

Molecular Dynamics Simulations of Ionic Interactions with Dodecyl Sulfate Micelles

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Specific ion effects on micelles have been addressed by molecular dynamics simulations of Li^+ , Na^+ , and NH_4^+ cations with dodecyl sulfate (DS) micelles in aqueous solution. Of the three systems, the most compact structure for a dodecyl sulfate micelle is observed in the case of Li^+ ions, which penetrate considerably deeper into the micelle than either Na^+ or NH_4^+ . Comparison of molecular trajectories of micellar solutions and those of methyl sulfate solutions with the same counterion demonstrates that the micelle surface is effective at disrupting the ionic hydration shells to allow direct cation–sulfate interaction. The structure of the second coordination shell of the sulfate groups on the micelle surface is, in turn, affected by the cations involved in contact ion pairs. The 4.9 Å peak in the sulfur–sulfur radial distribution function (rdf) in the LiDS micelle was attributed to direct coordination of two or more headgroups to a lithium ion. A second peak in the rdf is 1.2 Å farther, corresponding to a water molecule intervening between Li^+ and one of the sulfates. The sulfur–sulfur rdfs for both NaDS and NH_4DS feature single peaks at distances that suggest a lesser role of these cations in headgroup structuring. The direct coordination of the ions to the headgroups requires their dehydration and shows that hydrated-ion radii are inadequate for models of the micelle interfacial region.

Introduction

Dodecyl sulfate (DS) is an amphiphile that forms micelles when its concentration in aqueous solution reaches a critical micelle concentration (cmc), which varies with different counterions. Molecular dynamics (MD) simulations of spherical NaDS micelles have provided insights into the shape, degree of water penetration into the interior, and degree of neutralization by counterions.^{1–4} NaDS micelles comprised of 60 monomers are very spherical, with an average ratio of their maximum to minimum moments of inertia $I_{\text{min}}/I_{\text{max}}$ of 1.05 and with a degree of counterion binding of 25% over a five nanosecond trajectory.^{3,4} Another, shorter (138 ps) trajectory of the 60-monomer NaDS micelle indicated a water-impenetrable core of 12 Å,² whereas a 217 ps simulation of a 42-monomer NaDS system showed a 9 Å impenetrable core. MD simulations have also characterized other anionic micelles, including sodium octanoate^{5–11} and cesium pentadecafluorooctanoate,^{12,13} as well as the cationic systems nonyl trimethylammonium chloride¹⁴ and decyl trimethylammonium chloride.¹⁵

In the majority of studies involving ionic micelles, counterions were found to form contact pairs with headgroups as evidenced by the maxima in the headgroup–ion radial distribution functions (rdfs) observed at positions corresponding to the sum of the van der Waals radii of the counterion and headgroup atoms. The number of such counterions is typically 0.3–0.6 per headgroup. It was observed in the case of an aqueous sodium octanoate micelle that incorporation of polarization effects precluded the formation of contact pairs.⁸ However, that study included only induced polarization in the amphiphiles while water molecules were not polarizable and water–octanoate interaction parameters were not readjusted for polarization effects. Similarly, counterions were found to be separated from headgroups by a hydration sheath when the simulation of a

dodecyl sulfate micelle² was performed with the CHARMM22 force field²¹ as well as in one simulation of a sodium octanoate micelle employing the AMBER force field.⁸ However, failure to detect contact ion pairs in the latter work does not agree with several previous studies of this system^{5–7} using similar interaction parameters and, in our view, could arise from a less-than-optimal choice for the starting configuration adopted by the authors, which was not fully equilibrated in the first 100 ps allotted.⁸ It must be pointed out that several studies^{1,2,7} encompassing only a few hundred picoseconds report a pronounced drift of the center of mass of counterions during the production run, suggesting that the ionic atmosphere was not yet in equilibrium with the micelle. In fact, from a recent work by Bruce et al.,³ it is evident that at least 1 ns of dynamics is required to reach a stable counterion distribution.

It is noteworthy that the studies of a cesium pentadecafluorooctanoate micelle by Balasubramanian et al.^{12,13} thus far represent the only example where an anionic micelle was neutralized by cations other than Na^+ . Taking into account the well-known dependence of the properties of ionic micelles upon the size, charge, and chemical identity of counterions, which is best studied for dodecyl sulfate micelles,^{22–26} we feel that molecular dynamics simulations of dodecyl sulfate micelles involving other cations are in order. The results can be compared with the already available MD data on the NaDS system and aid in the interpretation of the experimental data.

