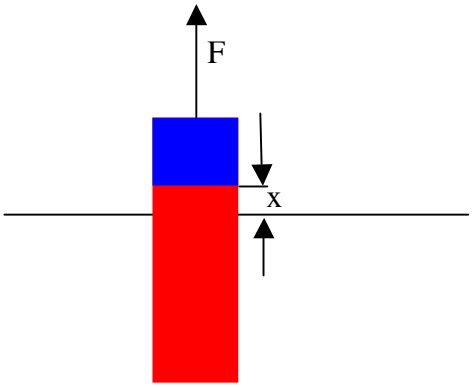
Reading for Lectures 30-32: PKT Chapter 11 (skip Ch. 10)

E. How much force does it take to "pull" a lipid (or a hydrophobically "belted" protein) out of a bilayer membrane?

The force F must provide the energy of hydrophobic contast as the lipid (or protein) is extracted:



$\Delta E = \sigma A = \sigma(2\pi r x) = Fx$, so

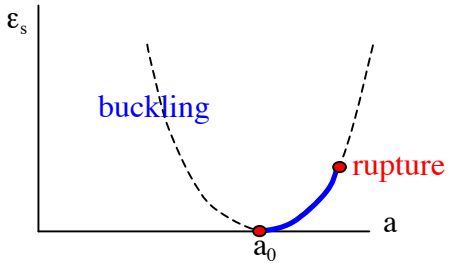
$F = \sigma(2\pi r) = 0.04(2\pi)0.4 \times 10^{-9} \sim 10^{-10}\ N = \boxed{100\ pN}$

This is a fairly large object.
Forces necessary to disrupt membranes ~1--100 pN.

F. How big is the lipid bilyer "stretching modulus" K_s?

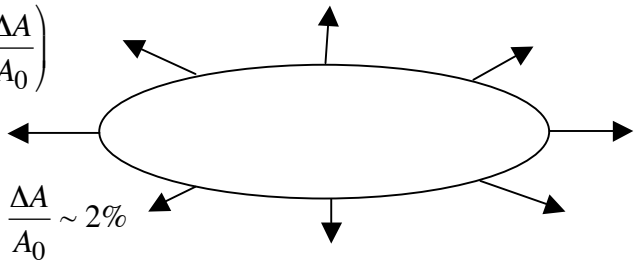
In the relaxed state, the area per lipid is a_0=0.5 nm^2. How much energy is required to increase that area to $a=a_0+\Delta a$ by pulling symmetrically outward at the edges?

- Basic membrane mechanics:
- areal "strain" = $\dfrac{\Delta a}{a_0} = \dfrac{(a-a_0)}{a_0} = \dfrac{\Delta A}{A_0}$ (dimensionless)
- strain energy/area $\equiv \varepsilon_s = \dfrac{1}{2}K_s\left(\dfrac{a-a_0}{a_0}\right)^2$



Note that dimensions of ε_s and K_s are E/A=F/L.

- membrane tension $\equiv \tau = \dfrac{d\varepsilon_s}{d\left(\dfrac{\Delta a}{a_0}\right)} = K_s\left(\dfrac{\Delta a}{a_0}\right) = K_s\left(\dfrac{\Delta A}{A_0}\right)$



- Experimentally, lysis/rupture typically occurs for $\dfrac{\Delta A}{A_0} \sim 2\%$

(and force is accurately harmonic to that point)

- so lysis/rupture occurs at a tension $\tau_{lysis} \approx 0.02 K_s$.

To understand where K_s comes from, we need to know the balance of forces that sets the equilibrium area/lipid:

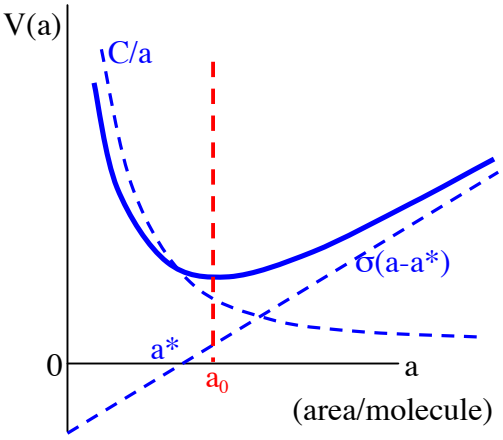
Attractive potential energy per lipid: $V_{attr}(a) = \sigma(a - a^*)$

Set by cost of hydrophobic exposure as heads are pulled apart.
There is some hydrophobic exposure at a_0.

Repulsive potential per lipid: $V_{repel}(a) = \dfrac{C}{a}$

Due to steric hinderance of lipid tails mainly entropy cost of restraining them. (form ~arbitrary)
both these terms are mainly entropic in origin; see this in temperature dependence, thus, both are of order k_BT.

