**Specific ion interactions with aromatic rings in aqueous solutions:
Comparison of molecular dynamics simulations with a thermodynamic solute
partitioning model and Raman hydration shell spectroscopy**

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ABSTRACT

Specific ion interactions of KF, and the Na^+ salts of SO_4^{2-} , F^- , Cl^- , NO_3^- , I^- , and ClO_4^- with benzene in aqueous solutions were investigated using molecular dynamics simulations and compared with experimental Raman multivariate curve resolution (Raman-MCR) and thermodynamic results. Good agreement is found with the hydration-shell partition coefficients of salts obtained from the thermodynamic analysis and of halogen anions obtained from the Raman-MCR spectra of benzene and pyridine. Larger discrepancies between the simulation and thermodynamic cation partitioning results point to the influence of counter-ion interaction on cation partitioning.

1. Introduction

In the late 1800s, Franz Hofmeister discovered that the extent to which proteins precipitated depends on the identity of the salts present in solution (1). Salt ions could be consistently ranked according to their effect on protein solubility in an order that is now referred to as the Hofmeister series. A representative ranking of anions, listed in decreasing order of ability to precipitate proteins is: $\text{CO}_3^{2-} > \text{SO}_4^{2-} > \text{F}^- > \text{Cl}^- > \text{Br}^- \sim \text{NO}_3^- > \text{I}^- > \text{ClO}_4^-$ (2). Ions on the left side of the series “salt out” (precipitate) proteins and those on the right “salt in” (dissolve/denature) proteins. An analogous series also exists for cations. Since its discovery, the Hofmeister series has been shown to arise in a wide variety of seemingly unrelated solution phenomena, including protein solubility, surface tension, water retention in wool, and bacterial growth, among many others (3,4).

Until fairly recently it was thought that the Hofmeister series followed from the “structure making” (kosmotropic) or “structure breaking” (chaotropic) effects of ions on water structure (3,5). However, more recent computational and Raman spectroscopic studies (6-8), as well as ultra-fast infrared pump-probe (9), x-ray absorption (10), and terahertz (11,12) spectroscopic measurements, demonstrated that the hydrogen-bond network in water is not affected much beyond the first hydration shell of the ions. In this paper, we will use the terms kosmotrope and chaotrope, not to imply structure water making/breaking effects, but rather to refer to where the ions lie in the Hofmeister series, kosmotropes being on the salting out (left) side and chaotropes on the salting in (right) side of the series.

Numerous computational and experimental studies, reviewed recently (2,13-16), have focused on specific ion effects at the air/water interface and at protein surfaces. Many factors have been correlated with the specificity of ions at these surfaces, including ion size,

polarizability, valency, and concentration, as well as the identity of other ions in solution. A spectroscopic and computational study recently showed that anion adsorption to the air-water interface is favored by enthalpy and opposed by entropy (17). A free energy partitioning approach suggested recently that the dominant thermodynamic driving forces for adsorption of an iodide to the air-water interface are the reduction of the size of the cavity that accompanies adsorption and a far-field electrostatic contribution corresponding to the ion interaction with the interfacial surface potential (18). Despite these many studies, the specificity and strength of the interactions between various ions and particular compounds or molecular sub-groups remain to be fully characterized. Here we focus on interactions between ions and aromatic rings, specifically, benzene and pyridine, in water, as such interactions are of both fundamental interest and potential biological relevance because of the prevalence of aromatic side chains in the hydrocarbon core of globular proteins.

Molecular dynamics (MD) simulations have played an important role in elucidating some of the mechanisms contributing to ionic specificity in aqueous interfacial processes (13,19). In this study we employ MD simulations to evaluate the affinity of various ions for benzene in several aqueous salt solutions. Furthermore, we compare our simulation results with those obtained from a recent thermodynamic analysis of the partitioning of ions between the benzene hydration layer and bulk aqueous solution (20), as well as with new Raman multivariate curve resolution (Raman-MCR) vibrational hydration-shell spectroscopic measurements of the affinity of halogen anions for both benzene and pyridine.

