Chapter 13. Ouellette, 2/e. Chemistry X402.

Ch 13. Lipids.

Skip. Sections 8-9.

Also read: p 86, Essay on Steroids. Introduces cholesterol and steroid hormones. (There is a follow-up essay on p 442; not required.)

Essays. Not required.

- p 372, Prostaglandins. As he notes, the prostaglandins are one type of eicosanoid, hormones made from the C_{20} fatty acid arachidonic acid. [Eicosane is the IUPAC name for the C_{20} alkane (Table 3.1)]. See Further reading and Computer resources for more.
- p 384, Sleep.

⇒ A **practice quiz** for Lipids is at the web site. Part of this quiz is somewhat advanced, but it deals with some interesting recent work on the role of cholesterol in heart disease.

Overview

Lipids are defined by a property, rather than by a structural feature.

There are several more-or-less distinct structural types of lipids (Fig 13.1). A useful start is to think of most lipids as either fatty acid-based or sterol-based. Ouellette also includes the terpenes (Sect 4.14) as a lipid class. This chapter emphasizes the fatty acid-based lipids, but we will also mention cholesterol and steroids.

Members of both fatty acid-type and sterol-type lipids are involved in two general biological roles: structural and hormonal. Fatty acid lipids are also used as storage material. We will discuss the role of lipids in the biological membrane. This is a key topic in biology, and it is also a good illustration of the properties of lipids.

Notes

Sect 1. Fig 13.1 is a good overview of lipids, especially the fatty acid lipids, but is more than we need here. We will discuss mainly the fatty acids, the triacylglycerols, and glycerophospholipids in general. The triacylglycerols (also called triglycerides) are typical of common storage fat. The glycerophospholipids are typical of membrane lipids. Fatty acids are the key lipid subunit of all of those.

Sect 3. To get the most out of Table 13.1 you need to recognize both the chain length and degree of unsaturation of each fatty acid. This is often represented by a shorthand. For example, oleic acid is 18:1, meaning that it is a C-18 fatty acid with 1 double bond. That shorthand is usually adequate, because the unsaturations follow a standard pattern. Using this shorthand, stearic acid plus the first three unsaturated fatty acids shown form a series: 18:0, 18:1, 18:2, 18:3.

Sect 4. One interesting oil is missing from Table 13.2. Coconut oil is quite liquid, like other plant oils, but contains only a small amount of unsaturated fatty acids (< 10%). How can it be a liquid if it is largely saturated? Because it contains high levels of short chain fatty acids; it is about 50% lauric acid (C_{12}). Therefore, coconut oil does not have whatever nutritional advantages are normally associated with plant oils, which are due to the unsaturated fatty acids.

> The question of health value is getting to be more complex. When the disadvantages of oils such as coconut oil, with high levels of short chain saturated fatty acids, were recognized, those oils were generally replaced with partially hydrogenated oils from "ordinary" plants. This has led to the use of high levels of "trans fatty acids" (fats with trans double bonds), now recognized as a problem in itself.
>
> Why do trans fatty acids occur in partially hydrogenated oils? Because the process of hydrogenation is reversible, to some extent. And when it reverses, it is more likely to make the trans double bond, which is more stable (p 226).
>
> Although trans fatty acids are now considered undesirable, one should realize that there is a low level (few percent) of trans fatty acids present normally in dairy products. These seem to occur as a result of bacterial metabolism in the rumen.

Sect 5. One way to broadly measure the amount of unsaturation in fats is to determine the "iodine value". The logic of this is the alkene addition reaction, from Ch 4; measuring the amount of addition tells the amount of unsaturation. Oddly, the value is expressed as "iodine value", as if I_2 were used as the addition reagent. However, you know from Ch 4 that I_2 itself does not react well with alkenes. In fact, the test is done with ICl (iodine monochloride), but then calculated as if it were done with I_2. In any case, the iodine number is a monotonic measure of the overall degree of unsaturation.

