ps, the first hydration shell consisted of six water molecules, the most probable hydration number as established by various simulations and experimental studies [2,7,15,16]. However, as can be seen from a plot of O–Mg–O angular distributions in Fig. 1, the geometry of the $\text{Mg}^{2+}(\text{H}_2\text{O})_6$ complex shows distortions with considerable variability of the O–Mg–O angles ($\sim \pm 20^\circ$).

The motions of water molecules in the hydration spheres of Mg^{2+} can be recognized from a plot of Mg–O distances versus the simulation time, as shown in Fig. 2. Re-arrangement of the hexahydrated Mg^{2+} can be observed, for example, at a simulation time of 11.8–12.0 ps, as depicted in Fig. 3a, in which the intermediate $\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$ is formed. One water molecule moved as far as 1 Å away from its optimal distance but it forms a hydrogen bond to an inner-shell water molecule. Figs. 2 and 3 reveal numerous other attempts of water ligands to dissociate and/or create another $\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$ complex, but none of them reaches the inter-shell region (>2.5 Å, cf. Fig. 4). The presence of $\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$ is in accordance with previous quantum chemical calculations, which reported that the $\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$ complex is only 3.7 kcal mol⁻¹ less stable than the $\text{Mg}^{2+}(\text{H}_2\text{O})_6$ species [31]. Experimental evidence for the existence of

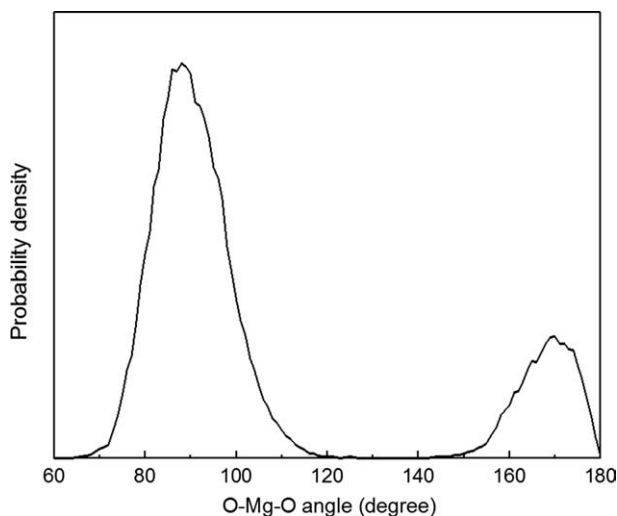


Fig. 1. Distribution of O–Mg–O angle, calculated up to the first minimum of the Mg–O RDF.

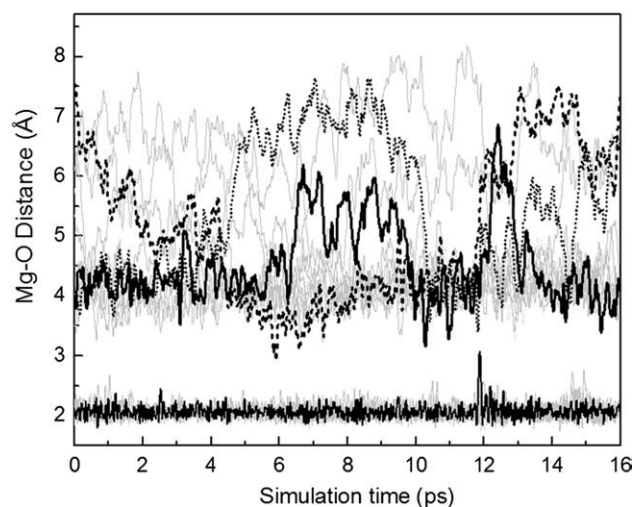


Fig. 2. Variations of Mg–O distances in the first and second hydration shells of Mg^{2+} obtained within the total simulation time of 16 ps.

