

Micellization, Solubilization, and Microemulsions

Volume 1

Edited by

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*IBM Corporation
East Fishkill Facility
Hopewell Junction, New York*

Plenum Press · New York and London

THERMODYNAMICS OF AMPHIPHILAR AGGREGATION INTO MICELLES AND VESICLES

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A unified thermodynamic treatment of self-aggregation into micelles and/or vesicles of amphiphiles with one or two hydrocarbon tails in aqueous media is developed. Empirical expressions provided by Tanford are used for the free energy of the aggregates to obtain the size distribution function and the type of aggregation for the two kinds of amphiphiles. Calculations have been carried out for different tail lengths and different repulsive interaction strengths between the polar head groups. They show that, for the range of parameters considered, the amphiphiles with one hydrocarbon tail aggregate as micelles, while those with two hydrocarbon tails aggregate as vesicles. A critical vesicle concentration (the analog of CMC) is calculated on the basis of a sharp change in the dependence of the total concentration of aggregates on the total amphiphilar concentration.

INTRODUCTION

Amphiphilar molecules in aqueous media achieve segregation of their hydrophobic parts by self-aggregation. The aggregates can be either in the form of micelles with an internal hydrocarbon core and a surface composed of polar groups or in the form of bilayers with two layers of amphiphiles in contact having the hydrocarbon tails inside, and the polar groups outside in contact with the aqueous medium. Micelles can be spherical, ellipsoidal or cylindrical, whereas bilayers can be either planar or spherical with an internal

cavity filled with solvent. Bilayers of the latter structure are called vesicles. Amphiphiles with single hydrocarbon tails form micelles¹ which grow in size as the length of the tail increases or as the ionic strength of the aqueous medium increases. Lipid molecules which possess a single polar head group and two long hydrocarbon tails form bilayers, both planar as well as spherical¹.

Aggregation of amphiphiles into micelles has been treated either as a stepwise association phenomenon or as a phase transition process^{2,3}. The formation of spherical vesicles from amphiphiles in solution has not yet been examined from a thermodynamic point of view. In an earlier paper⁴ micellization was treated, assuming that micellar aggregates of all possible sizes coexist. At low amphiphilar concentrations, the size distribution of the aggregates was predicted to decrease monotonically with size. As the total concentration was increased, the size distribution was found to change from a monotonic decreasing function to one exhibiting two extrema, a minimum and a maximum. A critical concentration was defined as the total amphiphilar concentration at which the change in the shape of the size distribution function occurs. This critical concentration was shown to be a close lower bound of the critical micelle concentration (CMC)⁵. In the region close to the CMC, the physico-chemical properties of the system were shown to change rapidly but continuously and the concentration of single amphiphiles was shown to increase slowly. Calculations showed that addition of surfactant above the CMC leads not only to an increase in the number of aggregates, but also to larger average sizes of the aggregates. These predictions are in agreement with experimental observations. It may be pointed out that this treatment was not based on any particular model of micellization. However, the treatment considered the existence of a single type of aggregate, the micelles.

The goal of the present paper is to determine the conditions under which micelles and/or vesicles form. It will be shown that a unified thermodynamic framework can be provided to describe the aggregation of amphiphiles with one or two hydrocarbon tails in aqueous solution into micelles and/or spherical vesicles.

In the next section the size distribution model is formulated for aggregates of arbitrary shape and kind. Explicit expressions for the free energy are introduced in section III. The types of aggregation of the amphiphiles with one and two hydrocarbon tails are considered in sections IV and V.

The main theoretical conclusion is that single chain amphiphiles aggregate generally as micelles and double chain amphiphiles as vesicles. As mentioned above, this is in agreement with experiment.

