

SELF-ASSEMBLY OF BOLA AMPHIPHILES

R. NAGARAJAN

*Department of Chemical Engineering
Pennsylvania State University
University Park, PA, 16802*

(Received November 15, 1986; in final form December 17, 1986)

A bola amphiphile is composed of two polar head groups attached to the ends of a hydrophobic tail. In this paper, the principles of molecular self-assembly of bola amphiphiles are quantitatively established by applying thermodynamic and geometric considerations developed earlier for the more common one-headed amphiphiles. Bola amphiphiles are found to aggregate into spheres, small spherocylinders, large cylinders, small and large discs and vesicles. Inside these aggregates, the hydrophobic tail is expected to assume both a folded and a fully stretched conformation. In general, the presence of the second polar group in a bola amphiphile causes an increase in the aqueous solubility of the amphiphile, an increase in the cmc and a decrease in the aggregation number when compared to the corresponding one-headed amphiphile. The quantitative principles of self-assembly established here can aid in deciding which bola amphiphiles should be synthesized in order to generate desired organized assemblies.

KEYWORDS Polar head groups Hydrophobic tail Self-assembly Bola amphiphiles

I. INTRODUCTION

Amphiphilic molecules are composed of a part that is soluble in water and a part that is insoluble in water. This dual nature is responsible for the ability of these molecules to organize themselves into various structures in an aqueous environment. Most common amphiphiles possess a hydrophobic tail and a hydrophilic head group. In contrast, bola amphiphiles refer to a class of molecules in which two hydrophilic head groups are connected to the ends of a hydrophobic tail. The name has its origin in the word 'bola' which stands for a weapon made of a long cord or thong with heavy balls at the end and used for throwing at and entangling cattle. The term 'bolaform electrolyte' was first introduced by Fuoss and Edelson for a hydrophobic chain connecting two ionic head groups [1]. Bola amphiphiles have also been referred to in the literature as bolaform detergents [2-5], two-headed amphiphiles [6, 7] and bipolar amphiphiles [8]. The two hydrophilic groups on a bola amphiphile can be either ionic or nonionic and they can be identical to or different from one another. The hydrophobic tail of the molecule may consist of one or more hydrocarbon chains. One may anticipate that the aggregation behavior of bola amphiphiles will differ somewhat from that of the one-headed amphiphiles because of the presence of the second hydrophilic group.

Very few investigations of the solution behavior of bola amphiphiles are to be found in the literature because these molecules are not widely obtainable as

commercial products. Available studies show that cationic bola amphiphiles with ammonium salt head groups and a single hydrocarbon chain consisting of less than ten methylene groups behave as normal electrolytes rather than as amphiphiles [9]. For dodecane-1,12-bis(trimethylammonium bromide) designated here as $\text{Me}_3\text{C}_{12}\text{Me}_3$, Menger and Wrenn [2] inferred that micelles form at concentrations between 0.02 and 0.05 M. They also interpreted their surface tension and dye spectral change measurements as reflecting extensive contacts between the hydrophobic portions of the micelle and water. However, a variety of chemical relaxation and equilibrium measurements carried out by Zana and coworkers [3-5] led to the conclusion that micellization does not occur in solutions of $\text{Me}_3\text{C}_{12}\text{Me}_3$ while for $\text{Me}_3\text{C}_{16}\text{Me}_3$ and for $\text{Me}_3\text{C}_{22}\text{Me}_3$, micelles of small aggregation numbers are generated. No definite inference was made as to the nature of the intramicellar conformation of the bola amphiphile, namely whether the hydrophobic tail is folded or fully stretched inside the micelle. Kunitake and coworkers [6, 7] synthesized a large number of two-headed amphiphiles and using electron microscopy determined the aggregate morphologies resulting in the solutions of these amphiphiles. They observed the occurrence of globules, rods, monolayer discs and vesicles from single chain amphiphiles with two head groups. The formation of vesicles from bola amphiphiles that are the derivatives of dimer acid has been reported by Fuhrhop and coworkers [10]. In a recent review Fuhrhop and Fritsch [8] have discussed the occurrence of bola amphiphiles in natural products and their importance to cell membrane function. More importantly, they have presented a variety of bola amphiphiles that have been synthesized in their laboratory and from which functional vesicle membranes could be constituted.

To realize the full advantage of synthetic bola amphiphiles which can be tailor-made to generate desired aggregate morphologies, it is necessary to elucidate the principles of molecular self-assembly governing these amphiphiles. It is natural to expect that the fundamental ideas that have been developed for one-headed amphiphiles can be applied to bola amphiphiles as well. It is generally recognized that one-headed amphiphiles form small spherical or globular micelles, large cylindrical micelles and spherical bilayer vesicles depending upon the molecular structure of the amphiphile and the solution conditions in which they are present. Significant progress has been made over the last fifteen years in our understanding of why amphiphiles aggregate into various structures. Mukerjee has shown [11-15] that cooperativity and anti-cooperativity are both important for the formation of aggregates which are large in size compared to molecular clusters like dimers, trimers, etc and yet finite in size. Utilizing the concept of cooperativity, he also established the conditions for the transformation of spherical aggregates into large cylindrical aggregates. Further, the formation of large cylindrical aggregates was shown to be always accompanied by a high polydispersity in the sizes of the aggregates. Tanford pioneered a model [16, 17] for the free energy of formation of micelles using a phenomenological approach. Based on this model, the cooperative growth of micelles was shown to be the consequence of hydrophobic interactions while the repulsions among the head

groups of the amphiphiles was shown to be responsible for the finite size of the micelles. This principle of opposing forces as formulated by Tanford has had a profound impact on all the subsequent studies of amphiphilar aggregation. The importance of geometric considerations in relating the aggregate shape to its size (namely, the aggregation number) was recognized in the work of Tartar [18] and Tanford [16]. However, a quantitative treatment of the relation between the pattern of aggregation and the molecular packing properties was clearly established only through the work of Israelachvili, Mitchell and Ninham [19]. From their treatment emerged a dimensionless molecular packing parameter involving the geometrical properties of the amphiphile as well as of the aggregate [19–21]. This packing parameter has been shown to be capable of describing various features of self-assembly of the one-headed amphiphiles without requiring any detailed consideration of the different intermolecular interactions operating in the system.

In our earlier work on one-headed amphiphiles, a detailed model for the free energy of aggregation was formulated using a statistical thermodynamic approach [22, 23]. This was necessary for the quantitative prediction of the surface area per amphiphile of the equilibrium aggregate and consequently, all the other features of aggregation. Using this free energy formulation, the critical micelle concentration, the size distribution of the aggregates and their average sizes were predicted for a number of nonionic, cationic, anionic and zwitterionic amphiphiles with either one or two hydrocarbon chains in their hydrophobic tail. This treatment has been extended to describe the formation of ideal and nonideal mixed micelles [24], formation of micelles in the presence of nonionic polymers [25], and the solubilization of single component and binary mixtures of hydrocarbons in micelles [26–28].

The main goal of this paper is to develop a quantitative treatment of the principles of self-assembly applicable to bola amphiphiles. The formulation of the free energy of aggregation follows from our earlier work on one-headed amphiphiles. The expression for the free energy of aggregation is cast in a form similar to that of Tanford [16] in order to emphasize the phenomenological origin of the various contributions to the free energy. Since the geometrical packing parameter introduced by Israelachvili, Mitchell and Ninham provides an intuitively pleasing picture of the patterns of aggregation, the aggregation behavior of bola amphiphiles is examined in this paper utilizing this concept of a packing parameter. While the treatment developed in this paper is applicable to bola amphiphiles with ionic or nonionic head groups which may be identical to or dissimilar from one another, only the results for amphiphiles with identical head groups are presented here. In the following section, the general thermodynamic principles of an aggregating system are briefly outlined. The geometrical properties of various aggregates resulting from bola amphiphiles are described in section III. In section IV, the model for the free energy of aggregation is formulated and the model parameters are presented. Illustrative results calculated on the basis of the present treatment are provided in section V. The last section contains the principal conclusions from this study.

