

## On the Mechanism of the Hofmeister Effect

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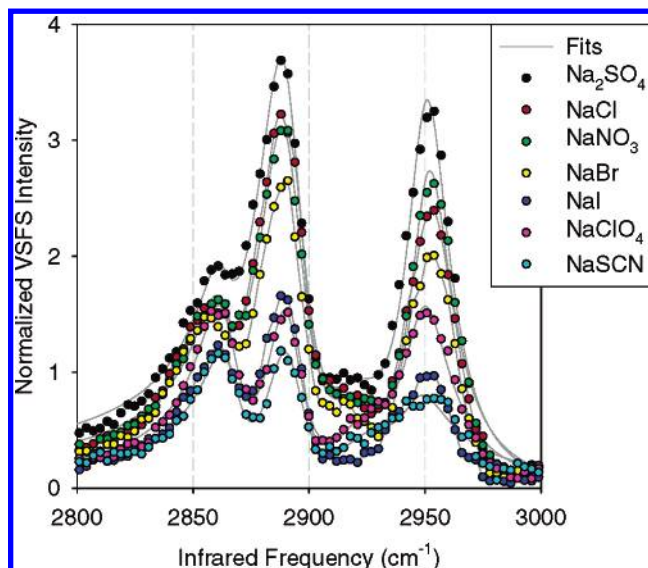
First proposed in 1888,<sup>1</sup> the Hofmeister series is a qualitative ordering of ions based originally on their propensity to salt-out proteins from aqueous solution.<sup>2–4</sup> It is now known that a variety of processes from enzymatic activity to polymer and protein folding also display a Hofmeister effect. However, despite the wide range of aqueous chemistries that follow this series, an underlying molecular level description of the mechanism is still far from complete. Two basic hypotheses have been put forward. The first one involves the various ions' ability to make and break hydrogen bonds (known as kosmotropic vs chaotropic behavior).<sup>5–8</sup> This idea has been called into question by recent experiments which indicate that the ions have little effect on the overall hydrogen bonding of water in bulk solution<sup>9</sup> and do not display the predicted thermodynamic behavior.<sup>5</sup> Another theory suggests that dispersion forces play a large role in the order of the Hofmeister series,<sup>10</sup> although this hypothesis has been largely examined theoretically rather than experimentally.

Herein we demonstrate a novel Hofmeister effect in an octadecylamine monolayer spread on salt solutions by using vibrational sum frequency spectroscopy (VSFS).<sup>11–16</sup> The advantage of VSFS is that both the interfacial water structure as well as the ordering of the monolayer can be followed directly. Specifically, because VSFS is sensitive to the alkyl chain conformation of the monolayer,<sup>17,18</sup> we can show the propensity of any given anion to induce gauche defects into the fatty amine film at constant temperature and pressure. The results clearly demonstrate that an anion's ability to disorder the alkyl chain region follows the Hofmeister series. Such a process is in line with the idea that dispersion forces play a critical role in determining this effect.<sup>4</sup> By contrast, the role of the ions in the hydrogen bonding and interfacial water structure were less clear-cut.

In a first set of experiments, VSFS data were collected from monolayers spread on D<sub>2</sub>O subphases containing various sodium salts. The vibrational spectra collected in the CH stretch range showed dramatic differences in the degree of ordering in the alkyl chains as a function of the specific anion in the subphase (Figure 1). As can be seen from Table 1, the ratio of oscillator strengths from the methyl symmetric stretch,  $\nu_s(\text{CH}_3)$  at 2891 cm<sup>-1</sup>, to the methylene symmetric stretch,  $\nu_s(\text{CH}_2)$  near 2863 cm<sup>-1</sup>, changed quite substantially. It is already well established that the higher this ratio, the more ordered the monolayer is under a given set of conditions.<sup>13,16,18,19</sup> The ratios for the anions follow a series from most ordered to least ordered monolayer as:



This is recognizable as the Hofmeister series. The basis for this ordering is related to an individual anion's ability to penetrate into the alkyl chain portion of the monolayer,<sup>20–22</sup> thereby disrupting the hydrocarbon packing. Sulfate, chloride, and nitrate ions show relatively little tendency to do this, while iodide, perchlorate, and



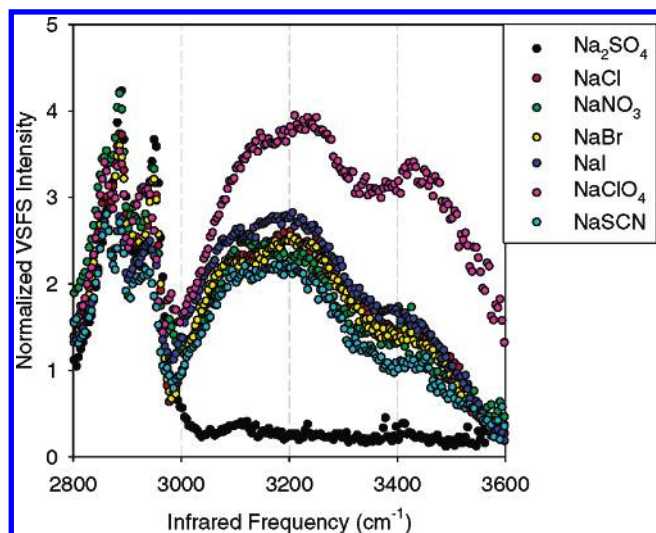
**Figure 1.** VSFS spectra of ODA monolayers ( $\Pi = 15$  mN/m) spread on D<sub>2</sub>O subphases at 20 °C. Each subphase contained 10 mM of a given salt as indicated in the legend. All spectra were recorded with the ssp (s - signal, s - visible, p - infrared) polarization combination and normalized to the signal from a piece of z-cut crystalline quartz.

