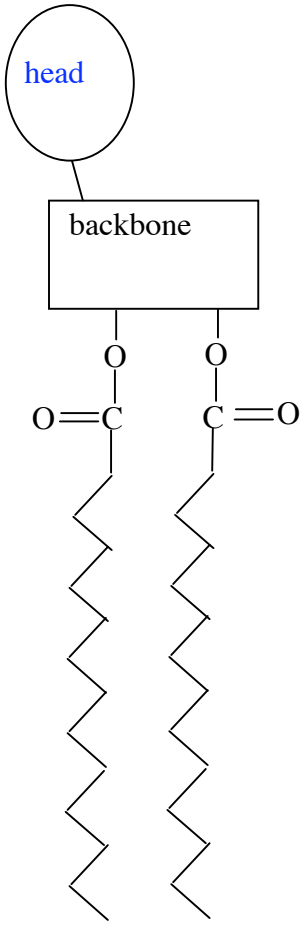
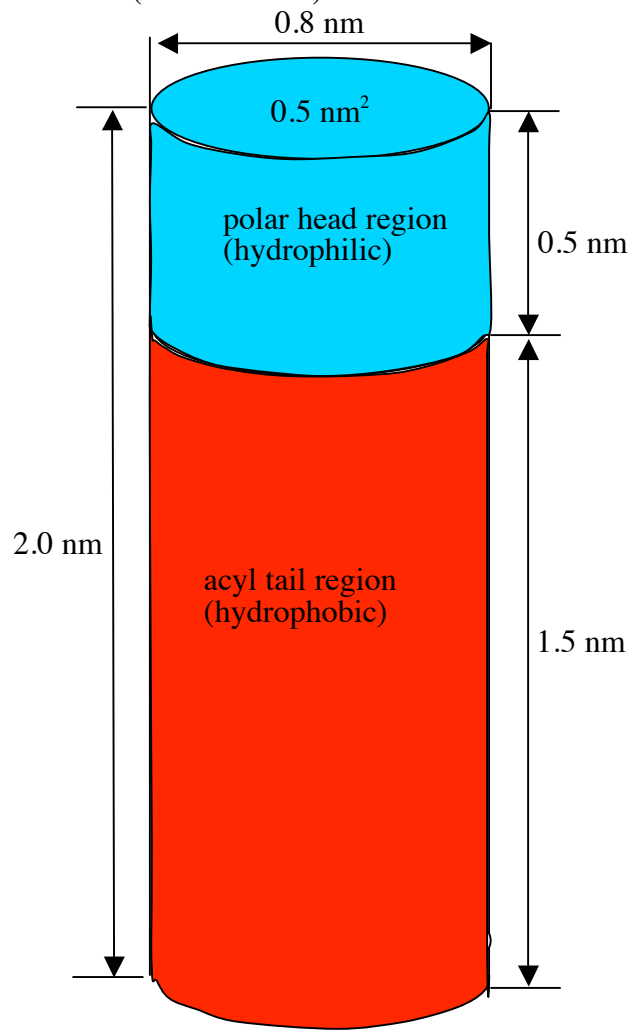
Reading for Lectures 30-32: PKT Chapter 11 (skip Ch. 10)

**Upshot of last lecture:**
Generic membrane lipid:
Can be cylindrical (equal head and tail diameters) or conical (small head/large tail or vv).
Length of the hydrophobic region depends on the lengths of the acyl chains.
Size of head region depends on head group.
Diameter of tail region depends on kinks (double bonds).




Hydrophobic repulsion organizes amphiphilic molecules: These scales are 5—10x$k_B$T:

| | |
|---|---|
| C=C double bond | 240 $k_B$T |
| C—C single bond | 140 $k_B$T |
| H-bond | 5--10 $k_B$T |
| trans-gauche ΔE | 5 $k_B$T |
| C---C van der Waals | 3 $k_B$T |

"soft" materials

The key number here is the free energy cost (σ=ΔF=ΔE-TΔS) of exposing a hydrophobic surface to water: $\sigma \approx 10\ k_B T/nm^2 = 0.04\ J/m^2$ **add to your list of numbers to remember!**

Obviously, this does depend somewhat on *which* hydrophobic surface:
Hydrocarbon—water interfacial tensions:

| | |
|---|---|
| benzene-water | 0.035 J/m$^2$ |
| saturated HC-water | 0.050 J/m$^2$ |

I am now going to do a series of estimates based on σ.
(it is like the Fermi energy in solids or the Rydberg in atomic physics)

**A. Why are single phospholipids molecules so insoluble in water?**

Calculate:

$\Delta F = \sigma A = \sigma\left[2\pi RL + \pi R^2\right] = 10\left[(2\pi)0.4(1.5) + 0.5\right] \approx 40\ k_B T$, since $0.05\ nm^2 = \pi R^2 \Rightarrow R = 0.4\ nm$.

