

# Characterization of Dynamics and Reactivities of Solvated Ions by *Ab Initio* Simulations

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**Abstract:** Based on a systematic investigation of trajectories of *ab initio* quantum mechanical/molecular mechanical simulations of numerous cations in water a standardized procedure for the evaluation of mean ligand residence times is proposed. For the characterization of reactivity and structure-breaking/structure-forming properties of the ions a measure is derived from the mean residence times calculated with different time limits. It is shown that *ab initio* simulations can provide much insight into ultrafast dynamics that are presently not easily accessible by experiment.

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**Key words:** solvated ions; *ab initio* simulations; dynamics

## Introduction

As one of the fundamental factors determining chemical reactivity, dynamics have always been the subject of intensive research. This is true, in particular for the dynamics of complex formation and dissociation reactions involving metal ions, solvent molecules, and other ligands, as such reactions determine not only industrial processes but also numerous essential biological systems.<sup>1–3</sup>

Experimental methods have been successively developed to get access to ever faster exchange reactions by physicochemical measurements such as stopped-flow kinetics or ultrasonic techniques as well as spectroscopic methods such as nuclear magnetic resonance. The time scale of these methods also sets the limits for the measurability of characteristic data for very fast reactions. NMR methods allow accurate direct measurements of velocity constants up to  $\sim 10^5 \text{ s}^{-1}$ , and estimations via line widths to  $\sim 10^9 \text{ s}^{-1}$ . However, numerous ligand exchange processes as well as other dynamic processes within the complexes such as the Jahn–Teller distortions, occur on a much faster time scale than presently accessible by experimental tools.<sup>4</sup>

Applying statistical mechanics to the processes in condensed systems at the molecular level has created the very successful tools of Monte Carlo (MC) and Molecular Dynamics (MD) simulations.<sup>5</sup> The latter method describes the time-dependent events in very small time steps (femtoseconds or fractions of femtoseconds) and thus supplies trajectories suitable to “measure” dynamics on the femtosecond and picosecond scale. This approach should be, therefore, the ideal tool to analyze ligand exchange reactions occurring so fast that experimental investigations are not yet feasible. However, methodical problems associated with the sim-

ulation technique have to be clarified and the evaluation of trajectories to be standardized before using the simulation-based kinetic data as reliable and realistic measures, in particular when they are lying beyond the experimentally accessible time scale.

In several previous works we have been able to demonstrate that classical, even three-body corrected MD simulations are capable of supplying fairly accurate data for structure and composition of the first coordination shell of main group<sup>6–8</sup> and transition metal ions,<sup>9–12</sup> but that they fail to predict correct data for librational/vibrational motions and for the composition of the second coordination shell. These data are of great importance, however, to describe dynamical processes, in particular ligand exchange reactions between both coordination spheres and with the bulk. Hybrid *ab initio* Hartree–Fock quantum mechanical/molecular mechanical simulations<sup>13,14</sup> proved to achieve the necessary accuracy, although at enormous costs in terms of computational effort, which increases by a factor of  $\sim 100$ . On the other hand, the use of simple density functionals as in the RIDFT method<sup>15,16</sup> or in Car–Parinello simulations<sup>17</sup> can lead to first-shell coordination numbers that are lower than almost all experimental and other theoretical data, for example, six for Ca(II) and five for Cu(II).<sup>6,18–20</sup> The more sophisticated B3LYP-DFT<sup>21</sup> formalism for the quantum mechanically treated region in QM/MM simulations leads to a similar degree of accuracy as the *ab initio* Hartree–Fock method, but without saving computer time.<sup>6</sup> The limits of the presently

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applicable quantum mechanical methods will be discussed in the final section of this article.

The need for *ab initio* simulations for the production of trajectories reliable enough for extracting sufficiently accurate dynamical data creates another problem, however, when aiming at the determination of mean ligand residence times: due to the computational effort of several months for a simulation of 10–20 ps, only a limited number of exchange processes can be observed, even if a typical case of ultrafast dynamics is investigated, and hence, the statistics for the evaluation of such data is poor. This problem makes the evaluation procedure crucial and the present article tries to derive conclusions that method and that parameters could provide the most acceptable values for these data, which are of great relevance for the interpretation of complex reactivities.