Sect 6. Recall Ch 12 Sect 9.

Sect 10. Cholesterol is a standard constituent of animal cell membranes. The role of cholesterol in the membrane is complex. Some of the "Further reading" items deal with cholesterol and related issues. Also see "Computer resources".

Errata

p 379, top. The 2nd sentence refers to esterification with choline, but the following structure shows serine. This isn't necessarily an error, but some people notice the inconsistency. Choline is more common in sphingolipids.

p 388, #31. There is an extra H in the formula. The C at the double bond should be CH not CH_2.

Suggested problems

Models. The three questions are best thought of as parts of one question. Do them all together, and emphasize what is different among the three.

Exercises. 1-2 are "advanced"; 3-34 look good; 35-42 are on skipped sections; 43-48 are good. For #23-24, see the note above for Sect 5.

Overview of skipped sections

Sect 8 & 9. These describe two additional classes of complex lipids. We will emphasize just the one class described in Sect 7, the glycerophospholipids. The additional classes introduce no new principles.

Further reading

> This is a chapter with a very broad scope. I have noted a variety of articles here, many well beyond course material, but perhaps of interest to some students.
>
> There is also an Org/Biochem web page, listing additional articles of general interest, but emphasizing those with medical relevance. The page is titled "Further reading: medical topics". That page is especially relevant to this chapter and to the Metabolism chapter. There is no clear distinction between what is included here and what is posted at that web page.

Books

> For more about these books, see my web page of book suggestions.

C Tanford, Ben Franklin Stilled the Waves: An informal history of pouring oil on water with reflections on the ups and downs of scientific life in general. 1989. The central scientific story -- announced in the subtitle -- is a simple one, one observed by many from ancient times onwards. Tanford discusses this story, from early observations, including those of Benjamin Franklin, through explanation in terms of molecules and polarity -- and up through its relevance to the nature of the cell membrane. Along the way he tells us about some key scientists of the 18th-20th centuries and about the scientific environment they worked in. A delightful book.

S Allport, The Queen of Fats - Why Omega-3s were removed from the western diet and what we can do to replace them. 2006. A book about the "omega -3" fatty acids: those with the last double bonds three carbons from the end. These are much in the news, and may be an important dietary issue. This book provides a good readable introduction to the story, with much historical development. It should not be considered an unbiased source of information on the dietary importance of these fatty acids, which I think is still an open issue. Also see Napier et al (2006), Lai et al (2006) and Nagahuedi et al (2009).

Articles

S A Farber et al, Genetic analysis of digestive physiology using fluorescent phospholipid reporters. Science 292:1385, 5/18/01. So how do you study lipid digestion in real animals? Use fluorescent lipids, and watch! It works, if the organism is transparent. The zebrafish larva has become an important model system precisely because it has that characteristic.

N V Chandrasekharan et al, COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: Cloning, structure, and expression. Proc Natl Acad Sci 99(21):13926-31, 10/15/02. Aspirin works by inhibiting cyclooxygenase (COX), a key enzyme in the synthesis of prostaglandins from arachidonic acid (p 372). More recently, we have understood that there are two COX enzymes, with different biological roles. This knowledge led to the development of a new class of anti-inflammatory drugs that preferentially inhibit COX-2 (e.g., Celebrex and Vioxx), thus avoiding some of the classic side effects of aspirin. But the discovery of COX-2 left a mystery: the common pain killer acetaminophen inhibited neither COX-1 nor COX-2. Now, we have the discovery of COX-3, which indeed is inhibited by acetaminophen. Interestingly, COX-3 is a variant of COX-1 (made from the same gene), and there are hints that there may be more COX enzymes remaining to be discovered. (There is a good news story about this in Nature 420:135, 11/14/02.)

