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Note

Proton magic-angle spinning–NMR investigation of surfactant aqueous suspensions

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Abstract

In this Note we present the advantages of ^{1}H magic-angle spinning nuclear magnetic resonance (MAS-NMR) for the investigation of surfactant suspensions via transverse relaxation rate (R_2) measurements. ^{1}H-relaxation rates can be determined by the classical CPMG method from high-resolution spectra obtained either under conditions of liquid-state NMR for monomers and small spherical micelles or by using MAS-NMR for larger aggregates. For a mixture of alkyl dioxyethylene sulfate and alkylbetaine (80:20, w/w), up to a percentage of surfactant in water of 20%, we found that R_2 increased, in accordance with an increased micellar size and very likely the formation of an H_I phase. However, above 25%, R_2 decreased. This result suggests a change from a hexagonal to a lamellar phase that would be difficult to observe by proton NMR without magic-angle spinning because the lines would be very broad, or by light scattering because of sample opacity. This NMR approach seems to have been overlooked by the community of surfactant physical chemists. It can be complementary to other analytical techniques and presents the advantage of not requiring isotopic labeling.

Keywords: Magic-angle spinning; Surfactants; Relaxation time; Micelles; Hexagonal phase

1. Introduction

A classical sequence of phase transformation of surfactants in water as the concentration of surfactant increases is the following: monomers → micelles → hexagonal H_I phase → lamellar phase → reverse H_{II} phase → inverse micellar phase [1–3]. Nuclear magnetic resonance (NMR) is one of the numerous techniques that provide structural information on surfactant phases. In general, broadband NMR is used with ^{31}P, ^{2}H, or ^{14}N due to the anisotropic magnetic properties of these nuclei and the partial averaging by rapid and anisotropic motions specific to each phase that allows one to discriminate the type of aggregation of surfactants in water from the lineshape [4–7]. However, ^{2}H requires labeling, ^{31}P is present in phospholipids but rarely in surfactants, and ^{14}N has a very low sensitivity due to its low gyromagnetic ratio. In addition broad lines are in general incompatible with a high sensitivity.

^{1}H, on the other hand, is an abundant and sensitive nucleus and its chemical shift allows one to differentiate molecules in a heterogeneous mixture if lines are narrow enough. In the case of small surfactant micelles, the rotation correlation time of the aggregates associated with rapid diffusion of the amphiphiles around the micelle and the rapid exchange between monomers and micelles generally suffice to efficiently average out the dipolar interactions between neighboring protons. As the micelles grow in size, their reorientation takes more time and, eventually, severe line broadening appears so that ^{1}H NMR spectra consist of broad lines from which very little information can be extracted. As a consequence ^{1}H NMR investigations of surfactants have been generally limited to the recognition of the transition from small micelles to large micelles by taking advantage of the sudden increase in linewidth that takes place at such transitions [8]. A possible quantitative analysis of ^{1}H broadband NMR spectra can be performed by using the moment analysis. For example, a ^{1}H NMR moment study has been used

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to show the transition from the gel to the liquid-crystalline phase of dipalmitoylphosphatidylcholine in water [9]. The flexibility of membrane proteins embedded in lipids has also been investigated by broad line proton NMR using moment analysis [10]. However, the usual advantage of ^{1}H NMR, besides its sensitivity and the universal presence of protons in organic materials, is that molecules can be differentiated by their chemical shifts. In a mixture of lipids or surfactants there can be a superposition of several phases (for example, fluid and rigid) and one may want to know the composition of the various phases coexisting. Broad lines do not permit one to sort out the composition of selective components in a multiphase system.

Magic-angle spinning (MAS), a technique that is used to narrow the NMR lines in solids, is in general inefficient in ^{1}H spectroscopy because dipolar ^{1}H–^{1}H couplings are very large (up to 40 kHz) and generally homogeneous. Averaging out the line broadening would require an unrealistic sample rotation speed of 100 kHz. However, it has been shown that the particular molecular conformations and motions of lipid alkyl chains in the fluid phase of membranes reduce these couplings and render them inhomogeneous, so that high-resolution ^{1}H NMR of lipids can be obtained with multilamellar vesicles at a relatively low spinning speed (≈2–4 kHz) [11].

We have reported elsewhere the poor efficiency of line narrowing for intermediate size lipid vesicles with a diameter of about 100 nm because of incoherent averaging due to the Brownian motion of the vesicles [12]. We show here that spinning at low speed narrows the ^{1}H lines of surfactants micelles. The possibility of resolving different compounds in a mixture by high-resolution spectra should give the opportunity of using relaxation rates to analyze the motions and to control the sample homogeneity through specific linewidth measurements. In this Note, we present data obtained with mixtures of surfactants commonly used at an industrial scale, in particular for cosmetic applications: sodium alkyl dioxyethylene sulfate and *N*-alkyl-*N*,*N*-dimethyl-*N*-methylcarboxy ammonium.