II. THERMODYNAMICS OF AGGREGATION

The amphiphilar solution is made up of singly dispersed amphiphiles, aggregates of various shapes and sizes and the solvent water. In this treatment, the aggregates of different shapes and sizes are considered as distinct chemical components each characterized by its own standard chemical potential. The standard states for the aggregates and the singly dispersed amphiphiles are taken to correspond to infinitely dilute solution conditions. The standard state of the solvent water is taken to be that of pure liquid. In this multicomponent solution, the interactions between the various components are considered negligible because the system is dilute in the concentrations of the constituent species. One should note that the interactions between the solvent and all the other species are properly taken into account since the standard chemical potentials of the various species already incorporate these interactions. The total Gibbs energy of this solution can be written as:

$$G = N_w \mu_w^0 + N_1 \mu_1^0 + \sum N_g \mu_g^0 + kT [N_w \ln N_w/F + N_1 \ln N_1/F + \sum N_g \ln N_g/F] \quad (1)$$

where

$$F = N_w + N_1 + \sum N_g \quad (2)$$

In the above equation, N refers to the number of chemical species of a given type, μ^0 is the standard Gibbs energy of the species, k is the Boltzmann constant, and T is the absolute temperature. The subscripts w , 1 , g refer to water, singly dispersed amphiphiles and an aggregate of aggregation number g , respectively. The solution entropy is written as for an ideal mixture because the mutual interactions among the constituent species have been considered negligible.

At equilibrium, the total Gibbs energy of the solution G is a minimum subject to the constraint that the total amphiphilar concentration is specified.

$$N_1 + \sum g N_g = \text{constant} \quad (3)$$

The minimization of G provides the following equilibrium condition,

$$\mu_g^0 + kT \ln N_g/F = g[\mu_1^0 + kT \ln N_1/F] \quad (4)$$

The above relation carries the meaning that the chemical potential of the amphiphile in the singly dispersed state is equal to that in each of the aggregate irrespective of the size and shape of the aggregate. The above relation can be recast in a form that provides the size distribution of the aggregates:

$$X_g = X_1^g \exp - [\mu_g^0 - g\mu_1^0]/kT \quad (5)$$

In this equation, X_g refers to the mole fraction of the aggregate of size g in the total solution while X_1 is the mole fraction of the singly dispersed amphiphile. Both mole fractions are expressed on the basis of a solution containing a total number of F chemical species. The quantity $\mu_g^0/g - \mu_1^0$ is the difference in the standard chemical potential between an amphiphile present in an aggregate of size g and one in its singly dispersed state. Given an explicit expression for this difference in the standard chemical potentials, one can compute the detailed size

distribution of the aggregates as well as all the other size dependent solution properties.

A convenient simplification useful for many amphiphilar solutions can be obtained from Eq. (4) if the aggregation number g is recognized to be sufficiently large. Near the critical micelle concentration, the concentration X_g of the aggregates is of the order of X_1 . Therefore, one may rewrite Eq. (4) as

$$\mu_g^0/g = \mu_1^0 + kT \ln X_1 \quad (6)$$

The above equation represents the description of aggregates as a pseudophase in equilibrium with the singly dispersed amphiphiles. One may note that the Gibbs energy per molecule of this pseudophase, μ_g^0/g , depends on the size of the phase. This is a characteristic feature for small systems like amphiphilar aggregates. In the framework of the pseudophase approximation, the equilibrium aggregate is defined by the condition of minimization of the standard Gibbs energy per molecule of the aggregate. This implies

$$d/dg[(\mu_g^0/g - \mu_1^0)/kT] = 0 \quad \text{at } g = g_e \quad (7)$$

The critical micelle (aggregate) concentration can be obtained from

$$\ln X_{\text{cmc}} = [\mu_g^0/g - \mu_1^0]/kT \quad \text{at } g = g_e. \quad (8)$$

The equilibrium size distribution of aggregates given by Eq. (5) consists of two factors. The first, X_1^g arises from the translational entropy of the various species in the entire solution. The second, $(\mu_g^0 - g\mu_1^0)$ originates from the difference in the standard Gibbs energy of an amphiphile in its aggregated state compared to that in its singly dispersed state. The entropic factor favors the formation of aggregates of small g since the system entropy is larger (and hence the total free energy is lower) for smaller aggregates present in larger numbers. This implies that for two different kinds of aggregates characterized by the same magnitude of the standard Gibbs energy difference per amphiphile, the aggregate of smaller aggregation number will be thermodynamically preferred. To obtain further information about the aggregation behavior of amphiphiles, it is necessary to formulate an explicit model for the standard Gibbs energy of aggregation per amphiphile. Also the relation between the shape of the aggregates and the aggregation number should be established.

III. GEOMETRICAL PROPERTIES OF AGGREGATES

For one-headed amphiphiles, various shapes of aggregates such as spheres, ellipsoids, discs, cylinders, and bilayer vesicles have been considered. Irrespective of the shape of the aggregates, the following geometrical conditions should be satisfied by all the aggregates [19]: (1) No point within an aggregate can be farther than l_0 from the hydrophobic core-water interface where l_0 is the extended length of the amphiphile. This implies that at least one dimension of the aggregate should be smaller than $2l_0$. (2) The total volume of the hydrophobic core of the aggregate should satisfy $V = gv_0$, where v_0 is the volume of the

hydrophobic tail of the amphiphile. This implies that there are no holes inside the aggregate and the entire core is filled with the hydrophobic part of the amphiphile. (3) The total surface area A of the hydrophobic core of the aggregate should satisfy $A = ga_e$. This implies that the average area per amphiphile of the hydrophobic core is equal to the equilibrium value a_e .

Israelachvili, Mitchell and Ninham [19] have clearly shown how an aggregate may satisfy the criteria $A/g = a_e$ on the average, while violating this equality everywhere on the surface of the aggregate. For example, if a spherocylindrical aggregate is considered, the area per amphiphile in the spherical ends of the aggregate and in the cylindrical middle of the aggregate are both different from the equilibrium area a_e while the average area per amphiphile of the aggregate is equal to a_e . Consequently, they have postulated a stronger local packing criterion to ensure that in each local region of an aggregate, the area per amphiphile A/g is equal to a_e . These considerations suggest that when a spherical micelle cannot accommodate all the amphiphiles, a spherocylindrical aggregate is not immediately generated but other intermediary shapes such as globules and toroids are formed.

In this paper, the following aggregate shapes are considered: spheres, cylinders, monolayer discs, monolayer vesicles, bilayer discs and bilayer vesicles (Figure 1a,b). The cylinders are assumed to have hemispherical ends while the discs are considered to possess hemicylindrical rims. In the case of cylinders and discs, it is evident that the average area per amphiphile of the aggregate will be different from the local areas per amphiphile in the spherical, cylindrical and planar parts of the aggregates. Consequently, the actual aggregates are likely to assume transition shapes such as distorted spherocylinders and non-planar discs. In this paper, the aggregation numbers of these transition shapes are considered equal to those of a spherocylinder (or of a disc with hemispherical rims) having the same average surface area per amphiphile of the aggregate.

The relation between the aggregation number g and the geometrical properties of the aggregate are presented below for each of the aggregate shape mentioned above. For one-headed amphiphiles and bola amphiphiles, the volume V of the aggregate is equal to gv_0 . In the case of one-headed amphiphiles, the area per amphiphile is the same as the area per polar head group. In contrast, for bola amphiphiles, the area per amphiphile is equal to twice the area per polar head group. In the treatment which follows, 'a' will be used to denote the area per polar head group. Therefore, for one-headed amphiphiles $A = ga$, $V = gv_0$. For bola amphiphiles, $A = 2ga$, $V = gv_0$.