II. SIZE DISTRIBUTION MODEL

The amphiphilar system considered here is composed of N_s solvent molecules, N_A single amphiphiles, and N_{gi} aggregates of type i (micelles or vesicles) and size g . Aggregates of different sizes are considered as distinct species, each characterized by its own standard chemical potential. The standard chemical potentials of the solvent molecule and of the single amphiphile are denoted by μ_s^0 and μ_A^0 respectively. The standard chemical potential per amphiphile of the aggregate of type i is separated into a size independent part denoted by μ_{Bi}^0 and a size dependent part μ_{gi}^0/g . As explained below the size independent part of the standard chemical potential per amphiphile μ_{Bi}^0 is the same for all types of aggregates and hence will be denoted by μ_B^0 . It is assumed that the solution is sufficiently dilute in amphiphiles and, therefore, that the interaction forces between the aggregates are negligible. For the total thermodynamic potential ϕ we use the expression:

$$\begin{aligned} \phi = & N_s \mu_s^0 + N_A \mu_A^0 + \sum_i \sum_g N_{gi} (\mu_B^0 g + \mu_{gi}^0) \\ & + kT [N_s \ln v_s + N_A \ln v_A + \sum_i \sum_g N_{gi} \ln v_{gi}] \quad , \quad (1) \end{aligned}$$

where the free energy of mixing has been written in terms of the volume fractions v_s , v_A and v_{gi} of the solvent molecule, single amphiphiles and aggregates of type i and size g to account for the large differences in sizes. Here k is Boltzmann's constant and T , the absolute temperature. The summation over g is carried out between 2 and ∞ for micelles and between the minimum size (as defined below) and ∞ for vesicles. The summation over i is carried out for all types of aggregates. Denoting by a the ratio of the volume of a single amphiphile to the volume of a solvent molecule, the total potential ϕ can be rewritten as

$$\begin{aligned} \phi = & N_s \mu_s^0 + N_A \mu_A^0 + \sum_i \sum_g N_{gi} (\mu_B^0 g + \mu_{gi}^0) \\ & + kT [N_s \ln \frac{N_s}{F} + N_A \ln a \frac{N_A}{F} + \sum_i \sum_g N_{gi} \ln a g \frac{N_{gi}}{F}] \quad , \quad (2) \end{aligned}$$

where

$$F = N_s + a N_A + \sum_i \sum_g a g N_{gi} \quad . \quad (3)$$

Since the total number of amphiphiles is a constant, F is also a constant. The equilibrium condition, corresponding to the minimum of the total potential ϕ subject to the constraint (3), yields

$$-g \mu_A^0 + g \mu_B^0 + \mu_{gi}^0 + kT \left[-g \ln a \frac{N_A}{F} - g + 1 + \ln a g \frac{N_{gi}}{F} \right] = 0 \quad (4)$$

Equation (4) can be rearranged to give the equilibrium size distribution for aggregates of type i

$$\frac{N_{gi}}{F} = \xi^g (aeg)^{-1} \exp(-\mu_{gi}^0/kT) \quad (5)$$

where

$$\xi = \left(\frac{N_A}{F}\right) a e \exp - \left(\frac{\mu_B^0 - \mu_A^0}{kT}\right) \quad (6)$$

and e is the base of the Napierian logarithm. It was shown⁴ that such a size distribution function is monotonically decreasing with size below a critical concentration and exhibits a minimum and a maximum above that concentration. From the size distribution function (5) one can compute any size dependent property of the system such as the true number average aggregation number

$$(\bar{g}_n)_i = \frac{\sum g N_{gi}}{\sum N_{gi}} \quad (7)$$

and the true weight average aggregation number

$$(\bar{g}_w)_i = \frac{\sum g^2 N_{gi}}{\sum g N_{gi}} \quad (8)$$

The dispersion in size of the aggregates of type i is measured by the variance σ_i^2 of the size distribution function

$$\sigma_i^2 = \frac{\sum (g - (\bar{g}_n)_i)^2 N_{gi}}{\sum N_{gi}} \quad (9)$$

or by the ratio

$$\frac{\sigma_i}{(\bar{g}_n)_i} = [(\bar{g}_w)_i / (\bar{g}_n)_i - 1]^{1/2} \quad (10)$$