2. Materials and methods

Sodium alkyl dioxyethylene sulfate, also named alkylether sulfate sodium salt (AES), and *N*-alkyl-*N*,*N*-dimethyl-*N*-methylcarboxy ammonium, also named alkylbetaine (AB), were provided by L'Oreal company and were dissolved in D_2O. Both surfactants have fatty chains containing 2/3 of dodecyl and 1/3 of tetradecyl alkyl chains. The average number of oxyethylene group per molecule was 2.2. NMR experiments were performed and processed on a Bruker Avance DMX 400-WB NMR spectrometer (^{1}H frequency of 400.13 MHz). Dilute solutions (up to 5% in weight of surfactant in water) were studied by solution NMR in a 5-mm-diameter glass tube. For more concentrated solutions (above 5%), the MAS equipment was necessary. The spinning speed of the 4-mm ZrO_2 MAS rotor was controlled to within 5 Hz at 8 kHz. The 90° pulses were 16 and 4.6 µs for the liquid probe and for the MAS probe, respectively. In all experiments, 4096 complex points were acquired. Prior to Fourier transformation, the data were zero-filled to 8192 points, exponentially multiplied with 10 Hz line broadening, and treated with automatic baseline correction. The reference frequency for ^{1}H was chosen such that frequency for chain terminal methyls was 0.9 ppm. Longitudinal relaxation T_1 ($T_1 = 1/R_1$) was measured by the classical inversion recovery sequence and transverse relaxation T_2 ($T_2 = 1/R_2$) by CPMG. 3D plots of linewidth and R_2 were made using Origin software.

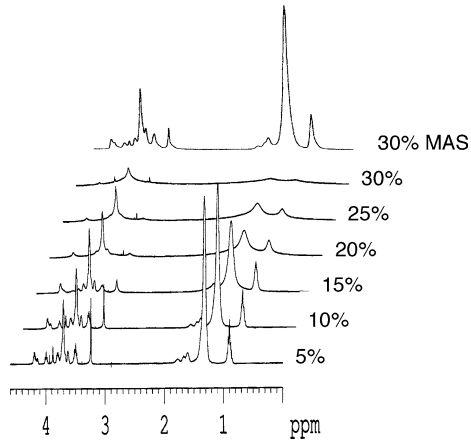

Fig. 1. ^{1}H NMR spectra of AES/AB (80/20) in D_2O as a function of surfactant concentration in D_2O (w:w). The lower six spectra are static, at 20 °C, and normalized to the same area. The upper spectrum is with 8 kHz magic-angle spinning, at 10 °C.

3. Results and discussion

3.1. Static vs magic angle-spinning ^{1}H NMR spectra

^{1}H NMR spectra of AES/AB (80/20, w:w) in D_2O are shown in Fig. 1, without MAS for several concentrations of surfactant, and with MAS for 30% surfactant. The critical micellar concentration (cmc) in water lies between 2.8 and 4.6 mM for AES [13] and 1.8 mM for AB [14] so that the first spectrum in Fig. 1 is already above the cmc. As the surfactant concentration increases, the number of visible peaks diminishes due to line broadening. The upper spectrum shows how magic-angle spinning affects the overall lineshape and restores the high resolution in ^{1}H NMR, in the case of a sample containing a high surfactant concentration. In our case, a spinning speed of 8 kHz is necessary to be able to separate well the methyl (0.9 ppm) from the methylene (1.3 ppm) resonance.

3.2. ^{1}H-linewidth vs ^{1}H-R_2 results

Fig. 2a shows the linewidth (LW) of the aliphatic CH_2 peak (1.3 ppm) plotted versus temperature and percentage