> There is much more to the COX story. There is evidence that aspirin -- and COX-2 inhibitors -- may have other effects, such as inhibition of cancer. And of course, 2004 brought a major re-evaluation of not only the newer COX-2 inhibitors but of NSAIDs (non-steroidal anti-inflammatory drugs) in general, due to side effects that had been unappreciated. More about this on my "Further reading: Medical topics" page. See Computer Resources for more. Also see Egan et al (2004), below.

A Wechsler et al, Generation of viable cholesterol-free mice. Science 302:2087, 12/19/03. By genetic engineering, they created mice in which cholesterol is replaced by a sterol with one double bond in the side chain (desmosterol). The resulting mice had relatively minor abnormalities. However, they were infertile. Humans with a similar genetic defect have more severe abnormalities; the authors suggest that the discrepancy here may be due to more maternal cholesterol being available in mice than in humans. In addition to the specifics here, this is an example of using genetic modification of an animal as a model system.

R S Watkins et al, Li–CaO catalysed tri-glyceride transesterification for biodiesel applications. Green Chem 6:335-340, 7/04. Biodiesel is a fuel prepared from renewable plant oils, including wastes, and consists largely of simple fatty acid esters. It is highly touted in some circles as a good way to reduce petroleum consumption. This paper explores better ways to make it.

J Daniel et al, Induction of a novel class of diacylglycerol acyltransferases and triacylglycerol accumulation in Mycobacterium tuberculosis as it goes into a dormancy-like state in culture. J

Bacteriol 186:5017-30, 8/04. One of the things that makes treatment of tuberculosis complicated is that the bacteria go into a dormant state, which is rather resistant to ordinary antibiotic treatment. In the dormant state, the bacteria use fat as their major energy source. Here Daniel et al find a novel enzyme involved in this stage of metabolism, and suggest that it may be a good target for treatment.

I A Chen et al, The emergence of competition between model protocells. Science 305:1474, 9/3/04. They show that membrane-bounded vesicles containing a charged polymer (such as a nucleic acid) will grow, because of osmotic pressure from the counter-ions. They suggest that this might be relevant to how living cells first arose.

D Tchernov et al, Membrane lipids of symbiotic algae are diagnostic of sensitivity to thermal bleaching in corals. PNAS 101(37):13531-5, 9/14/04. Coral bleaching is due to loss of its symbiotic algae. Here they show a correlation of sensitivity to bleaching with the degree of unsaturation of the algal chloroplast membranes.

M C Mansilla et al, Control of membrane lipid fluidity by molecular thermosensors. J Bacteriol 186:6681-8, 10/04. Minireview. Some bacteria can grow over a wide temperature range. They adjust the fatty acid composition of their membranes so that the fluidity is very similar regardless of T. This paper reviews how the T is sensed and the membrane composition regulated. Interestingly, the details vary for different bacteria.

F Backhed et al, The gut microbiota as an environmental factor that regulates fat storage. PNAS 101:15718-23, 11/2/04. The complexity of regulation of food intake and storage is being increasingly realized. It has long been known that the gut bacteria process carbohydrates. This paper reports changes in digestive proteins as a result of the gut bacteria. This may be an interesting area to follow, but caution: the work here is done with germ-free mice.

R P Evershed et al, Archaeology: Formulation of a Roman cosmetic. Nature 432:35, 11/4/04. They analyze a “face cream” that has been dated to 2nd century AD. In particular, they analyze the fatty acid composition, which leads them to suggest that the cream was made from heated animal fat.

K M Egan et al, COX-2-derived prostacyclin confers atheroprotection on female mice. Science 306:1954, 12/10/04. In this mouse model system, they get evidence to suggest why COX-2 inhibitors may promote heart disease -- and also why heart disease is less in pre-menopausal women. Also see Chandrasekharan et al (2002), above. See Computer Resources for more.

M J Francis & R M Pashley, A study of de-gassed oil in water dispersions as potential drug delivery systems. Colloids and Surfaces A: Physicochem Eng Aspects 260:7-16, 6/15/05. Many drugs are quite hydrophobic, and delivery is a practical problem. This article shows a new approach: more stable emulsions are possible if the oil is de-gassed first. The article includes a good overview of drug delivery issues. Also see De Geest et al (2006).