Record and coworkers have applied thermodynamic models to interpret and predict Hofmeister ion effects on surface tension at the air/water interface (21,22) and ion interactions with nonpolar and amide groups (20). The model assessed in the present work is a two-phase

equilibrium solute partitioning model (SPM) (20), in which the ions in an aqueous salt solution are assumed to act independently as they partition between a local hydration layer of the nonelectrolyte (e.g., benzene) solute and the bulk solution. The key parameters extracted from the SPM are ion partition coefficients, $K_{p,i} = m_i^{local} / m_i^{bulk}$, where m_i^{local} and m_i^{bulk} , are the local (i.e., vicinity of the solute) and bulk molal concentrations, respectively, of ion i . $K_{p,i}$ provides a quantitative measure of the affinity of an ion for the solute. In this paper we will compare partition coefficients computed from our MD simulations and Raman hydration-shell spectroscopic measurements with those obtained by applying the SPM to benzene solubility data (20).

2. Methods

2.1. System setup and simulation protocols

We performed MD simulations of a single benzene molecule dissolved in aqueous salt solutions containing approximately 1 M KF, NaCl, Na₂SO₄, NaNO₃, NaI, NaClO₄, or neat water. Nonpolarizable force fields with the TIP3P water model (23) were employed in all of the simulations. For benzene, we utilized a force field developed by Jorgensen and Severance (24). The ion parameters, along with their respective references are summarized in Table 1.

Each simulation was run for 100 ns with a 1 fs time step. Coordinates were saved every 1 ps, yielding 100,000 frames for analysis. The simulation box was approximately 26.3 x 26.3 x 26.3 Å³ and contained approximately 400 water molecules, one benzene molecule, 7 cations, and 7 anions, so that the benzene concentration was ~0.09 M and the salt concentration was ~1 M. Three-dimensional periodic boundary conditions were applied and long-range electrostatic interactions beyond 8 Å were treated using the smooth particle mesh Ewald method (25). The

Berendsen thermostat with a coupling constant of 1 ps and barostat with a coupling time of 1 ps were used to maintain a temperature of 300 K and a pressure of 1 atm (26). Bonds to hydrogen atoms were constrained using the SHAKE algorithm (27). All of the MD simulations were performed using the Amber 8 program (28).

2.2. Calculation of partition coefficients from MD simulations

Mass densities of salt ions and water molecules were averaged over 9,800 frames sampled evenly over the 100,000 frames and binned using the VMD (29) *VolMap* tool with bin volumes of $0.2 \text{ \AA}^3$. The density data were binned relative to the benzene molecular center-of-mass placed at the origin, with the benzene six-carbon plane parallel to the Cartesian x - y plane. Interactions between benzene and the ions/solution were assumed to be cylindrically symmetric about the benzene six-fold symmetry axis. Thus, for fixed cylindrical (r, z, θ) coordinates, volumetric mass densities of salt ions and water molecules were averaged over the azimuth (θ), and subsequently projected onto a grid in a two-dimensional (r, z) coordinate system.

For the purpose of calculating ion partition coefficients, a “local” region was defined around the benzene molecule as the cylindrical volume defined by $r \leq 6.5 \text{ \AA}$ and $|z| \leq 5 \text{ \AA}$; this region encapsulated the first hydration shell around benzene in neat water. The remaining volume of the simulation box constitutes the “bulk” region. The ion partition coefficients, $K_{p,i}$ were calculated from the ion and mass densities within the local and bulk regions using the following relation:

$$K_{p,i} = \frac{m_i^{local}}{m_i^{bulk}} = \frac{\rho_i^{local} \rho_{wat}^{bulk}}{\rho_i^{bulk} \rho_{wat}^{local}}, \quad (1)$$

where m_i^j is the molality of ion i in the j th region ($j = local$ or $bulk$), ρ_i^j and ρ_{wat}^j are the corresponding ion and water mass densities, respectively. For a salt consisting of monovalent

ions, the salt partition coefficient is defined as $K_p = K_{p,+} + K_{p,-}$, where $K_{p,+}$ and $K_{p,-}$ are, respectively, the cation and anion partition coefficients (20).