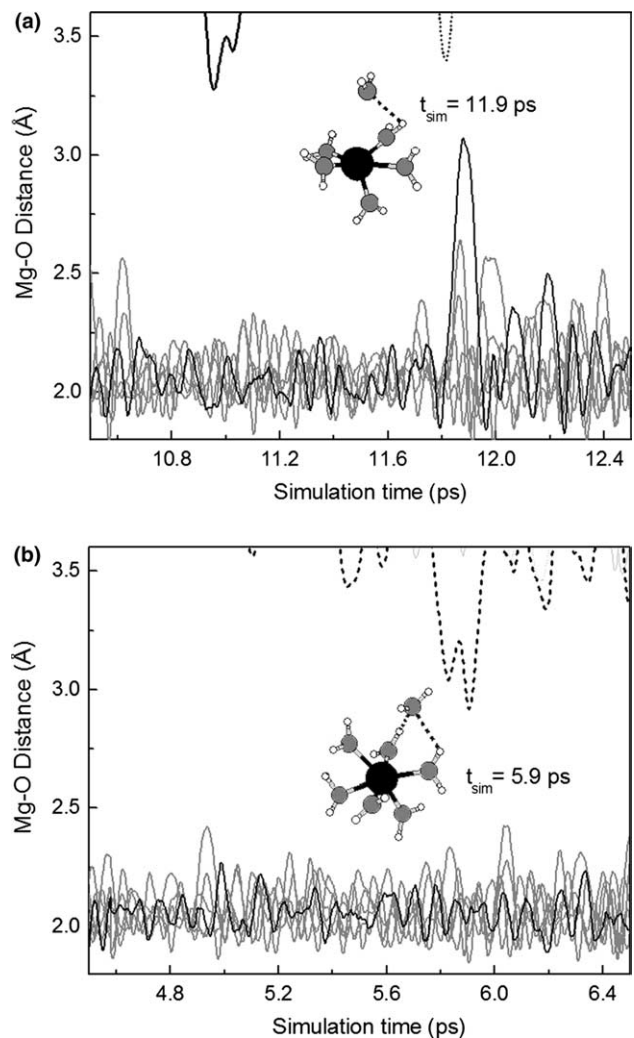


Fig. 3. Selected parts of Fig. 2, focussed at the Mg–O distance of 3.2 Å: (a) time interval between 10.5 and 12.5 ps and (b) time interval between 4.5 and 6.5 ps.

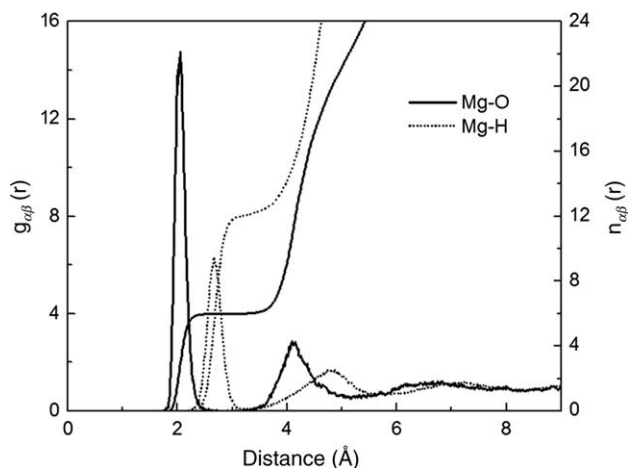


Fig. 4. Mg–O and Mg–H radial distribution functions obtained from the ab initio QM/MM MD simulation.

$\text{Mg}^{2+}(\text{H}_2\text{O})_5(\text{H}_2\text{O})$ or even $\text{Mg}^{2+}(\text{H}_2\text{O})_4(\text{H}_2\text{O})_2$ isomers in the gas phase comes from the BIRD measurements [18].

In addition, transition complexes of the type $\text{Mg}^{2+}(\text{H}_2\text{O})_6(\text{H}_2\text{O})$ also appear in aqueous solution, e.g., at a simulation time of 5.8–6.0 ps as shown in Fig. 3b, in which one water molecule from the second shell approaches as close as 3 Å to the ion and forms hydrogen-bonds to two inner-shell water molecules. This phenomenon can be ascribed to the strongly polarized first-shell water ligands [7], whose hydrogens can form strong hydrogen bonds to the outer-shell water molecules, if they happen to be in a suitable geometrical position.

