

Micelle Formation and the Hydrophobic Effect[†]

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The tendency of amphiphilic molecules to form micelles in aqueous solution is a consequence of the hydrophobic effect. The fundamental difference between micelle assembly and macroscopic phase separation is the stoichiometric constraint that frustrates the demixing of polar and hydrophobic groups. We present a theory for micelle assembly that combines the account of this constraint with a description of the hydrophobic driving force. The latter arises from the length scale dependence of aqueous solvation. The theoretical predictions for temperature dependence and surfactant chain length dependence of critical micelle concentrations for nonionic surfactants agree favorably with experiment.

I. Introduction

This paper concerns the formation of micelles, which are the simplest form of amphiphilic assemblies. Our treatment of this phenomenon is based upon the length scale dependence of hydrophobic effects.^{1,2} Namely, the free energy to solvate small hydrophobic molecules scales linearly with solute volume, whereas that to solvate large hydrophobic species scales linearly with surface area. The crossover from one regime to the other occurs when the oily species presents a surface in water extending over about 1 nm². Due to these contrasting scalings, the free energy to solvate a collection of small oily species that are well separated in water can exceed that of solvating a large cluster of these same species. The resulting free energy difference is the hydrophobic driving force for assembly. Although this force that derives from this scaling difference is surely the mechanism that drives oil–water phase separation, one may wonder if it is also applicable in the case of amphiphilic assembly where interfaces between solute clusters and water contain polar or charged headgroups as well as oil. In this paper, we argue that it is indeed applicable.

The primary difference between oil–water phase separation and amphiphilic assembly is due to stoichiometry. Each amphiphilic molecule contains an oily species that is constrained to remain within a molecular length of a hydrophilic species. For large clusters of amphiphiles, this constraint leads to an entropic cost for clustering oily components that grows faster than cluster volume. Thus, unlike simple oil–water phase separation which forms macroscopic domains, growth of amphiphilic assemblies is limited to mesoscopic domains. Our treatment of this effect uses an estimate of entropy³ obtained from an electrostatic analogy for stoichiometric constraints.^{4–6} In the next section, we describe this estimate along with the other factors that contribute to micelle formation. The resulting expression for the critical micelle concentration, ρ_{cmc} , is then compared with experiments in section III. In particular, we show that our expression yields good predictions of this concentration, changing with temperature and with amphiphile chain length

in accord with experimental observations. An appendix is used to augment the discussion in section II.

II. Theory

A. Law of Mass Action. We consider an aqueous solution of neutral amphiphilic molecules (i.e., nonionic surfactants), each of which has a single alkyl chain as its hydrophobic tail. In general, amphiphiles can form aggregates of various sizes and shapes. We will assume each micelle is spherical and neglect the effects of fluctuations in micelle size and shape. Thus, we imagine that each surfactant molecule exists either as a monomer or as part of a spherical n -mer. We denote the number densities of the monomers and n -mers by ρ_1 and ρ_n , respectively, so that the total surfactant concentration is given by $\rho = \rho_1 + n\rho_n$.

The concentrations of monomers and micelles are related by the law of mass action⁷

$$\rho_n a^3 = (\rho_1 a^3)^n \exp(-\beta \Delta G) \quad (1)$$

where β denotes inverse temperature (i.e., $\beta^{-1} = k_B T$), a is a microscopic length that specifies the standard state convention, and

$$\Delta G = f_n - n f_1 \quad (2)$$

is the driving force for assembly, namely, the free energy of the n -mer, f_n , relative to that of n monomers, $n f_1$. We take a to be approximately the girth of a surfactant molecule, see Figure 1.

For large n , eq 1 implies the existence of a threshold concentration of surfactant molecules ρ_{cmc} , at which the density of aggregates becomes significant. Because this crossover is precipitous, its location is almost independent of the specific definition of the threshold as long as it is physically sensible. Specifically, to within corrections of order $n^{-1} \ln n$

$$\ln \rho_{\text{cmc}} a^3 = \beta \Delta G / n^* \quad (3)$$

The driving force per surfactant, $\Delta G/n$, is a function of n , and it is to be evaluated at the most probable aggregation number, n^* . This number is the value of n that minimizes $\Delta G/n$. Equation 3 is discussed further in the Appendix.