Methods

To understand the interaction of counterions with micelles, we performed a series of classical molecular dynamics simulations. Two types of systems were treated in the simulations. The first system consisted of a DS micelle solvated with water and neutralized by Li^+ , Na^+ , or NH_4^+ ions. The second system was not micellar but rather an aqueous solution of methyl sulfate with the same counterions. LiDS and NaDS micelles contained 60 monomers. This is the aggregation number for which the

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most recent MD data are available in the literature on the NaDS system.^{2–4} Adopting the same value for LiDS is based on the closeness of the critical micelle concentrations for the two systems²⁷ and the fact that at this surfactant concentration in the absence of added salt the aggregation numbers for LiDS and NaDS are the same.²⁸ The NH₄DS micelle consisted of 80 monomers. The choice for the micelle size is somewhat arbitrary since this system has been studied to a much lesser extent than NaDS. However, the experimental data currently available indicate that a lower concentration of ammonium salt is required to induce the sphere–rod transition of sodium dodecyl sulfate compared to sodium or lithium salts²⁹ and that at the same added salt concentration the aggregation number of DS micelles is higher for NH₄⁺ than for Na⁺.^{30,31} For each counterion, the same number of methyl sulfate anions was introduced into the second system, and its size was chosen so that the equilibrated volume was approximately equal to that of the corresponding micellar solution.

Molecular trajectories were calculated using the AMBER 6 program package.³² The simulations were performed for the pressure of 1 atm while maintaining the temperature at 300 K with the help of the Berendsen temperature coupling method.³³ The time step was 2 fs. Nonbonded interactions were cut off at 10 Å. Long-range electrostatic forces were handled using the Particle Mesh Ewald technique³⁴ implemented in AMBER 6. Stretching motion was removed from bonds involving hydrogen atoms using the SHAKE algorithm.³⁵ In DS and methyl sulfate anions, the oxygen atoms were numbered starting from the ester oxygen; the first carbon atom was the one closest to the sulfate group. Values for the parameters were taken from the parm94 force field of AMBER 6 and supplemented by those of Huige and Altona.³⁶ Atomic charges for the dodecyl sulfate anion were those found in the study of Bruce et al.³

The starting micelle, consisting of all-trans dodecyl sulfate chains, was created as previously described.³⁷ In a series of successive energy minimization cycles the radius of the micelle was gradually brought down from 25.0 to 19.6 Å. Then the micelle was neutralized by counterions followed by addition of TIP3P³⁸ water molecules. To simulate an infinite solution, simple cubic periodic boundary conditions were applied to the system. To equilibrate the water subsystem, 25 ps of dynamics was performed when only the water molecules were allowed to move and the coordinates of the micelle and counterions were frozen. The entire system was subsequently equilibrated during a 75 ps dynamics run whereupon the overall density stabilized around 1.0 g/cm³ (simulation box dimensions are approximately 65 × 65 × 65 Å³). After that, 2 ns of production dynamics were performed, saving the system's coordinates every 400 fs. Simulation protocol for methyl sulfate solutions was chosen so as to match the corresponding micelle runs, except for a shorter production segment (1 ns).

Results and Discussion

When the micelle and counterions were allowed to move, the total energy and density of the system reached stable values after about 50 ps. Nonetheless, following the suggestion of Bruce et al.,³ only the last 1 ns portion of the 2 ns production trajectory was analyzed in each case in order to ensure that the equilibrium counterion distribution was attained. Equilibrated micelles had a slightly ellipsoidal shape (Table 1), with I_{\min}/I_{\max} close to the values reported by MacKerell² and Bruce et al.³ for the NaDS system. The size of the micelles, given by the radius of gyration R_g (Figure 1), increases in the series LiDS < NaDS < NH₄DS. Another measure of micelle size is the average position $R(S)_{\text{av}}$