At a critical value $(\frac{N_A}{F})^*$ of the concentration of non-aggregated amphiphiles, phase separation occurs. At this point the non-aggregated amphiphiles and the aggregates in aqueous solution are

in thermodynamic equilibrium with the bulk amphiphilic phase. The phase equilibrium is

$$\mu_{\text{bulk}} = \mu_A = \mu_A^0 + kT \left[\ln a\left(\frac{N_A}{F}\right)^* + 1 - a\left(\frac{N+N_A}{F}\right)^* - \sum_i \sum_g a\left(\frac{N_{gi}}{F}\right)^* \right], \quad (11)$$

where μ_{bulk} is the chemical potential per amphiphile of the bulk amphiphilic phase and μ_A is the chemical potential of the non-aggregated amphiphiles in solution. The asterisk denotes phase separation conditions. The concentration $\left(\frac{N_A}{F}\right)^*$ of the non-aggregated amphiphiles is a limiting value below which aggregation of any added amphiphile is favored and above which phase separation into one phase containing aggregates and a bulk amphiphilic phase occurs. The equations derived so far can be applied to different kinds of amphiphiles and types of aggregation by using suitable expressions for the free energy terms μ^0 . In the next section we describe one such expression.

III. EXPRESSIONS FOR THE FREE ENERGY

For illustrative purposes, Tanford's empirical expressions¹ are used. In that treatment the standard free energy of formation of an aggregate, per amphiphile, is separated into attractive and repulsive components. The attractive component arises from the hydrophobic effect which seeks to minimize the hydrocarbon-water contact. This component is assumed to be independent of the nature of the head group and contains both size independent and size dependent parts. The size independent part represents the free energy change of the hydrocarbon chain from an aqueous environment to complete immersion in the micellar core. Because the hydrocarbon environment and the translational and rotational constraints are similar for micelles and vesicles, this part can be assumed to be the same for all types of aggregates. However, it differs for different types of amphiphiles. The size dependent part is due to the interfacial interaction between the aqueous medium and the exposed hydrocarbon surface and is a function solely of the (size dependent) aggregate surface area A per head group. The repulsive component of the free energy depends both on the nature of the amphiphilic head group as well as on the separation between the head groups. The surface area A is used as a measure of this separation. In the present paper the standard free energy of formation of an aggregate is decomposed into size independent and size dependent terms. Since the size dependence occurs through A alone, the size dependent part of the free energies of different kinds of amphiphiles and aggregates can be expressed by the same function of A .

For amphiphiles consisting of a single hydrocarbon tail, the size independent part of the standard free energy of aggregation is

$$\frac{\mu_B^{\circ} - \mu_A^{\circ}}{kT} = \frac{-2000 - 700 (n_c - 1)}{RT} \quad (12)$$

where n_c is the total number of carbon atoms in the hydrocarbon tail and R is the gas constant in cal/mole $^{\circ}$ K. The size dependent part of the free energy is given by

$$\frac{\mu_g^{\circ}}{kT} = \frac{25 (A_H - 21) g}{RT} + \frac{\alpha g}{A_R RT} \quad (13)$$

where α is a constant in cal \AA^2 /mole representing the repulsion between the polar head groups, A_H and A_R are the surface areas per amphiphile in \AA^2 corresponding to an aggregate surface containing the bases or centers of the head groups respectively. For simplicity, A_H and A_R have been considered equal and denoted by A . The parameter α is dependent on the nature of the polar head group and on the ionic strength of the medium. The use of this expression implies that the surface area A per amphiphile is uniform throughout the aggregate surface. The area A per amphiphile is different for different types of aggregates and different types of amphiphiles and depends on g .

For amphiphiles with two hydrocarbon tails, the two tails have some degree of mutual association, thus decreasing the area of their exposure to the aqueous medium. Consequently, the free energy change of transfer of amphiphiles from an aqueous medium to an aggregate phase for a double chain amphiphile can be expected to be not quite twice that of the corresponding single chain amphiphile. This has, in fact, been observed experimentally¹. For amphiphiles with two hydrocarbon tails, Tanford¹ has estimated that addition of a second tail increases the energy change by only 60%. Using this estimate, the size independent part of the free energy of transfer for such amphiphilar aggregates is given by

$$\frac{\mu_B^{\circ} - \mu_A^{\circ}}{kT} = 1.6 \left[\frac{-2000 - 700 (n_c - 1)}{RT} \right] \quad (14)$$

The size dependent part of the free energy is given by the same equation as for a single chain amphiphile, since as mentioned earlier the influence of the two tails is incorporated in the area A per amphiphile.

$$\frac{\mu_g^{\circ}}{kT} = \frac{25 (A - 21) g}{RT} + \frac{\alpha g}{A RT} \quad (15)$$

The interactions between the two polar surfaces of vesicles makes a negligible contribution to the free energy⁶.