Spheres

The spherical aggregates are considered to have a hydrophobic core of radius r_0 . For an aggregate containing g amphiphiles,

$$V = 4\pi r_0^3/3, \quad A = 4\pi r_0^2 \quad (9)$$

For one-headed amphiphiles, the radius r_0 should be less than or equal to the

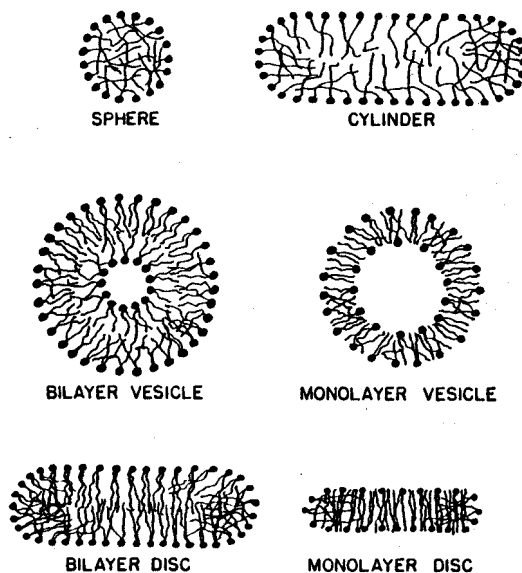


FIGURE 1a Patterns of aggregation of one-headed amphiphiles.

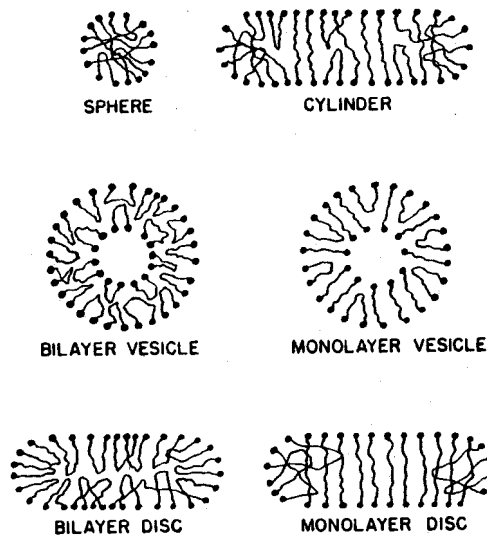


FIGURE 1b Patterns of aggregation of bola amphiphiles.

extended length l_0 of the hydrophobic chain. In this case

$$g = 36\pi v_0^2/a^3, \quad v_0/al_0 < 1/3. \quad (10)$$

For bola amphiphiles the radius r_0 should be less than or equal to $l_0/2$, irrespective of whether the hydrophobic chain has a bent or extended conformation inside the spherical aggregate. For this case,

$$g = 9\pi v_0^2/2a^3, \quad v_0/al_0 < 1/3. \quad (11)$$

Cylinders

The cylindrical aggregates are assumed to have a cylindrical middle part of radius r_0 and axial length L and hemispherical end caps of radius r_0 . For an aggregate containing g amphiphiles, the core volume V and the core surface area A are given by

$$V = \pi r_0^2 L + 4\pi r_0^3/3, \quad A = 2\pi r_0 L + 4\pi r_0^2 \quad (12)$$

For one-headed amphiphiles, the radius r_0 equals the extended length l_0 of the hydrophobic tail. Consequently,

$$g = (4\pi l_0^2/3)(a - 2v_0/l_0)^{-1}, \quad 1/3 < v_0/al_0 < 1/2 \quad (13)$$

For bola amphiphiles, $r_0 = l_0/2$. Consequently,

$$g = (\pi l_0^2/6)(a - 2v_0/l_0)^{-1}, \quad 1/3 < v_0/al_0 < 1/2. \quad (14)$$

Bilayer Vesicles

The bilayer vesicles are considered to be spherical with a hydrophobic shell of inner radius R_i and outer radius R_0 . The total volume and the surface area of the spherical hydrophobic shell of the bilayer vesicle are given by

$$V = 4\pi(R_0^3 - R_i^3)/3, \quad A = 4\pi(R_0^2 + R_i^2) \quad (15)$$

The amphiphiles distribute themselves between the inner and the outer layers in such a way as to ensure that the surface area per polar group at the inner surface is identical to that at the outer surface. If g_i and g_0 denote the number of amphiphiles in the inner and the outer layers of the bilayer vesicle respectively, then

$$g_i/g_0 = R_i^2/R_0^2. \quad (16)$$

For one-headed amphiphiles, the thickness of the hydrophobic shell is less than or equal to twice the extended length of the hydrophobic tail of the amphiphile. Taking $(R_0 - R_i) = 2l_0$, the following geometrical relations are obtained:

$$R_0 = [(gv_0/8\pi l_0) - (l_0^2/3)]^{1/2} + l_0, \quad R_i = R_0 - 2l_0 \quad (17)$$

$$g = (16\pi l_0^2/3)(a - v_0/l_0)^{-1}, \quad 1/2 < v_0/al_0 < 1 \quad (18)$$

In addition, if the volume of the polar head group of the amphiphile is v_p , then the formation of the vesicle is allowed only when the volume of the interior aqueous cavity of the vesicle is sufficiently larger than the total volume of the polar groups in the inner layer of the vesicle, namely

$$4\pi R_i^3/3 > g_i v_p \quad (19)$$

For bola amphiphiles, the formation of bilayer vesicles implies that the hydrophobic tails of all the amphiphiles assume a folded conformation. Correspondingly, the thickness of the hydrophobic shell of the bilayer vesicle is equal to the extended length l_0 of the hydrophobic tail of the amphiphile. For a vesicle

with hydrophobic shell thickness equal to l_0 , one may write

$$R_0 = [(gv_0/4\pi l_0) - l_0^2/12]^{1/2} + l_0/2, \quad R_i = R_0 - l_0 \quad (20)$$

$$g = (2\pi l_0^2/3)(a - v_0/l_0)^{-1}, \quad 1/2 < v_0/al_0 < 1. \quad (21)$$

Monolayer Vesicles

Spherical monolayer vesicles with a hydrophobic shell of inner radius R_i and outer radius R_0 are considered here. The total volume and the total surface area are given by

$$V = 4\pi(R_0^3 - R_i^3)/3, \quad A = 4\pi(R_0^2 + R_i^2) \quad (22)$$

The amphiphiles have to orient themselves in such a way that the area per polar head group at the inner and the outer surfaces of the monolayer vesicles are identical. If g_i and g_0 denote the number of polar groups that are oriented towards the inner aqueous core and the outer aqueous interface of the vesicle respectively, then

$$g_i/g_0 = R_i^2/R_0^2 \quad (23)$$

For one-headed amphiphile, the thickness of the hydrophobic shell can not exceed the extended length l_0 of the hydrophobic tail. Therefore,

$$R_0 = [(gv_0/4\pi l_0) - l_0^2/12]^{1/2} + l_0/2, \quad R_i = R_0 - l_0 \quad (24)$$

$$g = (4\pi l_0^2/3)(a - 2v_0/l_0)^{-1}, \quad 1/3 < v_0/al_0 < 1/2 \quad (25)$$

For bola amphiphiles, the monolayer vesicle is characterized by a hydrophobic shell thickness equal to l_0 . However, in a truly monolayer vesicle all the amphiphiles have to assume a fully stretched conformation. In such a structure, the number of head groups at the inner and the outer surfaces of the vesicle are equal to one another and are the same as the aggregation number g . Consequently, if the area per polar head group at the inner and the outer vesicular surfaces are to be equal, then a completely monolayer vesicle is not possible. Thus monolayer vesicles of bola amphiphiles must include certain number of molecules with a folded conformation in addition to the others with a fully stretched conformation. Indeed, no differentiation between monolayer and bilayer vesicles is necessary and the same geometrical relations hold in both the cases. Therefore,

$$R_0 = [(gv_0/4\pi l_0) - l_0^2/12]^{1/2} + l_0/2, \quad R_i = R_0 - l_0 \quad (26)$$

$$g = (2\pi l_0^2/3)(a - v_0/l_0)^{-1}, \quad 1/2 < v_0/al_0 < 1. \quad (27)$$

Bilayer Discs

The bilayer discs are assumed to consist of a planar part whose boundary is made up of a hemicylindrical rim. The thickness of the planar part and the diameter of the hemicylindrical rim are both equal and are of magnitude $2r_0$. The planar part

is a circular disc of radius R . The total volume and the total surface area of the bounded bilayer disc are given by

$$V = 2\pi R^2 r_0 + \pi^2 R r_0^2 + 4\pi r_0^3/3 \quad (28)$$

$$A = 2\pi R^2 + 2\pi^2 R r_0 + 4\pi r_0^2 \quad (29)$$

The amphiphiles are distributed equally between the two layers so as to ensure equal surface area per polar head group at both the surfaces of the bilayer.