T G Redgrave et al, Case report: Treatment with a dietary fat substitute decreased Arochlor 1254 contamination in an obese diabetic male. Journal of Nutritional Biochemistry 16:383-

384, 6/05. The fat substitute Olestra is made by esterifying sucrose with fatty acids. All the parts and the linkages are quite natural, but this particular combination cannot be digested by your esterases or lipases, so it is non-nutritive. A known issue is that people using Olestra may become deficient in the fat soluble vitamins, which stay in the Olestra and pass through you. Here they make use of the same idea -- to decontaminate a person with high levels of a fat-soluble toxin. Also see Computer Resources, below.

G K Beauchamp et al, Phytochemistry: Ibuprofen-like activity in extra-virgin olive oil. Nature 437:45, 9/1/05. "Enzymes in an inflammation pathway are inhibited by oleocanthal, a component of olive oil." Whether the level of this compound is enough to be physiologically relevant for those who consume considerable amounts of olive oil is open.

A Segura et al, Proteomic analysis reveals the participation of energy- and stress-related proteins in the response of Pseudomonas putida DOT-T1E to toluene. J Bacteriol 187:5937-45, 9/05. Bacteria use multiple mechanisms to develop resistance to membrane-soluble solvents. For example, some bacteria isomerize regular cis fatty acids to trans fatty acids (TFA; p 374), thus making the membrane more rigid. See Doyle (1997) at the web site "old articles" page for some basic background on TFA. This article discusses the resistance mechanisms, and focuses on efflux pumps. (An FDA rule now requires TFA content to be shown on nutrition labels. See Computer Resources, below.)

H Pilcher, Microbiology: Pipe dreams. Nature 437:1227, 10/27/05. A feature article about the anammox bacteria. A major gap in our understanding of the global nitrogen cycle has been how ammonia gets oxidized in anaerobic environments. Recent work has shown that the oxidation is due to bacteria carrying out an anaerobic oxidation reaction, now called anammox, using nitrate ions. So what does this have to do with lipids? Well, the anammox reaction produces hydrazine as an intermediate. The hydrazine would probably kill the bacteria, except that the reaction is done within a special intracellular compartment, surrounded by a novel lipid. This lipid contains a series of fused cyclobutane rings. The novel "ladderane" lipid makes such a dense membrane that it substantially reduces the diffusion of small molecules, such as hydrazine, through it. And the presence of this unusual lipid now serves as a marker for these bacteria.

G Frühbeck, Obesity: Aquaporin enters the picture. Nature 438:436, 11/24/05. News. The 2003 Nobel prize in chemistry was awarded, in part, for work on the water channels called aquaporins. As work on these membrane channels continues, more and more roles for them are found or postulated. The aquaporin studied here also transports glycerol, and its deficiency leads to obesity -- in mice. Also see Computer Resources, below.

A G Lee, Cell biology: A greasy grip. Nature 438:569, 12/1/05. News. "How do the lipids and proteins of the cell membrane interact to create a functioning barrier for the cell? A high-resolution structure of a membrane protein reveals intimate contacts with its lipid neighbours."

D M Engelman, Membranes are more mosaic than fluid. Nature 438:578, 12/1/05. Start of feature section on Membranes. Fig 1 from this article is included with class slides; it shows how our view of membrane structure has evolved to recognize a greater role for the proteins.

S M Hurtley, Crossing the bilayer. Science 310:1451, 12/2/05. Introduction to feature series on Crossing Membranes. After this introduction, there are three nice articles, on "Protein translocation across biological membranes", "The ins and outs of DNA transfer in bacteria", "Principles of selective ion transport in channels and pumps".

