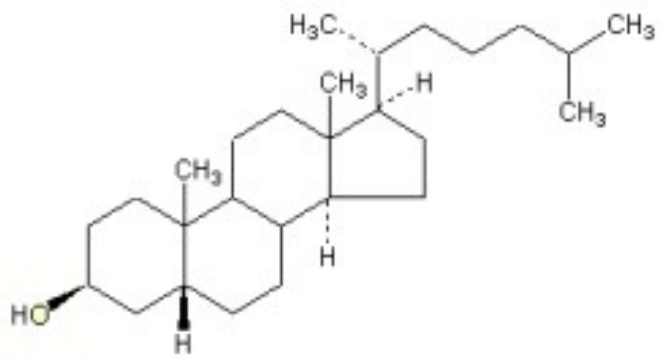
PROBLEMS
(Week of 17 Feb 09)

1. Try your hand at problem 1 in Chapter 12 of the text book. And while you're there, add in the following additional issue. If the membrane you're thinking about in this problem is a biological membrane, there is protein in the membrane as well. Assume that the membrane is about 30% by weight protein. Then assume that the average molecular weight of membrane proteins is 60,000, and that the proteins are all nonhydrated cylinders with a density of 1.35 g/cm^3 and with about 1/3 of their mass imbedded in the membrane. How many molecules of protein are there per 1 μm^2, and what fraction of that surface is protein rather than lipid?

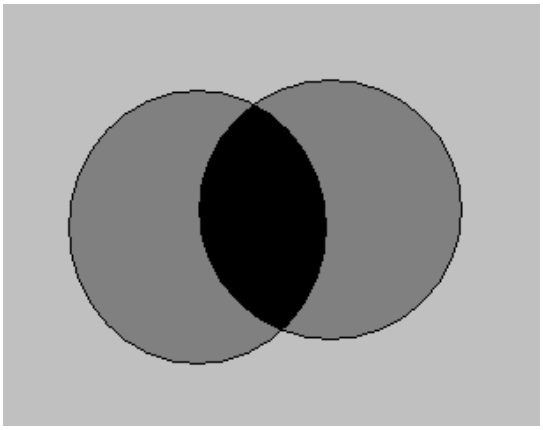
2. Try your hand at problems 2 and 5 as well.

3. In a competing textbook (Lehninger), the following problem is presented. A London doctor, Johann Thudicum, isolated and studied brain lipids about a century ago. Many years after his death, his vials were rediscovered, neatly labeled as, for example, "sphingomyeline" and "cerebroside". The question posed was how you might verify (using modern techniques) whether these were in fact the lipids in these vials corresponded to the names on the labels. The answer to this question does assume that you can guess at the efficacy of various separation techniques with only limited practical experience. But consider the following conundrum:. In the absence of modern techniques, what simple test might Thudichum have used to distinguish sphingomyelin from phosphatidylcholine.

4. The formation of domains implies that cholesterol interacts more favorably with some phospholipids than with others. An ongoing argument is whether it is the headgroup or the side chains of the phospholipids that is critical for these favorable interactions. In a study of domains like those seen by Veatch and Keller, Samsonov et al showed that enzymatic conversion of cholesterol to coprostanol (shown to the right) by cholesterol oxidase resulted in the disappearance of domains. Does this support one side or the other in the argument about what's important in the phospholipids?



5. Speaking of puzzles, in looking at the dark patches in those cholesterol domain experiments, the following pattern is never observed:



Why might you expect patches to occasionally overlap in this fashion? What do you conclude from the fact that this pattern is never seen?

6. Compare the time required for a lipid to diffuse in the membrane from one edge of a fibroblast to the other edge (ca 30 micrometerss) if the membrane contains cholesterol compared to if it doesn't (and is not in the solid phase).

7. As noted in lecture, a difference in the area of the two leaflets of the bilayer will result in membrane bending. In real cells, the tightest turn that membranes seem to take has a radius of about 25 nm. Calculate the fraction of phospholipids that would have to be moved from the outer to the inner layer in such a bent membrane to accommodate (or induce) such a curvature. (To make it simpler, do the calculation in two dimensions, not in three).

8. Draw the DSC profiles you would expect for mixtures of dilauroylPC (C12) and distearoylPC (C18) at molar ratios of 1:3, 2:2, and 3:1.

9. The following sequence appears in the Ca-ATPase from rabbits (the one whose structure can be found as 1SU4.pdb, for example).

...STEIGKIRDQMAATEQDKTPLQQKLDEFGEQLSKVISLICVAVWLINIGHFNDPVHGGS
WIRGAIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGC...

a) Calculate the hydrophobicity of this sequence, using a window size of 19. You can do this by hand (or using Excel) starting from the solvent transfer energies given in lecture, or you can have it done for you using the hydrophobicity plotter at

http://athena.bioc.uvic.ca/tools/Hydrophobicity

b) From this plot, predict the parts of the sequence which are transmembrane domains.

c) Recalculate the profile using a window size of 8 (in the plotter, there is a box on the plotting page that allows you to select the window size). Explain the difference in the profile that results from the change in window size.

d) The amino acids ...PEGL... in this sequence are highly conserved among cation-transporting P-type ATPases. Suggest why this might be so.

10. The small unilamellar vesicles (SUVs) used by Hamilton's lab have a diameter of about 30 nm.

a) Calculate the surface area of these vesicles at the outer surface of the membrane, at the center of bilayer (where the tips of the phospholipids meet), and at the inner surface of the bilayer.

b) The phospholipids that make up biological membranes (with interesting and important exceptions) are generally shaped like cylinders (rather than cones). What does this fact suggest about the spacing of the headgroups in the outer and inner leaflets of SUVs?

c) Given your answer to the last question, suggest an explanation for the increased flip rate of oleate in SUVs compared to LUVs (Large Unilamellar Vesicles).

11. If you haven't already brought up the structure of the K channel (1BL8.pdb) in Protein Explorer on your own, it's too late - now this problem requires it. So bring it up, and compare what you see with Figure 13.21 in the text.

a) There are 4 objects in the selectivity filter, but one of them seems to be different from the other three. What is the different one?

b) There's something really strange about two of the potassium ions. How could this strange situation be explained while retaining what we know about the laws of chemistry and physics?

c) Reconsider the final sentence in the legend to Figure 13.21 in light of the observed distribution of ions in the structure of the channel. Is that conclusion still valid? Is there any interesting differences in the conclusion which are suggested by the observed structure?