

Formation of Self-Assembling Structures: Micelles, Bilayers, and Vesicles

CHE 385M Surface Phenomena Project

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Objectives

The goal of this project will be to work through the derivation of several well-known equations that relate molecular features of amphiphilic molecules to the stability, size, and shape of the various aggregate structures that they form. An outline of the problem is as follows:

- a. Show that the surface energy for aggregate structures of amphiphilic molecules reaches a minimum when the average surface area per headgroup is at an optimum value. Express this optimal headgroup area as a function of the interfacial tension between the hydrocarbon tail/water interface and the repulsive energy between hydrophilic headgroups.
- b. Show how the form of the aggregate structure depends on the optimal headgroup area, chain volume, and critical chain length. Show how the dimensionless packing parameter (v_c/a_0l_c) determines whether the aggregates form spherical micelles, nonspherical micelles, vesicles or bilayers, or inverted micelle structures.
- c. Derive equations relating the size of micelles and vesicles to the chain volume, chain length, and optimal headgroup area of the amphiphile.
- d. Perform example calculations for the predicted micelle size of sodium dodecyl sulfate (SDS) and for the predicted vesicle size of phosphatidylcholine.
- e. Compare the predicted vesicle size for phosphatidylcholine to those measured by Tim Young in the laboratory. If the experimental data do not agree with the model predictions, propose an explanation to account for the differences.

Introduction

Amphiphilic molecules have both polar and nonpolar characteristics. The headgroup typically contains a hydrophilic functional group, and the tail usually consists of a hydrophobic hydrocarbon chain. When the concentration of these molecules in a solution is raised above a critical level known as the critical micelle concentration (CMC), the molecules can reduce their free energy by assembling into aggregated structures. Below the CMC, the entropy of mixing dominates and the molecules simply form a solution. By aggregating, the hydrophobic tail groups are largely able to avoid the unfavorable surface energies associated with contacting the water molecules.

Micelles are the simplest form of self-assembled structure. In these structures, the molecules are arranged with the tails in the center and the headgroups around the surface. Micelles may be in the form of spheres, flattened spheres, or cylinders. A bilayer is a planar sheet of two layers of molecules arranged with the tails in the middle and the headgroups on the surface. When a bilayer curves into a spherical structure it is called a vesicle. Vesicles may also contain many more than two layers as additional bilayers add to the surface analogous to the many layers of skin on an onion.

The size and shape of the aggregates that form are determined by the characteristics of the molecules that form them. The following discussion shows how the optimum headgroup area and tail length can be expressed as a dimensionless packing parameter. The packing parameter then determines which structures will form. Example calculations are then given for sodium dodecyl sulfate micelles and phosphatidylcholine vesicles.

Optimal Headgroup Area

Surface energy is minimized when headgroups on the structure occupy an optimum area. A balance exists between the interfacial energy of the hydrophobic tails exposed at the surface, and repulsive energy between headgroups (See Figure 1 below). As the surface area of the structure is decreased, the interfacial energy is lowered. However, the repulsive energy between headgroups is increased as the headgroups are crowded into a smaller surface area.

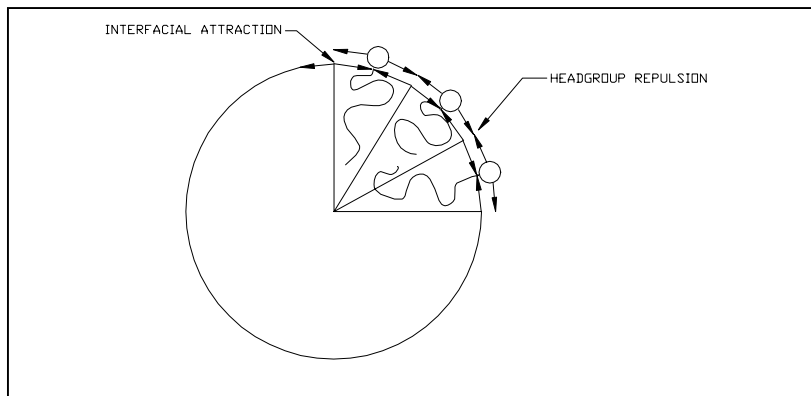


Figure 1: Schematic of Headgroup Surface Forces

A simple model of the total surface energy is given below (Israelachvili, p. 369):