2.3. Raman-MCR spectroscopy

High signal-to-noise Raman spectra were collected using a 514.5 nm Ar-ion laser excitation source with approximately 15 mW laser power at the sample. The backscattered Raman photons were collected using a fiber optic cable and dispersed onto a CCD camera using a 300 grooves/mm grating, as previously described (30). Some of the experiments were performed with a higher resolution grating (1200 grooves/mm); however, the results were independent of resolution. Self-modeling curve resolution (SMCR) (31), which requires no assumptions regarding the spectral shape or component concentrations of the input Raman spectra, was used to obtain the solute-correlated (SC) spectra of benzene and pyridine in aqueous KF, NaCl, and NaI solutions. Vibrational features arising from the solute (benzene or pyridine) appear in the SC spectra, as well as perturbed water molecules that differ in structure from bulk water. The three component system consisting of water, salt, and benzene (or pyridine) was reduced to a two component system by varying the concentration of only one component at a given time, as previously described (8). CH stretching frequencies were obtained by fitting the CH stretching mode at $\sim 3070\text{ cm}^{-1}$ to a Gaussian function. The ion-induced frequency shifts in this work are reported as a difference in frequency between the salt solution and salt-free solution.

The following chemicals were obtained from Sigma-Aldrich: pyridine (anhydrous, 99.8%), potassium fluoride (ACS reagent, $\geq 99.0\%$), sodium iodide (ACS reagent, $\geq 99.5\%$), sodium nitrate (ACS reagent), sodium perchlorate (ACS reagent, $\geq 98.0\%$), sodium sulfate (anhydrous, powder, ACS reagent, $\geq 99.0\%$) and sodium fluoride (BioXtra, $\geq 99\%$). Benzene and sodium chloride (Analytical Reagent) were purchased from EM Science and Mallinckrodt, respectively.

All of the above chemicals were used as received. Aqueous samples were prepared using ultrapure water (Milli-Q UF Plus, 18.2 m Ω ·cm resistance, Millipore).

3. Results and discussion

3.1. Comparison of MD and SPM results

Fig. 1a and 1b show, respectively, cation and anion K_p values obtained from the MD simulations (black bars) and the SPM thermodynamic study (red bars) (20). Due to the variability of the Na⁺ K_p values computed from the simulations, there is no discernable difference in the behavior of Na⁺ and K⁺ in the vicinity of benzene. The qualitative ordering of the cation K_p values (Fig. 1a) mirrors that of the anions (Fig. 1b). In all of the salt solutions the cations have K_p values less than 0.72, indicating their overall propensity for solvation in the bulk solution. The cation K_p data are, however, inconsistent with the thermodynamic study (SPM) by up to an order of magnitude discrepancy.

It is remarkable that the anion K_p values (Figure 1b) follow the same qualitative trend as the SPM data, except in the case of iodide. The K_p values computed from the simulations for the chaotropic anions nitrate and perchlorate are greater than 1. However, the typically strong chaotropic anion iodide has a $K_p \approx 0.8$, indicating a slight preference for solvation in the bulk solution. This atypical behavior of iodide may be a consequence of the nonpolarizable force field used in this study. In previous work, polarization has been shown to enhance the propensity of heavy halides for nonpolar solute surfaces (32), and it is now well established that explicit inclusion of electronic polarization in MD simulations enhances the propensity of heavy halides for the air/water interface (13).

For the most part, the anion K_p values calculated from the MD simulations are substantially lower than those extracted from the SPM analysis (Fig. 1b). In the case of sulfate, Pegram and

Record assumed $K_p = 0$ (20). Although our simulations show a very high degree of exclusion of sulfate from the benzene hydration layer, this exclusion is not absolute. Moreover, we find that the strong kosmotrope fluoride also has a small K_p value, whereas Pegram and Record find a value close to 1, indicating nearly equal preference of fluoride for the bulk water and the benzene hydration layer. Our simulations also yield a small K_p for chloride indicating a preference for its solvation in bulk solution, while the SPM predicts a value greater than unity, indicating an affinity for the benzene surface.