3.2. Dynamical properties of water molecules surrounding Mg^{2+}

Table 1 lists some important dynamical parameters of water molecules in the bulk and in the hydration spheres of Mg^{2+} , comparing them to the available experimental data. According to the self-diffusion coefficients, as reported in Table 1, it is obvious that water molecules in the first hydration shell are strongly attached to the ion, while water molecules in the second hydration shell diffuse only slightly slower than those in the bulk.

Frequencies for the librational motions of water molecules in the bulk and in the hydration spheres of Mg^{2+} (see Table 1) show a clear order of $R_y > R_x > R_z$. In comparison to pure water, the R_z frequencies of water molecules in the first and second hydration shells are slightly red-shifted. These red-shifts of R_z values are to be expected, since the rotation around the C_{2v} -axis is not energetically restricted by the binding to the ion. In contrast, the rotations accompanied by a change in dipole orientation toward the ion, i.e., R_y and R_x , are clearly inhibited due to the strong ion–water interactions. The relative shifts of $R_y > R_x$ frequencies, both

Table 1

Self-diffusion coefficients (in $\text{cm}^2 \text{s}^{-1}$), librational and vibrational motions (in cm^{-1}) and reorientation times (in ps) of water molecules in the bulk and in the first and second hydration shells of Mg^{2+}

	First shell	Second shell	Bulk ^a	H_2O (exp.) ^b
D	1.67×10^{-5}	3.16×10^{-5}	3.31×10^{-5}	2.30×10^{-5}
R_x	650	511	478	–
R_y	790	668	546	–
R_z	426	420	430	–
Q_2	1575	1622	1638	1645
Q_1	3440	3506	3563	3345
Q_3	3565	3610	3676	3445
$\tau_{1,x}$	6.5	1.9	2.3	–
$\tau_{1,y}$	6.2	1.7	1.6	7.5
$\tau_{1,z}$	33.9	5.2	1.9	–
$\tau_{2,x}$	5.1	1.1	0.8	–
$\tau_{2,y}$	3.7	1.1	0.6	2.5
$\tau_{2,z}$	11.0	1.9	0.6	–

^a Values obtained from a QM/MM MD simulation of pure water [13].

^b Experimental values of liquid water; D [32], Q_i [33] and τ_i [2].

in the first and second hydration shells, indicate that rotations around the x -axis occur more easily than around the y -axis.

Detailed information on the reorientation time of water molecules in solution can be viewed as probe for the strong ion–water interactions, i.e., water molecules around the ion can be expected to have relatively longer orientational correlation time (longer than if the ion was not present). The reorientational times around the three principal axes x , y and z of first and second order of water molecules in the bulk and in the hydration spheres of the ion are summarized in Table 1. It is obvious that rotations around the z -axis exhibit the longest relaxation times, which are consistent with the librational motions. Thus, besides the translation in each case, a rotation around the dipole axis is the most probable movement.

The vibrational spectra of water molecules in aqueous Mg^{2+} solution have been evaluated in order to describe the ion's influence on the hydrogen-bond structure of liquid water. The three quantities Q_2 , Q_1 and Q_3 , calculated from the VACFs of hydrogens for describing symmetric bending and stretching and asymmetric stretching motions, are summarized in Table 1. In pure water, a peak maximum at 1638 cm^{-1} is found for the symmetric bending and peak maxima at 3563 and 3676 cm^{-1} are observed for symmetric and asymmetric stretching, respectively. In the first hydration shell of Mg^{2+} , the bending and stretching frequencies of water molecules are largely red-shifted, i.e., by 63, 123 and 111 cm^{-1} for Q_2 , Q_1 and Q_3 , respectively. The rather large red-shift for both bending and stretching modes can be ascribed to the strong Mg–O attraction and Mg–H repulsions that elongate the O–H bond length and hence reduce the H–H repulsion. The vibrational frequencies of water molecules in the second hydration shell still show considerable red-shifts, by 16, 57 and

66 cm⁻¹ for the corresponding Q_2 , Q_1 and Q_3 . The associated structural changes of water molecules in this shell prove a significant influence of the ion up to this shell, causing enhanced hydrogen bonding between both solvation layers.

