

Solutions to Soft Matter exercise, Chapter 4: Vesicles

1. CMC of surfactants

- Surfactants have a hydrophobic and a hydrophilic part. The hydrophilic part has a high solubility in water. This hydrophilic part helps solubilizing the hydrophobic part. Hence, 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.
- The addition of a CH₂ group to a single chained amphiphile increases the length of the hydrophobic part of the surfactant more than if the CH₂ group is added to a double chained amphiphile. If added to a single chained amphiphile, it directly increases the length of the hydrophobic part of the molecule by the length of a C-C bond, corrected by the angle between the atoms. Hence, 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.
- Smaller counter ions structure water more strongly. This results in a stronger imbalance of the intermolecular forces at the interface and hence in an increase in the interfacial tension, γ . As a result, the decrease in CMC is more pronounced.

2. CMC of phospholipids

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

We first calculate the length of the C16 chain that has one CH₃ group and 15 CH₂ groups:

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

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 such that $r_2 = 0.4$ nm. For a phospholipid with two C16 chains, we obtain

$$CMC = e^{-\frac{2\pi r l \gamma}{k_B T}} = e^{-\frac{2\pi \times 0.4nm \times 1.918nm \times 10^{-18} \frac{m^2}{nm^2} \times 0.03 \frac{J}{m^2}}{1.38 \times 10^{-23} \frac{J}{K} \times 298K}} = 5.3 \times 10^{-16} M$$

- If we remove one of the chains, we replace r_2 by r_1 and obtain

$$CMC = e^{-\frac{2\pi r l \gamma}{k_B T}} = e^{-\frac{2\pi \times 0.2nm \times 1.918nm \times 10^{-18} \frac{m^2}{nm^2} \times 0.03 \frac{J}{m^2}}{1.38 \times 10^{-23} \frac{J}{K} \times 298K}} = 2.3 \times 10^{-8} M$$

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 10^8 times lower for DSPC than for the analogue that has the same head group but only one C16 chain, τ_R is 10^8 times higher 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 sphere and obtain for $\alpha = 1 \rightarrow$

$$\frac{\pi r_{DPPC}^2}{a_0} = 1 \text{ where } a_0 \text{ is the optimum head group area.}$$

To determine a_0 , we must determine r_{DPPC} .

The CMC is defined as $CMC = e^{-\frac{2\pi r l \gamma}{k_B T}}$.

Therefore, we can calculate r using

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

$$r = 3.22 \times 10^{-10} m$$

for the molecule with only one C16 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. Hence, the addition of a second hydrocarbon-based chain to amphiphiles does not only change their CMC but it also changes the shape of micelles that form.

3. Temperature dependence

- a. The CMC is defined as $CMC \approx e^{-\frac{2\pi r l \gamma}{k_B T}}$. An increase in temperature would increase the solubility of the molecule and thus increase the CMC.

$$\tau_R = \frac{\tau_0}{e^{-\frac{\mu_0^0 - \mu_N^0}{k_B T}}} \approx \frac{55\tau_0}{CMC}$$

- b. The exchange rate is given by $e^{-\frac{\mu_0^0 - \mu_N^0}{k_B T}}$. Because the CMC would increase, τ_R would decrease.
- c. It would make the vesicle more fluid. Because the exchange rates would be much faster, the system would be more dynamic and less stable.
- d. To decrease the CMC, one could
1. add CH_2 groups to the chain, to prolong l
 2. introduce unsaturated bonds to the hydrophobic part of the vesicle to increase r .

4. Vesicles

- a. Vesicles of this size are most often formed using 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 most 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 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). Because vesicles have a very similar density to water, they do not sediment, thereby facilitating the measurement. However, it is important to dilute the vesicles to minimize the risk that light is scattered on multiple vesicles. This would alter the results.

5. **Rigid vesicles**

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

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

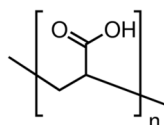
and the bending modulus: $k_b = -4\gamma hD$

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 become prone to rupture because they are fragile.

6. pH-responsiveness

- a. Poly(acrylic acid) has a carboxy group that is deprotonated at $\text{pH} > \text{pK}_a$ and protonated at $\text{pH} < \text{pK}_a$.



- b. The degree of hydration changes around the pK_a of poly(acrylic acid), which is around 4.2. Hence, at $\text{pH} < 4.2$, PAA is protonated and collapsed. At $\text{pH} > 4.2$, PAA is deprotonated and swollen.
- c. At high pHs ($\text{pH} > \text{pK}_a$), PAA is deprotonated and therefore hydrated.

7. 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 analysis 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. (For more details, see slides)