It should be mentioned that the empirical equations of Tanford are used here because of their simplicity and their ability to predict reasonably the micellar aggregation^{1,4,5}. Expressions with a clearer physical significance for various terms can be obtained⁷ and a treatment based on them will be published elsewhere. In addition to the well established terms representing cohesive interactions and electrostatic repulsions, that treatment accounts for the interfacial free energy and for the translational and rotational constraints on amphiphiles following their incorporation into an aggregate.

For amphiphiles with a single hydrocarbon tail, the volume v_o and extended length l_o of the hydrocarbon chain are¹:

$$v_o = 27.4 + 26.9 (n_c - 1) \text{ in } \text{Å}^3 \quad (16)$$

and

$$l_o = 1.5 + 1.265 (n_c - 1) \text{ in } \text{Å} \quad , \quad (17)$$

respectively. For amphiphiles with two hydrocarbon tails, the corresponding equations are

$$v_o = 2 [27.4 + 26.9 (n_c - 1)] \text{ in } \text{Å}^3 \quad (18)$$

and

$$l_o = 1.5 + 1.265 (n_c - 1) \text{ in } \text{Å} \quad . \quad (19)$$

For micellar aggregates of spherical shape and size g , the surface area per amphiphile is

$$A = \frac{1}{g} 4 \pi \left[\left(\frac{3gv_o}{4\pi} \right)^{1/3} + \delta \right]^2 \quad , \quad (20)$$

where δ accounts for the surface roughness. For micellar aggregates of cylindrical shape with hemispherical ends, the surface area per amphiphile is

$$A = \frac{1}{g} [2 \pi L (l_o + \delta) + 4 \pi (l_o + \delta)^2] \quad , \quad (21)$$

where l_o is the core radius of the cylinder and the sphere and L is the length of the cylindrical section given by

$$L = (gv_o - \frac{4}{3} \pi \ell_o^3) / \pi \ell_o^2 \quad (22)$$

For aggregates in the form of spherical vesicles, the hydrocarbon shell volume is

$$gv_o = \frac{4\pi}{3} (R_o^3 - R_i^3) \quad (23)$$

where R_o and R_i are the outer and inner radii of the hydrocarbon shell. The thickness of the hydrocarbon shell is taken to be twice the length of the extended hydrocarbon tail, i.e.

$$R_o - R_i = 2\ell_o \quad (24)$$

Then the outer radius R_o and the inner radius R_i of the hydrocarbon surfaces are related to g , v_o and ℓ_o through

$$R_o = \left[\frac{gv_o}{8\pi\ell_o} - \frac{\ell_o^2}{3} \right]^{1/2} + \ell_o \quad (25)$$

and

$$R_i = \left[\frac{gv_o}{8\pi\ell_o} - \frac{\ell_o^2}{3} \right]^{1/2} - \ell_o \quad (26)$$

The average surface area per amphiphile at a distance δ from the core surface is calculated from

$$A = \frac{1}{g} 4\pi [(R_o + \delta)^2 + (R_i - \delta)^2] \quad (27)$$

The computations have been carried out assuming $\delta = 3 \text{ \AA}$ and a value of 30 \AA^3 for the volume of a solvent molecule. Obviously the minimum size of the vesicles will correspond to $R_i = \delta$.

IV. AGGREGATION OF AMPHIPHILES WITH SINGLE HYDROCARBON TAILS

The aggregation of single chain amphiphiles into micelles and vesicles was examined for hydrocarbon chain lengths varying from $n_c = 6$ to $n_c = 12$ and for values of the repulsive parameter α between 6×10^4 and $8 \times 10^4 \text{ cal \AA}^2/\text{mole}$. In the case of micelles, since the spherical shape cannot be maintained beyond a critical radius equal to the length ℓ_o of the extended hydrocarbon tail, the computations were carried out for spherical micelles up to this critical radius. Beyond this, the shape was assumed cylindrical with hemispherical ends. The concentrations of non-aggregated

amphiphiles and the corresponding equilibrium concentration of aggregates in the form of micelles and of vesicles are presented in Table I for the four sets of values of α and n_c . The computations show that as the total concentration of amphiphiles is increased the number of micellar aggregates keeps increasing and the concentration of vesicles is almost zero in the whole range of parameters examined.