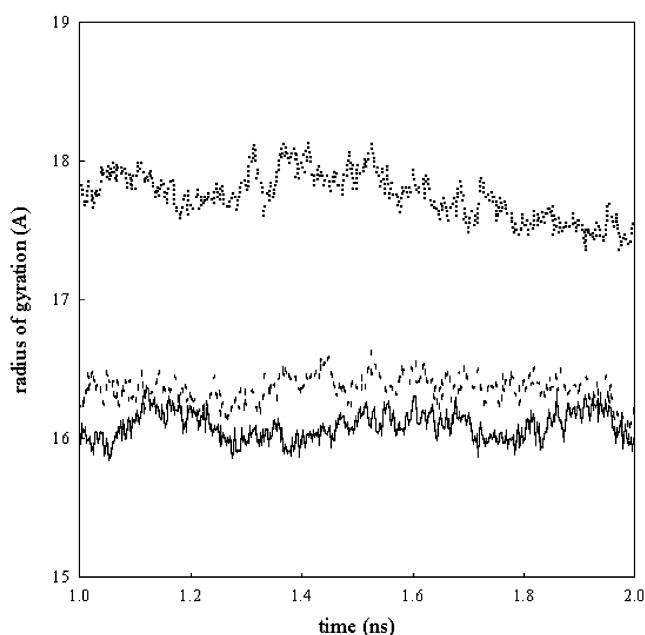


Figure 1. Radii of gyration of micelles during the second nanosecond of the production run. Solid line, LiDS; dashed line, NaDS; dotted line, NH₄DS.

TABLE 1: Structural Characteristics of Micelles

parameter	LiDS	NaDS	NH ₄ DS
I_{\min}/I_{\max}	1.08	1.09	1.10
R_g (Å)	16.1	16.4	17.8
$R(S)_{\text{av}}$ (Å)	19.5	19.9	21.2

of the headgroup sulfur atoms with respect to the micelle center of mass (COM), which follows the same trend as R_g with changing the counterion (Table 1). In their simulations of the NaDS micelle, Bruce et al. found $R_g = 16.2$ Å and $R(S)_{\text{av}} = 19.6$ Å, whereas MacKerell² cites an R_g of 16.0 Å and an $R(S)_{\text{av}}$ of 19.7 Å. The experimentally determined R_g for lithium dodecyl sulfate micelles³⁹ is 15.3 Å, in reasonable agreement with our value of 16.1 Å. As seen in Figure 2, apart from being the farthest from the micelle COM, the peak in the sulfur atom distribution for NH₄DS also exhibits a greater width compared to those for the smaller dodecyl sulfate micelles with Li⁺ and Na⁺ as counterions. Overall, it appears that, of the three counterions studied, Li⁺ leads to the most compact structure for a dodecyl sulfate micelle. Whereas swelling of the NH₄DS micelle can be attributed to the increased number of monomers comprising the micelle as compared to the LiDS and NaDS micelles, for the latter two, we observe clear evidence of the counterion effect upon micellar shape.

It is noteworthy that rdfs presented below were calculated by binning only the smallest distance out of all distances from the atom of choice to other atoms of the same type or to atoms of a different type. Integration of such an rdf provides the average number of atoms that can be found within a certain distance away from the atom of choice. Sulfur–sulfur rdfs for both NaDS and NH₄DS micelles feature single peaks positioned at 6.2 and 6.0 Å, respectively (Figure 3). In the case of Li⁺ counterions, there are two peaks of equal height in the S–S rdf, at 4.9 and 6.1 Å. The 1.2 Å difference between the peaks is close to the van der Waals radius of a water molecule. One could therefore surmise that the peak at 4.9 Å is due to headgroup arrangements where a lithium cation is directly coordinated to two or more headgroups at the same time, whereas the 6.1 Å peak arises when coordination to one of the headgroups is water-mediated and still direct to the other(s).

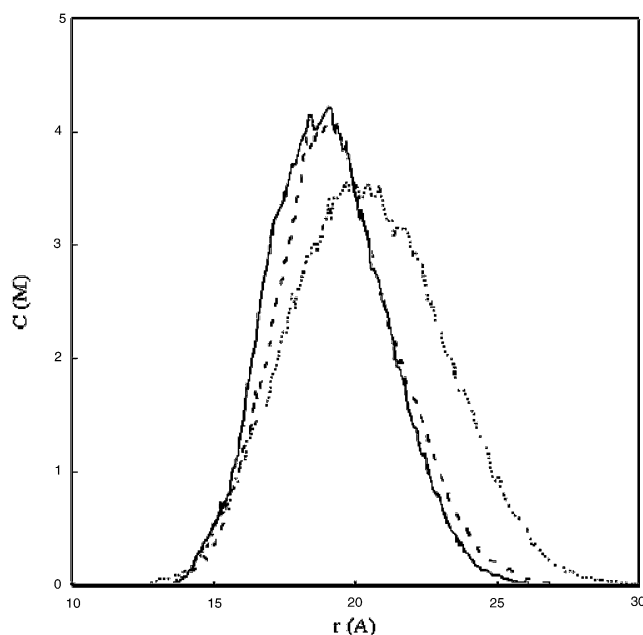


Figure 2. Concentration profiles of the headgroup sulfur atom with respect to the micelle center of mass. Solid line, LiDS; dashed line, NaDS; dotted line, NH₄DS.

