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Selected biologically relevant ions at the air/water interface: A comparative molecular dynamics study

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Abstract

Interfacial behavior of selected biologically and technologically relevant ions is studied using molecular dynamics simulations employing polarizable potentials. Propensities of choline, tetraalkylammonium (TAA), and sodium cations, and sulfate and chloride anions for the air/water interface are analyzed by means of density profiles. Affinity of TAA ions for the interface increases with their increasing hydrophobicity. Tetramethylammonium favors bulk solvation, whereas cations with propyl and butyl chains behave as surfactants. The choice of counter-anions has only a weak effect on the behavior of these cations. For choline, sodium, chloride and sulfate, the behavior at the air/water interface was compared to the results of our recent study on the segregation of these ions at protein surfaces. No analogy between these two interfaces in terms of ion segregation is found.

Keywords: Tetraalkylammonium; Polarizable potential; Surfactant; Molecular dynamics

1. Introduction

Organic ions containing long aliphatic chains naturally segregate to aqueous surfaces due to their hydrophobicity, behaving as typical ionic surfactants [1,2]. In contrast, classical theories predict that simple inorganic ions are repelled from the air/water interface towards the aqueous bulk by electrostatic image forces [3–6]. Recent molecular dynamics simulations [7–11] supported by surface selective experiments [12–15] indicate, however, that large polarizable atomic ions, such as bromide and iodide, exhibit an appreciable propensity for the aqueous surface. Somewhere in between simple inroganic ions and organic surfactants lay small organic ions (e.g., choline or smaller tetraalkylammonium (TAA) cations), the interfacial solvation of which is significantly less explored.

TAA cations are important ionic species the hydration properties of which can be tuned by the choice of the length of the alkyl chains [16]. Smaller TAA cations are also used in technology as phase transfer catalysts (e.g., tetrabutylammonium (TBA) cations) [17]. As such they can transport small ions across biological tissues, which explains their potential toxicity, and they can also block cellular ion channels [18,19]. The solubility of TAA cations in water drops upon increasing the length of the alkyl chain and the larger ions behave as ionic surfactants [16]. Bulk and interfacial aqueous solvation of TBA cations with different halides as counter-ions has been investigated by photoelectron spectroscopy and molecular dynamics (MD) simulations recently [20–22]. These studies quantified the significant surface propensity of TBA and also concentrated on the varying interfacial behavior of the different halide counter-anions. While bromide and particularly iodide strongly co-adsorb at the surface, fluoride rather resides in the subsurface and bulk regions of the solution. This behavior was rationalized in terms of increasing anionic size and polarizability upon moving down the periodic table.

Choline represents another organic cation with important biological implications. In the body, it is mainly found in phospholipids and it serves as a precursor for acetylcholine and betaine (trimethylglycine) [23]. It can also affect enzyme activity. For example, a recent study of horseradish peroxidase showed that choline chloride can counterbalance

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the superactivity of this enzyme induced by sulfate salts [24]. Based on molecular dynamics simulations of horseradish peroxidase in solutions of choline chloride or sodium sulfate, we have suggested that this effect can be connected with the sizable affinity of choline for the protein surface including its hydrophobic parts close to the enzymatic reaction center [25].

In the present study, we explore the interfacial behavior of TAA (with one to four carbons in each of the alkyl chains) and choline cations with chloride or sulfate counter-ions. This is accomplished by performing MD simulations of aqueous solutions in slab geometry, employing a polarizable force field. The results are analyzed in terms of density profiles (i.e., histogrammed abundancies of the individual species from the bulk across the air/solution interface into the gas phase) and compared to the behavior of these ions at the protein/solution interface.

2. Computational methods

Molecular dynamics simulations using Amber software package (version 8) [26] were performed consistently with our previous work [20,21]. A polarizable force field [27] together with the parm99 parameter set [28] and modified anion polarizabilities [29] was employed. These potential parameters were previously tested against experiments and ab initio calculations [28]. A self-consistent iterative procedure was used to converge the induced dipoles.

Simulation cells were created from a box of 863 POL3 water molecules [30] with approximate dimensions $31 \times 31 \times 30$ Å^3 by elongating the z-dimension to 100 Å. Application of 3D periodic boundary conditions produced an infinite water slab in the xy-plane with two independent air/water interfaces perpendicular to the z-axis. Ions were initially placed into the gas phase with the same amount of both cations and anions on each side of the water slab. 5000 steps of the steepest descent minimization removed potential bad contacts introduced during the system construction. Afterwards, temperature was raised to 300 K during a 50 ps heating period. An equilibration period of 500 ps, followed by a 1 ns production run, was then performed for each of the simulated systems.