$$\mu = \gamma a + K/a \quad [1]$$

where

μ = Chemical potential at interface

γ = Interfacial energy between hydrocarbon tails and aqueous phase

a = Surface area occupied per headgroup

K = Proportionality constant for repulsion of headgroups

In this model, the surface energy is proportional to the interfacial area, and the repulsive energy is inversely proportional to the surface area. The minimum energy is found by differentiating equation [1] with respect to (a), setting the derivative equal to zero, and solving for the optimal headgroup area, a_0 :

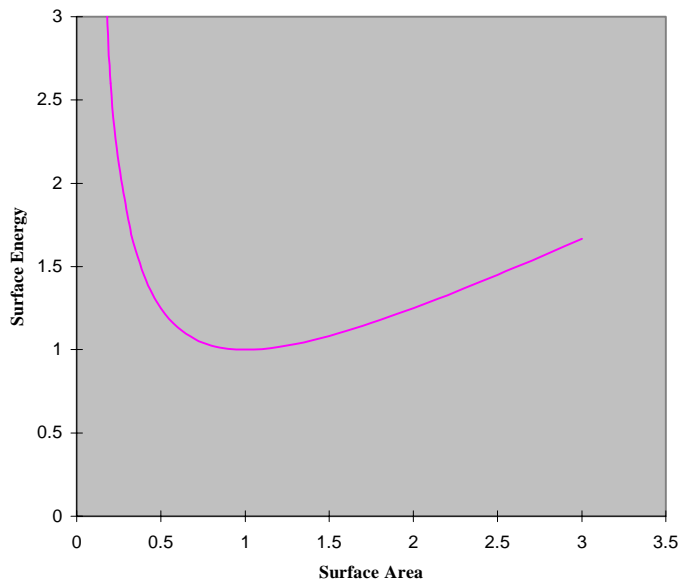
$$d\mu/da = \gamma - K/a^2 \quad [2]$$

$$\gamma = K/a_0^2 \quad [3]$$

$$a_0 = (K/\gamma)^{1/2} \quad [4]$$

Figure 2 shows a graph of this function. In this graph, the parameters have been normalized. The y axis is μ/μ_{minimum} and the x axis is a/a_0 .

Figure 2. Normalized Surface Energy Function



Packing Characteristics

Aggregate structures have a lower energy than the non-aggregated molecules in solution. However, molecular geometry constraints determine the actual shape of the aggregate. The analysis of molecular packing characteristics is facilitated with the use of the dimensionless packing parameter:

$$v_c/a_0l_c \quad [5]$$

where:

v_c = chain volume

a_0 = optimal headgroup area

l_c = critical chain length

The chain volume is simply the volume of the hydrocarbon tail. The critical chain length is the longest effective length that the chain can be extended in the fluid. It is slightly less than the actual length of the molecule based on bond length and angles (Israelachvili p 370).

The packing parameter can be thought of as a measure of the curvature of the molecular aggregate. It is the ratio of the tail volume to the volume projected by the optimal head group area. In other words, a small packing parameter indicates a small tail attached to a large head, and a large packing parameter indicates a large tail connected to a smaller head. Therefore, small packing parameters lead to highly curved aggregates (e.g. spheres) whereas larger packing parameters lead to aggregates with less curvature (e.g. vesicles or bilayers). The relationship between the packing parameter and aggregate shapes is described in the following sections.

Spherical Micelles

For spherical micelles composed of N molecules, the total micelle volume V and surface area S are given by:

$$V = Nv_c = (4/3)\pi r^3 \quad [6]$$

$$S = 4\pi r^2 \quad [7]$$

where r = the radius of the micelle.