Add these terms together: $V(a) = \sigma(a - a^*) + \dfrac{C}{a}$



Equilibrium occurs at minimum: $0 = \dfrac{dV}{da} = \sigma - \dfrac{C}{a_0^2} \Rightarrow \boxed{a_0^2 = \dfrac{C}{\sigma}}$

Comment: $\frac{C}{a_0} = \sigma a_0 = 10(0.5) = 5\ k_B T$, which reflects *entropic* elasticity of tails.

Having the potential, we now can calculate K_s:

$$\varepsilon_s = \frac{2}{a_0} V(a) \equiv \text{Const} + \frac{1}{2} K_s \left(\frac{a - a_0}{a_0} \right)^2 + \ldots \text{ near minimum}$$

Note: 2 leaves of lipid layer plus energy/lipid $\rightarrow$ energy/area.

Thus, taking two derivatives, $\frac{2}{a_0} \frac{d^2 V(a)}{da^2}\bigg|_{a_0} = \frac{K_s}{a_0^2} \Rightarrow$ $\boxed{K_s = 2a_0 \left(\frac{2C}{a_o^3} \right) = 4\sigma = 4(0.04) = 0.16\ J/m^2}$

Comments:

This modulus is 10^3 times smaller than for a typical "hard" solid; these are "soft materials."

For future reference, this makes the lysis tension $\boxed{\tau_{lysis} = 0.02 K_s = 3.2 \times 10^{-3}\ N/m.}$

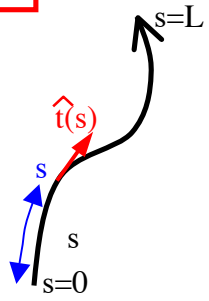
G. Membrane bending energy; the bending modulus κ_b:

A symmetric membrane (leaflets identical) is flat in its relaxed, unstressed state.

It costs energy to bend it away from this flat state.

1D Analog: Bending of stiff polymer

$E_{bend} = \frac{\kappa}{2} \int_0^L ds \frac{1}{R^2(s)} = \frac{\kappa}{2} \int_0^L ds \frac{d\hat{t}}{ds} \cdot \frac{d\hat{t}}{ds}$, where κ is the rigidity modulus.



As in the 1D case, membrane bending energy is related to local material deforamtions or "strain."

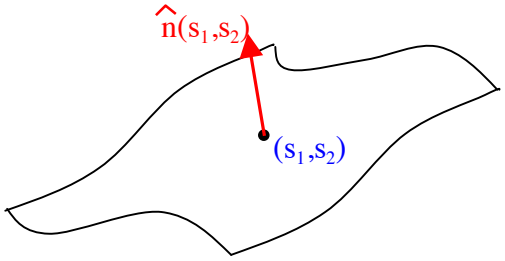
To describe those deformations, we will need a language/picture for describing the local membrane shape, just as we did in the 1D case:

Now, the surface needs two coordinates to locate the point.

Here we will designate the unit normal vector $\hat{n}(s_1, s_2)$.

At each point, there are now two radii of curvature $R_{1,2}(s_1, s_2)$, which refer to perpendicular "principle-axis" directions.

Examples: Sphere, cylinder.



The Monge representation:

To look at a local patch of surface S around a particular point P, construct the tangent plane at P and represent the local region by looking at its perpendicular "height" z(x,y) above/below the tangent plane.

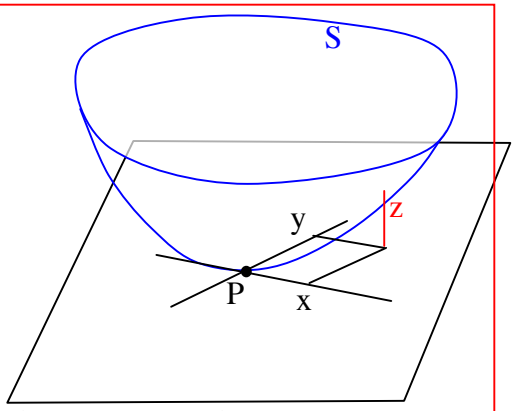
Because S is tangent to the plane at P,

$z(x,y) = a_{xx} x^2 + a_{xy} xy + a_{yy} y^2 + O\left(x^3, x^2 y, xy^2, y^3\right)$

with no constant term and no linear terms.

This is general: a_{xx}, a_{xy}, and a_{yy} can be +ive, -ive, or 0.

By appropriate rotation of axes (or of S) it is always possible to remove the cross term and write $z(x,y) = \frac{1}{2R_1} x^2 + \frac{1}{2R_2} y^2 + O\left(x^3, x^2 y, xy^2, y^3\right)$.



These axes are called "principal axes."

The quantities R_1 and R_2 are called the "principle radii of curvature".