Fig. 1c shows a comparison of the calculated overall salt K_p values from this study (black bars) with those from the SPM study (red bars) (20). The ordering of the salt K_p values from the MD simulations follows that of the cations and anions, which is consistent with Pegram and Record, except for the case of NaI. Excepting sodium sulfate, it is remarkable that the overall salt K_p values derived from simulations are in near quantitative agreement with those derived from the thermodynamic study (Fig. 1c). Although sodium cations and sulfate anions are highly excluded, our simulations clearly show that neither ion is completely excluded from the hydration layer of benzene.

Given the chosen parameters defining the hydration layer about benzene, and assuming that the solvent-accessible surface area of benzene is $212 \text{ \AA}^2$ (20), we find that there are approximately $0.17 \text{ H}_2\text{O \AA}^{-2}$, which is in good agreement with the $0.18 \text{ H}_2\text{O \AA}^{-2}$ assumed in the SPM (20).

The agreement between the MD and SPM salt K_p values suggests that the thermodynamic model correctly predicts the salt K_p . However, the MD results suggest that the SPM may overestimate the anion K_p values and underestimates the cation K_p values, as the SPM may not properly account for counter-ion interactions. Indeed, to derive ionic K_p values from the SPM

analysis it was necessary for Pegram and Record to assume the ions did not interact (20).

3.2. Comparison of MD and Raman-MCR results

Fig. 2 shows experimental results obtained from an SMCR analysis of Raman spectra of solutions containing either benzene or pyridine dissolved in aqueous KF, NaCl, NaBr, or NaI solutions (with salt molalities between 0.1 and 1). The unprocessed spectra of the benzene solutions are virtually indistinguishable from those of the corresponding solvent (because the solubility limit of benzene is $\sim 0.02\text{ m}$), while the higher concentration pyridine solutions show clear evidence of pyridine vibrational bands. However, in both cases SMCR analysis may be used to obtain solute-correlated spectra that clearly reveal the CH stretch band of the solute (33). For example, Fig. 2 compares the solute-correlated spectra (in the CH and OH stretch region) of 0.5 *m* pyridine in pure water and in 1 *m* NaI (compared with the OH stretch band of pure water). Fig. 2a shows a close up view of the CH peak of pyridine which reveals a small but measureable red-shift of $\Delta\nu \sim 2\text{ cm}^{-1}$ in the salt solution (virtually identical to that obtained for benzene in the same salt solution). Note that the measured red-shift is independent of pyridine concentration (over a 0.2 *m* to 0.5 *m* range), which implies that the shifts are not due to salt-induced pyridine aggregation, but rather to direct ion-solute interactions. Additionally, the measured frequency shift is insensitive to the specific cation used, as $\Delta\nu \sim 2\text{ cm}^{-1}$ in both aqueous NaI and KI solutions. No such salt-induced red-shift was found in similar measurements performed using aqueous KF (in which $\Delta\nu \sim 0 \pm 0.2\text{ cm}^{-1}$), thus implying that neither K^+ nor F^- have any detectable interaction with either benzene or pyridine (up to a salt concentration of 1 *m*). Previous Raman-MCR studies further indicate that Na^+ does not interact with non-aromatic hydrophobic groups (8). Thus, the above results imply that the aromatic CH shifts that we have observed in NaI

solutions are primarily due to the interaction between Γ^- and benzene (or pyridine).

