On Micelle Formation and Phase Separation

David P. Cistola*,† and Donald M. Small*

Departments of Biophysics, Biochemistry, and Medicine
Housman Medical Research Center
Boston University School of Medicine
Boston, Massachusetts 02118

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The issue of whether micelles can be treated theoretically and experimentally as a distinct phase has been debated for over four decades. Some early investigators observed fairly abrupt changes in a number of physical properties at or near the critical micelle concentration (cmc) and concluded that micelle formation had at least some of the properties of a phase change. As a result, a "phase-separation" or "two-phase" model was often used to describe the thermodynamics of micelle formation.[1-4] Hutchison et al. coined the term "pseudophase" and argued that the aggregation number of most micelles was too small to consider them a true phase.[2,4]

More recently, other investigators have questioned the treatment of micelles as a phase or pseudophase.[5-8] The two-phase model predicts an abrupt and discontinuous change in physical properties at a unique, truly critical concentration. In addition, the model predicts a homogeneous monodisperse micellar phase and a constant monomer concentration above the cmc. However, careful experimental measurements using highly purified systems revealed that somewhat gradual and continuous changes in physical properties occurred near the cmc,[6,7,9,10] that micelles appeared to be polydisperse,[11] and that monomer activities changed above the cmc.[6,12] For example, gradual and continuous decreases in the equivalent conductance of sodium dodecyl sulfate in water[9,13] and changes in the heats of micelle formation for alkyl carboxylates[10,14] in water have been observed. In addition, a significant decrease in surface tension was observed for sodium dodecyl sulfate in water above the cmc, indicative of a change in monomer activity.[6] Because of the apparent incongruities between experimental data and the two-phase model, it has been argued that the model is probably inappropriate[7] and that micelle formation is not equivalent to phase separation.[8]

The purpose of this communication is to present experimental data that provide further insight into this issue and to propose an explanation for the apparent incongruities between theory and experiment.

Carbon-13 NMR chemical shift and pH data were collected for two nearly identical samples of carboxyl ^{13}C-enriched potassium dodecanoate in H_2O as a function of concentration. To the first sample was added a small amount of KOH to prevent "hydrolysis",[15] i.e., the protonation of a small fraction of potassium laurate molecules by H_3O^+ ions. The sample was then diluted with H_2O from 45 to 10 mM, in increments of 2.5 mM. NMR carboxyl carbon chemical shift and pH measurements were made at each increment. As shown in Figure 1A, plots of carboxyl chemical shift and pH as a function of concentration exhibited changes in slope near the reported cmc for potassium laurate (26 mM).[16,17] However, these changes in slope were somewhat continuous and gradual, and a unique cmc value could not be defined by using graphical methods. The gradual and continuous changes observed near the cmc in Figure 1A were similar, for example, to those observed for the equivalent conductance of sodium lauryl sulfate in water as a function of concentration (cf. Figure 3 of ref 13).

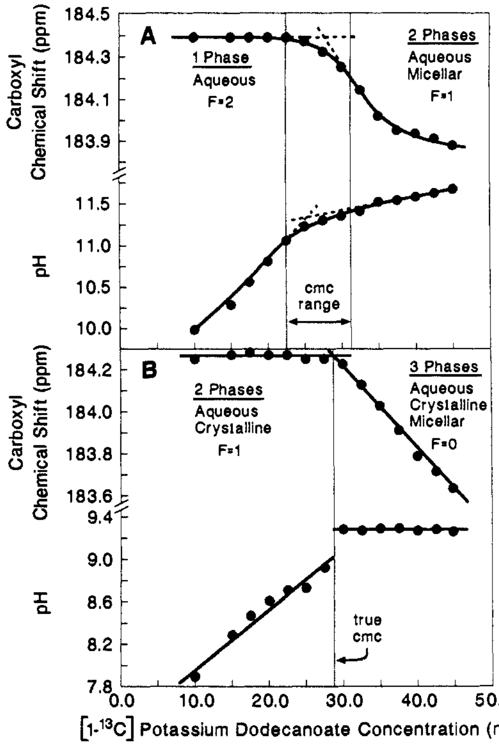

Figure 1. ^{13}C chemical shift and pH values as a function of concentration for samples of [1-^{13}C]potassium laurate (dodecanoate) (99% ^{13}C) in water at 25 °C. In A, a 45 mM sample of potassium dodecanoate was prepared and 20 μL of 1 N KOH was added to a final volume of 1.333 mL. NMR and pH measurements were made, and the sample was diluted to 42.5 mM. Subsequent dilutions and NMR and pH measurements were made at 2.5 mM increments. In B, a 45 mM sample of potassium dodecanoate was prepared as in A except that 4 μL of 1 N HCl was added, rather than KOH. Subsequent incremental dilutions and NMR and pH measurements were made as in A. Chemical shift values are reported in parts per million from external tetramethylsilane and have estimated uncertainties of ±0.05 ppm; pH measurements have estimated uncertainties of ±0.05 pH units. Abbreviations: *F*, number of degrees of freedom; cmc, critical micelle concentration.

The second sample of ^{13}C-enriched potassium laurate in water was identical with the first, except that a small amount of 1 N HCl was added. The sample was then diluted with H_2O from 45 to 10 mM, in increments of 2.5 mM, as above. Addition of 1 N HCl ensured that a small fraction (7%) of the potassium laurate molecules became protonated to form lauric acid. Under these sample conditions, potassium laurate and lauric acid combined to form 1:1 acid–soap crystals,[18,19] which added an additional

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† Present address: Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, 660 S. Euclid Ave., St. Louis, MO 63110.