E J Behrman & V Gopalan, Cholesterol in plants. J Chem Educ 82:1791, 12/05. It is often said that plants do not contain cholesterol. However, that is not really true. Cholesterol is one of many sterols in plants, usually at a fairly low level. This article broadly discusses plant sterols, and some of the implications for human nutrition. Of particular interest is how the various sterols are distinguished at a secondary stage of uptake. In fact, there is a genetic disease in which the major plant sterol, sitosterol, is not discriminated against; in these individuals sitosterol is efficiently used -- as cholesterol.

B G De Geest et al, Self-exploding lipid-coated microgels. Biomacromolecules 7:373-379, 1/06. See Francis & Pashley (2005) for some background. Another approach to drug delivery: vesicles that partially degrade, then swell and "explode".

L Anson, Ion channels. Nature 440:439, 3/23/06. Introduction to a Nature Insight feature section. Among the articles: From molecule to malady; Glutamate receptors at atomic resolution; hERG potassium channels and cardiac arrhythmia; K_{ATP} channels as molecular sensors of cellular metabolism; The ABC protein turned chloride channel whose failure causes cystic fibrosis.

S Tricon & P Yaqoob, Conjugated linoleic acid and human health: a critical evaluation of the evidence. Curr Opin Clin Nutr Metab Care 9:105-110, 3/06. Conjugated linoleic acids (CLA) are isomers of linoleic acid (18:2) with the double bonds conjugated, i.e., without a $-CH_2-$ between them (Section 4.13). They are minor components of ruminant animal fat and dairy products. There is some debate about whether they may have health benefits. Tricon & Yaqoob review the evidence; they are skeptical. There are several complexities, and the article is worth a browse for those interested in such nutritional questions.

J A Napier et al, Progress towards the production of very long-chain polyunsaturated fatty acid in transgenic plants: plant metabolic engineering comes of age. Physiologia Plantarum 126:398-406. 3/06. Review. They discuss recent work on developing plants, by genetic engineering, to make the polyunsaturated fatty acids that are normally considered typical of fish. Also see the book listed at the start of this section and Lai et al (2006).

L Lai et al, Generation of cloned transgenic pigs rich in omega-3 fatty acids. Nature Biotechnology 24(4):435 4/06. + Exchange of letters: 24:1472, 12/06 and 25:505 & 506, 5/07. One classification of the polyunsaturated fatty acids (PUFAs) is by the position of the last double bond. If we call the last carbon ω (omega), then the last double bond is typically at ω-6 (linoleic) or ω-3 (linolenic). There is considerable interest in the merits of the ω-3 fatty acids, which are less common and which mammals cannot make. Here, they develop pigs that can make ω-3 fatty acids, by genetic engineering, using an enzyme from the worm Caenorhabditis elegans. Does it work? Yes. Is it a good idea? See the lively exchange of letters. Also see the book listed at the start of this section and Napier et al (2006).

J T Groves, Chemistry: Unveiling the membrane domains. Science 313:1901, 9/29/06. News. A brief discussion of the use of mass spectrometry -- and of atomic force microscopy -- in exploring the details of membrane structure.

G Di Paolo & P De Camilli, Phosphoinositides in cell regulation and membrane dynamics. Nature 443:651, 10/12/06. Review. Discussion of the regulatory roles of one class of lipids, those with inositol attached to the glycerol phosphate.

A G Lee, Ion channels: A paddle in oil. Nature 444:697, 12/7/06. News. “How do voltage-gated ion channels in cell membranes open? The latest work suggests that the process depends on having the correct lipid molecules in the membrane, with phosphate groups being mandatory.”

F Seebacher & S A Murr, Transient receptor potential ion channels control thermoregulatory behaviour in reptiles. PLoS One 2(3):e281, 3/07. Online journal, open access: http://www.plosone.org/article/fetchArticle.action?articleURI=info%3Adoi%2F10.1371%2Fjournal.pone.0000281. This paper shows that reptiles (cold-blooded animals) sense temperature with ion channel receptors similar to -- though distinct from -- those found as thermosensors in mammals (e.g., Nilius & Voets, 2007 -- the next item).