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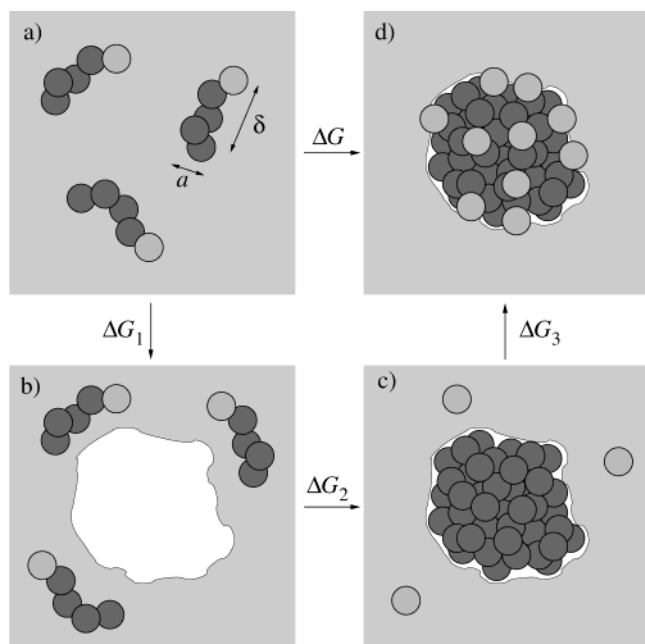


Figure 1. Thermodynamic cycle of micelle formation. The process of assembling n separated amphiphiles (a) to a micelle (d) can be performed in three steps: (1) Creating a cavity in the solvent (light gray) (b); (2) Transferring the hydrophobic chains (dark gray) from the aqueous solution into the cavity (c); (3) Distributing the polar units (gray) over the surface of the cavity and reconnecting them to the hydrophobic groups (d).

B. Driving Force. The contributions to ΔG can be found in three steps, employing the thermodynamic cycle illustrated in Figure 1.

(1) *Creation of a Cavity.* A micelle will fill a region vacated by water. Assuming the extent of the surface is at least 1 nm^2 , the free energy to create this cavity is

$$\Delta G_1 = \gamma A \quad (4)$$

where A denotes the surface area of the cavity and γ is the water–vapor surface tension. In general, there is also pressure–volume work for forming a cavity in a liquid. For water at standard conditions, pressure is sufficiently small that this contribution is negligible for cavities with diameters less than 5 nm . We will limit our consideration to sizes within this range.

(2) *Filling the Hydrophobic Core.* Imagine disconnecting each hydrophobic tail in a surfactant from its respective hydrophilic headgroup and moving the hydrophobic tail from water into the micelle core (we will reconnect the heads and tails in step 3). A total of n tails must be moved to fill the cavity formed in step 1. As such, one part of the free energy to fill the cavity is $-n\Delta\mu$, where $-\Delta\mu$ is the free energy change in transferring the hydrophobic tail (e.g., an alkane chain) from water into the oily hydrophobic core. An additional part of the free energy for filling the cavity is an interfacial contribution due to the presence of van der Waals attractions between oil and water. These interactions cause the oil–water surface tension, γ_{ow} , to be lower than the water–vapor surface tension, γ (see, for instance, ref 8). Thus, the free energy for filling the cavity is

$$\Delta G_2 = -n\Delta\mu - \Delta\gamma A \quad (5)$$

where $\Delta\gamma = \gamma - \gamma_{\text{ow}}$.

The interior of a micelle is densely packed and much like a hydrocarbon liquid.⁹ Thus, $\Delta\mu$ is close to the transfer free energy for moving the associated alkane chain from oil into water.

However, it is slightly smaller than this value because the environment of an alkane chain in a micelle interior is more confining than that in bulk oil.⁹ The numerical consequence of this small difference will be discussed in section III. To the extent that the micelle is spherical, $A = 4\pi L^2$, where L is the micelle radius. Since the interior is densely packed, L is given by $4\pi L^3/3 = n\delta a^2$, where δ is the mean length over which a polar headgroup is separated from an alkyl group within a surfactant molecule, see Figure 1. From these considerations

$$\Delta G_1 + \Delta G_2 = -n\Delta\mu + gn^{2/3} \quad (6)$$

where $g = (36\pi)^{1/3}(\gamma_{\text{ow}}a^2)(\delta/a)^{2/3} \approx 4.8 \times (\gamma_{\text{ow}}a^2)(\delta/a)^{2/3}$.