The size distribution of micellar aggregates formed from amphiphiles with a tail length of 12 carbon atoms is shown in Figure 1. As discussed earlier⁴, the size distribution function undergoes a transition in shape from a monotonic decreasing one to one exhibiting extrema. The dispersion of sizes of the micellar aggregates at the CMC is found to be relatively small ($\sigma/\bar{g}_n=0.19$). A similar behavior is exhibited when $n_c = 6$ to 12 and $\alpha = 6 \times 10^4$ to 8×10^4 cal $\text{\AA}^2/\text{mole}$.

For $\alpha = 4 \times 10^4$ cal $\text{\AA}^2/\text{mole}$ a peculiar result was obtained. Although the calculated size distribution of vesicles was found to be a monotonic decreasing function of size, the number of vesicles was much larger than that of micelles. There are, however, no experimental results indicating the formation of vesicles from single

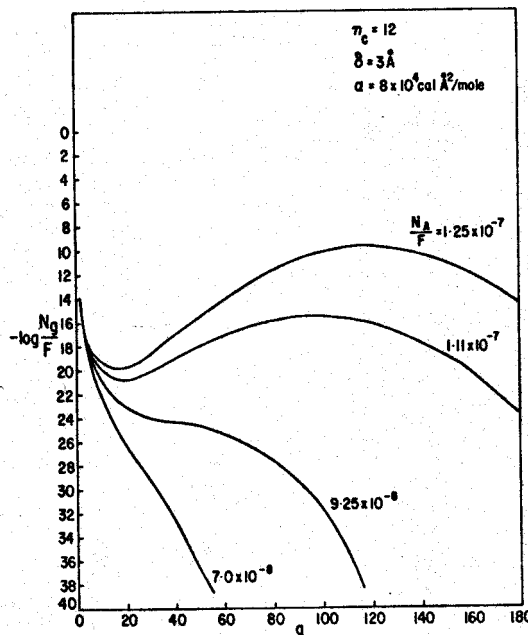


Figure 1. Micellar Size Distribution for Various Concentrations of Non-Aggregated Single Chain Amphiphile with $n_c = 12$ and $\alpha = 8 \times 10^4$ cal $\text{\AA}^2/\text{mole}$.

Table I. Equilibrium Concentrations of Non-Aggregated Amphiphiles, Micelles and Vesicles for Single Chain Amphiphiles^a

	$\alpha = 6 \times 10^4 \text{ cal } \text{\AA}^2/\text{mole}$			$\alpha = 8 \times 10^4 \text{ cal } \text{\AA}^2/\text{mole}$		
	$\frac{N_A}{(-F)}$	$\left(\frac{\sum \frac{N}{g F}\right)$ micelles	$\left(\frac{\sum \frac{N}{g F}\right)$ vesicles	$\left(\frac{N}{F}\right)$	$\left(\frac{\sum \frac{N}{g F}\right)$ micelles	$\left(\frac{\sum \frac{N}{g F}\right)$ vesicles
$n_c = 6$	1.515×10^{-4}	2.076×10^{-9}	1.003×10^{-24}	2.10×10^{-4}	5.46×10^{-10}	9.82×10^{-75}
	1.710×10^{-4}	1.108×10^{-6}	1.002×10^{-18}	2.55×10^{-4}	5.23×10^{-8}	2.36×10^{-60}
	1.785×10^{-4}	1.481×10^{-3}	1.560×10^{-15}	3.00×10^{-4}	1.14×10^{-4}	2.59×10^{-48}
$n_c = 12$	6.75×10^{-8}	2.01×10^{-14}	1.01×10^{-90}	1.17×10^{-7}	2.40×10^{-12}	~ 0
	7.05×10^{-8}	3.23×10^{-11}	6.98×10^{-81}	1.26×10^{-7}	1.10×10^{-8}	5.32×10^{-176}
	7.30×10^{-8}	7.42×10^{-7}	5.37×10^{-73}	1.35×10^{-7}	7.91×10^{-4}	2.11×10^{-160}

^a The size distribution of vesicles is monotonically decreasing for all values of α , n_c and $\frac{N_A}{F}$ used in the Table.

chain amphiphiles. We feel that the expressions for the free energies μ^0 used to obtain this anomaly are not adequate enough to draw definite conclusions.