## Methods

### Simulation Protocol

All simulations were performed with nearly the same simulation protocol.<sup>8,22,23</sup> The systems contained 1 ion and 199 to 499 solvent molecules in a cubic box, at a temperature of 298 K in a canonical *NVT* ensemble. The temperature was kept constant utilizing the Berendsen algorithm<sup>24</sup> with a relaxation time of 0.1 ps, and the density was assumed to be 0.997 g/cm<sup>3</sup>, which is the density of pure water at the simulation temperature. Periodic boundary conditions were applied to the simulation box and the reaction field procedure was employed in all simulations to correct the cutoff of long-range interactions. The flexible BJH water model<sup>25,26</sup> consisting of intermolecular and intramolecular potentials was used to describe the water–water interactions. The cutoff for non-Coulombic interactions between H and between H and O was set to 3.0 and 5.0 Å, respectively, and all other pair interactions were cut off at 9–12 Å. The pair potentials and forces were calculated within the spherical cutoff limit, and to avoid discontinuity of the potential function at the cutoff distance the shifted-force potential was used. The Newtonian equations of motion were treated by a general predictor–corrector algorithm and a time step of 0.2 fs was chosen, because the BJH-CF2 water model allows for explicit hydrogen movements. The QM/MM MD simulations were started from classically equilibrated systems and after an appropriate reequilibration time (1 to 2 ps) sampling was performed for 10 to 30 ps. To define first and second hydration shell from radial distribution functions (RDFs) in most cases clear minima can be identified, and in the few less unambiguous cases the evaluation of the first and second derivate of the RDF proved helpful.

### Evaluation of Dynamics

Trajectories of a large number of *ab initio* QM/MM MD simulations of metal ions in aqueous solution<sup>6,9–12,16,20</sup> were evaluated with respect to ligand exchange processes. First-shell exchange processes within the given simulation time can be observed only for a few weakly solvated ions, whereas in all cases second shell ligands are subject to exchange within the picosecond time scale.

Two evaluation methods have been employed, namely the “direct” method, accurately accounting for all actually incoming

and outgoing ligands, and the procedure suggested by Impey et al.,<sup>27</sup> varying in both cases systematically the time parameter  $t^*$  defining a “real” exchange process by the minimum duration of the ligand’s displacement from its original coordination shell.

The Impey procedure<sup>27</sup> is based on a “survival function” determining the number of ligands remaining in a given coordination shell after a time interval  $t$  and estimating the MRT from an exponential fit, extrapolating to the time when all ligands of a given shell have been exchanged. To be considered as a “real” exchange, a ligand has to cross the shell boundary for a time span  $\geq t^*$ , which should “eliminate short-lived fluctuations.”<sup>27</sup> The  $t^*$  value was set to 2 ps for hydrated ions by Impey et al., with the argument that this should approximately correspond to the reorientational time of a water molecule, calculated, however, for the simple rigid MCY water model at 286 K as 1.8 ps.<sup>27</sup> Higher temperatures shorten the MRT values considerably.<sup>28</sup> In investigations on biomolecules  $t^*$  is often set to 0,<sup>29</sup> thus counting all ligand displacements irrespective of their duration. It should be mentioned that this procedure does not account for associative processes, where the first step is an increase of the coordination number, but only for dissociative processes starting from a “maximal” coordination number.

The “direct” method scans the whole trajectory for movements of ligands, either leaving or entering a coordination shell. Whenever a ligand crosses the boundaries of this shell, its further path is followed, and if its new placement outside/inside the shell lasts for more than  $t^*$ , the event is accounted as “real” exchange process. The MRT is computed as the product of the average number of ligands in that shell with the duration of the simulation, divided by the number of events. This method has the advantage that it equally treats exchange processes starting with an associative or dissociative step, respectively, and that ions with quite irregular hydration structure such as Ag(I),<sup>9</sup> where coordination numbers between 4 and 7 occur within very small time intervals do not pose any problems.

In addition, graphical tools for analysis of the dynamics have been employed, in particular the MOLVISION package,<sup>30</sup> which allows the visualization of all processes registered on the trajectory files, to calculate RDFs for the whole system and subsystems of it, and to highlight ligands in different shells by specific atom definitions. Distance plots for exchanging ligands were another helpful tool for the investigation of the underlying mechanisms.

Besides the definition of coordination shell limits, which can be somewhat arbitrary in cases, where the RDF shows only shallow minima or intershell peaks, the  $t^*$  value is most “critical” for the determination of MRTs. It seemed most important, therefore, to investigate the influence of the value for  $t^*$  on MRT values resulting from both methods, and to determine the optimal choice of this parameter. The evaluation of the trajectories of numerous *ab initio* QM/MM MD simulations presented here is aiming at a decision that  $t^*$  choice(s) could be accepted in terms of solution physics, helping in a standardization procedure for the determination of MRT data obtained by any kind of MD simulation.