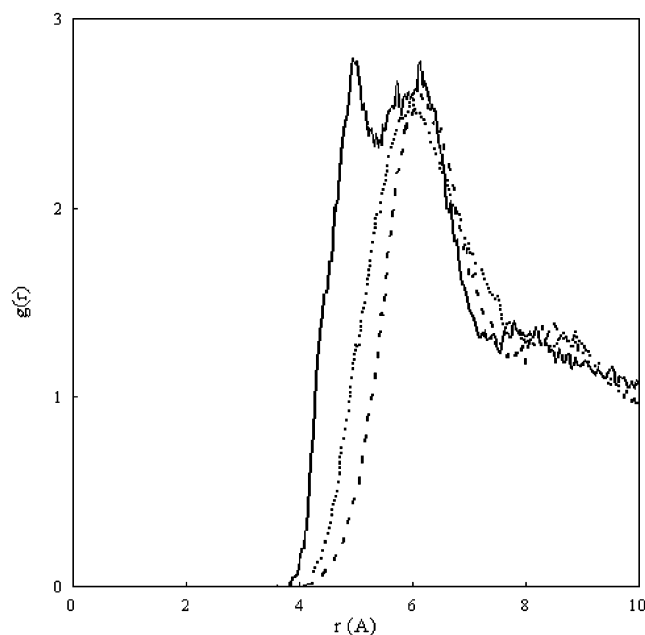


Figure 3. Sulfur-sulfur radial distribution functions. Solid line, LiDS; dashed line, NaDS; dotted line, NH₄DS.

Water-mediated bridging of headgroups by counterions may also explain the peaks near 6 Å observed for NaDS and NH₄DS.

To quantitatively characterize micelle-water and methyl sulfate-water interactions, we have calculated hydration numbers of their atoms (Table 2). This was done by integration of the rdfs of water oxygens around S and O₁₋₄ out to the first minimum (4.8 and 3.7 Å, respectively) and around C₁₋₁₂ out to 3.5 Å. In accordance with earlier results, we find that a sulfate headgroup in a micelle is coordinated on average to about eight water molecules, which are located predominantly near the anionic oxygens O₂₋₄. The level of headgroup hydration is somewhat higher in the NaDS system compared to LiDS or NH₄DS, and this is also true of the first four methylene groups. Hydration numbers for C₁₂ indicate that terminal chain segments in all of the micelles spend more time near the micelle-water

TABLE 2: Hydration Numbers of Dodecyl Sulfate and Methyl Sulfate Atoms

atom	LiDS	CH ₃ SO ₄ Li	NaDS	CH ₃ SO ₄ NH ₄	NH ₄ DS	CH ₃ SO ₄ NH ₄
S	8.7	11.8	9.4	11.7	8.3	11.5
O ₁	1.7	2.7	1.8	2.7	1.6	2.7
O ₂₋₄	7.7	9.7	8.4	9.7	7.4	9.5
C ₁	0.34	1.6	0.39	1.6	0.34	1.5
C ₂	0.24		0.26		0.23	
C ₃	0.12		0.14		0.13	
C ₄	0.07		0.08		0.06	
C ₅	0.06		0.06		0.07	
C ₆	0.04		0.05		0.05	
C ₇	0.05		0.05		0.04	
C ₈	0.04		0.04		0.04	
C ₉	0.04		0.04		0.05	
C ₁₀	0.04		0.04		0.05	
C ₁₁	0.06		0.05		0.06	
C ₁₂	0.14		0.13		0.15	