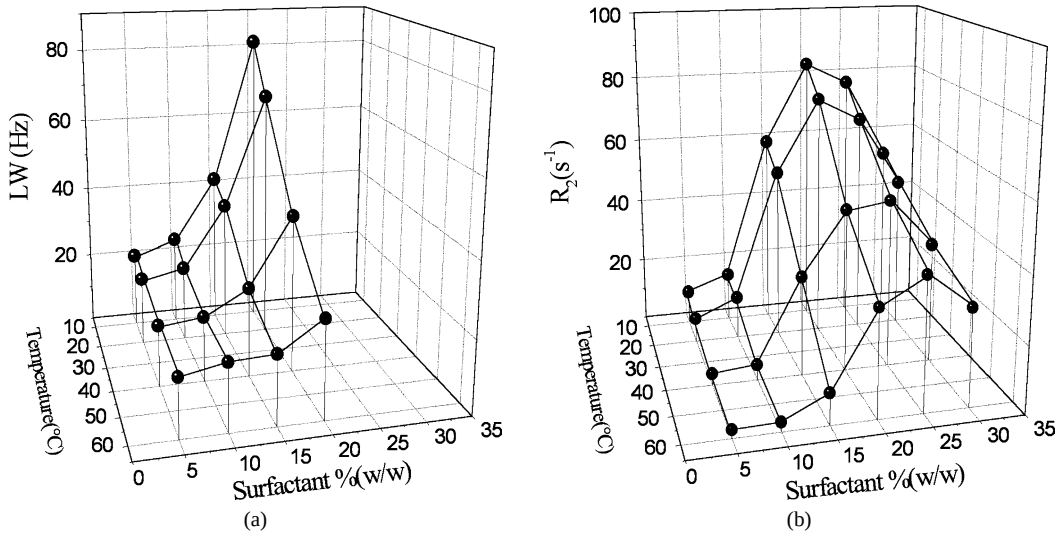

Fig. 2. (a) Linewidth of the CH_2 protons (1.3 ppm) measured on static samples as a function of surfactant concentration and temperature; (b) transverse relaxation rates R_2 of the CH_2 protons measured with MAS at 8 kHz, except for the very dilute samples where no spinning was applied. In (a) the uncertainty associated with the reproducibility of the measurement is 5% and only the points corresponding to peaks for which a meaningful measurement could be done are represented. In (b) the uncertainty is 0.5 s^{-1} for dilute samples and 5 s^{-1} for the more concentrated samples.

of surfactant. Without MAS, above 15% surfactant, LW is practically impossible to measure for each specific line, at least at temperatures below 60 °C. In these experiments, the physical parameter implicitly associated with LW is the mobility of the surfactant molecules and LW is likely to change drastically when the structure of the aggregates changes cooperatively [8,15]. Thus the rapid increase of LW between 10 and 20% surfactant is indeed indicative of a modification of micellar organization.

A more rigorous approach involves actual R_2 measurements and, for high surfactant concentrations, MAS is necessary to obtain narrow lines. One might be concerned about a possible perturbation of MAS on the CPMG method due to 180° pulses that could act as recoupling pulses for dipolar interaction [16]. However, we compared R_2 measurements carried out with a static liquid NMR probe and with magic-angle spinning in the case of a relatively low concentration of surfactant (5% in water) without seeing significant differences (data not shown). In Fig. 2b, R_2 values measured for the methylene peak are presented for the mixture of AES/AB (80/20) for different temperatures and concentrations. Similar results were obtained for the methyl (0.9 ppm) and the methyl ammonium (3.2 ppm) resonances.

Experiments with pure AES were also carried out (not shown). In the absence of AB, R_2 remained below 10 s^{-1} in the whole range of temperatures and concentrations. This suggests that there was no segregation of molecules in the original mixture, in particular no artificial segregation associated with the rapid spinning of the sample. Nevertheless, the detection of sample heterogeneities corresponding, for example, to a thermodynamic equilibrium involving the coexistence of several phases remains an interesting possibility offered in principle by this technique.

3.3. ^1H-R_2 vs ^1H-R_1 results

Fig. 3a shows R_1 and R_2 variations of methylene protons (1.3 ppm) with surfactant concentration at 40 °C while Fig. 3b indicates R_1 and R_2 variations as a function of temperature for a surfactant concentration of 20%. As shown in Fig. 3a, R_1 variation was very limited in the range of concentrations investigated, i.e., 0.1 to 20%, while R_2 increased by more than one order of magnitude in the same concentration range. By contrast R_1 and R_2 both decreased by a factor close to 3 when covering a range of temperatures between 10 and 60 °C (Fig. 3b).

3.4. Interpretation of the data

The increase in R_2 values when the surfactant concentration varies between 15 and 30% cannot be caused by a sudden very large increase of diameter of spherical micelles. In fact, the radius of a spherical micelle is roughly determined by the length of the hydrophobic stretch of the surfactant and *not* by the number of molecules [17]. Furthermore, the volume occupied by spherical micelles at a surfactant concentration of about 20% is not very large because micelles themselves form a condensed state. Thus, the most likely explanation of the increased apparent viscosity, hence of MAS efficiency, is a shape change of the micelles from spheres to tubules. Indeed, when the concentration of surfactants increases, micelles do not simply become more numerous, they interact and eventually fuse to form larger structures, with tubular shapes.

