

Contact Ion Pair Formation is not Necessarily Stronger than Solvent Shared Ion Pairing

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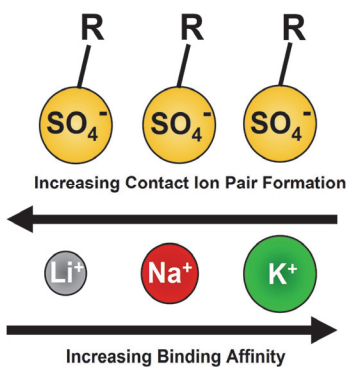
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Abstract

Vibrational sum frequency spectroscopy (VSFS) and pressure-area Langmuir trough measurements were used to investigate the binding of alkali metal cations to eicosyl sulfate (ESO_4) surfactants in monolayers at the air/water interface. The number density of sulfate groups could be tuned by mixing the anionic surfactant with eicosanol. The equilibrium dissociation constant for K^+ to the fatty sulfate interface showed ten times greater affinity than for Li^+ and approximately three times greater than for Na^+ . All three cations formed solvent shared ion pairs when the mole fraction of ESO_4 was 0.33 or lower. Above this threshold charge density, Li^+ formed contact ion pairs with the sulfate headgroups, presumably via bridging structures. By contrast, K^+ only bound to the sulfate moieties in solvent shared ion pairing configurations. The behavior for Na^+ was intermediate. These results demonstrate that there is not necessarily a correlation between contact ion pair formation and stronger binding affinity.

TOC Graphic



In 1921 Fajans reported that alkali metal cations (M^+) and halide anions with similar hydration enthalpies (ΔH_{Hyd}) gave rise to sparingly soluble salts in water.^{1,2} As ΔH_{Hyd} for the cation and anion diverged, the corresponding salt was found to be more soluble. More recently, Collins proposed the Law of Matching Water Affinities (LMWA) as an extension of Fajans' observations to include biologically relevant ions, such as those that are pendant groups of polymers and proteins.³⁻⁶ He further suggested that contact ion pair formation should be more favorable between free cations and biologically relevant anionic functional groups with similar ΔH_{Hyd} or free energies of hydration (ΔG_{Hyd}) values. By contrast, he hypothesized that solvent shared ion pairing would be expected if there were significant differences.

Numerous studies of specific alkali metal cation interactions with pendant carboxylate and sulfate groups have been performed for binding to micelles,⁷⁻¹⁵ polyelectrolytes,¹⁶ proteins,^{17,18} and monolayers.¹⁹⁻²² These investigations found that weakly hydrated cations paired better with pendant sulfate groups, while strongly hydrated cations paired better with carboxylate. Collins' hypothesis would suggest, for example, that K^+ would be more likely to form a contact ion pair with sulfate moieties compared with Li^+ because it binds more strongly and has a more similar ΔG_{Hyd} (**Section S1**). Unfortunately, previous studies have not addressed the question as to whether the binding to sulfate pendant groups occurs through solvent shared or contact pair formation. As such, it remains unknown as to whether contact pair formation is associated with stronger binding or not.

Herein, ion pairing was investigated with closely packed anionic monolayers of eicosyl sulfate (ESO_4) with LiCl , NaCl , and KCl in the subphase. Details concerning the experimental methods, fitting procedures, and fitting parameters are provided in **Section S2**. Vibrational sum frequency spectroscopy (VSFS) measurements of ordered water in the double layer confirmed the binding affinity order predicted by the LMWA. However, VSFS studies of the pendant sulfate $\nu_{\text{ss}}(\text{SO}_3^-)$ resonance revealed significant dehydration of a closely packed ESO_4 monolayer by Li^+ , but not by K^+ . Specifically, these results demonstrated an order of magnitude greater affinity for K^+ with ESO_4 monolayers compared to Li^+ . Nevertheless, Li^+ could bind through contact ion pair formation, while K^+ binding occurred through solvent shared ion pairing (**Figure 1**). Moreover, contact ion pairs between Li^+ and