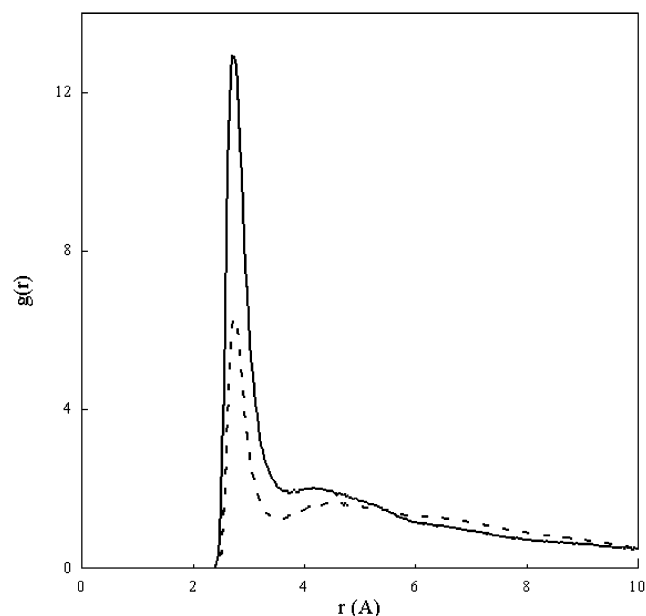
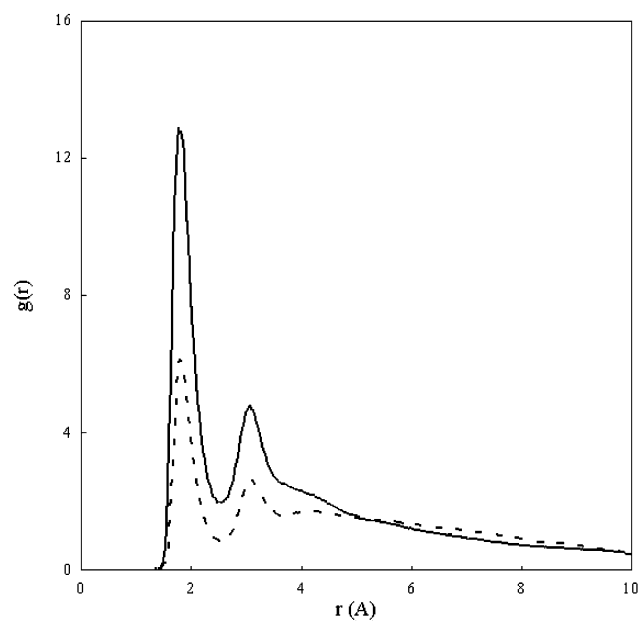
interface than do the central carbons, C₄-C₁₁. Table 2 shows that a sulfate group loses about three water molecules upon micellization. In contrast to cation-specific headgroup hydration in micelles, water coordination to methyl sulfates is almost insensitive to the cation nature. Another point of distinction is that the position of the second peak in O₂₋₄-O_{water} rdfs in all micellar systems is 0.3–0.5 Å closer to the anionic oxygens compared to methyl sulfate solutions (Figure 4a). At the same time, in O₂₋₄-H_{water} rdfs (Figure 4b), the peak positions are identical in both cases.

In Figure 5, the concentrations of the three counterions are plotted as a function of distance from the micelle COM. The concentration profiles peak at 19 Å (Li⁺), 20 Å (Na⁺), and 21 Å (NH₄⁺); no ions could be detected closer than 13 Å from the COM. The Li⁺ peak is the tallest one in Figure 5, but because of a steeper decay with distance, in the region between 22 and 28 Å from the micelle COM the concentration of lithium ions is smaller than that of sodium or ammonium ions.

We have also calculated radial distribution functions of counterions around the sulfur atoms of dodecyl sulfate (Figure 6) and methyl sulfate (not shown). These rdfs indicate that sulfur-ion separations in the contact (first peak) and solvent-separated (second peak) ion pairs increase in the series Li⁺ < Na⁺ < NH₄⁺ in both micellar and methyl sulfate solutions, which is consistent with their ionic radii. Except for NH₄DS, micellization appears to have little effect on the structure of the first ion coordination shell of sulfate as it leaves unchanged the position of the first peak in sulfur-ion rdfs. At the same time, judging from the second peak position in sulfur-ion rdfs, 0.3–0.5 Å contraction of the solvent-separated coordination shell of the ions is observed for dodecyl sulfate micelles compared to methyl sulfate solutions. The degree of counterion binding, estimated as the fraction of counterions under the first peak (from 0 Å to the first minimum) of the sulfur-ion rdfs, grows in the sequence Na⁺ < Li⁺ < NH₄⁺ (Table 3) in both simple electrolyte and polyelectrolyte, being roughly three times higher in the latter case. The steep increase in the number of cations directly bound to the sulfate groups in micellar as opposed to simple electrolyte solutions suggests an explanation to the observed shifts in the positions of the second peaks in the O₂₋₄-O_{water} and sulfur-ion rdfs. Water dipoles in the second coordination shell of the micelle change their orientation under the influence of the cations forming contact ion pairs with the headgroups. In the simple electrolyte solution, this change of water orientation occurs to a lesser extent owing to a smaller number of bound ions. The movement of the water molecules causes a corresponding decrease in the distance to the headgroup