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phase to the system. As shown in Figure 1B, plots of carboxyl chemical shift and pH values as a function of concentration exhibited abrupt and discontinuous changes at a unique concentration (29 mM). This unique concentration value was unequivocally defined by the intersection of the two least-squares straight lines observed for carboxyl carbon chemical shift values as a function of concentration (Figure 1B, top). Above 29 mM, pH values remained constant and carboxyl chemical shift values decreased linearly from the value expected for monomeric laurate (184.25 ppm) toward a value expected for predominately micellar laurate ($<$183.1 ppm).[18]

To facilitate the interpretation of these data, the Gibbs phase rule was applied. The formation of micelles in the system shown in Figure 1B resulted in thermodynamic invariance ($F = 0$), as demonstrated by the invariance in pH values and the linear change in chemical shift values above 29 mM.[20,21] Since the system in Figure 1B contained three components (potassium laurate, water, and HCl),[22] the phase rule indicated that, at constant temperature and pressure, two and three phases were present below and above 29 mM, respectively (Figure 1B). Therefore, the micelles formed in this system exhibited the characteristics of a true thermodynamic phase, and a unique cmc value was obtained.

In contrast, the system shown in Figure 1A contained one less phase (no acid-soap crystals) at all concentration values examined. This system contained three components and at least 1 degree of freedom at constant temperature and pressure. This degree of freedom, composition or concentration, had to be defined in order to fix the state of the system. Therefore, the composition and properties of the micellar phase, and hence the true cmc value, could change as a function of concentration, and a unique cmc value could be defined *only at a particular concentration value.* As a result, the measured parameters exhibited gradual and continuous changes as a function of concentration, and an approximate *range* of cmc values was obtained (Figure 1A).

Because of thermodynamic invariance, the micellar phase in Figure 1B had a fixed composition and, by deduction, was homogeneous and monodisperse. This deduction, which was based on the Gibbs phase rule and equilibrium thermodynamics, did not require any special knowledge of the atomic or molecular factors governing the size and shape of micelles. In contrast, in the system shown in Figure 1A, the properties of the micellar phase could have changed as a function of concentration, giving rise to inhomogeneity and polydispersity.

On the basis of the above comparisons, we propose that the gradual and continuous changes often observed near the cmc for ionic amphiphiles in water as a function of concentration[6-10] probably resulted from the presence of 1 or more degrees of freedom in the system. Because of this degree of freedom, such experimental measurements have provided only an approximate range of nonunique cmc values. As suggested by the results shown in Figure 1B, a unique cmc value can be determined if care is taken to work with an experimental systm that is thermodynamically invariant at and above the cmc.

The significance of these findings is 3-fold. First, at least some micelles do exhibit the properties of a true thermodynamic phase and can be treated as such in appropriate theoretical models. Second, cmc values, which have been ill-defined entities[17] and measured by using experimental systems analogous to that shown in Figure 1A, should be redefined as unique values and remeasured by more appropriate experimental systems. Third, systems such as the one shown in Figure 1B, which contain a micellar phase and 0 degrees of freedom above the cmc, provide an opportunity for careful measurements of the properties of a homogeneous and monodisperse micellar phase of well-defined composition. Such studies should facilitate careful comparisons between theory and experiment and clarify our understanding of the molecular factors that govern the size, shape, and formation of micelles.

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(20) Each chemical shift value represented the weighted average of laurate molecules in fast exchange between the monomer and micellar phases. The linear decrease in chemical shift values with increasing concentration represented an increase in the relative *amounts* of laurate molecules in the micellar vs monomer (aqueous) phases. However, the composition and physical properties of each of these phases did not change above the cmc and were considered invariant.

(21) Independent evidence that micelle formation can result in thermodynamic invariance has been presented elsewhere (ref 18).

(22) In the Gibbs phase rule, it is the *number* of components, rather than the identity of components, that is of importance. Hence, choice of the identity of components is somewhat arbitrary. If the components are chosen as potassium laurate, water, and HCl, then lauric acid is not a chemically indendent species (component). Alternatively, if the components are chosen as potassium laurate, water, and lauric acid, then HCl is not a chemically independent species.

Relative Hydrogen-Bonding Affinities of Imides and Lactams

K.-S. Jeong, T. Tjivikua, and J. Rebek, Jr.*

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

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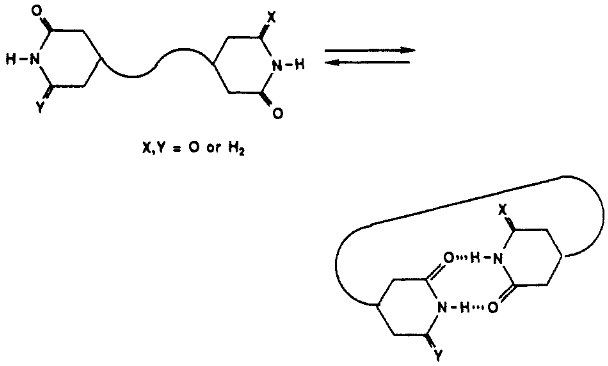
Intermolecular forces, particularly hydrogen bonds, lie at the heart of molecular-recognition phenomena. Synthetic receptors for biorelevant targets provide a means by which the relative hydrogen-bonding capacities of donor and acceptor pairs can be addressed.[1] We compare here imides with lactams and find that the latter show greater hydrogen-bonding affinities. The reduced affinity of imides is apparently related to destabilizing interactions involving the spectator carbonyl.

Previous work[2] with such functionality has established that, in $CDCl_3$, the self-association, or dimerization, is so weak that it is difficult to measure. It is possible, by arranging an intramolecular system (cyclization) (eq 1), to magnify the association to a conveniently measurable level and assess differences at the subkilocalorie level.



(1)

The new molecules are derivatives of Kemp's triacid,[3] and their uneventful synthesis[4] is outlined in Scheme I.

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