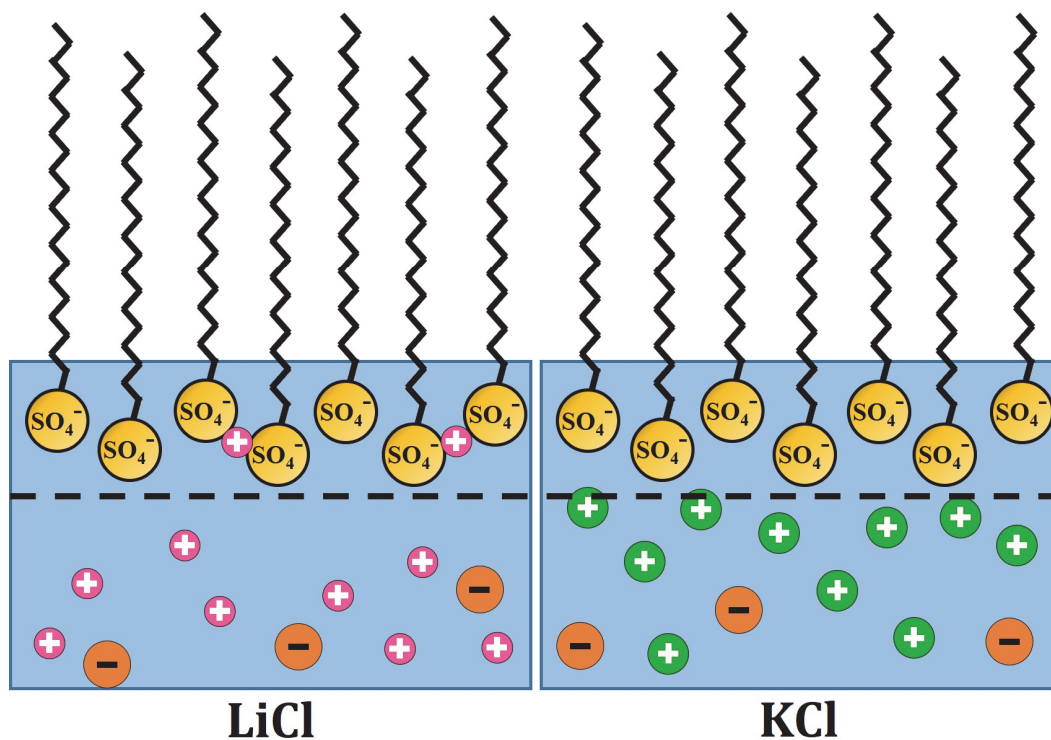


Figure 1. A densely packed ESO_4 monolayer displays opposite trends for cation specific binding and contact ion pair formation with alkali metal cations. K^+ (green) pairs more strongly than Li^+ (pink), yet strictly through solvent shared interactions, while Li^+ can interact with the interface through contact ion pairing.

pendant sulfate occurred when two ESO_4 headgroups were packed closely enough together to allow Li^+ to bind bivalently. This finding does not support Collins' postulate regarding contact ion pair formation. Instead, it would appear that Li^+ has a greater propensity than larger cations to form contact ion pairs with sulfate and that ion hydration enthalpies and binding constants are not particularly useful indicators as to the mode of pairing.

In a first set of experiments, ESO_4 monolayers were formed at the air/aqueous solution interface on a Langmuir trough and VSFS titrations in the OH stretch region were performed as a function of salt concentration (**Figure 2(A-C)**). The two sharp peaks seen in the spectra at 2877 cm^{-1} and 2941 cm^{-1} correspond to the $\nu_{\text{ss}}(\text{CH}_3)$ and its Fermi resonance with the CH_3 bending mode, respectively, in agreement with previous studies.²³⁻²⁵ By contrast, the $\nu_{\text{ss}}(\text{CH}_2)$ peak at 2850 cm^{-1} and the $\nu_{\text{as}}(\text{CH}_2)$ peak at 2920 cm^{-1} from methylene groups were quite small. These results are consistent with the idea that all three monolayers were well packed and contained relatively few gauche conformations.^{26,27} Nevertheless, the methylene group signatures were lower over KCl solutions compared with NaCl and LiCl, indicating that the monolayer over KCl was relatively better ordered.

The OH stretch region between $3000\text{-}3800\text{ cm}^{-1}$ gave rise to three much broader peaks. The two prominent OH stretch resonances near 3200 cm^{-1} and 3400 cm^{-1} represent water molecules beneath the negatively charged headgroups of the monolayer and should be oriented such that the hydrogen atoms face upward towards the negatively charged monolayer.^{25,28-31} These peaks correspond to water molecules with more (3200 cm^{-1}) and less (3400 cm^{-1}) tetrahedral ordering, respectively.³²⁻³⁴ A much smaller OH stretch resonance near 3600 cm^{-1} represents water molecules situated just above the headgroup in

