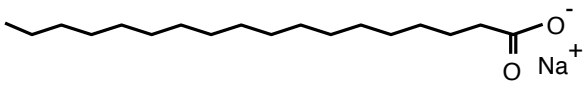
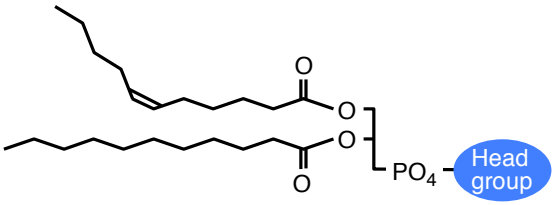
PHYS 4xx Mem 1 - Composition and self-assembly of biomembranes

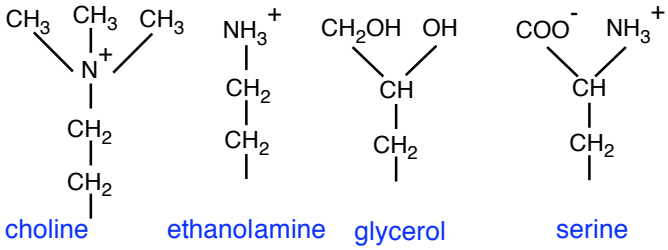
To construct a cell boundary, materials are needed that can self-assemble into a two-dimensional sheet, rather than the three-dimensional solids so familiar to us. There are a limited number of systems that can do this, and some of these are shear-resistant sheets that are poorly suited for cell division. Among those systems that assemble into fluid sheets are amphiphilic molecules in an aqueous medium:



Sodium stearate has a single hydrocarbon chain terminating at a carboxyl group.



Phospholipids of the cell's membranes generally have a pair of inequivalent hydrocarbon chains. Polar head groups commonly found on phospholipid molecules in cellular membranes include

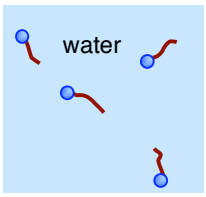


Chain lengths of fatty acids in rat liver membranes, where n_c is the number of carbon atoms in the hydrocarbon chain, including the COO group

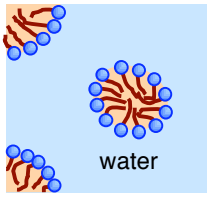
Membrane	Percent by weight					
	n_c = 14	15	16	17	18	20
mitochondrial (outer)	<1	27	25	14	14	16
mitochondrial (inner)	<1	27	22	16	16	19
plasma membrane	1	37	31	6	13	11
Golgi apparatus	1	35	23	9	18	15

The distributions are a percent of the total fatty acid content by weight; not all values of n_c are listed and n_c = 20 includes only arachidonic acid. Note that the fatty acids are generally bound as phospholipids and other molecules (from Gennis, 1989).

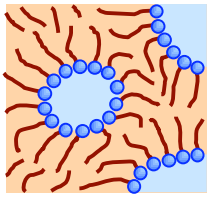
Phases of short-chain fatty acids in water



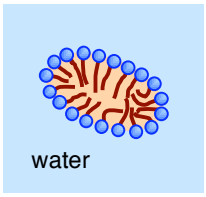
homogeneous solution



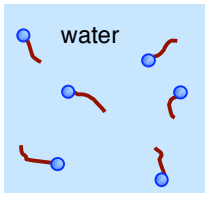
micelles


inverted micelles

A simple model for the concentrations of amphiphiles needed to create a condensed phase considers only two states:



condensed



dispersed

We use an energy vs entropy argument to determine which phase is favoured.

Condensed phase
Neglect all motion of the blob and define its entropy $S = 0$.

Assume the hydrocarbon region is a cylinder of radius R_{hc} and length $n_c \ell_{cc}$, where n_c is the number of carbon atoms along the hydrocarbon chain and ℓ_{cc} = 0.126 nm is the average C-C bond length projected on the chain.
---> the area of the hydrophobic region is approximately $2\pi n_c R_{hc} \ell_{cc}$.

Hence, the energy for a single amphiphile to escape from the blob is roughly

$$E_{bind} = 2\pi n_c R_{hc} \ell_{cc} \gamma,$$

where the *interfacial energy per unit area* approximately equals the *water/hydrocarbon surface tension* γ.

Dispersed phase
Assume the amphiphiles behave like an ideal gas.

The entropy per molecule S_{gas} of an ideal gas at number density ρ is

$$S_{gas} = k_B \left\{ 5/2 - \ln(\rho \bullet [h / \{2\pi m k_B T\}^{1/2}]^3) \right\},$$

where m = mass of each molecule h = Planck's constant.
Length scale $h/\{2\pi m k_B T\}^{1/2}$ is provided by the translational motion.