Classical Newton equations of motion were solved numerically with a time step of 1 fs. van der Waals and electrostatic interactions were cut off at 12 Å. A smooth particle mesh Ewald procedure [31] was used for accounting for the long-range electrostatic interactions. All bonds involving hydrogen atoms were frozen using the SHAKE algorithm [32]. The temperature was maintained at 300 K using the Berendsen temperature coupling scheme [33]. All the simulations were performed in the canonical (NVT) ensemble. Coordinates were dumped every 500 steps, i.e., every 0.5 ps. Every nanosecond of the production run thus produced 2000 frames for analysis.

3. Results and discussion

For each of the cations we investigated the interfacial behavior for a 1 M concentration, which corresponded to 16 TAA or choline cations per unit cell. The positive charge was compensated by an appropriate number of chloride or sulfate anions. The surface propensity of TAA and choline cations was examined in terms of density profiles for individual salt solutions, showing distribution of ions across the aqueous slab. We also addressed the effect of counter-ions by employing either Cl^- or SO_4^{2-}.

3.1. Tetraalkylammonium cations

We simulated aqueous tetraalkylammonium salts and investigated the propensity of TAA cations for the interface as

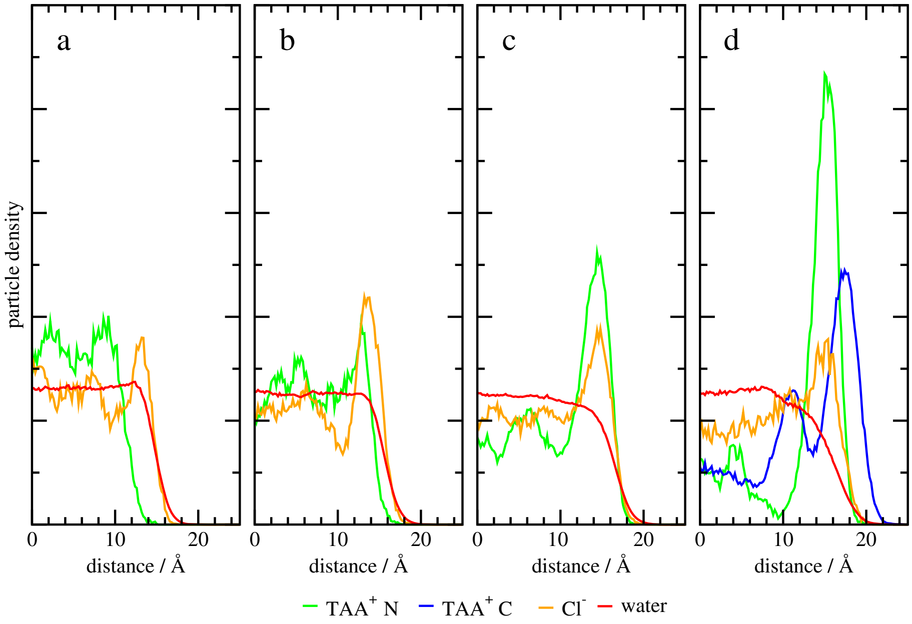

Fig. 1. Averaged density profiles for tetraalkylammonium cations with chloride counterions.

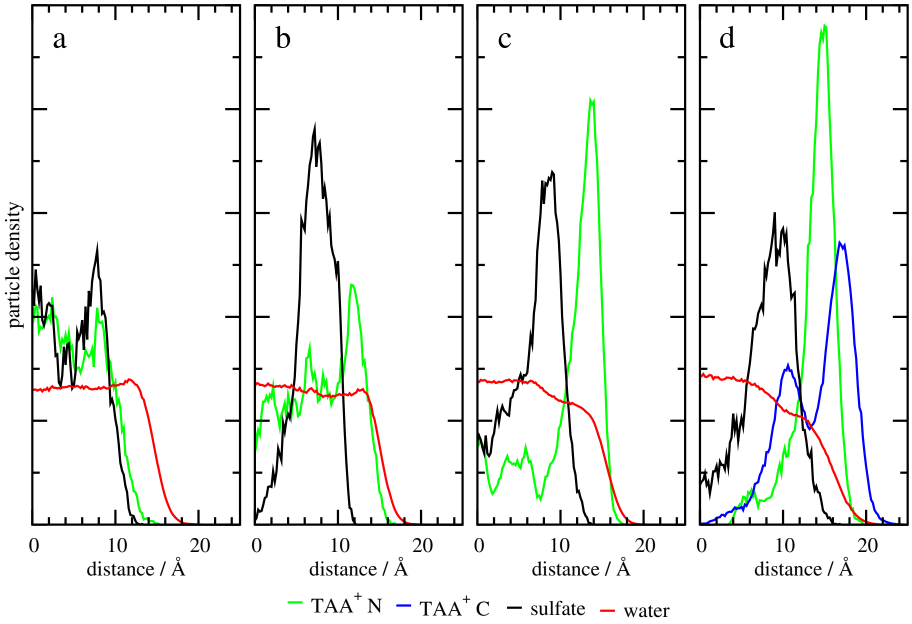

Fig. 2. Averaged density profiles for tetraalkylammonium cations with sulfate counterions.

a function of the length of the alkyl chain. We studied the four smallest TAA cations, i.e., tetramethyl (TMA^+), tetraethyl (TEA^+), tetrapropyl (TPA^+), and tetrabutyl ammonium (TBA^+).