V. AGGREGATION OF AMPHIPHILES WITH TWO HYDROCARBON TAILS

The formation of micelles and of vesicles by double chain amphiphiles was examined for hydrocarbon tail lengths in the range $n_c = 6$ and $n_c = 12$ and for values of the repulsive parameter α between 4×10^4 cal $\text{\AA}^2/\text{mole}$ and $\alpha = 8 \times 10^4$ cal $\text{\AA}^2/\text{mole}$. The equilibrium concentration of all aggregates in the form of micelles and of vesicles corresponding to given concentrations of non-aggregated amphiphiles is presented in Table II for four sets of values of α and n_c . The computations show that as the total concentration is increased, enormous numbers of vesicles are formed and the concentration of micellar aggregates is practically zero in the whole range of parameters studied.

The size distributions of spherical vesicles formed of amphiphiles with $n_c = 12$ and $n_c = 6$ are shown in Figures 2 and 3 for different values of α . The minimum in the size distribution function

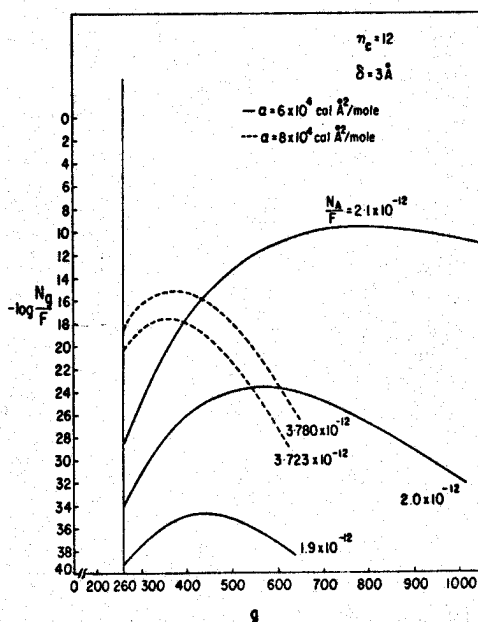


Figure 2. Vesicle Size Distribution for Various Concentrations of Non-Aggregated Double Chain Amphiphile with $n_c = 12$ and $\alpha = 6 \times 10^4$ and 8×10^4 cal $\text{\AA}^2/\text{mole}$.

Table II. Equilibrium Concentrations of Non-Aggregated Amphiphiles, Micelles and Vesicles for Double Chain Amphiphiles^a

	$\alpha = 4 \times 10^4 \text{ cal } \text{Å}^2/\text{mole}$			$\alpha = 8 \times 10^4 \text{ cal } \text{Å}^2/\text{mole}$		
	$\frac{N_A}{F}$	$\left(\frac{\sum g}{F}\right)$ micelles	$\left(\frac{\sum g}{F}\right)$ vesicles	$\left(\frac{N_A}{F}\right)$	$\left(\frac{\sum g}{F}\right)$ micelles	$\left(\frac{\sum g}{F}\right)$ vesicles
$n_c = 6$	1.504×10^{-7}	4.193×10^{-16}	5.579×10^{-16}	5.46×10^{-7}	5.34×10^{-15}	3.75×10^{-9}
	1.540×10^{-7}	4.419×10^{-16}	2.773×10^{-12}	5.73×10^{-7}	5.98×10^{-15}	1.29×10^{-6}
	1.572×10^{-7}	4.624×10^{-16}	3.329×10^{-6}	6.00×10^{-7}	6.66×10^{-15}	6.17×10^{-4}
$n_c = 12$	1.0032×10^{-12}	2.233×10^{-22}	9.528×10^{-16}	3.62×10^{-12}	2.698×10^{-21}	3.65×10^{-18}
	1.0036×10^{-12}	2.235×10^{-22}	1.282×10^{-14}	3.71×10^{-12}	2.844×10^{-21}	2.00×10^{-14}
	1.0041×10^{-12}	2.237×10^{-22}	8.000×10^{-13}	3.80×10^{-12}	2.995×10^{-21}	1.50×10^{-10}

^a The size distribution of micelles is monotonically decreasing for all values of α , n_c and $\frac{N_A}{F}$ used in the Table.