Cross-over density between the two phases is at $E_{bind} = TS_{gas}$. Solving:

$$\rho_{agg} \cdot [h / \{2\pi m k_B T\}^{1/2}]^3 = \exp(5/2 - E_{bind}/k_B T)$$

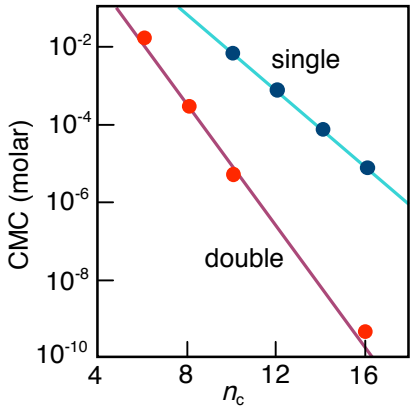
We have called this the aggregation threshold ρ_{agg}. Experimentally, the threshold for creating a condensed state is called the *critical micelle concentration*, or CMC. Substituting for E_{bind} gives the theoretical expression

$$\rho_{agg} = [\{2\pi m k_B T\}^{1/2} / h]^3 \, e^{5/2} \exp(- 2\pi n_c R_{hc} \ell_{cc} \gamma / k_B T)$$

This predicts that

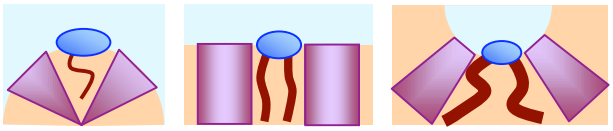
ρ_{agg} decreases exponentially with increasing chain length
dual chain lipids have lower CMC than single chain.

DATA: The single-chain lipids are lyso-phosphatidylcholines and the double-chain ones are di-acyl phosphatidylcholines. The straight lines are 690 exp(-1.15n_c) molar and 570 exp(-1.8n_c) molar for the single- and double-chain lipids, respectively. The exponents can be fit by the theoretical expression using $\gamma = 0.03$ J/m^2, in the measured range of γ.



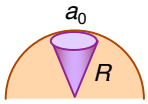
Molecular shape and phase behavior

Interface shape is related to molecular geometry. (a) Single-chain fatty acids tend to form micelles, while (b) dual-chain phospholipids with moderate size head groups prefer bilayers. (c) Phospholipids with small head groups may form inverted micelles.

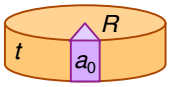


(a) (b) (c)

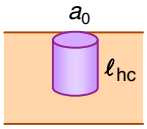
We can use understand this on the basis of molecular geometry. The cross sectional area of a head group is denoted by a_o, while the radius and thickness of the molecular shape are R and t, as applicable; the volume of its hydrocarbon chain(s) v_{hc}.



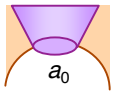
spherical micelle



cylindrical micelle



bilayer



inverted micelle.

Spherical micelles

A spherical micelle has a surface area $4\pi R^2$ and volume $4\pi R^3/3$.

The number of molecules in the micelle is either $4\pi R^2/a_o$ by area or $(4\pi R^3/3)/v_{hc}$ by volume. For these expressions to give the same number of molecules, R must obey

$$R = 3v_{hc}/a_o. \qquad \text{(S1)}$$

The interior of the cluster cannot contain a void, so the distance from the centre to the surface cannot exceed the length of one amphiphile. Thus, the radius of the micelle must be less than or equal to the projected length of the hydrocarbon chain: $R \le \ell_{hc}$. Eq. (S1) becomes

$$v_{hc}/a_o\ell_{hc} \le 1/3. \qquad \text{(S2)}$$

Cylindrical micelles

Referring to the figure, the surface area of this section around the ring is $2\pi Rt$, and the volume is $\pi R^2 t$.

The number of molecules in the cylindrical section is either $2\pi Rt/a_o$ by area or $\pi R^2 t/v_{hc}$ by volume. Equating these two expressions, the radius must obey

$$R = 2v_{hc}/a_o. \qquad \text{(C1)}$$

Substituting $R \le \ell_{hc}$, as before, leads to

$$1/3 < v_{hc}/a_o\ell_{hc} \le 1/2. \qquad \text{(C2)}$$

Bilayers

The packing geometry of the bilayer is best satisfied by cylindrical molecules, whose hydrocarbon volume is given by $v_{hc} = a_o\ell_{hc}$, as shown in Fig. 7.10(c). Hence, the "ideal" bilayer satisfies $v_{hc}/a_o\ell_{hc} = 1$, and the range of the shape factor favored for bilayers is

$$1/2 < v_{hc}/a_o\ell_{hc} \le 1. \qquad \text{(B1)}$$

Dual chain lipids are more cylindrical than single chain because v_{hc} is larger for a given a_o.

Inverted micelles

Suppose the hydrocarbon volume $v_{hc} > a_o\ell_{hc}$, so the shape factor $v_{hc}/a_o\ell_{hc} > 1$. Here, the head group is relatively small, and lies near the apex of a truncated cone. Such molecules form inverted micelles, with the head groups on the "inside" of the micelle, and the hydrocarbon regions radiating away from the aqueous core. Thus, the range of shape factor favoring inverted micelles is

$$v_{hc}/a_o\ell_{hc} > 1. \qquad \text{(IM.1)}$$