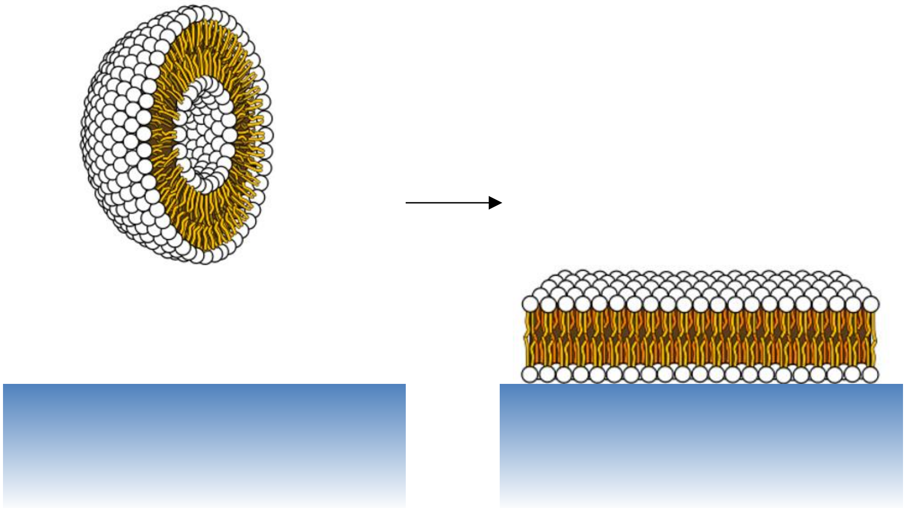
Lipid Vesicles and Supported Bilayers

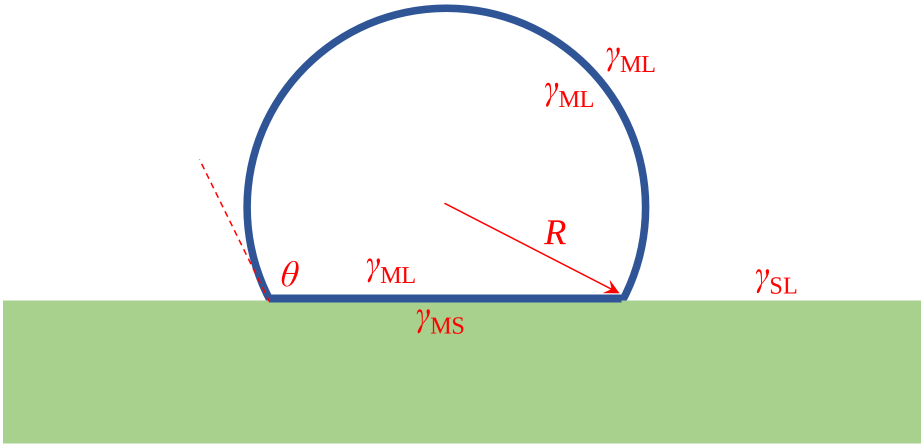
Vesicles can be made artificially by self assembly of phospholipids. They are usually not particularly stable in the long run because the curvature of the bilayer imposes a penalty in free energy. Vesicles can be used to form *supported phospholipid bilayers* on solid surfaces. The process is spontaneous for the right surface and the right phospholipid composition. The vesicles first adsorb intact to the surface and then rupture to form a planar bilayer on the surface when a high enough surface coverage has been reached. This is an important method for forming artificial cell membranes that are used in many biosensor applications. The exact mechanism of supported phospholipid bilayer formation is complicated and has occupied the minds of many researchers for many years. In this assignment you will make some relatively simple arguments in terms of interfacial energy in an attempt to understand some aspects of bilayer formation.



(A) Assume the free energy change of vesicle adsorption ΔG_{ads} (not bilayer formation) can be expressed only in terms of changes in interfacial energy. The interfacial tensions are γ_{ML}, γ_{MS} and γ_{SL} (M for membrane, L for liquid and S for solid). When a vesicle has adsorbed it is <u>not</u> spherical but deformed into a shape that can be assumed to be a truncated sphere with radius R (together with a planar region in contact with the surface). Use suitable physical reasoning to express ΔG_{ads} in terms of γ_{ML}, γ_{MS}, γ_{SL} and R. It can be assumed that R is much higher than the bilayer thickness and that the phospholipid packing density remains constant. (Note that the vesicle has two interfaces, one inner and one outer.)

(B) To form a bilayer after adsorption one would like the vesicles to rupture. One can suspect that this occurs by a pore forming in the bilayer at the top of the adsorbed vesicle, after which the vesicle spreads out on the surface. Do you expect a membrane that bends more easily will increase or reduce the chance of forming a supported bilayer? (Discuss briefly and motivate your opinion, the answer is not necessarily known…)

(A) The vesicle will look something like this:



There will be a certain contact angle θ. The change in interfacial energy occurs from contact of the vesicle to the surface but also due to the change in vesicle shape. We denote the membrane-solid area and the membrane-liquid area for the truncated sphere as A_{MS} and A_{ML}.

If the phospholipids are equally closely packed the sum of A_{MS} and A_{ML} must be equal to the initial area before adsorption. Considering that there are two interfaces, the initial interfacial energy for the spherical vesicle in solution must be $2[A_{MS} + A_{ML}]\gamma_{ML}$. The change in interfacial energy is then:

$$\Delta G_{ads} = 2A_{ML}\gamma_{ML} + A_{MS}[\gamma_{ML} + \gamma_{MS} - \gamma_{SL}] - 2[A_{MS} + A_{ML}]\gamma_{ML} = A_{MS}[\gamma_{MS} - \gamma_{SL} - \gamma_{ML}]$$

Using the geometry of a truncated sphere we replace A_{MS}:

$$\Delta G_{ads} = \pi R^2 \sin^2(\theta)[\gamma_{MS} - \gamma_{SL} - \gamma_{ML}]$$

From Young's equation we have a balance of interfacial tension at the triple point. However, there are also additional interfaces <u>inside</u> the vesicle, so the balance should include two more terms:

$$\gamma_{SL} = \gamma_{ML}\cos(\theta) + \gamma_{MS} + \gamma_{ML} + \gamma_{ML}\cos(\theta) = \gamma_{MS} + \gamma_{ML}[1 + 2\cos(\theta)]$$

Rewriting this expression:

$$\cos(\theta) = \frac{\gamma_{SL} - \gamma_{MS}}{2\gamma_{ML}} - \frac{1}{2}$$

Thus we get:

$$\Delta G_{ads} = \pi R^2[1 - \cos^2(\theta)][\gamma_{MS} - \gamma_{SL} - \gamma_{ML}] = \pi R^2\left[1 - \left[\frac{\gamma_{SL} - \gamma_{MS}}{2\gamma_{ML}} - \frac{1}{2}\right]^2\right][\gamma_{MS} - \gamma_{SL} - \gamma_{ML}]$$

(B) The problem with the expression for ΔG_{ads} is that it does not take into account the energy needed to deform the vesicle. In reality, even if vesicle deformation is favorable with respect to the interfacial energies it will be countered by an increase in free energy due to the increased bending of the membrane at the circumference. The probability that the vesicle ruptures likely increases if it is more deformed, i.e. low θ. This is easier to achieve if the membrane bends easily.

On the other hand, the total free energy change for bilayer formation is more negative for a stiff vesicle membrane because it has a high bending energy to begin with. However, the process could be hampered by a large activation energy.

Note: In summary, the answer is not obvious when taking kinetic considerations into account but one can at least make some intellectual comments and educated guesses…