For one-headed amphiphiles, the thickness $2r_0$ of the bilayer disc is less than or equal to twice the extended length of the amphiphilar tail. Taking $2r_0 = 2l_0$, the bilayer disc is defined by the approximate relations given below:

$$R = (gv_0/2\pi l_0)^{1/2} - (\pi l_0/4), \quad 2r_0 = 2l_0 \quad (30)$$

$$g = (16\pi v_0 l_0/3)(a - v_0/l_0)^{-2}, \quad 1/2 < v_0/al_0 < 1 \quad (31)$$

For bola amphiphiles, the occurrence of a bilayer disc implies that the hydrophobic tails of the amphiphiles are in a folded conformation rather than in a fully stretched conformation. This is identical to the situation considered earlier for the bilayer vesicles of bola amphiphiles. The thickness $2r_0$ of the bilayer disc is equal to the extended length l_0 of the amphiphile. As for vesicles, it is not necessary to distinguish between the bilayer discs and the monolayer discs since the latter also have a hydrophobic core of thickness equal to l_0 . A truly bilayer disc with all the amphiphiles in a folded conformation and a truly monolayer disc with all the amphiphiles in a fully stretched conformation are both possible since both these types of discs possess identical geometrical properties and both can satisfy the criterion of equal surface area per polar head group on the two disc surfaces. (This is in contrast to the case of vesicular aggregates where a truly monolayer vesicle will violate the condition of equal surface area per polar head group at the two surfaces). Taking $2r_0 = l_0$, one obtains the approximate relations

$$R = (gv_0/\pi l_0)^{1/2} - (\pi l_0/8), \quad 2r_0 = l_0 \quad (32)$$

$$g = (2\pi v_0 l_0/3)(a - v_0/l_0)^{-2}, \quad 1/2 < v_0/al_0 < 1. \quad (33)$$

Monolayer discs

Monolayer discs are characterized by a planar part of thickness $2r_0$ with hemicylindrical rims of diameter $2r_0$. The planar part has a radius R . The total volume and the total surface area of the hydrophobic core of the aggregate is given as before by the relations:

$$V = 2\pi R^2 r_0 + \pi^2 R r_0^2 + 4\pi r_0^3/3 \quad (34)$$

$$A = 2\pi R^2 + 2\pi^2 R r_0 + 4\pi r_0^2 \quad (35)$$

For one-headed amphiphiles, the amphiphiles must orient themselves in such a way that equal number of polar head groups are on either sides of the disc. The thickness of the monolayer disc is less than or equal to the extended length of the amphiphilar tail. For $2r_0 = l_0$, the following approximate equations for R and g

are obtained.

$$R = (gv_0/\pi l_0)^{1/2} - (\pi l_0/8), \quad 2r_0 = l_0 \quad (36)$$

$$g = (8\pi v_0 l_0/3)(a - 2v_0/l_0)^{-2}, \quad 1/3 < v_0/al_0 < 1/2 \quad (37)$$

For bola amphiphiles, as mentioned earlier, there is no distinction between the properties of the bilayer and monolayer discs. Therefore,

$$R = (gv_0/\pi l_0)^{1/2} - (\pi l_0/8), \quad 2r_0 = l_0 \quad (38)$$

$$g = (2\pi v_0 l_0/3)(a - v_0/l_0)^{-2}, \quad 1/2 < v_0/al_0 < 1 \quad (39)$$

In addition to the shapes of the aggregates discussed above, one can consider other shapes such as cylindrical vesicles as well. Once again it should be noted that the present analysis is focused on bola amphiphiles with identical polar head groups. Examples of bola amphiphiles with dissimilar head groups will be considered in a later paper. However, it may be mentioned here that if one of the polar groups is very weak such as a hydroxyl group then this polar group could possibly be accommodated within the hydrophobic region of the aggregate. In such a case, the bola amphiphile behaves identically to a one-headed amphiphile.

The geometrical properties discussed above are summarized in Table I for convenient reference. The aggregation numbers for various shapes are presented in terms of the packing parameter v_0/al_0 and the molecular constants v_0 and l_0 denoting the size of the amphiphile. If the area per polar head group for the optimal aggregate (favored by equilibrium conditions discussed in section II) is a_e , then the type of aggregates resulting from amphiphiles are summarized in Table II. If for the same value of the equilibrium packing parameter $v_0/a_e l_0$ more than one type of aggregate is indicated as possible, then equilibrium favors the aggregate of smaller aggregation number g as long as it is geometrically allowed. This latter geometrical restriction specifically refers to vesicular aggregates for which the inner aqueous core volume should be larger than the volume of all the polar groups located at that inner interface.

For all allowed shapes of the aggregates, the relations summarized in Table I can be used to obtain the ratios of aggregation numbers when v_0 , l_0 and a_e are specified.

TABLE I

Geometrical properties of aggregates

Aggregate	One-headed amphiphile	Bola amphiphile
Sphere	$g = (36\pi l_0^3/v_0)(v_0/al_0)^3$	$g = (9\pi l_0^3/2v_0)(v_0/al_0)^3$
Cylinder	$g = (4\pi l_0^3/3v_0)(al_0/v_0 - 2)^{-1}$	$g = (\pi l_0^3/6v_0)(al_0/v_0 - 2)^{-1}$
Monolayer vesicle	$g = (4\pi l_0^3/3v_0)(al_0/v_0 - 2)^{-1}$	$g = (2\pi l_0^3/3v_0)(al_0/v_0 - 1)^{-1}$
Bilayer vesicle	$g = (16\pi l_0^3/3v_0)(al_0/v_0 - 1)^{-1}$	same as monolayer vesicle
Monolayer disc	$g = (8\pi l_0^3/3v_0)(al_0/v_0 - 2)^{-2}$	$g = (2\pi l_0^3/3v_0)(al_0/v_0 - 1)^{-2}$
Bilayer disc	$g = (16\pi l_0^3/3v_0)(al_0/v_0 - 1)^{-2}$	same as monolayer disc

TABLE II

Equilibrium packing parameter and allowed aggregates

Packing parameter	One-headed amphiphile	Bola amphiphile
$0 < v_0/a_l_0 < 1/3$	Spheres	Spheres
$1/3 < v_0/a_l_0 < 1/2$	Cylinders	Cylinders
$1/2 < v_0/a_l_0 < 1$	Bilayers vesicle Bilayer disc	Vesicle disc

For one-headed amphiphiles

$$g(\text{cylinder}) = g(\text{monolayer vesicle})$$

$$g(\text{cylinder}) < g(\text{monolayer disc})$$

$$g(\text{bilayer vesicle}) < g(\text{bilayer disc})$$

For bola amphiphiles

$$g(\text{bilayer vesicle}) = g(\text{monolayer vesicle})$$

$$g(\text{bilayer disc}) = g(\text{monolayer disc})$$

$$g(\text{vesicle}) < g(\text{disc})$$

In order to obtain further quantitative information about the aggregates, it is necessary to estimate the equilibrium area a_e per polar head group of the aggregate. This is carried out in the following section on the basis of a consideration of the free energy of aggregation.