Besides mean residence times, simulation data can provide other characteristics of ions in terms of “lability” of the hydration shell, measurable by the number of exchange events occurring within a standard time interval, and by the “sustainability” of exchange processes, measuring the “rate of success” of exchange

**Table 1.** Mean Ligand Residence Times  $\tau_d$  and  $\tau_l$  for Direct and Impey's Method in Picoseconds as a Function of  $t^*$ ;  $N_{\text{ex}}$  is the Number of Accounted Exchange Events,  $t_{\text{sim}}$  the Simulation Time in ps, and CN the Average Coordination Number of a) the First and b) the Second Shell.

	CN	$t_{\text{sim}}$	$t^* = 0$ ps			$t^* = 0.5$ ps			$t^* = 1.0$ ps			$t^* = 2.0$ ps			Ref.
			$N_{\text{ex}}^0$	$\tau_d^0$	$\tau_I^0$	$N_{\text{ex}}^{0.5}$	$\tau_d^{0.5}$	$\tau_I^{0.5}$	$N_{\text{ex}}^{1.0}$	$\tau_d^{1.0}$	$\tau_I^{1.0}$	$N_{\text{ex}}^{2.0}$	$\tau_d^{2.0}$	$\tau_I^{2.0}$	
a)															
Water															
H <sub>2</sub> O	4.1	10.0	269	0.2	4.7	24	1.7	3.7	13	3.2	4.1	3	13.7	4.5	16
1 <sup>st</sup> Shell															
Cs(I)	8.0	9.3	151	0.5	2.0	91	1.8	2.5	21	3.5	4.0	7	10.6	4.2	16
Ag(I)	5.5	16.0	66	1.3	1.8	17	5.5	13.3	7	12.7	27.2	7	12.7	26.8	9
Au(I)	4.3	12.2	55	1.0	3.6	17	3.1	5.6	11	4.8	7.5	7	7.6	7.5	16
Ca(II)	7.8	21.8	8	21.3	22.0	4	42.6	22.0	4	42.6	22.0	1	170	22.0	6
Hg(II)	6.2	15.3	10	9.4	88.7	4	23.6	88.2	4	23.6	88.2	1	94.5	88.2	12
b)															
2 <sup>nd</sup> Shell															
Cs(I)	25.6	9.3	675	0.4	1.3	144	1.7	3.0	77	3.1	4.4	24	9.9	9.3	16
Ag(I)	17.3	16.0	670	0.4	2.2	105	2.6	6.0	47	5.9	7.9	25	11.1	11.0	9
Au(I)	33.1	12.2	547	0.7	5.2	88	4.6	9.4	34	11.8	15.1	16	25.1	21.2	16
Ca(II)	18.9	21.8	791	0.5	3.9	94	4.4	5.2	56	7.2	8.2	35	11.8	9.7	6
V(II)	15.8	10.0	361	0.4	3.9	21	7.5	10.8	15	10.5	11.7	11	14.3	13.7	10
Mn(II)	15.9	8.1	273	0.5	3.9	19	6.8	31.7	8	16.1	45.3	4	32.2	51.7	10
Fe(II)	14.4	14.0	359	0.6	3.7	31	5.4	24.7	23	8.7	27.5	14	14.3	32.9	11
Co(II)	15.7	11.6	395	0.5	6.5	27	6.8	20.8	13	14.0	30.0	7	26.0	36.0	16
Cu(II)	11.7	30.1	660	0.5	4.0	46	7.7	11.9	32	11.0	12.6	20	17.6	12.6	20
Cd(II)	11.6	13.1	572	0.3	0.8	33	4.6	7.6	23	6.6	7.8	8	19.0	8.4	16
Hg(II)	22.1	15.3	655	0.5	9.5	70	4.8	15.9	30	11.3	23.0	20	16.9	27.9	12
Cr(III)	15.4	16.0	337	0.7	8.6	33	7.5	14.3	15	16.4	19.9	11	22.4	20.0	16
Fe(III)	14.0	8.5	157	0.8	9.9	6	19.8	43.9	5	23.8	43.4	3	39.7	53.7	11
Co(III)	15.7	12.0	182	1.0	20.4	18	11.0	45.1	10	18.8	44.2	3	62.8	69.3	16

events in leading to longer lasting changes in the hydration structure, for example, by comparing the number of all transitions through a shell boundary,  $N_{\text{ex}}^0$ , to the number of changes persisting after 0.5 picoseconds,  $N_{\text{ex}}^{0.5}$ . A sustainability coefficient can be defined as:

$$S_{\text{ex}} = N_{\text{ex}}^{0.5}/N_{\text{ex}}^0$$

and its inverse  $1/S_{\text{ex}}$  lists how many border-crossing attempts are needed to produce one longer lasting change in the hydration structure of an individual ion.