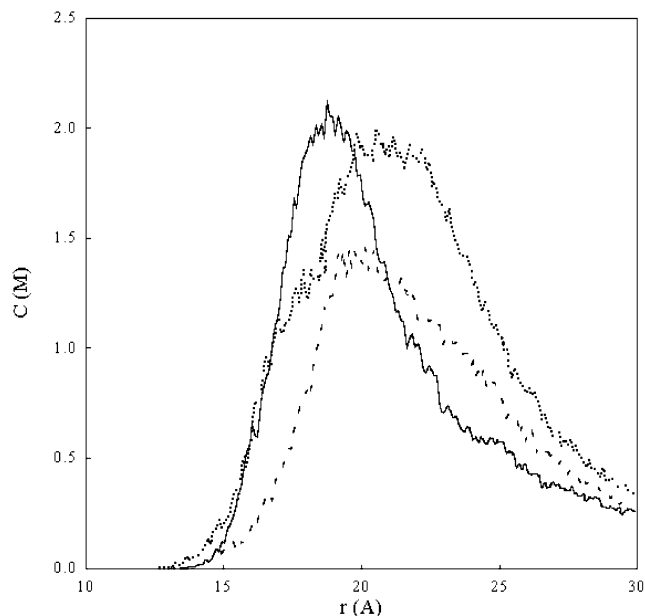
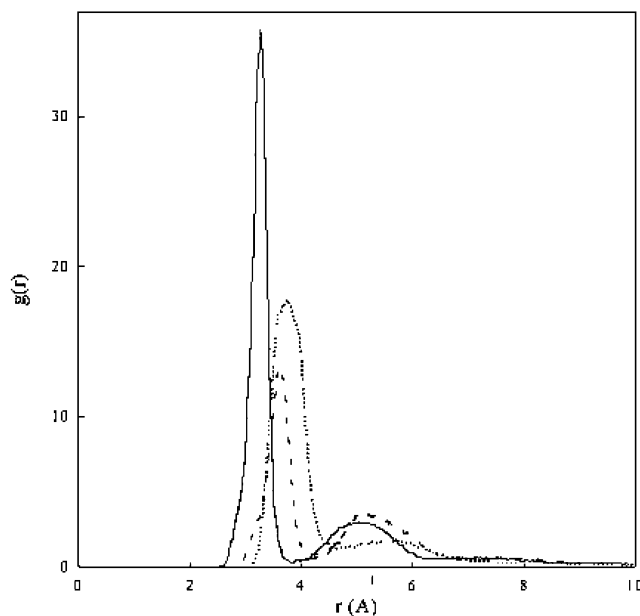
TABLE 3: Counterion Binding to Dodecyl Micelles and Methyl Sulfate Anions

system	LiDS	CH ₃ SO ₄ Li	NaDS	CH ₃ SO ₄ Na	NH ₄ DS	CH ₃ SO ₄ NH ₄
degree of counterion binding (%)	28	8	17	6	44	16
ions bound to one headgroup (%)	41		78		48	
ions bridging two headgroups (%)	28		20		28	
ions in 3-fold coordination (%)	31		2		24	

**a****b****Figure 4.** Radial distribution functions: (a) O₂₋₄-O_{water}; (b) O₂₋₄-H_{water}. Solid line, LiDS micelle; dashed line, CH₃SO₄Li solution.

of the second-shell cations, which are directly coordinated to those waters.

The percentages of the first-coordination-shell ions that simultaneously interact with one, two, and three headgroups are also reported in Table 3. Around 60% of Li⁺ and NH₄⁺ ions are engaged in the bridging of two or three headgroups with an almost equal probability of the bridging modes. These findings confirm our suggestion regarding the origin of the 4.9 Å peak in the S-S rdf for LiDS as being due to Li⁺ intercalation among

**Figure 5.** Ion concentration profiles with respect to the micelle COM. Solid line, Li⁺; dashed line, Na⁺; dotted line, NH₄⁺ (N).**Figure 6.** Sulfur-ion radial distribution functions in solutions of dodecyl sulfate micelles. Solid line, Li⁺; dashed line, Na⁺; dotted line, NH₄⁺ (N).

the headgroups. The high bridging propensity of lithium cations stems from their small radii, while it is likely that ammonium cations form multiple hydrogen bonds with anionic oxygens of adjacent headgroups. Also, in agreement with the results of Bruce et al.,³ we find that nearly three-quarters of Na⁺ ions are singly coordinated and the rest are bound almost exclusively to two headgroups. Our findings for the alkali metal ions are in line with the experimental observations²³ that Li⁺ interacts more strongly with the micellar surface than does Na⁺.