The right-hand side of eq 6 is essentially the free energy for nucleating oil clusters in water.¹⁰ It is the hydrophobic driving force identified in the Lum–Chandler–Weeks theory.¹ The first term is proportional to the volume of hydrophobic units. The second term is proportional to the area of the interface. The first term is extensive in n and dominates at large n . Thus, if only ΔG_1 and ΔG_2 were significant, the strength of the driving force would grow without bound leading to macroscopic clusters. However, these contributions are counter balanced by a third term that we consider now.

(3) *Placing Hydrophilic Headgroups on the Micelle Surface.*

In the final step, the hydrophilic headgroups are reconnected to the hydrophobic tails, placing them at the water–oil interface so as to maintain a favorable solvation energy. This positioning is to be done while simultaneously enforcing the connectivity between heads and tails and while also maintaining the densely packed interior. These conditions result in an entropic cost that increases super-extensively with aggregate size. The form of this third contribution to the driving force is conveniently estimated from the electrostatic analogy of stoichiometric constraints.^{4,5} The result is³

$$\Delta G_3 = hn^{5/3}/\beta \quad (7)$$

where $h = (3/(4\pi))^{2/3}(96/49)(a/\delta)^{4/3} \approx 0.75 \times (a/\delta)^{4/3}$. In employing this analogy, it is important to note that the micelle volume is essentially that of the densely packed alkyl chains.

C. Micelle Size and Critical Micelle Concentration. Combining the three contributions discussed above gives the driving force in units of $k_B T$

$$\beta\Delta G \approx -n\beta\Delta\mu + \beta gn^{2/3} + hn^{5/3} \quad (8)$$

Minimization of $\Delta G/n$ therefore gives

$$n^* \approx \beta g/2h = (49\pi/48)\beta\gamma\delta^2 \quad (9)$$

With this aggregation number, eqs 3 and 8 yield

$$\ln\rho_{\text{cmc}}a^3 = c(\beta\gamma_{\text{ow}}a^2)^{2/3} - \beta\Delta\mu \quad (10)$$

where $c = (5832/49)^{1/3} \approx 4.9$.

III. Comparison with Experiment

Equation 10 is the principal result of this paper. It expresses the critical micelle concentration in terms of measured quantities and one adjustable parameter, the molecular length scale a . As such, its validity is easily checked. Here we do so by considering m -alkyl hexaoxyethylene glycol monoethers, C_mE_6 , i.e., $(\text{CH}_3)-(\text{CH}_2)_{m-1}(\text{OCH}_2\text{CH}_2)_6\text{OH}$. The critical micelle concentrations for this class of nonionic surfactants have been determined experimentally.

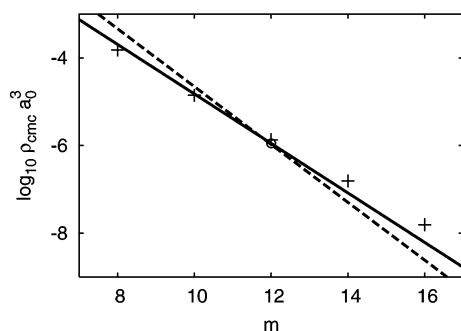


Figure 2. Critical micelle concentration of $C_{12}E_6$ as a function of the length of the hydrophobic tail at room temperature. Crosses and circle are experimental data from refs 19 and 20, respectively. A reference length $a_0 \approx 3 \text{ \AA}$ was chosen to transform the reported values into dimensionless units. The curves show the results of eq 10 using the transfer free energy $\Delta\mu$ (solid line) and the bulk approximation $\Delta\mu_0$ (dashed line). The length a is chosen such that the experimental value at $m = 12$ from ref 20 is recovered. Solid line, $a/a_0 = 1$; dashed line, $a/a_0 = 1.3$ or $a/a_0 = 1.6$ if the correction $\Delta\gamma$ to the surface tension is neglected.