This is a solvation energy, so there is a factor in the phospholipids density in water which goes as

$n_{phospho} \sim e^{-40} \sim 4 \times 10^{-18}$ ($<10^{-11}$ M)

this increases with chain length: for each $-CH_2-$ you get about 1 $k_BT$

Comment: Of course, lipid chain would reorganize and become a bit more "spherical" in water solution. This does not change the conclusion significantly.

Message:

Isolated biolipid molecules do not occur in water solution.

Lipids only go into water solution when they can organize in such a way as to prevent exposure of hydrophobic "tails".

This produces a whole "zoo" of what are called "lyotropic" structures: (see Figures, next page)

- micelles
- bilayers, multi-lamellar phases
- liposomes
- hexagonal/columnar phases
- cubic phases
- micellar crystals, etc.

plus "inverted versions", when the solvent is hydrocarbon and it is the polar regions that want to be hidden.

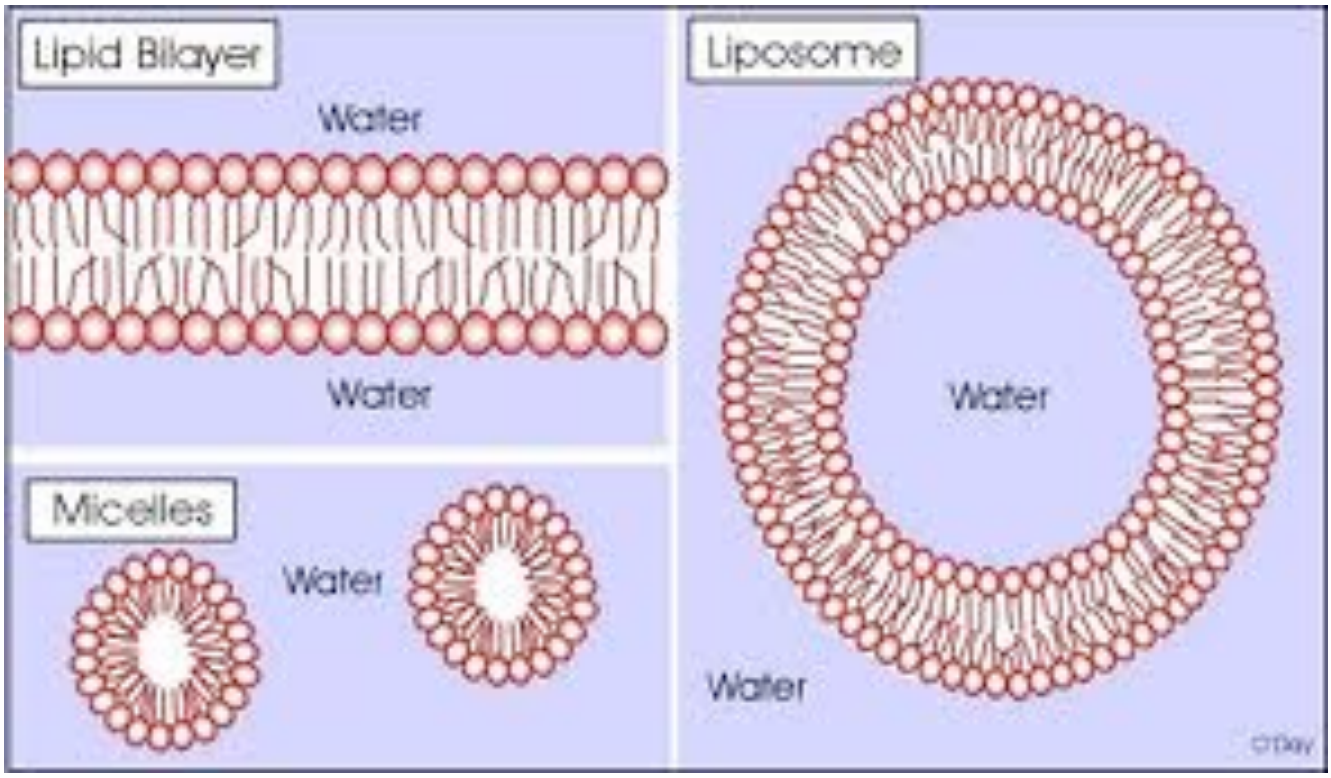
Comment: The shape of the molecule makes a big difference here; packing is important:

- Molecules with big heads and small tails like micellar shapes.
- Molecules with small heads and big tails like inverted micelles.
- Molecules that are cylindrical like the bilayer form.