Conclusions

Our calculations are in general agreement with the results of the previous simulations of ionic micelles. For all of the counterions studied, the micelle remains nearly spherical on the nanosecond time scale and its core is devoid of water. Of the three counterions, Li^+ leads to the most compact structure for a dodecyl sulfate micelle. The 4.9 Å peak in the sulfur–sulfur rdf of the LiDS system is due to ion-bridged headgroup arrangements. For NaDS and NH_4DS , direct ion bridging plays a lesser role in the headgroup structuring at the micelle surface. The sulfur-ion distances in the contact and solvent-separated ion pairs increase in the series $\text{Li}^+ < \text{Na}^+ < \text{NH}_4^+$ in micellar and methyl sulfate solutions, which is consistent with their ionic radii.

Except for ammonium ions, micellization appears to have little effect on the structure of the first coordination shell of sulfate. At the same time, judging from the second peak positions in the $\text{O}_{2-4}-\text{O}_{\text{water}}$ and sulfur-ion rdfs, a 0.3–0.5 Å contraction of the second coordination shell of the headgroups is observed for dodecyl sulfate micelles compared to methyl sulfate solutions. One can conclude that water dipoles in the second coordination shell of dodecyl sulfate micelles change their orientation under the influence of cations forming contact ion pairs with the micelle headgroups, causing a concomitant contraction of the second coordination shell of counterions as compared to methyl sulfate solutions.

The loss of waters of hydration from the simple electrolyte ions and their intimate interaction with the headgroups implies that models of the interfacial region cannot simply rely on hydrated ion radii (e.g., derived from electrokinetic measurements) to describe the surface of ionic micelle. On the contrary, judging from our data, it appears that bare (crystallographic) ion radii are a better measure of the ion size in this case.