3.3. Water exchange in the second hydration sphere of Mg^{2+}

According to Fig. 2, no water exchange processes were observed between the first and second hydration shell, as expected from the experimental water exchange rate at 25 °C of 5.3×10^5 [34]. Exchange processes were observed, however, between the second hydration shell and the bulk. As can be seen in Fig. 2, a large number of such processes occurred and most of them display associative character. The MRT data, calculated as a function of t^* , of water molecules in the second hydration shell and in the bulk are summarized in Table 2. The time parameter t^* is defined as a minimum duration of the ligand's displacement from its original coordination shell to count an exchange process. In general, a value of 0.0 ps is a good choice for the estimation of H-bond lifetimes, and a value of 0.5 ps is considered as a good measure for ligand exchange processes [12]. The MRT values of water molecules in the second hydration sphere are about 2.5 times higher than the corresponding values of bulk water. In terms of lability, the sustainability coefficient, S_{ex} , as well as the average number of processes needed for one successful water exchange, $1/S_{ex}$, have rather similar values as those obtained for the bulk. These data demonstrate a significant 'structure-making' ability of the Mg^{2+} beyond its first hydration sphere, which correspond to the experimental observation that the presence of small divalent cations like Mg^{2+} causes the distance between the first and second shell water molecules to decrease relative to pure water [35].

With respect to the role of Mg^{2+} in RNA stability [19,20], it is known that this ion can, in principle, stabilize RNA in several distinct ways, including diffuse binding and site binding, mostly distinguished by its hydration properties. In diffuse binding, hydrated Mg^{2+} interacts with RNA via non-specific long-range electrostatic interactions, while in site binding (partially) dehydrated Mg^{2+} interacts with donor sites, in particu-

lar anionic ligands specifically arranged by the RNA fold to act as coordinating ligands for the ion. In this context, the detailed analysis of the structural arrangement and the dynamics of hydrated Mg^{2+} provides the basis for a more detailed interpretation of the relationship between diffuse and site binding, in particular concerning the flexibility of the hydrated Mg^{2+} structure and possible pathways to interact with other ligands.

4. Conclusion

The QM/MM results concerning the structural arrangement and the dynamics of hydrated Mg^{2+} have provided numerous details for the characteristics of this ion in aqueous solution. Although the first hydration shell of Mg^{2+} is stable with six water molecules, this hexahydrate forms intermediates such as $Mg^{2+}(H_2O)_5(H_2O)$ and $Mg^{2+}(H_2O)_6(H_2O)$, even on the picosecond scale. These intermediates give clear indications on the possible reaction pathways for first-shell water exchange processes and the interaction of the hydrated ion with other ligands, in particular with biomolecules. On the other hand, the results obtained for the second hydration shell provide a good explanation of the structure-forming property of the Mg^{2+} ion and thus for the observations of its physico-chemical behavior in aqueous solution.

Acknowledgements

Financial support for this work by the Thailand Research Fund is gratefully acknowledged. B.M.R. acknowledges support by the Austrian Science Foundation (FWF Project P16221-N08).

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Table 2

Mean residence times and sustainability of migration processes to and from the second hydration shell of Mg^{2+}

Solute/ion	CN	t_{sim}	$t^* = 0$ ps		$t^* = 0.5$ ps		S_{ex}	$1/S_{ex}$
			N_{ex}^0	$\tau_{H_2O}^0$	$N_{ex}^{0.5}$	$\tau_{H_2O}^{0.5}$		
Mg^{2+}	14.0	16.0	476	0.47	53	4.23	0.11	8.98
Bulk ^a	4.6	12.0	292	0.19	31	1.78	0.11	9.42

^a Values obtained from a QM/MM MD simulation of pure water [13].

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