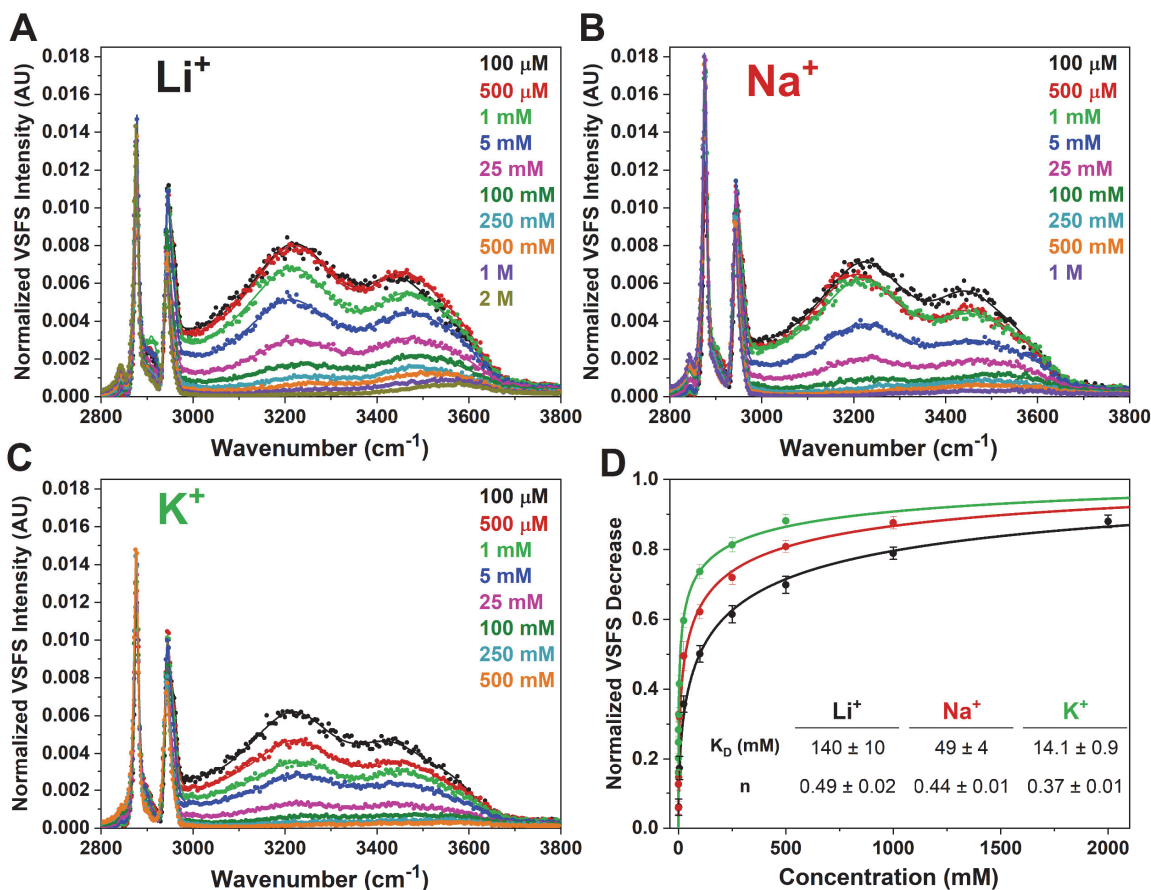


Figure 2. VSFS spectra in the OH stretch region of an ESO₄ monolayer over subphases containing (A) LiCl, (B) NaCl, and (C) KCl at a constant mean molecular area (MMA) of $23 \pm 1 \text{ \AA}^2$ with the SSP polarization combinations. The MMA was determined from Langmuir trough pressure-area (Π -A) isotherms (**Section S3**). All subphases contained 100 μM MOH with enough MCl added to achieve the listed alkali metal ion concentrations. In all cases where the salt concentration was $\geq 1 \text{ mM}$, 4 μM EDTA was included to chelate trace metal contaminants. The pH determined after each experiment was 9.3 ± 0.1 for all conditions at $21 \pm 1 \text{ }^\circ\text{C}$. At this pH, the monolayers were fully deprotonated (**Section S4**). The colored circles are experimental data points representing the average of at least 3 trials and the solid lines are fits to the spectra. (D) The relative decrease in the summed amplitudes of the 3200 cm⁻¹ and 3400 cm⁻¹ peaks are presented as colored circles. These data were fit to binding isotherms with the corresponding dissociation constants and cooperativity terms listed in the inset table. Additional details for the binding isotherm fitting procedures are provided in **Section S5**. The effect of interference at salt concentrations $< 100 \text{ } \mu\text{M}$ is described in **Section S6**.^{35–38}

a weaker hydrogen bonding environment.^{28,31,39} In this case, the water molecules are adjacent to the alkyl chains and the hydrogen atoms face downward toward the bulk solution. This interpretation is consistent with previous spectra of highly charged anionic monolayers obtained by both heterodyne-detected VSFS (HD-VSFS)^{25,28,31} as well as computational results employing the maximum entropy method (MEM)³⁰ to extract the relative phase associated with each of the three peaks.