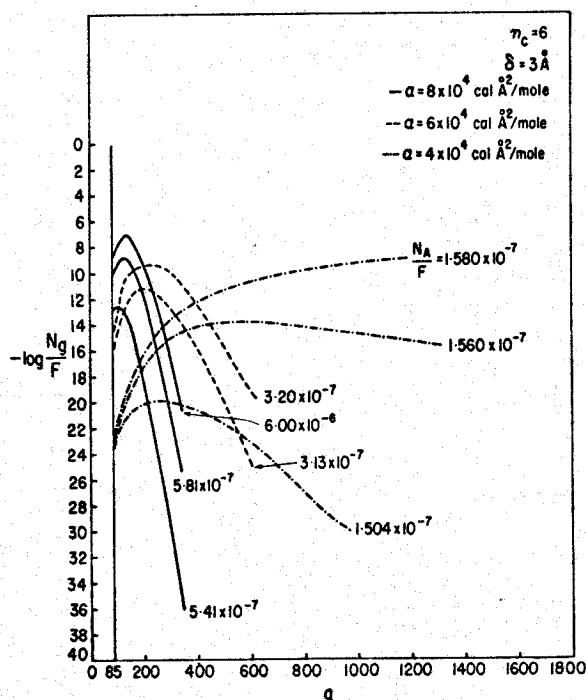


Figure 3. Vesicle Size Distribution for Various Concentrations of Non-Aggregated Double Chain Amphiphile with $n_c = 6$ and $\alpha = 4 \times 10^4$, 6×10^4 and 8×10^4 cal $\text{\AA}^2/\text{mole}$.

is not plotted in the figure since it occurs in a size range wherein vesicles cannot exist. The size distribution function representing the transition from a monotonic decreasing function to one exhibiting extrema is also not plotted in the figure, because the corresponding aggregate concentrations are almost zero. The shape of the size distribution functions in Figure 3 shows that as the value of α increases, the size distribution function tends to become a monotonic decreasing function of size, while as its value decreases, the size distribution function tends to become an increasing function of size leading to phase separation.

The dependence of the concentration of spherical vesicles on the single amphiphilic concentration N_A/F is presented in Table III for amphiphiles with $n_c = 12$ and for $\alpha = 6 \times 10^4$ cal $\text{\AA}^2/\text{mole}$. The table also contains the number average and weight average aggregation numbers and the dispersion in size. Over a large range of concentrations of the aggregates the change in the degree of aggregation is small and the size dispersion is quite narrow.

Table III. Dependence of the Concentration of Aggregates on the Concentration of the Non-Aggregated Double Chain Amphiphile^a

$\frac{N_A}{F} \times 10^{12}$	$\Sigma \frac{N}{F} \frac{g}{F}$	\bar{g}_n^b	\bar{g}_w^b	\bar{g}_w / \bar{g}_n	σ / \bar{g}_n
2.010	3.82×10^{-18}	585	591	1.0102	0.1010
2.020	7.51×10^{-17}	603	609	1.0104	0.1020
2.030	1.60×10^{-15}	622	629	1.0105	0.1024
2.040	3.69×10^{-14}	643	650	1.0105	0.1024
2.045	1.84×10^{-13}	654	661	1.0107	0.1034
2.050	9.36×10^{-13}	665	673	1.0108	0.1039
2.055	4.89×10^{-12}	677	685	1.0108	0.1039
2.060	2.62×10^{-11}	690	698	1.0110	0.1049
2.070	8.16×10^{-10}	716	724	1.0115	0.1072
2.100	5.27×10^{-5}	811	821	1.0123	0.1109

^a $n_c = 12$, $\delta = 3 \text{ \AA}$, $\alpha = 6 \times 10^4 \text{ cal \AA}^2/\text{mole}$