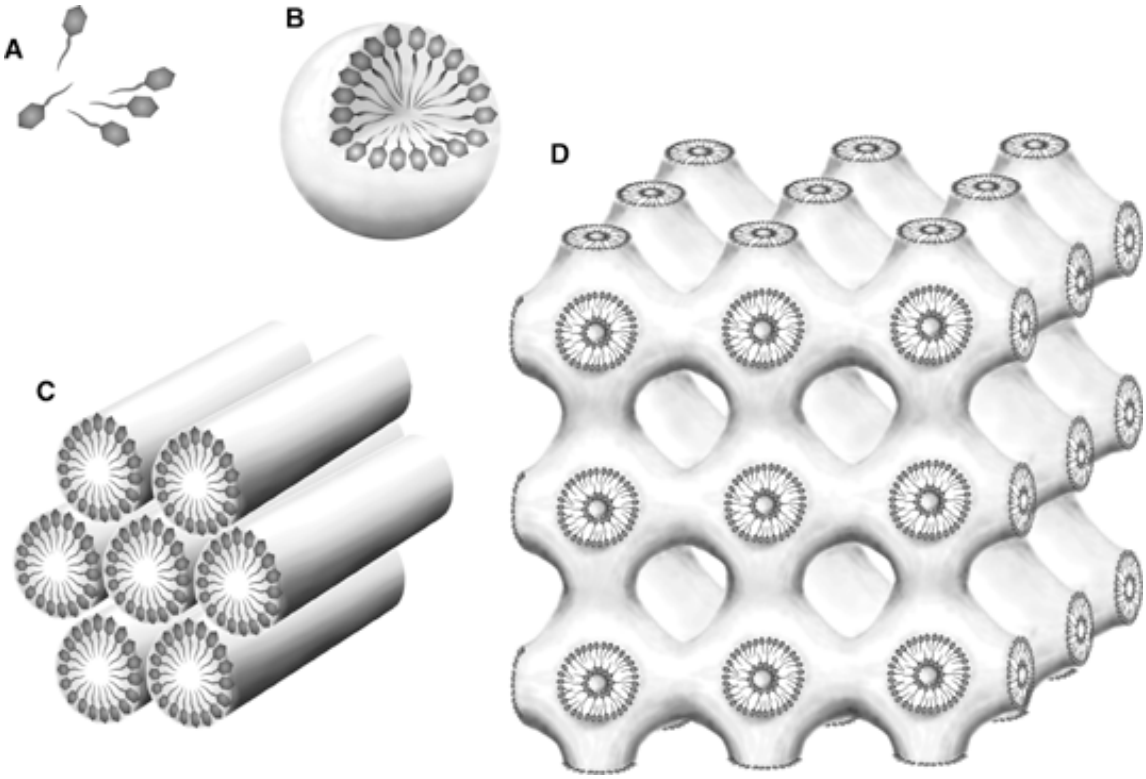
Within the bilayer class, adding molecules with big heads or big tails preferentially to one of the bilayer leaves will cause the membrane to prefer a curved shape. This is called "spontaneous curvature." (see lect. 32)

Comment: Lamellar structures can be in many different "phases":

- The common biological phase is called the fluid or $L_\alpha$ phase. It is characterized by the molecules on average being perpendicular to the plane and rotationally symmetric about this axis. It is a 2D fluid—which is good for 2D chemical mobility.
- At lower temperatures, below what is called the "main transition" (temperature $T_m$), one finds for model systems the "gel" phase. This is basically a 2D solid; it supports shear rigidity. The chains are strongly aligned and have few kinks (gauche configurations). Low mobility, not used by biology, although for reasons not fully understood, many biological systems are only slightly above the main transition.
- There are additional "smectic" phases in which the molecules are tipped away from the perpendicular, phases with periodic undulations called "ripple phases," etc/




http://www.utm.utoronto.ca/~w3bio315/lecture2.htm




http://www.currentprotocols.com/protocol/ps0408

**B. Isolated lamellar sheets do not have edges. They tend to close up into vesicles/liposomes. Why?**

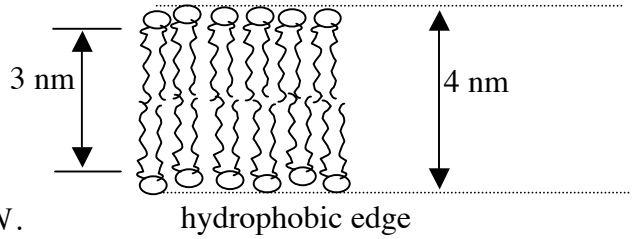
Note: This means that as soon as you create lipids, you automatically get "cellular" structures.