Interfacial water ordered by a charged surface can be separated into two populations.^{23,35,36,38,40–46} First, a chemically bound water population primarily interacts with the surface through hydrogen bonding. Second, a physically aligned water population is ordered by the electric field permeating into the solution from the interface.⁴⁰ At the surface charge density employed herein, nominally 0.7 C/m² without ion pairing (**Section S7**), the electric field-oriented water dominates both the 3200 and 3400 cm⁻¹ peaks.^{47,48} Formation of ion pairs between cations in the subphase and the anionic functional groups present in the monolayer decrease the effective surface charge density and attenuate the VSFS signal in the OH stretch region. The extent of attenuation of the VSFS signal enables a quantitative comparison amongst the various cations that are employed.

The summed amplitudes of the 3200 cm⁻¹ and 3400 cm⁻¹ peaks are employed herein as a metric of ion affinity. It should be noted that the intensity of the 3600 cm⁻¹ peak is omitted from this analysis, as this peak was found to be relatively insensitive to the subphase environment under the conditions used herein. As can be seen, the 3200 cm⁻¹ and 3400 cm⁻¹ peaks decrease monotonically in each case while the adjacent CH peaks remain essentially unchanged. Ion specific effects are already present at 100 μ M M⁺, with the

intensity in the OH stretch region increasing in the order $K^+ < Na^+ < Li^+$. The apparent equilibrium dissociation constants, $K_{D,app}$, were determined by fitting the normalized decrease in the VSFS amplitude of the 3200 cm^{-1} and 3400 cm^{-1} peak region to a Hill-Langmuir binding isotherm with a cooperativity coefficient, n (**Figure 2D** inset).⁴⁹

$$I_{VSFS,Norm} = \frac{B_{max}[M^+]^n}{K_{D,app}^n + [M^+]^n} \quad (1)$$

As can be seen, the value of n is less than 1 in each case, which indicates that the binding is anti-cooperative.⁴⁹ Indeed, decreasing affinity should be expected because of charge neutralization. While binding between a charged group at the surface and a cation in solution decreases the surface potential, increasing ionic strength also lowers the surface potential through screening of the interfacial electric field.⁵⁰ Both processes lead to a decrease in the VSFS signal in the OH region.^{35,51} As such, the $K_{D,app}$ values are apparent binding constants that arise from a combination of binding and screening. Nevertheless, K^+ should have a binding affinity that is 10 times stronger than Li^+ , and about 3 times stronger than Na^+ . Integration of Langmuir trough surface pressure-area (Π -A) isotherms confirmed the $K^+ > Na^+ > Li^+$ affinity order for ESO_4 monolayers (**Section S8**).

The data in **Figure 2** and **Section S8** demonstrated that the affinity of cations for packed ESO_4 monolayers follow the LMWA prediction.³⁻⁶ Unfortunately, neither Π -A isotherm measurements nor VSFS measurements in the OH stretch region provide direct insight as to whether alkali metal cations bind to the surfactant headgroups via contact ion pair formation or through solvent shared ion pairing. To obtain this information, VSFS spectra of the $\nu_{ss}(SO_3^-)$ mode of ESO_4 monolayers were obtained in the presence of increasing subphase concentration of LiCl, NaCl, and KCl (**Figure 3A-C**). The hydrated $\nu_{ss}(SO_3^-)$ mode