IV. FREE ENERGY OF AGGREGATION

An explicit expression to estimate the free energy of aggregation may be formulated by taking into consideration all the changes experienced by an amphiphile when transferred from water into an aggregate. Firstly, the formation of the aggregate involves the transfer of the hydrophobic tail of the amphiphile from water to a hydrocarbon liquid like region of the aggregate. This region differs somewhat from a liquid hydrocarbon when the state of the amphiphilar tail is compared to that of an equivalent molecule in bulk liquid. In the former, one end of the hydrophobic tail (which is attached to the head group) is constrained to remain at the aggregate-water interface. This constraint induces some ordering of the hydrocarbon tail inside the aggregate. After accounting for this internal ordering, the net contribution to the free energy of aggregation arising from the transfer of the hydrophobic tail of the amphiphile from water to an aggregate is negative. This constitutes the principal driving force for the aggregation. This contribution when expressed per amphiphile is independent of the size of the aggregate.

Secondly, the formation of the aggregate is accompanied by the generation of an interface between the hydrophobic region of the aggregate and water. The corresponding free energy of formation of the interface provides a positive contribution to the free energy of aggregation. In general, the larger the aggregation number, the smaller the aggregate surface area per polar group of the amphiphile. Consequently, the positive contribution per amphiphile from the aggregate-water interfacial free energy decreases with the increasing size of the aggregate. Thus this contribution is responsible for the positive cooperativity favoring the growth of aggregates.

Finally, the formation of the aggregate results in the polar groups of the amphiphiles being brought into close proximity of one another at the aggregate surface. This gives rise to steric interactions among them. Additionally, if the polar groups are dipolar or ionic, then electrostatic interactions among the head groups are also present. These mutual interactions among the head groups provide a positive contribution to the free energy of aggregation. The head group repulsions per amphiphile increase when the aggregate area per head group decreases, i.e. when the aggregation number increases. Hence, this contribution is responsible for the negative or anti-cooperativity which limits the aggregates to finite sizes.

Taking into account all the contributions mentioned above to the free energy of aggregation, one can write the following expression for $(\mu_g^0 - g\mu_1^0)/kT$ for one-headed amphiphiles:

$$\begin{aligned} (\mu_g^0 - g\mu_1^0)/kT = & g \Delta\mu_w^0/kT + g \Delta\mu_{ex}^0/kT + g\sigma(a - a_0)/kT - g \ln(1 - a_p/a) \\ & + (g^2 e^2 \beta / 2\epsilon k T r) [(1 + \kappa a_i) / (1 + \kappa a_i + \kappa r)] \end{aligned} \quad (40)$$

In the above expression, the first term represents the free energy change associated with the transfer of the amphiphilar tail from water to a hydrocarbon liquid phase. The second term provides the free energy corrections to the above transfer energy because of the ordering of the tails inside the aggregates. The third term refers to the free energy of formation of an interface between the hydrophobic region of the aggregate and water. Here, σ is the macroscopic interfacial tension between hydrocarbon and water, a is the surface area of the hydrophobic region of the aggregate per polar head group and a_0 is the area per polar group of the surface that is shielded from contact with water because of the presence of the head group in the amphiphile. The fourth term provides an estimate of the steric interactions among the polar head groups at the aggregate surface. It is written in a form suggested by the van der Waals equation of state. Here a_p is the geometrical cross-sectional area of the polar group impenetrable by other head groups. The last term accounts for the electrostatic interactions between the ionic head groups at the aggregate surface. It is written as equal to the work of charging a sphere of radius r with g net charges and invoking the Debye-Hückel approximation. Here, e is the electronic charge, ϵ is the dielectric constant of water, $r = r_0 + \delta$ where δ is the distance from the hydrophobic surface where the ionic charges are located, κ is the reciprocal Debye length, and a_i is the radius of the counterion of the surfactant. β is an empirical constant which

corrects for the overestimation of the ionic interaction energy by the Debye-Hückel approximation. Following Tanford's observation [16] and our earlier calculations for a variety of amphiphiles [24], β is taken equal to 0.46 for all ionic amphiphiles. The last term could be used to estimate the electrostatic interaction energy among dipolar head groups as well. In this case, a_i refers to the length of the dipole, κ tends to infinity and β is taken equal to unity.

For bola amphiphiles, the free energy of aggregation can be written in a similar form taking into consideration the presence of two head groups in each amphiphile.

$$\begin{aligned} (\mu_g^0 - g\mu_i^0)/kT = & g \Delta\mu_{ir}^0/kT + g \Delta\mu_{ex}^0/kT + 2g\sigma(a - a_0)/kT - 2g \ln(1 - a_p/a) \\ & + \{(2g)^2 e^2 \beta / 2\epsilon k T r\} [(1 + \kappa a_i)/(1 + \kappa a_i + \kappa r)] \end{aligned} \quad (41)$$

The free energy of aggregation per amphiphile can be written in a simplified form by introducing the geometrical relation between g and r given in Eq. (9) to (11) for spheres. This yields, for one-headed amphiphiles

$$(\mu_g^0/g - \mu_i^0)/kT = \Delta\mu_{ir}^0/kT + \Delta\mu_{ex}^0/kT + \sigma(a - a_0)/kT - \ln(1 - a_p/a) + \Phi/a^2 \quad (42)$$

and for bola amphiphiles

$$(\mu_g^0/g - \mu_i^0)/kT = \Delta\mu_{ir}^0/kT + \Delta\mu_{ex}^0/kT + 2\sigma(a - a_0)/kT - 2 \ln(1 - a_p/a) + \Phi/a^2 \quad (43)$$

In the above equations, Φ is given approximately by the relation

$$\Phi = 6\pi v_0 e^2 \beta / (\epsilon k T) [(1 + \kappa a_i)/(1 + \kappa a_i + \kappa(l_0 + \delta))] \quad (44)$$

for one-headed amphiphiles and

$$\Phi = 6\pi v_0 e^2 \beta / (\epsilon k T) [(1 + \kappa a_i)/(1 + \kappa a_i + \kappa(l_0/2 + \delta))] \quad (45)$$

for bola amphiphiles. The functional form of the electrostatic interaction energy between the polar head groups Φ/a^2 , is retained for the other shapes of the aggregates as well. Alternately, one could write specific expressions suitable for each aggregate shape [24] but this refinement in detail is unnecessary for the purposes of this paper. Consequently, the free energy of formation per amphiphile of all shapes of aggregates can be calculated from Eqs. (42) and (44) for one-headed amphiphiles and from Eqs. (43) and (45) for bola amphiphiles.

Given the explicit expression for the free energy of aggregation, one may apply the pseudophase equilibrium condition Eq. (7) to obtain the equilibrium aggregation number g_e and the equilibrium aggregate area per polar head group a_e . The minimization of Eqs. (42) and (43) can be done with respect to the variable a . The equilibrium area a_e per head group is obtained from the solution of

$$a_e = [(a_p/a_e)/(1 - a_p/a_e) + 2\Phi/a_e^2]/(\sigma/kT) \quad (46)$$

for one-headed amphiphiles, and from the solution of

$$a_e = [(a_p/a_e)/(1 - a_p/a_e) + \Phi/a_e^2]/(\sigma/kT) \quad (47)$$

TABLE III

Some molecular constants for amphiphiles

Head group	Symbol	a_p (Å ²)	a_0 (Å ²)	a_i (Å)	δ (Å)
N(CH ₃) ₃ Br	Me ₃	35	21	2.2	1.5
(OCH ₂ CH ₂) ₇ OH	E ₇	36	21	0	0
(OCH ₂ CH ₂) ₁₅ OH	E ₁₅	50	21	0	0
(OCH ₂ CH ₂) ₂₂ OH	E ₂₂	60	21	0	0

for bola amphiphiles. The corresponding critical micelle (aggregate) concentrations are calculated using Eqs. (8), (42) and (43) in which the area a is replaced by the equilibrium area a_e per polar head group. The calculated equilibrium aggregate area a_e per polar head group, in conjunction with the packing criteria summarized in Table II allows one to determine the type of aggregate generated by an amphiphile.