References and Notes

- (1) Shelley, J.; Watanabe, K.; Klein, M. L. *Int. J. Quantum Chem.: Quantum Biol. Symp.* **1990**, *17*, 103–117.
- (2) MacKerell, A. D. *J. Phys. Chem.* **1995**, *99*, 1846–1855.
- (3) Bruce, C. D.; Berkowitz, M. L.; Perera, L.; Forbes, M. D. E. *J. Phys. Chem. B* **2002**, *106*, 3788–3793.
- (4) Bruce, C. D.; Senapati, S.; Berkowitz, M. L.; Perera, L.; Forbes, M. D. E. *J. Phys. Chem. B* **2002**, *106*, 10902–10907.
- (5) Jönsson, B.; Edholm, O.; Teleman, O. *J. Chem. Phys.* **1986**, *85*, 2259–2271.
- (6) Watanabe, K.; Ferrario, M.; Klein, M. L. *J. Phys. Chem.* **1988**, *92*, 819–821.
- (7) Shelley, J.; Watanabe, K.; Klein, M. L. *Electrochim. Acta* **1991**, *36*, 1729–1734.
- (8) Shelley, J. C.; Sprik, M.; Klein, M. L. *Langmuir* **1993**, *9*, 916–926.
- (9) Kuhn, H.; Rehage, H. *Ber. Bunsen-Ges. Phys. Chem.* **1997**, *101*, 1485–1492.
- (10) Kuhn, H.; Rehage, H. *Ber. Bunsen-Ges. Phys. Chem.* **1997**, *101*, 1493–1500.
- (11) Kuhn, H.; Breitzke, B.; Rehage, H. *J. Colloid Interface Sci.* **2002**, *249*, 152–161.
- (12) Balasubramanian, S.; Bagchi, B. *J. Phys. Chem. B* **2001**, *105*, 12529–12533.
- (13) Balasubramanian, S.; Bagchi, B. *J. Phys. Chem. B* **2002**, *106*, 3668–3672.
- (14) Maillet, J.-B.; Lachet, V.; Coveney, P. V. *Phys. Chem. Chem. Phys.* **1999**, *1*, 5277–5290.
- (15) Böcker, J.; Brickman, J.; Bopp, P. *J. Phys. Chem.* **1994**, *98*, 712–717.
- (16) Wendoloski, J. J.; Kimatian, S. J.; Schutt, C. E.; Salemme, F. R. *Science* **1989**, *243*, 636–638.
- (17) Marrink, S. J.; Tieleman, D. P.; Mark, A. E. *J. Phys. Chem. B* **2000**, *104*, 12165–12173.
- (18) Wymore, T.; Gao, X. F.; Wong, T. C. *J. Mol. Struct.* **1999**, *485*–486, 195–210.
- (19) Tieleman, D. P.; van der Spoel, D.; Berendsen, H. J. C. *J. Phys. Chem. B* **2000**, *104*, 6380–6388.
- (20) Bogusz, S.; Venable, R. M.; Pastor, R. W. *J. Phys. Chem. B* **2000**, *104*, 5462–5470.
- (21) MacKerell, A. D.; Bashford, D.; Bellott, M.; Dunbrack, R. L.; Evanseck, J. D.; Field, M. J.; Fischer, S.; Gao, J.; Guo, H.; Ha, S.; Joseph-MacCarthy, D.; Kuchnir, L.; Kuczera, K.; Lau, F. T. K.; Mattos, C.; Michnick, S.; Ngo, T.; Nguyen, D. T.; Prodhom, B.; Reiher, W. E.; Roux, B.; Schlenkrich, M.; Smith, J. C.; Stote, R.; Straub, J.; Watanabe, M.; Wiórkiewicz-Kuczera, J.; Yin, D.; Karplus, M. *J. Phys. Chem. B* **1998**, *102*, 3586–3616.
- (22) Mukerjee, P.; Mysels, K. J.; Kapauan, P. *J. Phys. Chem.* **1967**, *71*, 4166–4175.
- (23) Jones, R. R. M.; Maldonado, R.; Szajdzinska-Pietek, E.; Kevan, L. *J. Phys. Chem.* **1986**, *90*, 1126–1129.
- (24) Gustavsson, H.; Lindman, B. *J. Am. Chem. Soc.* **1978**, *100*, 4647–4654.
- (25) Ropers, M. H.; Czichocki, G.; Brezesinski, G. *J. Phys. Chem. B* **2003**, *107*, 5281–5288.
- (26) Aswal, V. K.; Goyal, P. S. *Phys. Rev. E* **2000**, *61*, 2947–2953.
- (27) Mukerjee, P. *Adv. Colloid Interface Sci.* **1967**, *1*, 241.
- (28) Bales, B. L.; Shanin, A.; Lindblad, C.; Almgren, M. *J. Phys. Chem. B* **2000**, *104*, 256–263.
- (29) Nguyen, D. T.; Bertrand, G. L. *J. Phys. Chem.* **1992**, *96*, 1994–1998.
- (30) Kumar, S.; David, S. L.; Aswal, V. K.; Goyal, P. S.; Kabir-ud-Din. *Langmuir* **1997**, *13*, 6461–6464.
- (31) Kumar, S.; Aswal, V. K.; Goyal, P. S.; Kabir-ud-Din. *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 761–764.
- (32) Cornell, W. D.; Cieplak, P.; Bayly, C. I.; Gould, I. R.; Merz, K. M.; Ferguson, D. M.; Spellmeyer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 5179–5197.
- (33) Berendsen, H. J. C.; Postma, J. P. M.; Vangunsteren, W. F.; Dinola, A.; Haak, J. R. *J. Chem. Phys.* **1984**, *81*, 3684–3690.
- (34) Essmann, U.; Perera, L.; Berkowitz, M. L.; Darden, T. A.; Lee, H.; Pedersen, L. *J. Chem. Phys.* **1995**, *103*, 8577–8593.
- (35) Vangunsteren, W. F.; Berendsen, H. J. C. *Mol. Phys.* **1977**, *34*, 1311–1327.
- (36) Huige, C. J. M.; Altona, C. *J. Comput. Chem.* **1995**, *16*, 56–79.
- (37) Rakitin, A. R.; Pack, G. R. *Colloids Surf. A* **2003**, *218*, 265–276.
- (38) Jorgensen, W.; Chandrasekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. L. *J. Chem. Phys.* **1983**, *79*, 926–935.
- (39) Bendedouch, D.; Chen, S.-H.; Koehler, W. C. *J. Phys. Chem.* **1983**, *87*, 153–159.