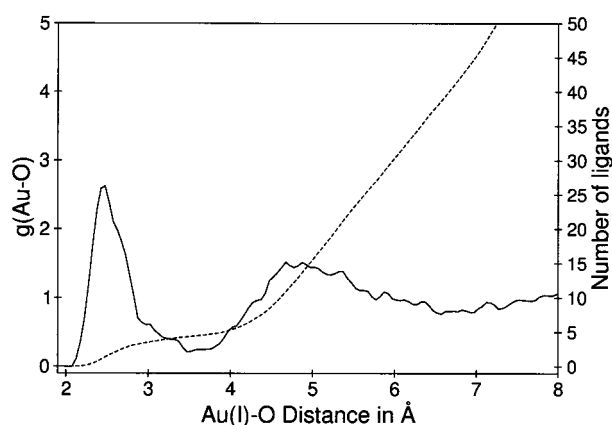
## Results and Discussion

### MRT Values

Table 1 lists the MRT values in picoseconds obtained by both procedures for  $t^*$  values of 0, 0.5, 1.0, and 2.0 ps, respectively. Figure 1 illustrates possible ambiguities of setting coordination shell limits in a difficult case [Au(I)] and Figure 2 problems

frequently encountered in fitting the Impey data to the required exponential form. Due to such problems, the methodical accuracy limit of the direct method and the Impey procedure can reach in some cases  $\pm 20\%$  and  $\pm 50\%$ , respectively, in average it is estimated as  $\pm 10\%$  and  $\pm 20\%$  for direct and Impey procedure. The accuracy further depends on the quality of statistics, i.e., on the number of events observed during the simulation time, which has been included, therefore, in Table 1.

As this number decreases with increasing  $t^*$ , MRT data for shorter  $t^*$  values are certainly more reliable, and when the number of observed exchange processes within a given  $t^*$  limit falls to values below 10, the corresponding MRT values should be considered with distinctly higher error limits. As the characteristics of the pure solvent represent the most important reference values for the discussion of solvated ions, the calculated MRT data from our most recent, still unpublished *ab initio* QM/MM MD simulation of pure water<sup>16</sup> are also listed in Table 1. The values according to Impey are nearly the same ( $\sim 4$  ps) for all  $t^*$  values and that appears very high compared to the experimental value of 0.5 ps obtained for the average lifetime of a hydrogen bond by the most accurate experimental technique, namely fs-laser pulse spectroscopy.



**Figure 1.** Radial distribution function for Au(I) in aqueous solution according to *ab initio* QM/MM-MD simulations.

copy.<sup>31</sup> The direct measurement of exchange processes supplies a value of 0.2 ps for  $t^* = 0$ , and 1.7 ps for  $t^* = 0.5$ . Accepting only ligand removals with at least 1- or 2-ps duration, MRT increases to 3.2 and 13.7 ps, but in the latter case only three processes are recorded making statistics poor.

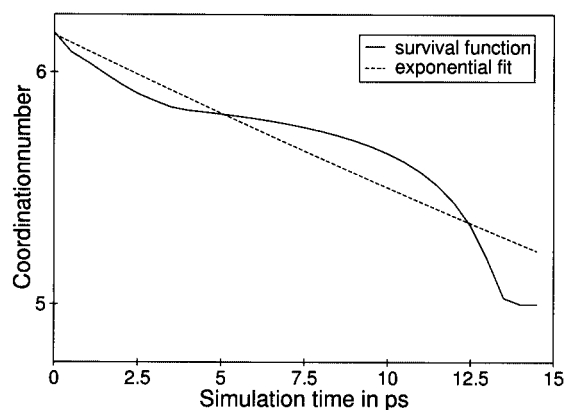
For ions, where first shell ligand exchange is observed within the ps scale, reasonable statistics are obtained for the monovalent ions up to  $t^* = 0.5$ , for Cs(I) even for  $t^* = 2$ . For divalent ions the number of observed processes is small, and the accuracy should, therefore, be considerably less. The deviation of directly measured values from Impey-based data is large and not systematic: comparing the  $t^* = 0.5$  values one finds a similar value for Cs(I), higher Impey values for Hg(II), Ag(I), and Au(I), but a much lower Impey value for Ca(II). For  $t^* = 0$  the picture is quite different: now the Ca(II) values are similar, while Cs(I) has a considerably higher Impey value. Figure 3 shows the movements for all first-shell water ligands of Ag(I) with minimum displacement times  $\geq 0.5$  and  $\geq 2$  ps. This plot indicates that 0.5 ps seems a reasonable value for MRT determination, as an increase to higher values not only makes the statistics worse but also seems to neglect too many significant structural changes, which in this case are also responsible for rapid changes in coordination.