The density profiles of the individual species of the studied systems are shown in Figs. 1 and 2. As expected, the cationic propensity for the surface increases with the growing length of the alkyl chains, which is directly connected with the hydrophobicity of the ion. TMA^+ is repelled from the air/water interface (Figs. 1a and 2a), similarly to alkali cations [7]. The density profiles of TEA^+ closely follow that of water (Figs. 1b and 2b). TEA^+ can thus be viewed as surface neutral, possibly with a small density peak at the air/water interface. In comparison, TPA^+ and even more so TBA^+ already exhibit strong surface activity, as demonstrated by the large density peaks at the air/water interface (Figs. 1c,d and 2c,d). This is consistent with our previous study which quantified by means of MD simulations and photoelectron spectroscopy the surfactant behavior of TBA^+ in aqueous solutions of tetrabutylammonium iodide and bromide [20,21]. The increasing cationic surface propensity with extending the length of the alkyl chain is also visualized in Fig. 3, which shows snapshots from simulations of the four investigated TAA chloride solutions.

For TBA^+ we show not only the density profile of the central nitrogen but also of the terminal carbon atoms of the butyl chains (Figs. 1d and 2d). The carbon density profile exhibits a double peak in the interfacial region. The larger carbon peak, which is shifted from the nitrogen peak towards the gas phase demonstrates the strong hydrophobicity of the butyl chains. However, due to bonding within TBA^+ at least one carbon chain has to reside closer to the aqueous phase than the central nitrogen atom, which rationalizes the smaller carbon peak in the subsurface.

The two employed counter-anions behave very different from each other. Chloride exhibits a weak propensity for the air/water interface due to its relatively large polarizability, while the doubly charged sulfate is strongly repelled from the surface by electrostatic forces. Nevertheless, the counter-ion

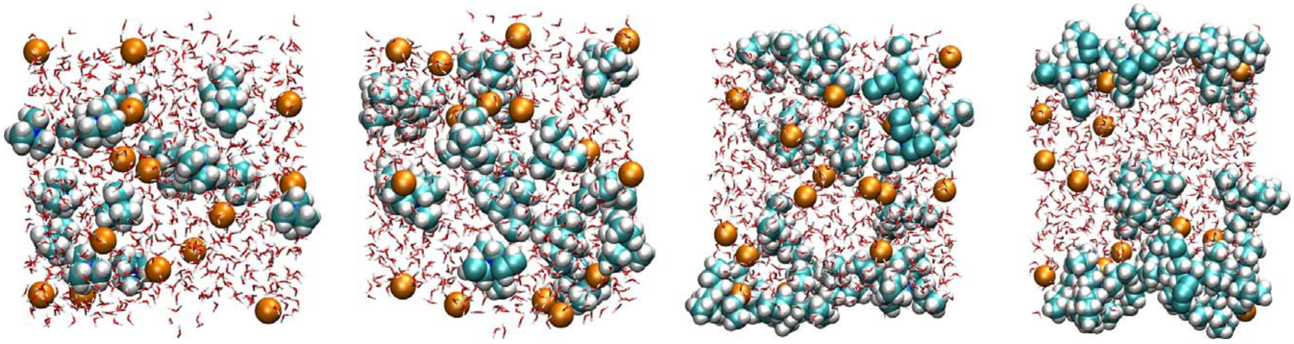

Fig. 3. Snapshots from the tetraalkylammonium chloride simulations, showing the side views of the unit cells with solution/vapor interfaces at the top and bottom of the figures. From left to right: TMA^+, TEA^+, TPA^+, and TBA^+.