Fig. 2b shows the Γ^- induced CH shift of both benzene and pyridine as a function of NaI concentration. These frequency shifts may be used to estimate the corresponding iodide partition coefficient K_p by assuming that the observed shifts reflect the probability that a single anion is present in the first hydration shell of the solute, combined with our experimental estimate that one iodide ion in the first hydration-shell induces an aromatic CH red-shift of $\Delta\nu_1 = 7 \pm 3 \text{ cm}^{-1}$. This iodide-induced shift was obtained from the frequency of the pyridine CH peak appearing in the iodide-correlated spectrum (and thus arising from pyridine molecules whose hydration shells contain an iodide ion), as described previously (8). The latter iodide-induced shift is quite similar to the iodide-induced shift in the CH stretch frequency of non-aromatic methyl groups of $\Delta\nu_1 = 9 \pm 3 \text{ cm}^{-1}$ (8). Thus, the K_p pertaining to the partitioning of iodide ions into the first hydration shell of benzene and pyridine may be estimated as follows:

$$K_p = \frac{1}{N_{HS}} \frac{(\Delta\nu / \Delta\nu_1)}{(m_i / m_{wat})} \approx 1.54 \left(\frac{\Delta\nu}{\Delta\nu_1} \right), \quad (2)$$

where m_i and m_{wat} are the molalities of Γ^- and water, respectively, and $N_{HS} = 36$ is the MD simulation-derived estimate of the number of water molecules in the first hydration-shell of benzene. The second approximate equality pertains to a 1 *m* salt solution.

The primary source of error in the resulting K_p values, as reflected in the hatched regions in Fig. 2c, derives from the uncertainty in the shift induced by a single first hydration-shell anion, $\Delta\nu_1$, which is significantly larger than the $\pm 0.5 \text{ cm}^{-1}$ maximum experimental uncertainty in $\Delta\nu$. Note that the Raman-MCR derived K_p values in Fig. 2c imply that both benzene and pyridine have approximately the same K_p values. The Raman-MCR derived K_p values for KF, NaCl, and NaBr were obtained assuming that $\Delta\nu_1 = 7 \pm 3 \text{ cm}^{-1}$ for all of the anions. Although the latter

assumption remains to be independently verified, it seems unlikely that the shift induced by a single halogen anion within the first hydration-shell could lie significantly outside this range. However, our preliminary measurements in molecular salt solutions (described below) may imply that these anions induce significantly smaller CH frequency shifts. The primary finding of our Raman-MCR derived results is that the partition coefficient of Γ is somewhat smaller than unity, in agreement with the MD simulation predictions, and significantly smaller than the thermodynamic SPM-based estimate that $K_p > 1.5$ for Γ (Fig. 1b). Moreover, since the Γ induced aromatic CH red-shift of $\sim 2 \text{ cm}^{-1}$ is approximately twice that found previously for non-aromatic CH groups, our Raman-MCR results imply that Γ ions have a higher affinity for the first hydration-shells of aromatic than non-aromatic hydrocarbon groups.

Although our most reproducible Raman-MCR results are those obtained in alkali halide solutions, we have also attempted to use Raman-MCR to quantify the aromatic CH stretch shift induced by molecular anions in Na_2SO_4 , NaNO_3 , and NaClO_4 solutions. Our results indicate that all of these molecular anions produce significantly smaller CH red-shifts than Γ . More specifically, for both benzene and pyridine the CH red-shifts range from $\Delta\nu \sim 0.2 \pm 0.3 \text{ cm}^{-1}$ in 1 *m* Na_2SO_4 to $\Delta\nu \sim 0.5 \pm 0.4 \text{ cm}^{-1}$ in 1 *m* NaClO_4 (with intermediate values obtained in 1 *m* NaNO_3). The small shift induced by SO_4^{2-} is consistent with the MD results, as well as the assumption of the SPM that SO_4^{2-} is strongly excluded from nonpolar surfaces (20). However, the small red-shift induced by ClO_4^- is rather surprising, as both the MD and SPM results suggest that this anion should have a substantial affinity for benzene. Thus, our Raman-MCR results may either imply that ClO_4^- has a quite low value of K_p (comparable to that of Cl^-) or that the red-shift induced by a single ClO_4^- anion in the first hydration-shell of benzene (or pyridine) is significantly smaller than that induced by an Γ anion.