Estimation of Model Parameters

To facilitate quantitative calculations, the values of parameters appearing in Eqs. (42) to (45) are needed. The values of various molecular constants appearing in these equations are listed in Table III for a number of amphiphiles. Other parameters appearing in the equations are estimated as described below. A more detailed discussion of these parameter values has been presented before [24, 29].

The free energy of transferring an alkyl chain from water to a bulk liquid hydrocarbon can be estimated from independent experimental data [16, 30–32] on the solubility of hydrocarbons in water. For an aliphatic hydrocarbon chain of length n_c with $(n_c - 1)$ methylene groups and a terminal methyl group, at 25°C,

$$\Delta\mu_{tr}^0/kT = -(2.05 + 1.49n_c) \quad (48)$$

In the hydrophobic tail of length n_c in a bola amphiphile, there are n_c methylene groups and no methyl group. For such a tail,

$$\Delta\mu_{tr}^0/kT = -(1.49n_c) \quad (49)$$

When the hydrophobic tail consists of two chains, the transfer free energy is not simply twice the value given by Eqs. (48) or (49). This is because of the presence of considerable intramolecular interactions among the two chains even in the singly dispersed state of the molecule [16]. The second chain makes a smaller contribution to the transfer free energy compared to the first chain. Based on available information [16], the transfer free energy of dialkyl hydrocarbon tails is taken to be equal to 1.5 times that of the monoalkyl tail.

The excess contribution to the above transfer free energy which arises from the ordering of the hydrophobic tails inside the aggregates can be roughly estimated based on one or another assumed model [22, 23]. However, this excess

contribution has been treated as an empirical quantity in our earlier work [24, 29]. For single alkyl chains containing $(n_c - 1)$ methylene and one terminal methyl group, at 25°C

$$\Delta\mu_{ex}^0/kT = -0.5 + 0.24n_c \quad (50)$$

Since the excess contribution is estimated on an empirical basis, no modification is made for the hydrophobic tail of a bola amphiphile in which there is no terminal methyl group. For a hydrophobic tail containing two hydrocarbon chains, the excess contribution to the transfer free energy is simply taken to be twice the value for a single chain. It may be mentioned that the empirical Eq. (50) has certain generality in the sense that the same equation is used for all hydrocarbon amphiphiles. For one-headed amphiphiles, the use of this empirical equation has been shown to provide good agreement between the experimental and calculated critical micelle concentrations when a homologous family of amphiphiles is considered [29]. Any uncertainty in using Eq. (50) for bola amphiphiles affects only the magnitudes of the critical micelle concentrations slightly but not any other feature of aggregation behavior discussed in this paper.

The interfacial tension σ between the hydrophobic core of the aggregate and water is treated to be the same as the macroscopic interfacial tension between liquid hydrocarbon and water. For aliphatic hydrocarbon tails, σ is taken to be 50 dyne/cm. The hydrophobic tail of the surfactant (which has a cross-sectional area of 21 \AA^2 for aliphatic chains) is shielded completely from water if the polar head group has a cross-sectional area a_p greater than 21 \AA^2 . For such an amphiphile, a_0 is taken to be 21 \AA^2 . If a_p is less than 21 \AA^2 , then the polar head group shields only a part of the cross-sectional area of the tail. In this case a_0 is taken equal to a_p .

In summary, the expression for the free energy of aggregation presented above mostly involves parameters which are independently known as well as a number of molecular constants. Two empirical quantities have been used, namely, Eq. (50) which accounts for the ordering of the tails inside the aggregates and the constant $\beta = 0.46$ which corrects for the overestimation of the inter-ionic interaction energy by the Debye-Hückel approximation. However, these two empirical quantities are not treated as adjustable parameters but as constants valid for all hydrocarbon amphiphiles and ionic head groups, respectively. Using the model parameters, one can examine the aggregation behavior of amphiphiles on the basis of Eqs. (42) to (47). In the following section, some illustrative results are presented for ionic as well as nonionic amphiphiles containing one or two chains in the hydrophobic tail.

V. RESULTS AND DISCUSSION

In this section, the aggregation behavior of bola amphiphiles is examined in comparison to that of one-headed amphiphiles having an equivalent hydrophobic tail. Two general results are evident from Eqs. (42) to (47) even without performing any model calculations. For the same polar head group, the

equilibrium area per amphiphile (a_e for one-headed amphiphiles and $2a_e$ for bola amphiphiles) is smaller for one-headed amphiphiles when compared to bola amphiphiles. This implies that the equilibrium aggregation number for the aggregates of bola amphiphile will be relatively smaller. Secondly, the presence of two head groups in the bola amphiphile results in larger positive contribution to the free energy of aggregation and consequently in higher values for the critical micelle (aggregate) concentrations. Both these aspects are intuitively understandable if one recognizes that the presence of the second polar head group increases the aqueous solubility of bola amphiphiles when compared to that of the corresponding one-headed amphiphiles. This stronger tendency towards molecular dissolution is coupled to the weaker tendency to self-associate. Specific results for a number of bola amphiphiles are discussed below.

Ionic Amphiphiles: Influence of Hydrophobic Tail

The aggregation behavior of cationic single chain amphiphiles with trimethyl ammonium bromide as the polar head group has been examined as a function of the hydrophobic chain length. These bola amphiphiles have been experimentally studied before [2–5]. One should note that for the same polar head group, the equilibrium area per head group a_e will be different for different hydrophobic chain lengths because the electrostatic inter-ionic interaction energy group Φ changes. The dependence of Φ on n_c is caused by the changes in v_0 , l_0 , and κ as can be seen from Eqs. (44) and (45). In the absence of any added electrolyte in the solution, κ depends upon the concentration of the singly dispersed amphiphile (cmc) which varies substantially with varying hydrophobic tails.

The results from the present calculations are summarized in Table IV. As mentioned above, the values of Φ increase with increasing n_c . This is consistent with the corresponding increase in v_0 and the decrease in the cmc (which decreases κ). When one-headed and bola amphiphiles having the same hydrophobic tail are compared, Φ for the bola amphiphile is smaller. This is primarily because of the larger cmc and the contribution to the ionic strength from both the ionic head groups of the bola amphiphile (which increase κ and hence decrease Φ). The one-headed amphiphiles form spherical micelles. The calculated aggregation numbers and the cmcs compare well with known experimental values [3, 16]. For all the bola amphiphiles the calculated aggregation numbers are small. This

TABLE IV

Aggregation behavior of single chain ionic amphiphiles: Influence of hydrophobic tail length

Amphiphile	Φ	a_e (\AA^2)	$v_0/a_e l_0$	Aggregate	g_e	cmc(M)
$C_{12}Me_3$	14067	65	0.323	Sphere	51	1.7×10^{-2}
$C_{16}Me_3$	22855	74.5	0.282	Sphere	58	6.9×10^{-4}
$C_{22}Me_3$	36577	86.3	0.243	Sphere	68	3.2×10^{-6}
$Me_3C_{12}Me_3$	6447	47.2	0.438	Cylinder	23	1.64
$Me_3C_{16}Me_3$	11725	52.1	0.403	Cylinder	21	9.3×10^{-2}
$Me_3C_{22}Me_3$	25256	62.8	0.334	Sphere	19	3.0×10^{-3}

TABLE V

Aggregation behavior of double chain ionic amphiphiles: Influence of hydrophobic tail length

Amphiphile	Φ	a_e (\AA^2)	$v_0/a_e l_0$	Aggregate	g_e	cmc(M)
$(C_{12})_2Me_3$	38450	87.6	0.479	Cylinder	324	5.5×10^{-4}
$(C_{16})_2Me_3$	55186	98.3	0.427	Cylinder	139	3.4×10^{-6}
$(C_{22})_2Me_3$	75416	108.7	0.386	Cylinder	146	6.0×10^{-10}
$Me_3(C_{12})_2Me_3$	18690	58.0	0.724	Disc	81	1.9×10^{-1}
$Me_3(C_{16})_2Me_3$	33155	68.1	0.620	Disc	55	8.0×10^{-3}
$Me_3(C_{22})_2Me_3$	68533	84.6	0.495	Cylinder	480	7.9×10^{-5}

means that the extent of cooperativity of association is weaker. Two general characteristics of systems showing weakly cooperative association are the occurrence of small oligomers (of amphiphiles) in appreciable concentrations and the decrease in the sharpness of transition of the various physical properties near the cmc [33]. For the bola amphiphile with the dodecyl chain, the calculated cmc is unreasonably large to be physically meaningful. This implies that the amphiphile behaves essentially as an electrolyte having considerable solubility in water. This may explain why at the concentrations at which experiments were performed by Menger and Wrenn [2] only small oligomers were observed and why the experiments of Zana *et al.* [3] failed to reveal a cmc. The calculated cmcs and aggregation numbers for the bola amphiphiles with C_{16} and C_{22} chains agree very well with the measured values of Zana *et al.* [4, 5].