The surface tension is required to compare eq 10 with experimental results. At room temperature, the oil–water surface tension is $\gamma_{ow} \approx 51 \text{ mN/m}$.¹¹ Were we to neglect $\Delta\gamma$, we would instead take the room-temperature value of the water–vapor surface tension, $\gamma = 72 \text{ mN/m}$.¹² The difference $\Delta\gamma = \gamma - \gamma_{ow}$ is mainly enthalpic.⁸ As such, a good approximation for the temperature dependence of the required surface tension is $d\gamma_{ow}/dT \approx d\gamma/dT \approx -0.17 \text{ mN/m/K}$.¹²

The transfer free energy, $\Delta\mu$, is also needed. To the extent that the micelle interior is like a bulk hydrocarbon liquid, it can be obtained from solubility measurements.^{13,14} This free energy change for transferring alkane chains with fewer than 12 carbons from oil to water depends linearly on the number of carbons, m . The linear fit to experimental data is $\Delta\mu_0(m) = (2.25 + 0.9m) \text{ kcal/mol}$ at room temperature. We have used the subscript “0” to indicate that this free energy for transferring between bulk phases must differ to some extent from that for transferring from a micelle interior to water. Indeed, experimental evidence for alkane chains with $m < 6$ [9] indicates that $\Delta\mu(m) \approx (1.9 + 0.77m) \text{ kcal/mol} \equiv \Delta\mu_0(m) + \Delta\Delta\mu(m)$.

The temperature dependence of $\Delta\mu$ can be estimated from the observation of convergence temperatures for transfer entropies and enthalpies, T_S^* and T_H^* , respectively.^{15,16} Namely

$$\Delta\mu(T, m) \approx \Delta C_p(m)[(T - T_H^*) - T \ln(T/T_S^*)] \quad (11)$$

where $T_S^* = 112 \text{ }^\circ\text{C}$ and $T_H^* = 22 \text{ }^\circ\text{C}$.¹⁷ The heat capacity $\Delta C_p(m)$ is chosen so as to fit the experimental $\Delta\mu(m)$ at room temperature, i.e.

$$\Delta C_p(m) = [\Delta\mu_0(m) + \Delta\Delta\mu(m)] / [(298 \text{ K} - T_H^*) - 298 \text{ K} \ln(298 \text{ K}/T_S^*)] \quad (12)$$

Equation 10 together with the dependence of transfer free energies on the alkyl chain length predicts that ρ_{cmc} varies exponentially with m . When plotted on a logarithmic scale, it should have the slope $-\partial\Delta\mu/\partial m$. Figure 2 compares this prediction with experimental data. The measured data is indeed linear over a range of concentrations spanning several orders of magnitude. The slope of the experimental data is approximately -0.7 kcal/mol , which is close to the value of -0.9 kcal/mol inferred by neglecting $\Delta\Delta\mu(m)$, and even closer to

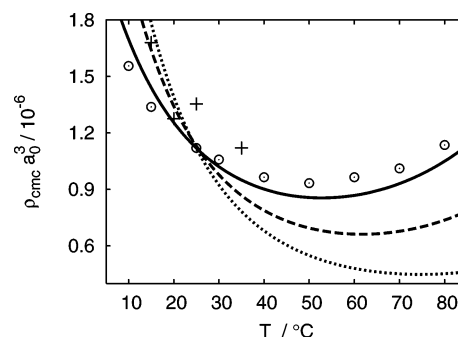


Figure 3. Temperature dependence of the critical micelle concentration of $C_{12}E_6$. The meanings of the symbols are the same as in Figure 2. The solid line is the prediction of eq 10. Disregarding the correction $\Delta\Delta\mu$ yields the dotted line, and additionally neglecting $\Delta\gamma$ results in the dashed line.

the value of -0.77 kcal/mol inferred by accounting for this correction to transfer free energies between entirely bulk phases.

Figure 3 concerns the temperature dependence of the critical micelle concentration. The experimental data for $C_{12}E_6$ show a minimum in the critical micelle concentration near $50 \text{ }^\circ\text{C}$. A similar minimum is found from eq 10. The excellent fit to experimental data is obtained by choosing a so as to match the experimental data at $T = 25 \text{ }^\circ\text{C}$. This method of choice gives $a = 3 \text{ \AA}$, which is not an unreasonable value for the microscopic length. Neglecting the corrections $\Delta\gamma$ and $\Delta\Delta\mu$ lead to similar lengths and similar though inferior fits to the data over the observed temperature range.

Since $\beta\gamma a^2$ is of order 1, and δ/a is of order 10, we see that eq 9 predicts aggregation numbers of order 100. This cluster size is consistent with our assumption of large n .

