Solutions to Soft Matter Exercise - Chapter 4: Vesicles

1. CMC of Surfactants

a. Surfactants have a hydrophobic and a hydrophilic part. The hydrophilic part has a high solubility in water. This hydrophilic part helps to solubilize the hydrophobic part. Thus, the solubility of surfactants is higher than that of the corresponding hydrophobic molecule with the same number of C atoms that lacks the hydrophilic part.

b. The addition of a CH_2 group to a single-chained amphiphile increases the length of the hydrophobic part of the surfacant more than if the CH_2 group is added to a double-chained amphiphile. If added to a single-chained amphiphile, it directly increases the length of the hydrophibic part of the molecule by the length of a C-C bond, corrected by the angle between hte atoms. Thus, it directly influences the CMC:

$$CMC \approx e^{\frac{-2\pi r l \gamma}{k_B T}}$$

If added to a double-chained amphiphile, it also increases the average length of the hydrophobic part. However, because it is the average length and one chain remains unchanged, the change in l used to calculate the CMC is smaller.

c. Smaller counter ions structure water more strongly. This results in a stronger imbalance of the intermolecular forces at the interface, causing an increase in the interfacial tension, γ. As a result, the decrease in CMC is more pronounced.

2. CMC of Phospholipids

a. We first calculate the length of the C_{16} that has one CH_3 group and 15 CH_2 groups:

$$l \approx (0.154 + 0.126(n-1)) = (0.154 + 0.126 \times 14) = 1.918 \text{ nm}$$

The radius of one chain is $r \approx 0.2$ nm. To estimate the lower limit for r of two chains, we approximate r_2 to be two times r, giving $r_2 = 0.4$ nm. For a phospholipid with two C_{16} chains, we obtain:

$$CMC = e^{-\frac{2\pi r l \gamma}{k_B T}} = e^{-\frac{2\pi \times 0.4\ nm \times 1.918\ nm \times 10^{-18}\ \frac{m^2}{nm^2} \times 0.03 \frac{J}{m^2}}{1.38 \times 10^{-23} \frac{J}{K} \times 298\ K}}$$

$$= 5.3 \times 10^{-16} \text{ M}$$

b. If we remove one of the chains, we replace r_2 with r_1 and obtain:

$$CMC = e^{-\frac{2\pi\times 0.2\ nm\times 1.918\ nm\times 10^{-18}\ \frac{m^2}{nm^2}\times 0.03\frac{J}{m^2}}{1.38\times 10^{-23}\frac{J}{K}\times 298\ K}}$$

$$= 2.3 \times 10^{-8}\ \text{M}$$

This is 8 orders of magnitude lower!

c. The residence time is inversely proportional to the CMC:

$$\tau_R \propto \frac{1}{CMC}$$

Because the CMC is 10^8 times lower for DSPC than for the analogue with the same head group but only one C_{16} chain, τ_r is 10^8 times greater for DSPC than for the one-chain analogue.

d. The packing parameter is the ratio of the cross-section of the head group to the cross-section of the hydrophobic tail. We approximate the cross-section of the hydrophobic tail to be a cylinder and obtain:

$$\text{for } \alpha = 1 \rightarrow \frac{\pi r_{DPPC}^2}{a_0} = 1$$

where a_0 is the optimal head group area.

To determine a_0, we must find r_{DPPC}. As CMC is defined as:

$$CMC = e^{-\frac{2\pi r l\gamma}{k_B T}}$$

We can calculate r using

$$r = -\ln(CMC)\frac{k_B T}{2\pi l\gamma} = -\ln(7\times 10^{-14})\frac{1.38\times 10^{-23}\frac{J}{K}\times 298\ K}{2\pi\times 1.918\times 10^{-9}\ m\times 0.03\frac{J}{m^2}}$$

$$= 3.22 \times 10^{-9}\ \text{m}$$

For the molecule with only one C_{16} chain:

$$\alpha_2 = \frac{\pi r_0^2}{a_0} = \frac{\pi r_0^2}{\pi r_{DPPC}^2} = \frac{0.2^2\ nm^2}{0.322^2\ nm^2} = 0.39$$

These molecules form micelles that are almost spherical. The addition of a second hydrocarbon-based chain to amphiphiles does not only change their CMC, but also the shape of micelles that are formed.

3. Vesicles

a. Vesicles of this size are most often formed using **rehydration and electroformation**.
Advantages:

- Relatively high yield
- Relatively fast production rates

Disadvantages:

- Low encapsulation efficiency
- A mixture of unilamellar and multilamellar vesicles is obtained
- The formation in the presence of sucrose works well, but the formation in the presence of salt is difficult
- Vesicles are polydisperse

b. Vesicles of this size are often formed through **rehydration and extrusion**.
Advantages:

- Fast production
- Experimentally easy to form vesicles
- Vesicles have an average size that is defined by the pore size of the membranes
- No oil residues remain in the membrane of vesicles because all of the oil is completely removed during the drying step. This is important if vesicles are intended to be used for food, cosmetic, or biomedical applications.

Disadvantages:

- Relatively broad size distribution
- Low encapsulation efficiency

c. The size of these vesicles is in a range that is easily accessible with dynamic light scattering (DLS). Since vesicles have a very similar density to water, they do not sediment, therby facilitating the measurement. However, it is important to dilute the vesicles to minimize the risk that light is scattered on multiple vesicles as this would alter the results.

4. Rigid Vesicles

a. The rigidity of vesicles is described by the expansion modulus:

$$k_a \approx 4\gamma \approx \frac{4k}{a_0}$$

and the bending modulus:

$$k_b = -4\gamma hD$$

The expansion and bending moduli increase with increasing interfacial tension. Thus, the rigidity increases with increasing interfacial tension.

b. The interfacial tension increases with increasing ion concentration. If this effect is insufficient, the rigidity can be tuned with the structure of the block-copolymers. For example, if hydrocarbon chains are employed that easily crystallize, the rigidity of the membrane strongly increases. This has been observed, for example, if poly(lactic acid) (PLA) is used as a hydrophobic block of block-copolymers that are assembled into polymersomes.

c. The main disadvantage is that rigid vesicles are fragile and become prone to rupture.

5. Characterization of Delivery Vehicles

a. **Dynamic light scattering** (DLS). 50-100 nm sized vesicles are within the size range that is well suited for DLS analysis. Moreover, DLS analzsis is experimentally easy and the instrumentation is readily available.

b. The scattering intensity is measured as a function of time. Scattering intensity patterns measured at time t_0 are compared to those measured at time $t_0 + \tau$, and the correlation between the two scattering patterns is determined. The correlation function is plotted as a function of τ and fitted using an exponential function to determine the diffusion coefficient of the particles. The hydrodynamic diameter of the micelles can be calculated using the Stokes-Einstein equation.