The calculated aggregation properties for cationic double chain amphiphiles are presented in Table V. The presence of the second chain causes some increase in the equilibrium area a_e per head group when compared to the single chain amphiphiles (because cmc is lower, κ is smaller, and hence Φ is larger) while doubling the chain volume v_0 . Consequently, the magnitude of the packing parameter is considerably increased and correspondingly larger aggregates are formed. One-headed amphiphiles form cylindrical aggregates while the bola amphiphiles form discs and cylinders. It may be noted that the discs could be of monolayer, bilayer or a mixed type since all these structures are geometrically and thermodynamically equivalent. For the bola amphiphile $Me_3(C_{12})_2Me_3$, the calculated cmc is physically unrealistic implying that no aggregates are formed.

The results presented in Tables IV and V suggest that in order to observe other aggregation patterns, the magnitude of the packing parameter has to be increased. This can be done by decreasing a_e for ionic amphiphiles through the addition of electrolytes. The limiting situation is that of a nonionic amphiphile. Therefore, examples of nonionic amphiphiles are examined below.

Nonionic Amphiphiles: Influence of Head Group

Nonionic amphiphiles with polyoxyethylene type head groups have been examined here. The hydrophobic tail is a hexadecyl alkyl chain while the polar head

TABLE VI

Aggregation behavior of single chain nonionic amphiphiles: Influence of the size of polar head group

Amphiphile	a_p (Å ²)	a_e (Å ²)	$v_0/a_e l_0$	Aggregate	g_e	cmc(M)
C ₁₆ E ₇	36	42.9	0.489	Cylinder	2097	0.8×10^{-6}
C ₁₆ E ₁₅	50	57.7	0.364	Cylinder	126	5.8×10^{-6}
C ₁₆ E ₂₂	60	68.3	0.307	Sphere	75	2.3×10^{-5}
E ₇ C ₁₆ E ₇	36	42.9	0.489	Cylinder	227	5.5×10^{-4}
E ₁₅ C ₁₆ E ₁₅	50	57.7	0.364	Cylinder	14	2.9×10^{-2}
E ₂₂ C ₁₆ E ₂₂	60	68.3	0.307	Sphere	8	4.7×10^{-1}

groups are varied from 7 to 22 ethyleneoxide units. The larger the number of ethyleneoxide units, the larger is the effective size of the head group (reflected in the value of a_p) and hence the magnitude of steric interactions among them. The calculated results for one-headed amphiphiles show the formation of a very large cylindrical micelle, a smaller spherocylinder and a small spherical micelle (Table VI). The calculated aggregation numbers and the values of the cmc are in satisfactory agreement with available experimental data [29]. For the bola amphiphiles, the equilibrium area per polar group is the same as for the one-headed amphiphiles since a_e depends only on a_p for nonionic amphiphiles. Thus one obtains micelles of bola amphiphiles that are smaller than those of the corresponding one-headed amphiphiles. One may note that the cmc calculated for E₂₂C₁₆E₂₂ is physically unrealistic, implying that no aggregation is possible. The presence of the two large ethyleneoxide head groups makes the molecule highly soluble in water and prevents its aggregation.

The results for nonionic amphiphiles with two hydrocarbon chains are presented in Table VII. The equilibrium area a_e does not change with the addition of a second tail, in contrast to the behavior of ionic amphiphiles. Consequently, the addition of the second tail results in the doubling of the magnitude of the equilibrium packing parameter. For the one-headed amphiphile with E₇ head group, bilayer vesicles are formed. In contrast, for the amphiphiles

TABLE VII

Aggregation behavior of double chain nonionic amphiphiles: Influence of the size of the polar head group

Amphiphile	a_p (Å ²)	a_e (Å ²)	$v_0/a_e l_0$	Aggregate	g_e	cmc(M)
(C ₁₆) ₂ E ₇	36	42.9	0.979	Bilayer vesicle	8741	5.4×10^{-11}
(C ₁₆) ₂ E ₁₅	50	57.7	0.728	Bilayer disc	1295	3.9×10^{-10}
(C ₁₆) ₂ E ₂₂	60	68.3	0.614	Bilayer disc	462	1.6×10^{-9}
E ₇ (C ₁₆) ₂ E ₇	36	42.9	0.979	Vesicle	952	1.0×10^{-7}
E ₁₅ (C ₁₆) ₂ E ₁₅	50	57.7	0.728	Disc	142	6.5×10^{-6}
E ₂₂ (C ₁₆) ₂ E ₂₂	60	68.3	0.614	Disc	51	8.7×10^{-5}

TABLE VIII

Aggregation behavior of nonionic bola amphiphiles: Influence of hydrophobic tail length

Amphiphile	a_p (\AA^2)	a_e (\AA^2)	$v_0/a_e l_0$	Aggregate	g_e
$E_7C_{10}E_7$	36	42.91	0.489	Cylinder	93
$E_7C_{20}E_7$	36	42.91	0.489	Cylinder	372
$E_7C_{30}E_7$	36	42.91	0.489	Cylinder	837
$E_7(C_{10})_2E_7$	36	42.91	0.979	Disc	16825
$E_7(C_{20})_2E_7$	36	42.91	0.979	Vesicle	1488
$E_7(C_{30})_2E_7$	36	42.91	0.979	Vesicle	3348

with E_{15} and E_{22} head groups, bilayer discs are preferred. It may be recalled that for a given value of a_e , the aggregation number of a bilayer vesicle will always be smaller than that of a bilayer disc. Thus the system entropy should favor the formation of bilayer vesicles. However, such vesicles are geometrically disallowed because the inner aqueous compartments of the vesicles do not possess a volume adequate to accommodate the polar head groups. Therefore, the bilayer discs are formed.

The calculated results for nonionic double chain bola amphiphiles show that vesicles and discs are formed. As mentioned earlier, no distinction needs to be made as to whether the vesicles and discs are of the monolayer or the bilayer type. For small polar groups, vesicles are formed. When the size of the polar group increases, the inner aqueous compartment of the vesicle becomes inadequate for accommodating the polar head groups and hence the vesicles are geometrically disallowed and discs are formed.

Nonionic Amphiphiles: Influence of Hydrophobic Tail

The calculated aggregation behavior of single chain and double chain bola amphiphiles with E_7 as the polar head group are summarized in Table VIII. For single chain amphiphiles, increasingly larger cylindrical micelles are formed with increasing chain length of the hydrophobic tail. One may note that the equilibrium packing parameter is identical in all the cases and the differences in the aggregation numbers are purely a consequence of the geometrical property of the aggregate. For double chain bola amphiphiles, discs and vesicles are predicted. When the hydrocarbon chain length is small, the size of the equilibrium vesicle is small. Since the inner aqueous cavity of the vesicle is smaller in volume than that of all the polar groups that should be accommodated inside, the vesicle is geometrically disallowed and the much larger disc is formed. For example, the calculated aggregation number of the equilibrium vesicle for $E_7(C_{10})_2E_7$ is 372 and the inner and outer radii of the hydrophobic shell are 28.74 and 41.39 \AA , respectively. Correspondingly, 502 polar groups should be at the outer surface while 242 should be at the inner surface. The calculated volume of the inner aqueous cavity per polar group is only 411 \AA^3 while the volume of a E_7 polar group is about 441 \AA^3 [29]. In contrast, as the hydrophobic chain length

increases, the size of the equilibrium vesicle increases and the vesicle becomes both the thermodynamically preferred and geometrically allowed aggregate. This is seen for the C_{20} and C_{30} double chain bola amphiphiles.