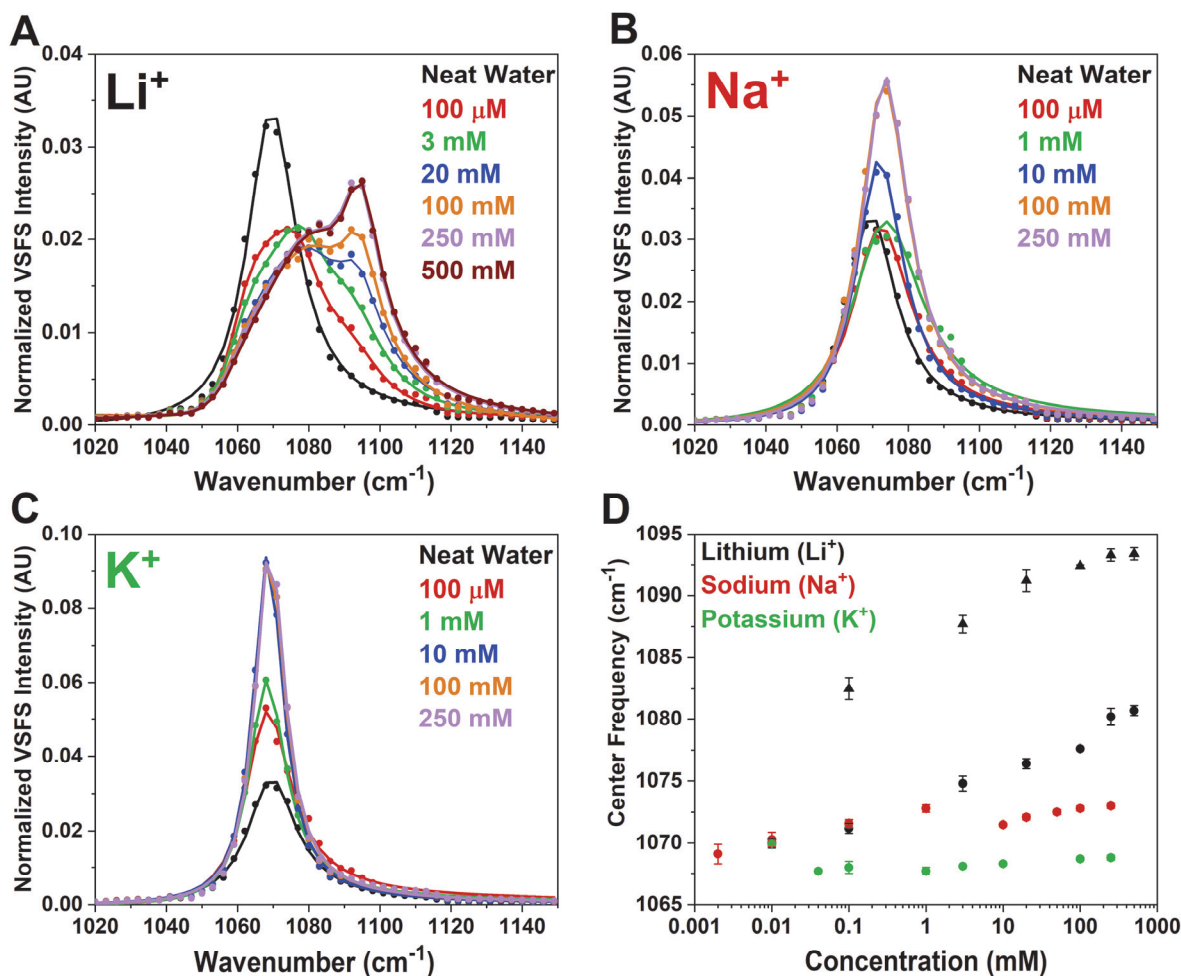


Figure 3. VSFS spectra of the $\nu_{\text{ss}}(\text{SO}_3^-)$ resonance from an ESO_4 monolayer over a subphase containing (A) LiCl , (B) NaCl , and (C) KCl at an MMA of $23 \pm 1 \text{ \AA}^2$ with the SSP polarization combination. The MMA was determined from Langmuir trough pressure-area (Π -A) isotherms (**Section S3**). All subphase contained 100 μM MOH with sufficient MCl to achieve the desired alkali metal ion concentration. In all cases where the salt concentration was $\geq 1 \text{ mM}$, 4 μM EDTA was included to chelate trace metal contaminants. All experiments were run at $21 \pm 1 \text{ }^\circ\text{C}$ and $\text{pH } 9.3 \pm 0.1$. The colored circles are experimental data points representing the average of at least 3 trials and the solid lines are fits to the spectra. (D) The center frequency of the spectral features are plotted against cation concentration. For Li^+ , the higher frequency peak is plotted with triangles and the lower frequency peak is plotted with circles. “Neat water” actually contains 2 μM Na^+ , due to its presence in the NaESO_4 salt used to form the monolayer and this data point is therefore plotted with the rest of the sodium data. Additional spectra are provided in **Section S9**. Additional analysis, including spectral measurement in PPP and SPS polarization, is provided in **Section S10**.