As the second hydration shell is much more labile than the first one, a much larger number of ions could be studied within the ps scale, and the number of exchange processes occurring ensures fairly good statistics for all ions up to  $t^* = 0.5$ , for most ions to  $t^* = 1$ , and for several of them even for  $t^* = 2$ . Counting all intershell border crossings ( $t^* = 0$ ) not much differentiation between the ions listed is obtained, and it seems more appropriate; therefore, to observe the more “sustainable” of these movements, with a minimum duration of 0.5 ps. In this case, monovalent, divalent, and trivalent ions can be quite well distinguished, although with remarkable exceptions such as Au(I) and Cr(III). In the Au(I) case, the exceptionally large second hydration sphere is supposed to cause the larger MRT, and in the case of Cr(III), the kinetically very inert (MRT  $\sim 24$  h!) first shell has recently been found to undergo long-lasting internal distortions that have a considerable influence on structure and dynamics of the second shell.<sup>16</sup> The experimental estimation of the MRT for the second

shell of Cr(III) of 128 ps is much higher than even the value for  $t^* = 2$ . Extending  $t^*$  further, one reaches an MRT of  $\sim 130$  ps for  $t^* = 6$  ps, which indicates that the experimental value rather corresponds to the lifetime of the complete second shell (15 times 8 ps) than to that of a single ligand.

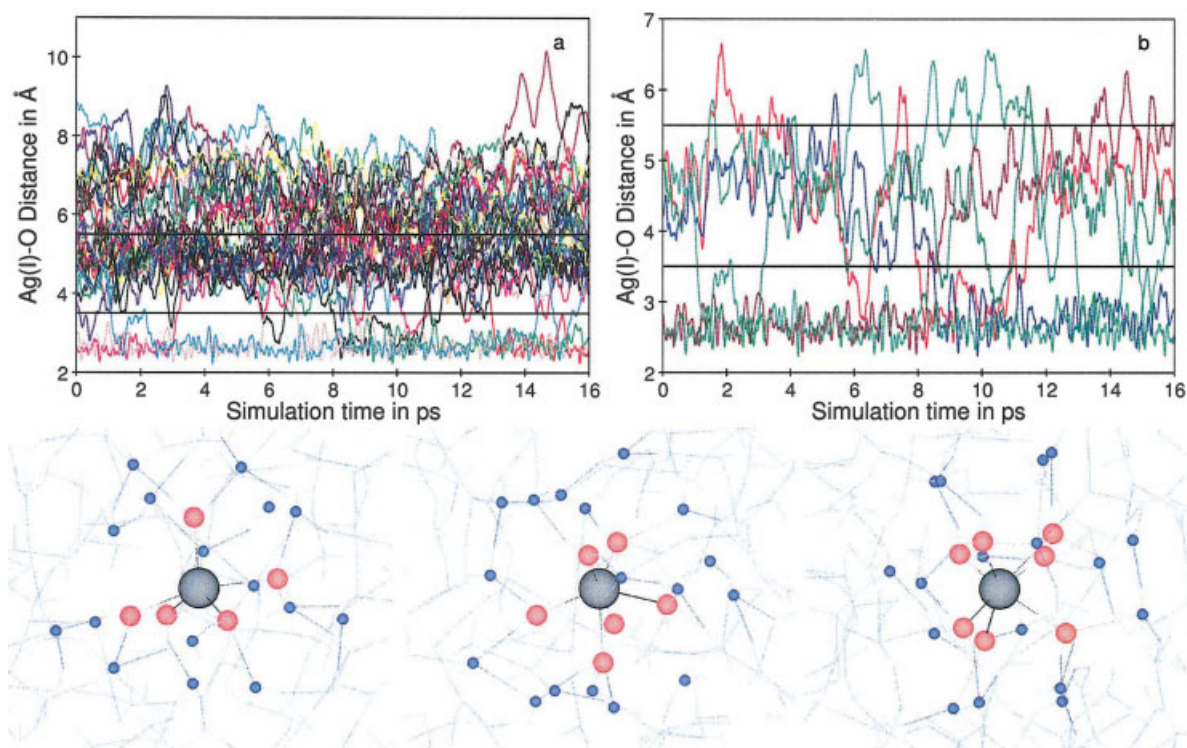
Another feature that can be extracted by comparing the values according to the Impey procedure to the directly counted ones is that the strongly reduced number of processes with increasing  $t^*$  is not always reflected in the Impey values. Although this procedure has been proposed as a convenient tool “to avoid elaborate book-keeping,”<sup>27</sup> it seems to have some serious limits, and as the accurate “bookkeeping” is not a fastidious procedure with present computational facilities (our evaluation program analyses a 1 Gigabyte trajectory within a few minutes), we therefore suggest the direct measurement as the more appropriate procedure for the determination of mean ligand residence times.