VI. CONCLUSIONS

The principles of molecular organization of bola amphiphiles are examined in this paper using thermodynamic and geometric considerations that have been successfully applied to one-headed amphiphiles. The bola amphiphiles are found to aggregate into spheres, small and large cylinders, small and large discs and vesicles. In all the aggregates, the amphiphiles are likely to have a combination of both the folded and the fully stretched conformations of the hydrophobic chain. In general, the presence of the second head group increases the solubility of the amphiphile in water, increases the cmc and decreases the aggregation numbers when compared to the corresponding one-headed amphiphiles. An increase in the repulsive interactions among the head groups (steric and/or electrostatic) and a shorter hydrophobic tail lead to the formation of small spherical and spherocylindrical micelles or discs. In a number of situations, aggregation does not occur at all and the amphiphile is dissolved in a singly dispersed state or as small oligomers. When the repulsive interactions among the head groups are reduced and for sufficiently long hydrophobic tails, very large cylinders or vesicles are formed. An analysis of the aggregation behavior of bola amphiphiles with dissimilar polar groups will be published in a later paper.

NOMENCLATURE

a	surface area of the hydrophobic core of the aggregate per polar head group.
a_e	surface area per polar head group of the hydrophobic core of the aggregate preferred by equilibrium conditions.
a_p	cross-sectional area of the polar head group.
a_0	area per polar head group shielded from contact with water because of the presence of the head group.
a_i	radius of the counterion of the ionic head group of the amphiphile.
C_1	molar concentration of the ionic head groups in the singly dispersed amphiphiles (equals the cmc for one-headed amphiphiles and twice the cmc for bola amphiphiles).
C_{add}	molar concentration of any added electrolyte.
e	electronic charge ($= 4.8 \times 10^{-10}$ esu).
E_x	nonionic polar head group with x units of ethylene oxide.
g	number of amphiphiles in an aggregate.

k	Boltzmann constant ($= 1.38 \times 10^{-16}$ erg/°K).
l_0	length of the hydrophobic tail of the surfactant ($= 1.265 \text{ \AA}$ for each methylene group and 2.765 \AA for the terminal methyl group).
L	Length of the cylindrical portion of the cylindrical aggregate having hemispherical ends.
n_c	number of methylene and methyl groups in the hydrophobic tail.
r_0	radius of the hydrophobic core of the spherical aggregate, the cylindrical aggregate, and the hemicylindrical rims of discs.
r	radius of the aggregate surface at which the ionic charges or the zwitterionic dipoles are located ($= r_0 + \delta$).
R_i	radius of the inner surface of the hydrophobic spherical shell of the vesicle.
R_0	radius of the outer surface of the hydrophobic spherical shell of the vesicle.
R	radius of the planar part of the disc with hemicylindrical rim.
T	absolute temperature of the solution ($= 298^\circ\text{K}$ in this paper).
v_0	molecular volume of the hydrophobic tail of the amphiphile ($= 27 \text{ \AA}^3$ for each methylene group and 54 \AA^3 for the terminal methyl group).
v_p	volume of the polar head group of the amphiphile.
X_1	mole fraction of singly dispersed amphiphiles.
X_g	mole fraction of aggregate containing g amphiphiles.
β	a constant which modifies the Debye-Hückel estimate of the interionic interaction energy ($= 0.46$).
δ	distance of separation between the hydrophobic core of the aggregate and the surface at which the ionic charges or dipoles are located.
ϵ	dielectric constant of water ($= 80$).
κ	reciprocal Debye length ($= (C_1 + C_{\text{add}})^{1/2}/3.08 \text{ \AA}^{-1}$ at 25°C).
σ	macroscopic hydrocarbon-water interfacial tension ($= 50$ dyne/cm).

REFERENCES

1. Fuoss, R.M., and Edelson, D.J., *J. Am. Chem. Soc.*, **73**, 269 (1951).
2. Menger, F.M., and Wrenn, S., *J. Phys. Chem.* **78**, 1387 (1974).
3. Yiv, S., Kale, K. M., Lang, J., and Zana, R., *J. Phys. Chem.* **80**, 2651 (1976).
4. Yiv, S., and Zana, R., *J. Colloid Interface Sci.*, **77**, 449 (1980).
5. Zana, R., Yiv, S., and Kale, K. M., *J. Colloid Interface Sci.*, **77**, 456 (1980).
6. Okahata, Y., and Kunitake, T., *J. Am. Chem. Soc.*, **101**, 5231 (1979).
7. Kunitake, T., Okahata, Y., Shimomura, M., Yasunami, S., Takarabe, K., *J. Am. Chem. Soc.*, **103**, 5401 (1981).
8. Fuhrhop, J.H., Fritsch, D., *Acc. Chem. Res.*, **19**, 130 (1986).
9. Brown, G.L., Grieger, P., Kraus, P.A., *J. Am. Chem. Soc.*, **71**, 95 (1949).
10. Fuhrhop, J.H., Kaufmann, W., Schambil, F., *Langmuir*, **1**, 387 (1985).
11. Mukerjee, P., *Adv. Colloid Interface Sci.* **1**, 241 (1967).
12. Mukerjee, P., *J. Pharm. Sci.*, **68**, 972 (1974).

13. Mukerjee, P., In *Micellization, Solubilization and Microemulsions*, Mittal, K.L., Ed., Plenum Press: New York, (1977).
14. Mukerjee, P., *J. Phys. Chem.*, **73**, 2054 (1969).
15. Mukerjee, P., *J. Phys. Chem.*, **76**, 565 (1972).
16. Tanford, C., *The Hydrophobic Effect*, Wiley: New York (1973).
17. Tanford, C., *J. Phys. Chem.*, **78**, 2469 (1974).
18. Tartar, H.V., *J. Phys. Chem.*, **59**, 1195 (1955).
19. Israelachvili, J.N., Mitchell, D.J., and Ninham, B.W., *J. Chem. Soc. Faraday Trans. II*, **72**, 1525 (1976).
20. Israelachvili, J.N., Mitchell, D.J., and Ninham, B.W., *Biochim. Biophys. Acta*, **470**, 185 (1977).
21. Israelachvili, J.N., Marcelja, S., and Horn, R.G., *Q. Rev. Biophys.*, **13**, 121 (1980).
22. Nagarajan, R., and Ruckenstein, E., *J. Colloid Interface Sci.*, **60**, 221 (1977).
23. Nagarajan, R., and Ruckenstein, E., *J. Colloid Interface Sci.*, **71**, 580 (1979).
24. Nagarajan, R., *Langmuir*, **1**, 331 (1985).
25. Nagarajan, R., *Colloids Surf.*, **13**, 1 (1985).
26. Nagarajan, R., and Ruckenstein, E., In *Surfactants in Solution*, Mittal, K.L., Lindman, B., Eds., Plenum Press, New York, (1984).
27. Nagarajan, R., Chaiko, M.A., and Ruckenstein, E., *J. Phys. Chem.*, **88**, 2916 (1984).
28. Nagarajan, R., and Ruckenstein, E., *Sep. Sci. Technol.*, **16**, 1429 (1981).
29. Nagarajan, R., *Adv. Colloid Interface Sci.*, **26**, 205 (1986).
30. Nemethy, G., and Scheraga, H.A., *J. Chem. Phys.*, **36**, 13401 (1962).
31. "American Petroleum Institute Technical Data Book"; American Petroleum Institute: Washington, DC (1979).
32. Abraham, M.H., *J. Chem. Soc. Faraday Trans. I*, **80**, 153 (1984).
33. Ruckenstein, E., and Nagarajan, R., *J. Phys. Chem.*, **85**, 3010 (1981).