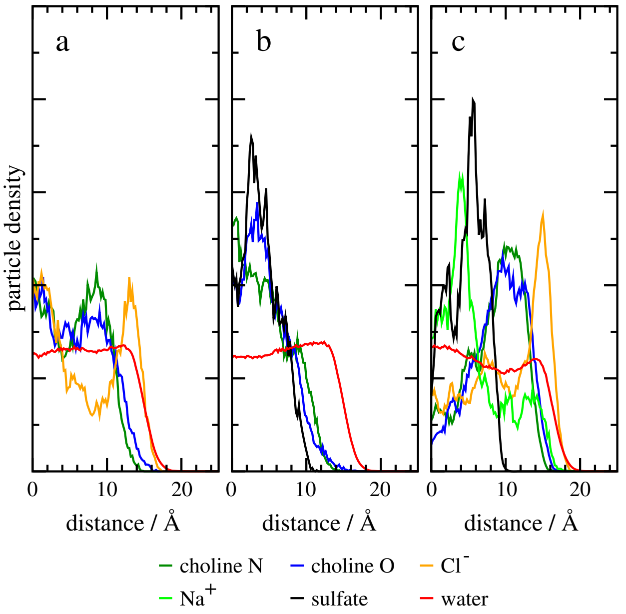

Fig. 4. Averaged density profiles of individual species in a slab of choline chloride, choline sulfate, and a mixture of choline chloride and sodium sulfate.

effect on the surface propensities of the TAA cations is weak (compare Figs. 1 and 2). This might seem rather surprising for highly non-ideal, 1 M solutions. Apparently, the weakly surface-attracted chloride ions cannot pull any appreciable amounts of TMA$^+$ towards the surface. Similarly, the bulk-bound sulfates are not able to pull surface active TPA$^+$ and TBA$^+$ into the aqueous bulk.

3.2. Choline cation

We investigated the interfacial behavior of choline cations in aqueous solutions with chloride or sulfate as counter-ions. Fig. 4 shows the density profiles of the individual species for a 1 M solution of choline chloride, choline sulfate, and a mixture of choline chloride and sodium sulfate. In none of the solutions does choline exhibit any propensity for the surface, which is in striking contrast with its sizable preference for the protein/water interface [25]. As a matter of fact, it is repelled from the surface despite its relatively large size. This is particularly true for the choline sulfate solution (Fig. 4b), while in the choline chloride solution the cations move somewhat towards the subsurface following the chloride anions, present at the interface (Fig. 4a).

An interesting situation occurs in the aqueous mixture of choline chloride and sodium sulfate (Fig. 4c). Chloride exhibits a weak propensity for the interface, similarly as in pure alkali chloride solutions [7,8]. Sulfate and sodium are found to be solvated in the bulk (sulfate dianions being particularly strongly repelled from the surface) and their charges tend to compensate. Choline is in this salt mixture solvated close to the surface (closer than in the case of choline chloride solution) and exhibits an appreciable subsurface peak, compensating the surface chloride charge. The behavior of the individual ionic species in all three solutions is also visualized as representative snapshots from the simulations in Fig. 5.

4. Summary

We have investigated by means of molecular dynamics simulations the interfacial behavior of selected biologically relevant cations in aqueous solutions with chloride or sulfate counter-anions. For small tetraalkylammonium cations we have demonstrated the transition from bulk to surface solvation upon increasing the length of the aliphatic chain. Namely, TMA$^+$ solvates in the aqueous bulk, TEA$^+$ exhibits an intermediate behavior, while TPA$^+$ and TBA$^+$ show an appreciable surfactant activity. The counter-ion effect on the surface propensity of these cations is relatively weak, the cationic density profiles being almost the same in chloride and sulfate solutions. Another small organic cation, choline, was shown to be repelled from the solution/vapor interface both for chloride and sulfate counter-ions. However, in the presence of chloride anions, choline exhibits a certain propensity for the subsurface region. The behavior of choline, sodium, chloride and sulfate ions at the solution/vapor interface was found to have no correlation with their segregation at the solution/protein interface.

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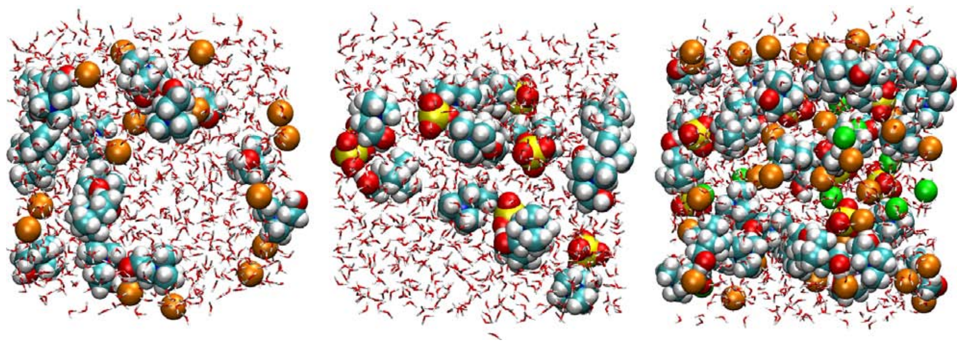

Fig. 5. Snapshots from the simulations of choline chloride, choline sulfate, and a mixture of choline chloride and sodium sulfate. The side views of the unit cells are displayed with solution/vapor interfaces at the top and bottom of the figures.

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