3.3. MD density distributions

Figs. 3a and 3b show mass density distributions of the cations and anions, respectively, about benzene, obtained from our MD simulations in a cylindrical coordinate system in which the center of the benzene ring is at the origin, and the z axis is normal to the plane of the ring. The anions show significant variability in their density distributions compared to the cations. This is consistent with the observation that cations generally exhibit less pronounced interactions with nonelectrolyte solutes relative to anions (34). The density distributions of potassium and sodium about benzene in KF, NaNO₃, NaI, and NaClO₄ are approximately uniform throughout the hydration layer and bulk water. However, the sodium distributions in the Na₂SO₄ and NaCl systems show some depletion in the vicinity of benzene. This is reflected in the calculated partition coefficients (K_p) for the cations shown in Figure 1a. Of the aqueous solutions studied here, K_p for sodium is smallest when in solution with sulfate or chloride. To account for sodium depletion in these two systems, consider the density distributions (Fig. 3a,b) and K_p data of sulfate and chloride (Figure 1b). In particular, sulfate is strongly excluded from the hydration layer of benzene, and correspondingly has the smallest K_p of all the anions and cations. This result is consistent with other MD studies of air/water and hydrophobic interfaces showing strong exclusion of sulfate (35,36). Furthermore, in Na₂SO₄ solution, sodium is observed to be withdrawn by sulfate from the air/water interface (35). Thus, the density depletion about benzene and the low K_p values for sodium in Na₂SO₄ solution are accounted for by interactions between the ions in solution. Chloride also shows depletion in the benzene hydration layer (Fig. 3b) as well as a relatively small K_p value (Fig. 1b). Its exclusion from a hydrophobic surface was also observed in a simulation study of methane in aqueous NaCl solution (36). Similar to the Na₂SO₄ system, a cation-withdrawing mechanism may account for the slight depletion of sodium in the

hydration layer. According to Collins' "law of similar water affinities" sodium is expected to pair with chloride in aqueous solution (37). A recent study on ion-pairing in sodium salts further corroborates this view (38).

K_p data (Fig. 1b) and density distributions (Fig. 3b) indicate exclusion of fluoride from the benzene surface, intermediate between sulfate and chloride. Fluoride exclusion from the air/water (39,40) and macroscopic and molecular hydrophobic interfaces (8,41,42) has been previously demonstrated both in simulations and experimentally. However, potassium, while in the presence of the strong kosmotrope fluoride, shows no appreciable depletion from the benzene surface (Fig. 3b). Ion-pairing would likely not play a role in potassium and fluoride interactions (37). This may account for the unperturbed density distribution of potassium about benzene. However, potassium has been considered a weak chaotrope (37), and hence is expected to show an affinity for the benzene surface. Further studies are needed to elucidate the effect of counter-anions on potassium behavior in the presence of nonpolar solutes.

The chaotropic anions nitrate, iodide, and perchlorate show an enhanced affinity for the benzene surface relative to the bulk water. Both the density distributions (Fig. 3b) and anion K_p values (Fig. 1b) allow for ordering of these anions in decreasing affinity for the benzene surface as $\text{ClO}_4^- > \text{NO}_3^- > \text{I}^-$. The affinity of perchlorate and iodide for air/water interfaces and hydrophobic surfaces is well established (13,39,41,43-48). While the sodium cation exhibits an overall preference for bulk water, K_p values of sodium positively correlate with those of the chaotropic anions (Fig. 1a,b).

Fig. 4 shows normalized density distribution functions, denoted $g(r,z)$, of the anions, cations and water oxygen (O_w) atoms around benzene in the (r,z) coordinate system for all six of the simulated salt solutions. The density distributions are normalized by the bulk density of the

respective species, and they have been symmetrized in the direction (z) normal to the benzene plane. The ion distributions in Fig. 4 are normalized versions of the data shown in Fig. 3. Plotting them along with the O_W distributions in Fig. 4 enables us to see how the ions are distributed in the benzene hydration shells.