The question that still has to be answered is which  $t^*$  value is “best,” on the one hand, to have a certain standardization, on the other hand, to obtain “realistic” data in physical terms. Unfortunately, not many experimental values are available, and even they are subject to severe limitations of accuracy in the ps scale, which is not accessible by either NMR or other presently used techniques. It is to be hoped that further fs laser pulse spectroscopic data will help to answer this question. Looking at the corresponding value for pure water, a  $t^*$  value between 0 and 0.5 seems appropriate. Comparing the values for the hydrated ions, 0.5 ps appears more suitable than 0, as it allows a better differentiation between the ions. Finally, it also appears conclusive and reasonable, to take the (experimental) average lifetime of a solvent–solvent hydrogen bond of 0.5 ps as a reference value for ligand lability in the surrounding of an ion. Based on these considerations we propose using the directly determined data with  $t^* = 0.5$  ps as a “standard” for the MRT determination from MD simulations. Further, it is important to state the temperature for which MRT values have been determined. As the majority of thermodynamic and kinetic data is available for 298 K, we have selected this temperature for all simulations, and the MRT values obtained, therefore, correspond to it.



**Figure 2.** Survival function according to Impey et al.<sup>27</sup> and attempted exponential fit for Hg(II) in aqueous solution according to *ab initio* QM/MM-MD simulations.<sup>12</sup>





**Figure 3.** Ag(I)–O distance plots<sup>9</sup> showing water ligand migration between first and second hydration shell. In (a), all processes with a minimum duration of  $\geq 0.5$  ps are shown; in (b), only those lasting  $\geq 2$  ps. The pictures illustrate 5-, 6-, and 7-coordinated Ag(I) hydrates interchanging within a few picoseconds. First-shell ligands are displayed with red, second-shell ligands with blue oxygen atoms; water in the bulk by bonds only (snapshots taken by MOLVISION<sup>30</sup>).

Accurate experimental measurements and methodically further improved *ab initio* simulations will prove whether the absolute values obtained by us need to be corrected, but at least we can be quite confident that the relative scale of ligand exchange rates obtained from our QM/MM MD trajectories give a quite realistic picture of the stability/reactivity of the investigated ions. This relative scale lists the second-shell MRTs of the ions in the following order from lowest to highest values:

direct method: Cs(I) < Ag(I)

< Ca(II) ~ Cd(II) ~ Au(I) ~ Hg(II) < Fe(II)

< Mn(II) ~ Co(II) < V(II) ~ Cr(III) ~ Cu(II)

< Co(III) << Fe(III)

A comparison with the ionic radii:<sup>32</sup> Cs(I)  $\gg$  Au(I) > Ag(I) > Ca(II) > Hg(II) > Cd(II) > Mn(II) > V(II) > Cu(II) > Co(II) ~ Cr(III) ~ Fe(II) > Fe(III) ~ Co(III) shows that a weak correlation between ionic radii and MRT values seems to exist (cf. Table 2), but that other factors should have a considerable influence. A comparison of the second-shell MRT values with the experimental hydration energies<sup>33</sup> does not show a strong correlation either (cf. Table 2):