The actual area per headgroup, a_a , is therefore given by:

$$a_a = 4\pi r^2/N \quad [8]$$

Substituting in equation [6] for N gives:

$$a_a = 3v_c/r \quad [9]$$

The ratio of the actual area to the optimum area (a_a/a_o) is given by:

$$a_a/a_o = 3v_c/ra_o \quad [10]$$

or equivalently,

$$a_a/a_o = (3l_c/r)(v_c/a_o l_c) \quad [11]$$

Noting that is not geometrically possible to form a micelle with $r > l_c$, the above equation shows that as long as the packing parameter ($v_c/a_o l_c$) is less than 1/3, it will be possible for the actual area a_a to equal the most optimum area. For packing parameters greater than 1/3, the actual area would be larger than optimum and these structures would be energetically unfavored.

Equation [11] above also shows that the size of the spherical micelles formed is given by the value of r that results in the minimum energy, or when $a_a/a_o = 1$. Solving for r gives:

$$r_{\text{sphere}} = 3l_c(v_c/a_o l_c) \quad [12]$$

Therefore, the size of the micelle is a function of the packing parameter and the critical chain length. Since larger or smaller micelles could form at the expense of higher surface energy, a distribution of micelle sizes will actually result, but the average size will be on the order of that given by equation [12].

Cylindrical Micelles

The analysis for cylindrical micelles follows the same method as that described for spherical micelles. For cylindrical micelles composed of N molecules, the total micelle volume V and surface area S are given by:

$$V = Nv_c = L\pi r^2 \quad [13]$$

$$S = 2\pi rL \quad [14]$$

where L = the length of the cylindrical micelle.

The actual area per headgroup, a_a , is therefore given by:

$$a_a = 2\pi rL/N \quad [15]$$

Substituting in the first equation for N gives:

$$a_a = 2v_c/r \quad [16]$$

The ratio of the actual area to the optimum area (a_a/a_o) is given by:

$$a_a/a_o = 2v_c/ra_o \quad [17]$$

or equivalently,

$$a_a/a_o = (2l_c/r)(v_c/a_o l_c) \quad [18]$$

Again, noting that is not geometrically possible to form a micelle with $r > l_c$, the above equation shows that as long as the packing parameter ($v_c/a_o l_c$) is less than 1/2, it will be possible for the actual area a_a to equal the most optimum area. For packing parameters greater than 1/2, the actual area would be larger than optimum and these structures would be energetically unfavorable.

Equation [18] above also shows that the size of the cylindrical micelles formed is given by the value of r that results in the minimum energy, or when $a_a/a_o = 1$. Solving for r gives:

$$r_{cyl} = 2l_c(v_c/a_o l_c) \quad [19]$$

At this point, it is interesting to note that for packing parameter values of less than 1/3, cylindrical micelles could still form while maintaining the optimum headgroup area. Therefore, while both spherical and cylindrical micelles could be formed based on energy considerations, the spherical micelles have fewer molecules per aggregate and are favored entropically.

Vesicles

The analysis for vesicles is slightly more complicated. Consider a vesicle with an outer layer and an inner layer. The radius of the outer layer is R_o and the thickness of the outer layer is t_o . We only need to consider the outer layer in the molecular packing considerations since this is where the geometrical constraints emerge.

For a vesicle with N_o molecules in the outer layer, the outer layer volume V_o and outer surface area S are given by:

$$V_o = N_o v_c = (4/3)\pi (R_o^3 - (R_o - t_o)^3) \quad [20]$$

$$S_o = 4\pi R_o^2 \quad [21]$$

The actual area per headgroup, a_a , is therefore given by:

$$a_a = 4\pi R_o^2 / N_o \quad [22]$$

Substituting in the first equation for N_o gives:

$$a_a = 3v_c R_o^2 / (R_o^3 - (R_o - t_o)^3) \quad [23]$$

The ratio of the actual area to the optimum area (a_a/a_o) is given by:

$$a_a/a_o = 3(v_c/a_o l_c) l_c R_o^2 / (R_o^3 - (R_o - t_o)^3) \quad [24]$$

This equation gives the area ratio as a function of the packing parameter, the chain length, the outer radius of the vesicle, and the thickness of the outer layer. If we examine the behavior of this function for a given molecule, i.e. a fixed packing parameter and chain length, we find that the area ratio increases with decreasing radius and decreases with increasing layer thickness t_o .