IV. Discussion

Elements of the theory we have presented here for micelle assembly can be found in earlier works. For instance, the surface energy and entropy terms, ΔG_1 and ΔG_3 , have been considered in ref 3. As a result, that paper obtains the same scaling of aggregate size as given by eq 9, namely, $n^* \propto \beta\gamma\delta^2$. By neglecting ΔG_2 , however, ref 3 errors in its treatment of the temperature dependence of ρ_{cmc} .

Detailed consideration of the transfer free energy contribution ΔG_2 and its linearity with m is found in Tanford's monograph.⁹ That work does not consider ΔG_1 and ΔG_3 which compete with ΔG_2 . Both ΔG_1 and ΔG_2 contribute significantly to the temperature dependence of ρ_{cmc} .

For the neutral surfactants we have considered, the net hydrophobic driving force, $\Delta G_1 + \Delta G_2$, is balanced by the super-extensive entropy term, ΔG_3 . It is remarkable how well ρ_{cmc} is described over a wide range of conditions with only these three terms. For ionic surfactants, an additional super-extensive term will limit the micelle size. It is an electrostatic contribution that opposes the clustering of like charge. For low concentrations of counterions, its scaling with n is identical to the entropic term, growing as $n^{5/3}$ for the case of spherical micelles. The size of this term will depend on ionic strength in a fashion not yet determined.

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Appendix

Here we consider further the law of mass action, considering the water–surfactant mixture as an ideal solution of surfactants

and surfactant aggregates. The free energy density is¹⁸

$$\beta F = \sum_n [\rho_n (\ln \rho_n a^3 - 1) + \rho_n \beta f_n - \beta \mu_s n \rho_n] \quad (13)$$

The first term accounts for the translational entropies of the aggregates. f_n is the internal free energy of an n -mer, and μ_s is the surfactant chemical potential that controls the total surfactant density $\rho = \sum_n n \rho_n$.

The equilibrium partitioning of densities is that which minimizes eq 13

$$\rho_n a^3 = \exp(-\beta f_n + n \beta \mu_s) \quad (14)$$

from which the law of mass action, eq 1, follows.

To the extent that micelles are monodisperse, $\rho_n \approx \rho_1 \delta_{n,1} + \rho_n^* \delta_{n,n^*}$. Here, δ_{n,n^*} refers to the Kronecker delta. Substituting this expression into eq 13 gives

$$\beta F \approx \rho_1 (\ln \rho_1 a^3 - 1) + \frac{\rho - \rho_1}{n^*} \left[\ln \left(\frac{\rho - \rho_1}{n^*} a^3 \right) - 1 \right] + \beta \rho_1 f_1 + \beta \left(\frac{\rho - \rho_1}{n^*} \right) f_{n^*} - \beta \mu_s \rho \quad (15)$$

In this approximation, the equilibrium partitioning of aggregated and unaggregated surfactants is obtained by minimizing this expression with respect to ρ_1 and n^* . That minimization gives again eq 1, and also

$$0 = \partial \beta F / \partial n^* = \left[\frac{\partial \beta \Delta G / n}{\partial n} - \frac{1}{n} (\ln \rho_1 a^3 - \beta \Delta G / n) \right]_{n=n^*} \quad (16)$$

The critical micelle concentration is identified as the lowest surfactant density at which a measurable fraction of surfactants, x , aggregate to form micelles. As such, $n \rho_n = x \rho_1$, and the law of mass action is $\exp(-\beta \Delta G) = (x \rho_1 a^3 / n) / (\rho_1 a^3)^n$. Therefore

$$\beta \Delta G / n = (1 - 1/n) \ln \rho_1 a^3 + (1/n) \ln(n/x) \quad (17)$$

and $\rho_{cmc} = \rho_1 [1 + \mathcal{O}(x)]$. Equation 3 with the condition that n^* minimizes $\Delta G / n$ thus follows from eqs 16 and 17 when n is large.

An alternative definition of the critical micelle concentration is the lowest density ρ_1 at which eq 16 has a nontrivial solution for n^* . This convention is used in ref 3. The free energy develops a local minimum for $n > 1$ at the concentration $\rho a^3 = \exp[c'(\beta \gamma_{ow} a^2)^{2/3} - \beta \Delta \mu]$, where $c' = (4320/49)^{1/3} \approx 4.45$, and the location of the minimum is at $n^* = \beta g / (5h)$. Comparison with eqs 10 and 9, respectively, shows that this convention is in close accord with the approach we have taken.

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