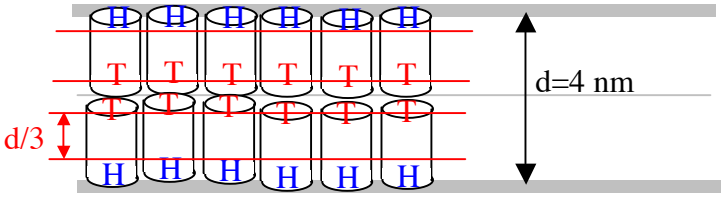
Geometrically, they are the radii of the circles which approximate the intersection of S with the xz and yz planes, respectively. (Proof: left to the reader or HW?)

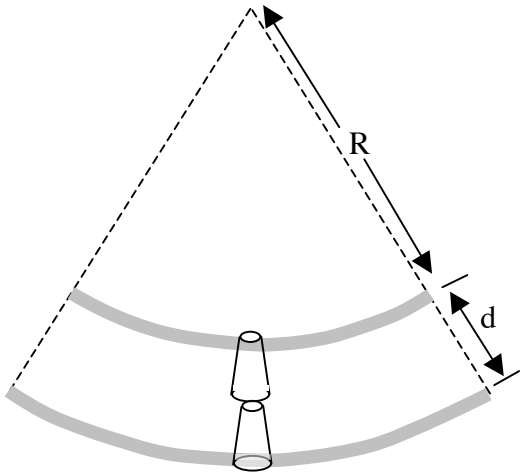
The quantity $H \equiv \frac{1}{2}\left(\frac{1}{R_1} - \frac{1}{R_2} \right)$ is called the "mean curvature".

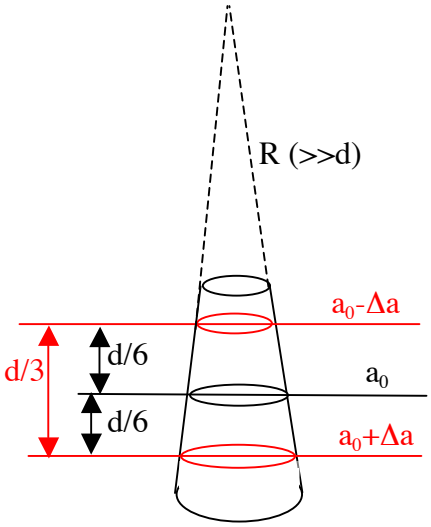
I claim that the bending energy/unit area now has the form: $\varepsilon_b(P) = \frac{\kappa_b}{2}\left(\frac{1}{R_1}+\frac{1}{R_2}\right)^2$ **32.3**

Note that κ_b has units of energy.
I will now show you the reason for this form of the energy and, at the same time, give you an estimate of κ_b based on the estimate of K_s from **F**.

When you bend this membrane, the layers slide over each other freely, the lipid molecules do not change their length, so they are forced to deform.
On the inner side of the bend, the molecular head are squeezed closer and the tails expand. On the outer side the tails are squeezed and the heads expand. (Four separate sublayers, two in each leaflet.)







The energy of this sublayer stretching/compression is just a modulus like K_s. I am going to simplify the problem by assuming that they are all the same. The overall stretching modulus is K_s, so the sublayer moduli are ~K_s/4.
The actual stress profile across the membrane is more complicated. There is compressive pressure in the head regions (caused by the hydrophobic energy) and a balancing expansive pressure in the tail regions (caused by the entropic tendency of the tails to expand).

Thus, the total stretching/compression energy per unit area in the bent layer is $\varepsilon_b \approx 4\times\frac{1}{2}\cdot\frac{K_s}{4}\left(\frac{\Delta A}{A_0}\right)^2$.

But, from the geometry, $\frac{\Delta a}{a_0}=\frac{\Delta A}{A_0}=\frac{d/6}{R}=\frac{d}{6R}$.

Thus, $\varepsilon_b \approx 4\times\frac{1}{2}\cdot\frac{K_s}{4}\left(\frac{\Delta A}{A_0}\right)^2 = 4\times\frac{1}{2}\cdot\frac{K_s}{4}\left(\frac{d}{6R}\right)^2 = \frac{1}{2}\left(\frac{K_s d^2}{36}\right)\left(\frac{1}{R}\right)^2$, from which we identify,

Note that we are in the "cylindrical" geometry, so $\left(\frac{1}{R_1}+\frac{1}{R_2}\right)=\left(\frac{1}{R}+0\right)=\left(\frac{1}{R}\right)$.

$$\kappa_b = \frac{K_s d^2}{36} = \frac{(0.16)\left(4\times10^{-9}\right)^2}{36} = 7.1\times10^{-20}\ J = 17\ k_BT.$$ (estimate)

The measured bending modulus of the human red cells is $25\ k_BT$. So, we are pretty close!