As discussed by Israelachvili [17], micelles comprising molecules with the proper packing factor, p, can be either spherical *or* tubular ($1/3 < p < 1/2$). Entropic considerations can explain the occurrence of spherical micelles at low

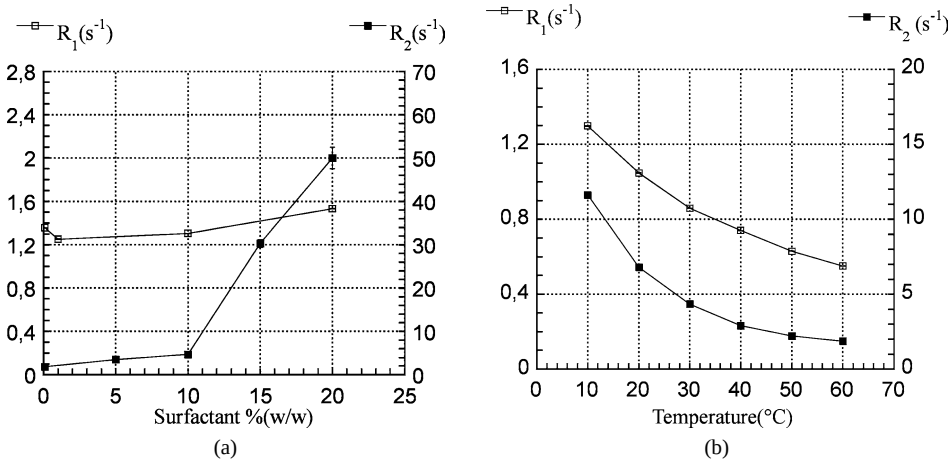

Fig. 3. R_1 and R_2 plots of CH_2 protons measured with MAS at 8 kHz: (a) as a function of surfactant concentration at 40 °C (data with 0.1 and 1% surfactant were obtained with no spinning); (b) as a function of temperature with 20% surfactant in D_2O.

concentrations while tubular micelles would be formed at high concentrations. The entanglement between elongated micelles reduces considerably their own mobility and raises the viscosity [18]. We interpret the R_2 increase, which took place at a surfactant concentration in water between 10 and 20% (Fig. 2b) as reflecting a transition from spherical micelles to tubular micelles, which is the expected evolution of the aggregation state of surfactants. Rods will eventually form an hexagonal H_I phase which is in fact a close packing of rods. The slow tumbling of free rods must be impeded by the packing and R_2 in the hexagonal phase, that is likely to replace the micellar phase, should continue to increase with the concentration of surfactants. Therefore the decrease of R_2 at high surfactant concentrations cannot be explained without assuming a completely new phase. This new phase is likely to be a lamellar phase. As pointed out by Thurmond et al. [19] one process of relaxation which is the rapid diffusion of amphiphiles around the axis of the tubules in elongated micelles or in a hexagonal phase disappears in the lamellar phase.

3.5. Comparison of R_1 and R_2 variations

R_1 generally reports on faster movement than R_2. Typically, molecular motions in the nanosecond time scale are responsible for changes of R_1 values. The fast motions are the *trans-gauche* isomerizations of the alkyl chains, i.e., motions that determine the microviscosity. Slow molecular motions (μs time scale) that are responsible for R_2 variations originate from the overall micellar tumbling, surfactant diffusion within micelles, and micellar undulations. Thus, increase in micelle size should affect R_2 but not R_1. In Fig. 3a, R_1 and R_2 are plotted as a function of surfactant concentration from 0.1 to 20%. The increase in R_2, as discussed above, is consistent with a modification of the micellar size and shape. The nearly constant R_1 value within this concentration range indicates that the viscosity within the micelles is not influenced by their overall shape. On the other hand, plots of R_1 and R_2 as a function of temperature between 10 and 60 °C (Fig. 3b) show that the relative variations of R_1 and R_2 are almost identical within this temperature range.

4. Conclusion

This study shows that high-resolution solid-state ^1H NMR can be useful for investigating the physical organization of surfactants in water, as it is to investigate membranes and liposomes. The high sensitivity and the natural abundance of ^1H make this nucleus attractive, in particular for opaque samples. We have shown that the residual internal mobility of surfactants in micelles, hexagonal phase, and lamellar phase rendered MAS efficient with protons, which is not common with real solids. Since ^1H MAS NMR spectra are of good quality, several magnetization transfer schemes could also be used to facilitate the observation of *other* nuclei under magic angle-spinning, especially ^{13}C MAS NMR [20].

Although this investigation was undertaken with a mixture of surfactants of industrial applications with a statistical distribution of chain lengths, physical transitions were visible when the temperature, the percentage of surfactant in water, the ionic strength, or the total surfactant composition was modified.

Note added in proof

Recent experiments carried out in our laboratory with the same surfactant mixture to which was added trace amounts of perdeuterated decane or of lysophosphatidylcholine as NMR probes for wide band ^2H and ^{31}P NMR have confirmed that the hexagonal phase appears only above 20% surfactant in water. They also show the existence of a lamellar phase at 30% surfactant in water.

Acknowledgments

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