^b aggregation numbers rounded off to integral values

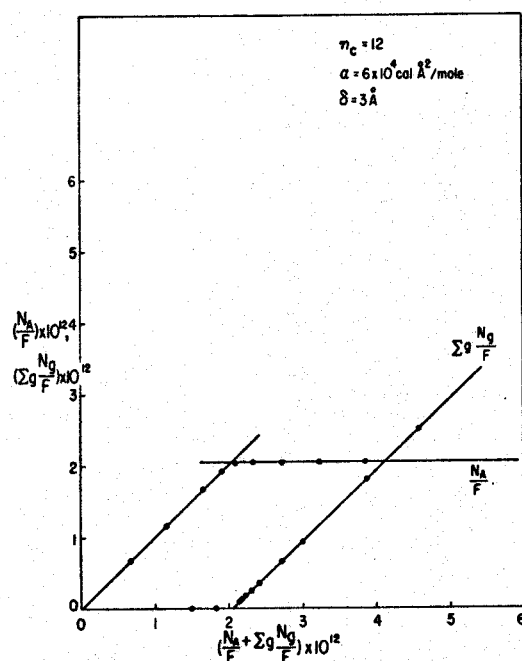


Figure 4. Dependence of Non-Aggregated Amphiphile and Vesicle Concentrations on the Total Concentration of Double Chain Amphiphiles with $n_c = 12$ and $\alpha = 6 \times 10^4 \text{ cal } \text{\AA}^2 / \text{mole}$.

The concentration of amphiphiles present as single amphiphiles and as aggregates is plotted against the total amphiphilar concentration in Figure 4 for vesicles formed of amphiphiles with $n_c = 12$ and for $\alpha = 6 \times 10^4 \text{ cal } \text{\AA}^2 / \text{mole}$. From the sharp change in the values of either of these two concentrations a CVC value (the analog of CMC) for formation of spherical vesicles can be determined. The plot shows that the changes are sharper than those in the case of micellar aggregates⁵. This indicates that spherical vesicles are almost monodispersed. Also the concentration of the single amphiphiles appears to remain almost constant beyond the CVC. An aggregation model assuming a single size of vesicles would be adequate to describe the system.

The CVC values, the average aggregation numbers and the variance in the size distribution of spherical vesicles are tabulated in Table IV for $n_c = 6$ and $n_c = 12$ and for three different values of α . The CVC values are much lower than those generally measured for micellization, but as in micellization the aggregates grow drastically to very large sizes as α is decreased. The dispersion of sizes

Table IV. Dependence of the Characteristics of Vesicles from Double Chain Amphiphiles on Tail Length n_c and Head Group Repulsion α^2

n_c	α^2 cal $\text{\AA}^2/\text{mole}$	CVC in molar fraction units	\bar{g}_n	\bar{g}_w	\bar{g}_w/\bar{g}_n	σ/\bar{g}_n
6	4×10^4	1.644×10^{-7}	690	742	1.0756	0.2750
	6×10^4	3.307×10^{-7}	190	195	1.0255	0.1596
	8×10^4	5.804×10^{-7}	117	119	1.0165	0.1285
12	4×10^4	1.062×10^{-12}	7466	8057	1.0791	0.2812
	6×10^4	2.14×10^{-12}	650	656	1.0106	0.1030
	8×10^4	3.90×10^{-12}	363	366	1.0080	0.0894

^a $\delta = 3 \text{ \AA}$, \bar{g}_n , \bar{g}_w and σ are calculated at the CVC.

of vesicles is small for larger values of α and increases as α decreases.

VI. CONCLUSIONS

In this paper it is shown that a general thermodynamic description of amphiphilar aggregation can describe adequately the formation of micelles and of spherical vesicles from amphiphiles with either one or two hydrocarbon tails. For a range of parameters $n_c = 6$ to $n_c = 12$ and $\alpha = 6 \times 10^4$ to 8×10^4 cal $\text{\AA}^2/\text{mole}$, amphiphiles with single hydrocarbon tails do not form spherical vesicles but only micelles.

Thermodynamically stable spherical vesicles are formed from amphiphiles with two hydrocarbon tails for n_c in the range of 6 to 12 and α in the range 4×10^4 to 8×10^4 cal $\text{\AA}^2/\text{mole}$. No stable micellar aggregates form from amphiphiles with two tails at least in the range of parameters considered.

ACKNOWLEDGEMENT

This work was supported by the National Science Foundation.

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