from a densely packed dodecyl sulfate monolayer occurs at $\sim 1070 \text{ cm}^{-1}$.⁵² Hydration of these negatively charged functional groups transfers a small amount of electron density into the

hydrating water molecules, which red shifts the vibrational mode to lower frequency relative to the gas phase peak or the one obtained with the solid salt.^{53,54} Contact ion pairs partially dehydrate the anionic functional group. However, alkali metal cations cannot accept excess electron density. As such, the frequency shifts back toward the blue upon contact ion pair formation with these metal cations.^{22,55–61}

The center frequency for the fitted data in **Figure 3(A-C)** is plotted in **Figure 3D** with the fitting parameters for 250 mM salt in **Table 1**. The spectra over LiCl subphases required 2 peaks to fit the data while the other spectra could be fit to a single peak. As can be seen, the center of mass for the Li⁺ spectra already shifted to higher frequency by introducing 100 μ M of the corresponding hydroxide salt and 2 distinct peaks were evident. The high frequency peak grew in continuously up to 250 mM LiCl, after which point little additional spectral changes were observed. The high frequency peak was blue-shifted by approximately 25 cm⁻¹ with respect to the reference peak over neat water as it approached the saturation point. By contrast, the lower frequency peak was blue-shifted by 12 cm⁻¹ at the highest concentration and this shift occurred over the entire concentration range. Next, the Na⁺ peak blue-shifted only 4 cm⁻¹ with respect to the reference peak. Moreover, the resonance frequency stopped changing by 100 mM NaCl. Finally, the peak associated with K⁺

Table 1. Fitting parameters for $\nu_{ss}(\text{SO}_3^-)$ resonance over 250 mM MCl.

	Water	LiCl	NaCl	KCl
Center Frequency (ω_n , cm ⁻¹)	1069.1 (0.8)	1081.5 (0.7) ^a 1093.7 (0.4) ^b	1073.2 (0.1)	1068.7 (0.1)
Half-Width at Half-Max (Γ , cm ⁻¹)	8.4 (0.3)	18 (1) ^a 6.6 (0.8) ^b	8.1 (0.2)	5.1 (0.1)

^aLow frequency peak

^bHigh frequency peak

maintained a center frequency within $\pm 1 \text{ cm}^{-1}$ of the reference peak over the entire concentration range. Nevertheless, this peak markedly increased in intensity and narrowed as KOH/KCl was added. This is consistent with an increase in environmental homogeneity of the pendant sulfate group at constant MMA when K^+ is present in the subphase relative to Na^+ or Li^+ .^{62,63} The same intensity trend is seen in the antisymmetric stretching mode (**Section S10**). It is also consistent with the relatively small methylene signatures over K^+ subphases found in **Figure 2C**. The peak shifts observed herein are surprising, as dehydration of pendant sulfate groups through contact ion pair formation follows the order $\text{Li}^+ > \text{Na}^+ > \text{K}^+$. This is opposite to the trend for the thermodynamic binding measurements in **Figure 2** and **Section S8**. Also, changing the identity of the anion from Cl^- to OH^- had no noticeable effect on these results (**Section S11**).

In a final set of experiments, the influence of surface charge density on the nature of ion pairing between the alkali metal cations and the ESO_4 monolayer was explored by replacing some of the fatty sulfate groups with fatty alcohols. VSFS data from the $\nu_{\text{ss}}(\text{SO}_3^-)$ mode of these mixed monolayers was collected over 250 mM LiCl, NaCl, and KCl at ESO_4 mole fractions (χ_{ESO_4}) of 0.20, 0.33, and 0.50 (**Figure 4**). As can be seen, there was little difference in the peak position or line shape amongst the cations at 0.20 and 0.33 χ_{ESO_4} and no indication of either ion specific dehydration or contact ion pair formation was found. However, the $\nu_{\text{ss}}(\text{SO}_3^-)$ spectra at 0.50 χ_{ESO_4} revealed significant dehydration of the pendant sulfate group when Li^+ was present in the subphase. A modest peak shift was also observed for Na^+ in comparison with K^+ . As such, the 0.50 χ_{ESO_4} spectra resembled the data obtained with pure ESO_4 monolayers (**Figure 3**).