The six different systems show remarkably similar O_W distributions with an enhanced affinity of water for the benzene surface, especially along the z axis. The solvation of benzene in our simulations is consistent with earlier studies on the hydration of benzene in pure water (49). All of the water distribution functions show a well-defined first hydration shell about benzene peaked at ~ 3 Å along the z axis and at ~ 5.5 Å along the radial (r) axis. The structure of the second and third benzene hydration layers depends on the particular anion present in solution. In the presence of the kosmotrope sulfate, there appears to be no water structure beyond the first hydration layer of benzene (Fig. 4a). On the other hand, the chaotrope iodide seems to enhance the water structure with a clear indication of a second hydration layer along the z axis, with a peak at ~ 6 Å above and below the benzene plane; however, along the radial axis there is no clear indication of a second hydration layer (Fig. 4e). The remaining salts show intermediate effects on the hydration characteristics of benzene.

The distributions of the ions depicted in Fig. 4 show markedly different behavior depending on the ions present in the solution. Of the systems simulated, sulfate and sodium in Na_2SO_4 show the greatest depletion in the first hydration layer of benzene relative to the other simulated ions (compare Fig. 4a to Fig. 4b-f). Remarkably, there is an enhanced sulfate and sodium density above and below the benzene plane at $|z| > 10$ Å, which is well outside of the first hydration layer. It is not known if this is system size artifact of our simulations or if it implies a long distance interaction between Na_2SO_4 and benzene. In the KF solution, the potassium ion

exhibits an enhanced affinity for the first hydration layer relative to fluoride, but both ions show an overall depletion relative to the bulk solution (Fig. 4b). Although chloride is excluded from the benzene surface, the distribution function indicates a slight increase in density slightly beyond the first hydration layer of benzene along the z axis.

The chaotropic anions exhibit an enhanced affinity for the hydration layer of benzene. In particular, nitrate and perchlorate density is enhanced at the first minimum of the O_W density distribution function along the z axis, with perchlorate exhibiting a two-fold enhancement in that region relative to nitrate (Fig. 4d,f). These anion densities are also enhanced along the radial axis coincident with the peak of the first hydration shell of benzene, with perchlorate again exhibiting an almost two-fold enhancement relative to nitrate. Iodide shows enhanced density coincident with the second hydration shell peak at ~ 6 Å along the z axis (Fig. 4e). However, iodide enhancement along the radial axis resides in the trough beyond the first hydration shell.

4. Conclusions

MD simulations of benzene, as well as Raman-MCR measurements of benzene and pyridine, in several salt solutions were performed. Distributions of ions and water around benzene, obtained from 100 ns simulations, were employed to directly compute ion and salt partition coefficients for comparison with a thermodynamic SPM. The partitioning of the cations into the hydration layer of benzene depended strongly upon the specific counter-anion in solution. The Raman-MCR measurements imply that only anions produce measurable salt induced shifts in the aromatic CH stretch frequencies of benzene and pyridine. The partition coefficient K_p of Γ obtained from these measurements is consistent with that found in the MD simulations, as is the decrease in K_p with decreasing size of halogen anions. Good agreement was found between the simulations and the thermodynamic model for the partitioning of salts between the hydration

layer of benzene and bulk solution. However, inconsistency between this study and the SPM regarding individual cation and anion partitioning suggests that an improved thermodynamic model must account for the interactions between the counter-ions. Greater disparities between the MD simulation results and those obtained using SPM and Raman hydration-shell measurements are found for the partition coefficients for molecular anions. These discrepancies may reflect the influence of molecular polarizability and/or shape on both ion-partitioning and ion-induced aromatic CH frequency shifts, and possibly also counterion interactions (whose effects were neglected in both the SPM and Raman-MCR analysis).

