They have no memories of their previous shapes — unlike solids.

When a bilayer bends, the heads on the outside layer must occupy Δa more area than a1. Assume the free energy has the expansion

\[ ΔF = c_0 + c_1 Δa + c_2 (Δa)^2 + \ldots \]

We can drop \( c_0 \). And \( c_1 \) must vanish because the minimum of \( F \) is at \( Δa = 0 \).

So, \( ΔF \) per PL is

\[ ΔF = \frac{1}{2} k (Δa)^2 \]

for small bends in which \( (Δa)^3 ≈ 0 \).

This Hooke's law describes the cost of exposing the lipids to \( \text{H}_2\text{O} \).
Suppose the PL bilayer is wrapped around a cylinder of radius $R$. If $\Delta a$ is the thickness of half the membrane, then since the perimeter at $R + d$ is $2\pi (R + d)$, while that at $R$ is $2\pi R$, it follows that the outer layer is stretched

\[
\frac{\Delta a}{a_n} = \frac{R + d}{R} \quad \text{or} \quad a_n + \Delta a = a_n (1 + d/R)
\]

so $\Delta a = a_n d/R$. The inner head areas are squeezed by $\Delta a = -a_n d/R$.

So the bending energy per head is

\[
\Delta F = \frac{1}{2} k (\Delta a)^2 = \frac{1}{2} k \left( \frac{d a_n}{R} \right)^2. \quad (8.36)
\]

So counting the inner heads and the outer ones, we get

\[
2 \frac{\Delta F}{\text{area}} = \frac{k}{a_n} \left( \frac{d a_n}{R} \right)^2 = \frac{k}{R^2} \frac{d^2 a_n}{R^2}
\]
\[ r \text{ with } k = 2kd^2a_n \]

\[ \frac{\Delta F}{an} = \frac{1}{2} k \frac{1}{R^2}. \]

\[ (8.37) \]

Spheres are different. Now

\[ \frac{a_n + \Delta a}{an} = \frac{(R + d)^2}{R^2} = \frac{R^2 + 2Rd}{R^2}. \]

Thus

\[ \Delta a = \frac{2a_n d}{R} \]

and so the per-head cost is

\[ \Delta F = \frac{1}{2} h (\Delta a)^2 = \frac{1}{2} h \frac{4a_n^2 d^2}{R^2} \]

\[ \frac{2 \Delta F}{an} = 4k \frac{a_n d^2}{R^2} \text{ for both heads of the PL.} \]

With \( k = 2kd^2a_n \),

\[ 2 \frac{\Delta F}{a_n} = \frac{2K}{R^2} \text{ is the cost per unit area.} \]
So for a sphere of radius $R$, with area $4\pi R^2$, the energy cost is

$$\Delta F = 8\pi K$$

which is independent of the radius $R$!

This is why PL bilayers can be of any size.

**Estimate of $K$:** Suppose $R \sim l_t$ length of a PL tail. Then

$$2\frac{\Delta F}{a_n} = \frac{2K}{R^2} = \frac{2K}{l_t^2} \approx 2\Sigma.$$ 

So if $\Sigma \sim 0.05 J/m^2$ and $l_t \sim 1.3$ nm, we have

$$K \sim \Sigma l_t^2 \sim 0.05 \frac{J(0.3)^2}{(nm)^2}$$

$$\sim 0.8 \times 10^{-19} J.$$
The measured value is

\[ k = 6 \times 10^{-19} \text{ J} = 15 \text{ kT} \]

for dimyristoyl PC (DMPC).

So \( \delta \approx 24 \), \( 15 \text{ kT} \approx 400 \text{ kT} \).

What's the energy of a corrugated (washboard) shape

\[ \Delta F = \frac{1}{2} k \frac{A}{R^2} \approx \frac{1}{2} \frac{1000(\mu \text{m})^2}{(15 \text{ mm})^2} \approx \frac{15 \text{ kT}}{30} \]

\[ \Delta F \approx 300 \text{ kT} \]

So thermal fluctuations will not corrugate a PL bilayer. But for \( A \approx 2\pi R^2 \), a round bulge of radius \( R \) would cost

\[ \Delta F \approx \frac{1}{2} k \frac{2\pi R^2}{R^2} \approx 45 \text{ kT} \]
which costs only 2 ATP dimer molecules.
So cells can crawl but can't get
'drops or pimples'.
Ph bilayer vesicles are used
inside cells for many purposes.

Protein folding to native state:
The primary structure (the sequence of aa)
of many proteins determines how they
fold and into what shapes under
suitable physiological conditions.
The native state is a minimum of
free energy.

But changes in the pH, the
temperature, or the concentrations of various ions can denature most proteins, causing them to unfold, to wander through a sequence of random coils, and to lose functionality. The net $\Delta G$ that drives the folding of a protein often is less than $20 \text{ kT}$, which is that of a few H-bonds. So protein folding is a delicate business. Kauzmann showed that both high ($T > 55 \text{ C}^\circ$) and low ($T < 20 \text{ C}^\circ$) temperatures can denature proteins. Recall that $F = E - TS$, so entropic gains lower $F$ by $\Delta F = -T \Delta S$, which is smaller at cold temperatures.
Adding a surfactant, even 1.7%, SDS, can unfold proteins by shielding their hydrophobic parts from water when unfolded.

But charges matter too. Charged residues like D, E, K, R try to be on the surface to be close to the water. And D & E seek K & R, while D & E avoid each other as do K & R. So charges matter, but the stability of a protein at its isoelectric pH is nearly independent of the salt concentration.

Aggregation: Recall how sickle-cell β-globin chains stick together due
to the glu 6p -> val mutatoin.
Fibrinogen is soluble in blood, but when the body is injured an enzyme clips off part of that molecule, exposing a hydrophobic patch. The clipped protein, called fibrin, polymerizes, forming a scaffold on which clot can clot.

The bases in DNA are hydrophobic disks that stack together in a helical stack. Hydrophobicity helps molecules adhere — including the adhesion of antibodies to antigens.

Milk is 40% fat, mostly water.
Milk also contains two classes of proteins: the casein complex and whey, which is mostly α-lactalbumin and β-lactoglobulin. The casein complexes form micelles with Rn 50 nm. Thin charged heads keep the micelles from aggregating further, so fresh milk is fluid. But the bacteria Lactobacillus bulgaricus and Streptococcus thermophilus secrete lactic acid whose protons reduce the negative charge on the micelles. The micelles then coagulate, forming the gel we call yogurt. Milk curdles when its pH drops from 6.5 to below 5.3. The casein network then
traps fat globules. These fat globules are coated by an amphiphilic membrane, and so they do not coalesce, but instead form an emulsion.

Cooking unfolds the proteins in eggs into random chains or coils whose aa interact with those of nearby chains. This cross-linked network is a solid gel — a cooked egg. Adding acid enhances the coagulation of unfolded egg proteins. After all, an acid HA supplies both H⁺ and A⁻, and so the acid can neutralize D & E as well as K & R.
Whipping air into raw eggs replaces water by air and so denatures egg proteins. The unfolded conalbumin gives chiffon pie and mousse their structural stability; these unfolded proteins point their hydrophobic ac to the air and their hydrophilic ac to the water. Other egg proteins, ovomucin and globulins make the raw eggs so viscous that their foam drains slowly enough for the conalbumin to form its interlocked networks. Ovalbumin foams if heat has unfolded it—or in the preparation of meringue and soufflé.