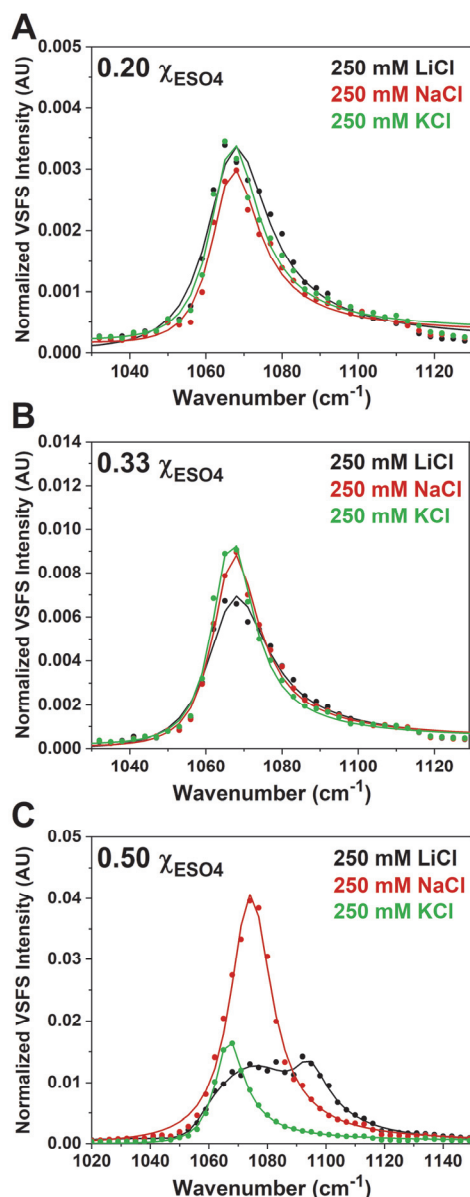


Figure 4. VSFS spectra of $\nu_{ss}(\text{SO}_3^-)$ resonance from mixed monolayers of ESO₄ and eicosanol at (A) 0.20 χ_{ESO_4} , (B) 0.33 χ_{ESO_4} , and (C) 0.50 χ_{ESO_4} at an MMA of $21 \pm 0.5 \text{ \AA}^2$ with the SSP polarization combination. The subphase contains 250 mM MCl and 100 μM MOH of the corresponding alkali metal hydroxide, in addition to 4 μM EDTA to chelate trace metal contaminants. The pH was 9.3 ± 0.1 at a temperature of $21 \pm 1 \text{ }^\circ\text{C}$ under all conditions. The colored circles are experimental data points representing the average of at least 3 trials and the solid lines are fits to the spectra. Additional details are provided in **Section S12**.

For hexagonal packing, a 0.33 χ_{ESO_4} monolayer is the highest concentration that would still allow every pendant sulfate to be completely surrounded by alcohol functional groups (**Figure 5**). Such isolation of the sulfate headgroups may be expected to occur since they are negatively charged and will repel each other. Moreover, since contact ion pair formation was not observed with LiCl at 0.33 χ_{ESO_4} , contact ion pairing between Li^+ and pendant sulfate presumably involves the bridging of adjacent headgroups by metal ions (**Figure 1**).

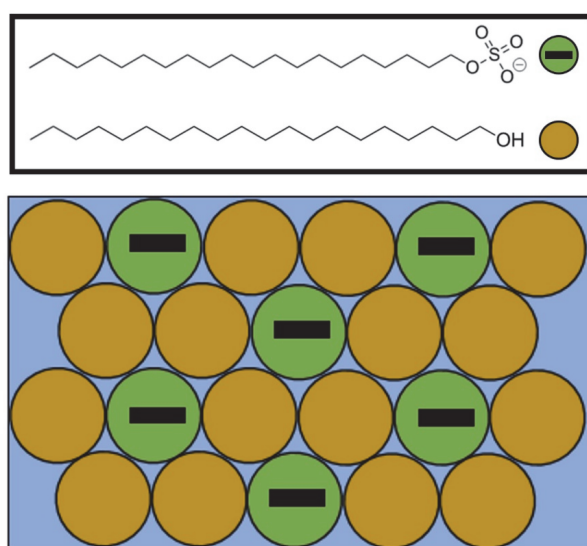


Figure 5. Overhead view of a mixed monolayer of ESO_4 and eicosanol at 0.33 χ_{ESO_4} .