Our MD simulations have provided an atomic-scale picture of specific-ion interactions with the nonpolar solute benzene. We have shown that nonpolarizable MD simulations are in reasonable (semi-quantitative) agreement with results obtained from both the thermodynamic SPM and Raman-MCR hydration-shell spectroscopic measurements.

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Table 1

Ion force field parameters

Atom	σ [Å] [†]	ϵ [kcal/mol] [‡]	q [e] [§]	reference
K ⁺	4.935	0.3280 x 10 ⁻³	1.00	(50)
Na ⁺	3.330	2.771 x 10 ⁻³	1.00	(50)
F ⁻	2.733	0.7200	-1.00	(51)
Cl ⁻	4.417	0.1180	-1.00	(52)
I ⁻	5.400	0.0700	-1.00	(51)
N (NO ₃ ⁻)	3.900	0.8368	0.86	(53)
O (NO ₃ ⁻)	3.154	0.6489	-0.62	(53)
Cl (ClO ₄ ⁻)	3.950	0.9489	1.20	(54)
O (ClO ₄ ⁻)	2.960	0.8782	-0.60	(54)
S (SO ₄ ²⁻)	3.550	0.2500	2.00	(55)
O (SO ₄ ²⁻)	3.150	0.2000	-1.00	(55)

[†]Lennard-Jones size parameter.[‡]Lennard-Jones well depth.[§]Atomic charge.

Figure captions

Fig. 1. (a) Cation, (b) anion, and (c) total salt partition coefficients, K_p , calculated from our MD simulations (black bars). The corresponding partition coefficients obtained from a thermodynamic solute partitioning model (SPM) (20) are shown as red bars. In panel (a), the MD values are for Na^+ in Na_2SO_4 , NaCl , NaNO_3 , NaI , and NaClO_4 , and for K^+ in KF ; the cation values do not depend on the identity of the counter anion in the SPM. In panel (b), the MD values are for SO_4^{2-} in Na_2SO_4 , F^- in KF , NO_3^- in NaNO_3 , I^- in NaI , and ClO_4^- in NaClO_4 ; the anion values do not depend on the identity of the counter cation in the SPM.

Fig. 2. Raman-MCR results for the salt-induced red-shift in aromatic CH vibrational bands of benzene and pyridine. The solute correlated spectra of 0.5 *m* pyridine (solid curves) in both pure water (blue) and 1 *m* NaI (red) are compared with the OH stretch band of pure water (dashed blue); (a) expanded view of the CH stretch peak of pyridine, (b) CH shift of both benzene and pyridine vs. NaI concentration, (c) K_p (from Eq. 2) plotted as a function of the salt induced frequency shift of both benzene and pyridine induced by KF , NaCl , NaBr , and NaI (see text for further details).

Fig. 3. Mass density distributions of the (a) cations Na^+ and K^+ , and the (b) anions SO_4^{2-} , F^- , Cl^- , NO_3^- , I^- , and ClO_4^- , around benzene for the six salt systems simulated in this study. The z coordinate runs perpendicular to the benzene plane, with the geometric center of benzene located at the origin. The radial coordinate, r , runs radially outward from the z -axis parallel to the benzene plane. The distribution at each point (r,z) is an average over the azimuth.

Fig. 4. Normalized density distribution functions of the ions and water oxygen atoms (O_w) about benzene. Each distribution is normalized by its bulk density. The z coordinate runs

perpendicular to the benzene plane, with the geometric center of benzene located at the origin. The radial coordinate, r , runs radially outward from the z -axis parallel to the benzene plane. The distribution at each point (r,z) is an average over the azimuth.

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Figure 1

Figure 2

Figure 3

Figure 4

Graphical Abstract

Jordan Vincent received his B. S. in Chemistry and B. A. in Mathematics from Saint Cloud State University in 2007, and an M. S. in Chemistry from the UC Irvine, in 2011. He is currently a Ph. D. candidate at UC Irvine. His research interests include development and application of ab initio non-adiabatic and classical molecular simulation techniques to aqueous interface chemistry problems and modeling photochemical reaction dynamics.

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