Cs(I) > Ag(I) > Au(I)  $\gg$  Ca(II) < V(II)

> Cd(II) ~ Hg(II) ~ Mn(II) > Fe(II) > Co(II)

> Cu(II)  $\gg$  Fe(III) > Cr(III) ~ Co(III)

Among the monovalent ions, however, increasing hydration energies correspond to longer MRTs, and among the divalent ions it is obvious that the shorter MRTs of the main group ion Ca(II) and the d10 ions Cd(II) and Hg(II) are associated not only with the largest radii, but also with the lowest hydration energies. The differences among the other transition metal ions are small, and do not allow an assignment to their specific electronic structure or the particular amount of charge transfer between ligands and central ion. For the trivalent ions one observes that higher hydration energies and shorter radii are related to lower MRT values. *Ab initio* ion–water binding energies are apparently much less correlated to MRT values and therefore, have not been included in this discussion. Summarizing, one would rather assume that the MRTs are determined by several factors simultaneously, i.e., by the ionic radius, ion–ligand interaction energy and charge transfer, as well as coordination numbers. Our data are not sufficient yet to analyze such a multifactorial correlation, and more simulations with increasing accuracy will be needed for this purpose.

**Table 2.** Comparison of MRTs in ps of the Second Shell with a Minimum Duration of 0.5 ps, Atomic Radii  $r$  in Angstroms and the Enthalpies of Hydration in kJ/mol.

Ion	$\tau_d^{0.5}$	$r^{32}$	$\Delta H_{\text{hyd}}^{0,33}$
Cs(I)	1.1	1.74	-283
Ag(I)	2.6	1.15	-483
Au(I)	4.6	1.37	-587
Ca(II)	4.4	1.12	-1602
V(II)	7.5	0.79	-1692
Mn(II)	6.8	0.83	-1874
Fe(II)	5.4	0.61	-1972
Co(II)	6.8	0.65	-2036
Cu(II)	7.7	0.73	-2123
Cd(II)	4.6	0.95	-1833
Hg(II)	4.8	1.02	-1853
Cr(III)	7.5	0.55	-4606
Fe(III)	19.8	0.61	-4462
Co(III)	11.0	0.55	-4691

#### Lability of Hydration Shells and Sustainability of Exchange Processes

To further elaborate the reactivity of the hydrated ions and the dynamics of the hydration shells, the “lability” of hydration shells and the “sustainability” of exchange processes have been evaluated as outlined in the Method section, by counting the number of ligand movements through shell borders and by comparing these values for  $t^* = 0$  and  $t^* = 0.5$ . Table 3 lists the normalised (to 10 ps)  $N_{\text{ex}}$  and  $S_{\text{ex}}$  values for all ions and for pure water, together with the average coordination number of the respective hydration shell. The last column ( $1/S_{\text{ex}}$ ) indicates how many border-crossing processes are performed in average, until a “sustainable” exchange process is achieved.

For the interpretation of these data, the values for pure water again serve as reference. Considering first the lability of the ligands in the immediate surrounding of a central molecule or ion, it is seen that only Cs(I) ligands cross the first-shell border nearly as often as water leaves the nearest neighbourhood of an arbitrary “central” water molecule in the pure solvent. In the case of the other monovalent ions, roughly five to six times less displacements occur, and in the first shell of the divalent ions their probability is about 50 times lower. In the second shell, ligand mobility is much higher, and varies considerably even within ions of the same charge. Only for trivalent ions is the lability less than for pure water. For Fe(II) it is similar to the solvent, and for all other di- and monovalent ions higher, peaking at Cs(I), followed by Au(I), Hg(II), and Cd(II). These data can be seen as a good measure for the “structure breaking” ability of these ions, which has been very well documented in particular for Cs(I) ion.<sup>34–36</sup>

The  $S_{\text{ex}}$  data, measuring the sustainability of such displacements, lead to quite an unexpected picture of the hydrated ions’ reactivity. Apparently, only every  $\sim 10^{\text{th}}$  attempt of a water molecule to leave its immediate environment for more than 0.5 ps is successful, while in the first hydration shell of monovalent ions, three to four attempts lead to one longer breakout from the shell. For the divalent ions, the “success rate” seems to be even higher.

The higher the  $S_{\text{ex}}$  value, the lower the probability becomes for another ligand to approach the ion and to bind to it. This value and its inverse  $1/S_{\text{ex}}$  should have some significance; therefore, for the ease of an ion to bind to another coordination site, for example, in complex chemistry or in biological processes.