In contrast to the results herein, fatty carboxylate monolayer systems show the same trend for binding and contact ion pair formation with the same alkali metal cations. Specifically, Li^+ binds the strongest^{14,16} and has the greatest propensity to form contact ion pairs.²² We performed a parallel set of studies with arachidic acid and found the binding constant and contact pair trends both followed the order: $\text{Li}^+ > \text{Na}^+ > \text{K}^+$ (**Section S13**). Since different systems can exhibit opposite trends, the question naturally arises as to when

contact pairing versus solvent shared pairing should be expected. Ion pairing in aqueous solutions is a relatively complex process compared to the analogous pairing process in the absence of water. Moreover, the gas phase interaction between Li^+ and the sulfate headgroup should be more free energy favorable than for K^+ , as Li^+ can sit closer to the anion. At the air/water interface, however, K^+ has a substantially greater affinity for sulfate. In aqueous solutions, both the cation and anion may shed hydration water during the binding process. These hydration waters are then released into the bulk solution where new water-water interactions are formed. Typically, there are free energy costs associated with shedding hydration water around each ion and free energy gains associated with the ion pairing event as well as with the formation of new water-water interactions.

When K^+ interacts with sulfate, the free energy dehydration penalty for removing water from around the cation should be smaller than with Li^+ , since the ion pairing interaction only involves solvent shared pairing. Moreover, K^+ is a larger ion that holds its waters less tightly. Nevertheless, the additional dehydration penalty is paid in the Li^+ system since a stronger contact pair can be formed. The dehydration costs associated with contact pair formation with Li^+ , however, are sufficiently high that the dissociation constant between Li^+ and sulfate is weaker. Li^+ only pays this cost when it is able to bridge two sulfate moieties. One possible reason for this could be the need to displace fewer hydration waters in a bridging geometry compared with one-to-one contact pair formation. Indeed, some hydration water between the anionic headgroups is already released through the compression of the monolayer by the trough barriers.

Since the work herein does not support the idea that stronger binding necessarily means contact pair formation, it might be tempting to conclude that smaller cations have a higher propensity to form contact pairs when the anion identity is kept constant. Indeed, the free energy gain with smaller cations should be enthalpically more favorable. However, there are counterexamples in the literature where it has been found that larger cations more easily form contact pairs with a common anion compared with smaller cations. For example, Ca^{2+} bridges phosphate moieties between adjacent phosphate groups on phosphatidylinositol 4,5-bisphosphate (PI(4,5)P₂) lipids in biomembranes, while the smaller Mg^{2+} ion forms more solvent shared structures.⁶¹ Undoubtedly, a general model for contact pairing in aqueous solutions will ultimately need to consider the hydration thermodynamics, the charge, as well as the chemical structure of the ions. Indeed, these are the same parameters that Fajans originally suggested would be decisive for predicting the solubility of salts 100 years ago.² In addition to these ideas, multivalency and the spatial positioning of the ions can also be decisive as indicated by the data in **Figure 4**.

In summary, the work herein demonstrates that stronger ion affinity does not necessarily correlate with a greater propensity to form contact ion pairs. Although the equilibrium dissociation constant for K^+ to pendant sulfate headgroups is an order of magnitude stronger than for Li^+ (**Figure 2**), K^+ interacts with the sulfate moiety exclusively through solvent shared interactions (**Figure 3C**). By contrast, Li^+ can form contact ion pairs above a threshold ESO_4 surface density (**Figures 3A & 4C**). This is significant, as it reveals specific circumstances under which contact ion pair formation does not follow the same order as the dissociation constant but instead follows a reverse trend.

Associated Content

Supporting Information

The Supporting Information is available free of charge at <http://pubs.acs.org/>.

Thermodynamic hydration values, materials and methods, VSFS fitting ranges, Π -A isotherms for all conditions, deprotonation of monolayers, binding constant fitting, interference of VSFS signal at low ionic strength, surface charge density calculations, compression free energy of Π -A isotherms, additional VSFS spectra of the $\nu_{ss}(\text{SO}_3^-)$ resonance, plotted fit parameters of the $\nu_{ss}(\text{SO}_3^-)$ resonance, SPS and PPP polarization combination VSFS spectra of the $\nu_{ss}(\text{SO}_3^-)$ resonance, interaction of MOH and ESO_4 , Π -A isotherms for mixed ESO_4 /eicosanol monolayers, plotted fit parameters for the $\nu_{ss}(\text{SO}_3^-)$ resonance of mixed ESO_4 /eicosanol monolayers, interaction of MOH and arachidic acid, and MATLAB fitting parameters with error ranges for all the VSFS spectra (PDF)

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Notes

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