**Table 1.** CH Symmetric Stretch Ratios and Surface Potentials for ODA Monolayers on Subphases Containing 10 mM Salt

salt	$\nu_s(\text{CH}_3)/\nu_s(\text{CH}_2)$	surface potential (mV $\pm$ 20)
Na <sub>2</sub> SO <sub>4</sub>	6.0 $\pm$ 0.6	635
NaCl	4.7 $\pm$ 0.4	606
NaNO <sub>3</sub>	4.1 $\pm$ 0.4	562
NaBr	3.3 $\pm$ 0.4	563
NaI	1.7 $\pm$ 0.3	365
NaClO <sub>4</sub>	1.1 $\pm$ 0.1	303
NaSCN	0.8 $\pm$ 0.1	193
no salt	4.4 $\pm$ 0.3	852

thiocyanate go in more facily. Bromide appears to display intermediate behavior.

Next, surface potential data were collected at the air/ODA/subphase interface for each respective anion using the vibrating capacitor method (Table 1). As expected, the surface potential was greatest for ODA on pure water. This positive potential was generated by the protonation of some of the surface amines under these conditions. The addition of the various salts caused an attenuation of the potential in the same order as that seen above for alkyl chain ordering. In other words, the anions that could most efficiently partition into the monolayer caused the greatest attenuation of the surface potential, while those that were excluded showed the least effect. This finding is in line with the notion that those anions which partition to the greatest extent into the monolayer had the highest interfacial concentration.



**Figure 2.** VSFS spectra of ODA monolayers ( $\Pi = 15$  mN/m) spread on  $\text{H}_2\text{O}$  subphases at 20 °C. Each subphase contained 10 mM of the salt indicated in the legend.

It was important to exploit VSFS's unique ability to probe interfacial water structure to correlate changes in monolayer ordering. This was carried out under the identical conditions as those shown in Figure 1, but with  $\text{H}_2\text{O}$  rather than  $\text{D}_2\text{O}$  in the subphase. In this case, CH stretches from the ODA molecules' alkyl chains as well as the OH stretches from the interfacial water were present in the spectra (Figure 2). Furthermore, a very weak band of intensity near  $3100\text{ cm}^{-1}$  came from the NH stretch mode of the partially aligned amine headgroups.<sup>15</sup>

As expected, two major broad water peaks were observed. The first one near  $3200\text{ cm}^{-1}$  corresponded to water molecules with tetrahedral coordination. The second one was caused by water with more disordered hydrogen bonding and was located just above  $3400\text{ cm}^{-1}$ .<sup>14,23–25</sup>

Figure 2 shows a partial Hofmeister-like trend in the water structure data, but it has significant deviations and does not follow the series nearly as rigorously as data from either the alkyl chain ordering or surface potential measurements. In fact, the relative intensities of the OH features show several anomalies inconsistent with a Hofmeister effect. For example, although  $\text{SCN}^-$  is at one end of the Hofmeister series, it shows OH signal intensities below  $\text{Br}^-$ . The  $\text{NO}_3^-$  signal is also somewhat out of place, while the OH stretch intensity from  $\text{Br}^-$  and  $\text{Cl}^-$  are nearly identical. It should also be noted that the  $\text{SO}_4^{2-}$  ions cause almost complete destruction of the water signal, which is consistent with the propensity of divalent ions to drastically attenuate water signal.<sup>23,26</sup> The observed differences between the way anions affect alkyl chain ordering and surface potential on the one hand and water structure on the other argues against the hypothesis that the Hofmeister effect is primarily due to the ions' ability to mediate water structure.

Water structure at an aqueous interface can be affected by several factors. These include surface potential and the ability to hydrogen bond to terminal functional groups at the adjacent surface. It is also generally accepted that raising the salt concentration in solution decreases the Debye length, resulting in the attenuation of interfacial water structure at a charged interface.<sup>15</sup> Furthermore, at greater surface potential, water alignment is normally expected to increase.<sup>15,27,28</sup> This last argument, however, is based upon the assumption that the interface is impenetrable in accordance with standard Gouy–Chapman theory.<sup>29</sup> This assumption generally applies for systems such as the silica/water interface but breaks

down in the present case where ions can penetrate past the amine headgroup region. In Figure 2, larger water features are frequently observed from ions responsible for lower surface potentials (Table 1). This result is not completely surprising, given the fact that a central tenet of Gouy–Chapman theory does not hold for this system.

It might also be anticipated that Gouy–Chapman theory would break down in biological systems where more hydrophobic ions can penetrate the hydrophilic shells of aqueous proteins so as to interact with the more hydrophobic portions of the macromolecules. As with these fatty amine monolayers, the penetration of the hydrophilic surface of a folded protein would lead to ion specific disruption of the structure. Such ion-induced changes in the conformation of the biomacromolecules are a more likely origin of the observed Hofmeister effect, rather than merely alteration in water structure.

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**Supporting Information Available:** Experimental procedures for VSFS and surface potential measurements. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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