In the second hydration shell, weakly solvated ions such as Cs(I), Ag(I), Au(I), Ca(II), and Hg(II) have  $S_{\text{ex}}$  values higher than that for pure water, indicating a high mobility and thus reactivity. Again, these values can be related to breaking of the solvent structure. For divalent transition metal ions, the values vary from nearly the same as water to about 1.5 times this value, showing a certain inertness and stability of the second hydration shell, or a “structure forming” ability of these ions beyond the first shell. Trivalent ions, however, do not seem to follow this trend, except for Fe(III). The values for Cr(III) and Co(III) are even slightly below the water value. Considering the strong interaction of these ions with the solvent, the quantum mechanical treatment of only the first shell might be methodically insufficient, and only more extended simulations including the full second shell within the QM region (and thus extending the computational effort by another factor of 10–20) will allow the decision, whether the differences between these three ions are indeed as large as indicated by our

**Table 3.** Values Indicating the Lability ( $N_{\text{ex}}$ ) of a Hydrated Ion, the Sustainability of Migration Processes ( $S_{\text{ex}}$ ), and the Number of Processes Needed for One Successful Ligand Exchange ( $1/S_{\text{ex}}$ ) for a) the First and b) the Second Hydration Shell.

	CN	$N_{\text{ex}}^0/10$ ps	$N_{\text{ex}}^{0.5}/10$ ps	$S_{\text{ex}}$	$1/S_{\text{ex}}$
a)	Water				
H <sub>2</sub> O	4.1	268	24	0.09	11.2
	1 <sup>st</sup> Shell				
Cs(I)	8.0	162	44	0.27	3.7
Ag(I)	5.5	41	11	0.25	3.8
Au(I)	4.3	45	14	0.30	3.2
Ca(II)	7.8	4	2	0.50	2.0
Hg(II)	6.2	7	3	0.40	2.5
b)	2 <sup>nd</sup> Shell				
Cs(I)	25.6	726	155	0.21	4.7
Ag(I)	17.3	418	66	0.16	6.4
Au(I)	33.1	448	72	0.16	6.2
Ca(II)	18.9	364	43	0.12	8.4
V(II)	15.8	361	21	0.06	17.2
Mn(II)	15.9	337	23	0.07	14.4
Fe(II)	14.4	257	22	0.09	11.6
Co(II)	15.7	339	23	0.07	14.6
Cu(II)	11.7	339	23	0.07	14.6
Cd(II)	11.6	437	25	0.06	17.3
Hg(II)	22.1	428	46	0.11	9.4
Cr(III)	15.4	211	21	0.10	10.2
Fe(III)	14.0	184	7	0.04	26.2
Co(III)	15.7	152	15	0.10	10.1

present data and how accurate MRT and  $S_{\text{ex}}$  data can be obtained by limiting the QM region to the first shell. First tests involving Cu(II) with two hydration shells in the QM region have shown that the MRT and the  $S_{\text{ex}}$  values may become still lower by this extension of the method.<sup>16</sup> Further tests have been made, to show what extent limited basis sets and the neglect of electron correlation could influence the results. The BSSE is in the order of 1 kcal/mol for the ion–water interactions with the basis sets used in our simulations,<sup>6,9–12,16</sup> and MP/2 corrections shorten the water–water hydrogen bonds (which in our simulation are located in the MM region or between the QM and MM regions where they are considered by a mixed term), but not the ion–ligand bonds.<sup>9</sup> DZP basis sets with relativistically corrected ECPs thus appear as a good compromise between accuracy and affordable computational effort, and to deliver a reliable description of the first shell.

## Conclusion

Based on the results of this work, the usage of a full accountancy of ligand movements seems advantageous for accurate MRT determinations from simulation data, irrespective of the simulation method. The most appropriate value for the time span of an “accountable” ligand displacement from its original coordination sphere appears to be 0.5 ps, i.e., the average lifetime of a hydrogen bond in the solvent. The proposed measures of “lability” and “sustainability” of ligand displacements are believed to supply useful information about the dynamics of ligand exchange processes and the reactivity of hydrated ions, and they can be utilized to characterize structure-breaking and structure-forming properties of the ions in water. The values for mean residence times collected from *ab initio* HF simulations with presently possible accuracy seem to be good indicators for the dynamics of the hydration shells, although a further increase of the QM region and the quantum mechanical accuracy level would inevitably lead to some corrections of the absolute values.

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