An "open" edge like this costs a free energy per unit length:

$\lambda = \sigma d = 10 \cdot 3 = 30\ k_B T / nm$

But, this [E]/[L] acts as a line tension:

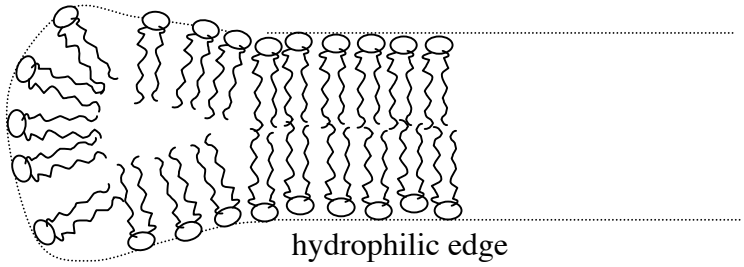
$$\frac{30\left(1.38\times10^{-23}\right)(300)}{10^{-9}}\ J/m = 1.2\times10^{-10}\ N = 120\ pN.$$




This is also the force which seals the broken plasma membrane after lysis.
It is the analog of surface tension in 3D, which makes raindrops spherical.

Comment: This same energy actually reforms the edge with some lowering of the line tension:

In this lipid rearrangement, the hydrophobic exposure decreases; however, there is a free energy cost to reorganize the lipid tails to fit in the space provided. This energy cost is comparable to that of the open, hydrophobic edge.




**C. Why does water pass easily through the membrane while ions do not?**

Think of water as a sphere of radius 0.15 nm. If a water molecule wants to enter the hydrophobic region of the bilayer, it needs to create an area of hydrophobic interface. This costs energy: "solvation energy" of water in hydrocarbon "solvent".

$\Delta F = \sigma A = \sigma \cdot 4\pi r^2 = 10(4\pi)(0.15)^2 \sim$ **$3\ k_B T$ per water molecule.**

This is easy to achieve by thermal fluctuations.

Compare to ions:
How much energy to create an ion of charge q?

Work to move the compensating charge from radius r to infinity = $\frac{1}{4\pi\varepsilon}\frac{q^2}{r}$.

Initially that ion is in water with dielectric constant D=80 $\varepsilon_w = D_w\varepsilon_0$, so, as we saw at Lect. 28.1, that energy is greatly decreased from what it would have been in vacuum, where D=1
But, in the hydrophobic (hydrocarbon) environment, where $\varepsilon_{HC} \approx 1$, that energy is 80x larger, i.e. right back at $\frac{1}{4\pi\varepsilon_0}\frac{e^2}{r} \sim 2.3\times10^{-18}\ J = 550\ k_B T$ for r = 0.1 nm (or a bit smaller for larger r), i.e., many times the thermal energy.

Of course, you would get back this energy, when the ion exits at the other side
Nature does transport lots of ions across membranes but only by the use of specialized protein channels and "pumps," which use ATP. When the transport goes via a channel, then this (large) extra energy is not required.

**D. What about lipid "flip-flop? Can this take place thermally?**

Answer: No, it can't, so lipids do not redistribute thermally between bilayer leaflets. Thus, absent specialized machinery, the number and type of lipids in the two leaflets remains fixed.

Why not?

Problem is that in order to flip, the polar head group must pass through the hydrophobic membrane interior region.

This costs energy $\Delta F = \sigma A = 10 \cdot \left[0.5 + 2\pi(0.4)0.5\right] \sim 18\ k_B T$, so $P \sim e^{-\beta \Delta F} = e^{-18} \sim 10^{-8}$, and this can at best happen slowly.

This will be important for red-cell shapes.

Note: The cell does have some specialized proteins that do this. That's how the leaflet asymmetry in the red cell is maintained. These special protein "flipases" can, e.g., simply cut off the head group on one side and reattach another on the opposite side.