Therefore, as R_o becomes increasingly smaller, a limit is reached where a_a/a_o will have to exceed unity. In other words, a limit is reached where vesicles cannot form without causing the headgroup area to exceed the optimum, resulting in unfavorable surface energies. This minimum value of R_o occurs when the thickness is at the maximum value, which is l_c . So, the minimum radius R_{min} occurs when $t_o = l_c$. Setting $a_a/a_o = 1$ and $t_o = l_c$ gives:

$$1 = 3(v_c/a_o l_c) l_c R_{min}^2 / (R_{min}^3 - (R_{min} - l_c)^3) \quad [25]$$

This equation is quadratic in R_{min} and can easily be solved to give:

$$R_{min} = \frac{3 + [3(4v_c/a_o l_c - 1)]^{1/2}}{6(1 - v_c/a_o l_c) l_c} \quad [26]$$

Equation [26] shows that the minimum size vesicle depends on the packing parameter and the critical chain length. Larger vesicles can also form without causing the headgroup area to exceed a_o , but these are not favored entropically.

Bilayers

Bilayers result when the packing parameter is unity. In this configuration, the lack of curvature results in unlimited size without unfavorable energy constraints. For packing parameter values less than unity, bilayers could form without curvature by folding up their hydrocarbon tails to a chain length less than the critical chain length, l_c . However, these structures would be entropically unfavorable compared to the formation of aggregates with the same energy but with less molecules.

Summary of Geometric Packing Analysis

The conclusions of the above analysis are summarized below:

- For packing parameter between 0 and 1/3, all structures could form while keeping the headgroup area at the optimum value, but spherical micelles are favored entropically.

- For packing parameters between $1/3$ and $1/2$, spherical micelles can no longer form with the optimal headgroup area. Cylindrical micelles are favored entropically over vesicles and bilayers.
- For packing parameters between $1/2$ and 1 , both cylindrical micelles and spherical micelles cannot be formed while maintaining the optimal headgroup area. Vesicles are entropically favored compared to bilayers.
- For packing parameters of 1 , vesicles become large and indistinguishable from planer bilayers. A planer bilayer can be thought of as an infinitely large vesicle.

For packing parameters larger than one, inverse micelles can form. Other more complex structures, including multilayered vesicles and bilayers are also possible. Cylindrical micelles may also pack together in a secondary close-packed hexagonal structure.

Example Calculations

For sodium dodecyl sulfate, Israelachvili reports the following molecular characteristics:

$$l_c = 1.67 \text{ nm}$$

$$v_c = 0.3502 \text{ nm}^3$$

$$a_o = 0.57 \text{ nm}^2$$

$$(v_c/a_o l_c) = 0.37$$

Substituting these values into equation [12] gives

$$r_{\text{sphere}} = 3l_c(v_c/a_o l_c) = 1.84 \text{ nm}.$$

In this case, the packing factor is just above 0.33 and therefore perfectly spherical micelles cannot form. This is also apparent above by noting that the estimated radius is slightly larger than the critical chain length. Therefore, we might expect cylindrical micelles to form. Instead, however, Israelachvili reports that the packing factor is close enough to 0.33 to allow formation of spherical micelles as long as the spheres flatten slightly to maintain the optimal headgroup area.

For phosphatidylcholine, Israelachvili reports the following molecular characteristics:

$$l_c = 1.75 \text{ nm}$$

$$v_c = 1.063 \text{ nm}^3$$

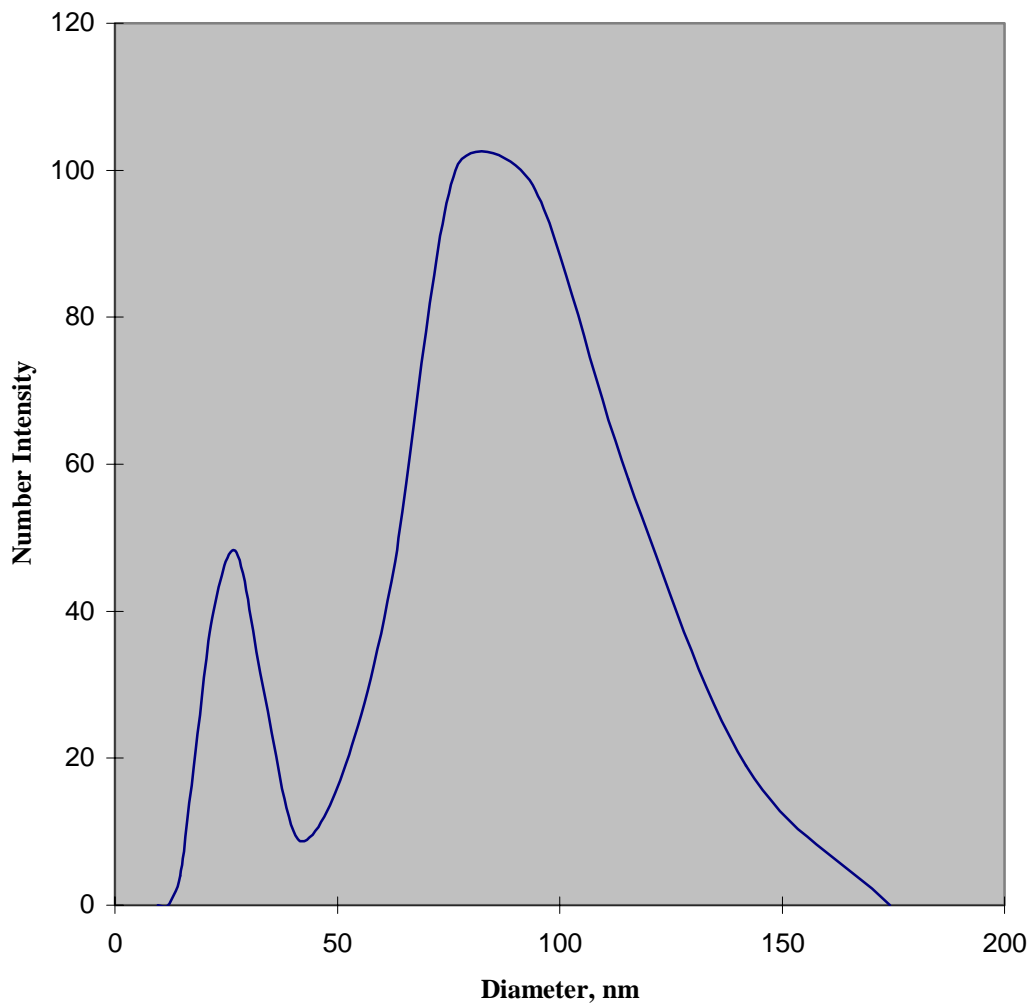
$$a_o = 0.717 \text{ nm}^2$$

$$(v_c/a_o l_c) = 0.85$$

Substituting these values into equation [26] gives a minimum vesicle diameter of 22 nm.

As part of his experimental research with Dr. Johnston's group, Tim Young has measured the diameter of phosphatidylcholine vesicles. Figure 3 shows the particle number distribution as measured using a light-scattering technique. As shown, the size distribution is bimodal. The first group of particles has a number-averaged diameter of 25 nm, in close agreement with the estimated value of 22 nm.

Figure 3. Phospholipid Vesicle Size Distribution



The additional particles ranging in size from 50 – 140 nm in diameter are thought to be multilayer vesicles. According to Tim, the solutions are first made up by dissolving solid phosphatidylcholine in water to form a suspension of large particles. These larger

particles consist of multi-layered vesicles along with some large single-layered vesicles. This solution is then sonicated and subjected to extremely high shear in a homogenizer to break up the particles into smaller vesicles. The process of sonication and homogenization decreases the particle size dramatically, but some multi-layered vesicles still remain as evidenced by the particle size distribution measurements.

References

Israelachvili, Jacob. Intermolecular and Surface Forces, Second Edition. Harcourt Brace & Company, New York, 1998.