B Nilius & T Voets, Neurophysiology: Channelling cold reception. Nature 448:147, 7/12/07. News. We sense temperature with T-responsive ion channels -- receptor proteins in the membrane. The main thrust of the work discussed here is to show that mice lacking a particular cold-sensing membrane protein indeed have the expected behavioral response. Incidentally, this cold-receptor is also the receptor for menthol, which we interpret as a “cool” chemical.

M A Hillmyer, Materials science: Micelles made to order. Science 317:604, 8/3/07. News. Discusses recent work on making a range of micelle structures, based on controlled synthesis of amphiphilic polymers; “amphiphilic” means that one end is polar and the other end is nonpolar. This is not only cute, but possibly useful; it is an example of the kind of synthetic work going on in nanotechnology.

S H White, Biochemistry: Crowds of syntaxins. Science 317:1045, 8/24/07. News. Discussion of how a protein forms clusters in the cell membrane -- by simple diffusion and physical association due to the usual quaternary interactions.

M P Cuajungco et al, TRP channels as candidates for hearing and balance abnormalities in vertebrates. Biochimica et Biophysica Acta - Molecular Basis of Disease 1772:1022-1027, 8/07. Review. Ion channels are involved in various kinds of sensory transduction. We have noted taste and odor receptors. Mechanosensory ion channels are involved in touch (including pain) -- and hearing. However, the identification of specific channels for hearing has been elusive so far, although there have been plenty of leads, some now known to be false. Good overview.

E W McCleskey, Neuroscience: A local route to pain relief. Nature 449:545, 10/4/07. News. This news story discusses some fascinating work on ion channels -- and their role in common biological processes. Some anesthetics work by blocking sodium ion channels of neurons;

they basically shut down nerve cell communication. In the work discussed here, a modified form of an anesthetic is targeted to specific cells: those responsible for pain. The anesthetic is modified so that it cannot cross cell membranes on its own; they do this by making it less lipophilic (it has a positive charge). And then it is delivered along with capsaicin -- which opens up the ion channels of the pain-sensitive cells that detect that hot pepper stuff. Thus the anesthetic specifically acts on pain-sensing neurons. The hope is that this approach can be developed as a treatment for pain.

S Lee & N D Spencer, Materials science: Sweet, hairy, soft, and slippery. Science 319:575, 2/1/08. News. As you might infer from the title, this news story discusses work on lubricants. The idea is to design synthetic lubricants using ideas learned from looking at biological lubricants, such as mucins. Thus the work explores bottle-brush structures, coated to achieve high interaction with solvent (e.g., sugars or similar hydrophilic substances if the lubricant is to work in water), and the role of soft surfaces, so often found in biological systems.

D W Deamer, Origins of life: How leaky were primitive cells? Nature 454:37, 7/3/08. News. Modern cells have bio-membranes that are quite impermeable; small charged molecules depend on transport proteins to cross the membrane. However, such transport proteins presumably were not present at the start. The work discussed here shows a plausible primordial membrane, solid enough to keep macromolecules in, but permeable enough to allow small molecules, even if charged, to cross.

H Cao et al, Identification of a lipokine, a lipid hormone linking adipose tissue to systemic metabolism. Cell 134:933-944, 9/19/08. An idea that has been developing in recent years is that adipose (fat) tissue is “active” -- that it sends out hormonal signals that affect metabolism. The first and most famous of the adipokines -- hormones made by adipose tissue -- is leptin. Now we have evidence, from mice, for an adipokine that is itself a fatty acid. The fatty acid is cis-9-hexadecenoic acid, popularly called palmitoleic acid. A news story on this work is listed on the course page of Internet Resources.

R P Evershed et al, Earliest date for milk use in the Near East and southeastern Europe linked to cattle herding. Nature 455:528, 9/25/08. An interesting paper, at several levels. The big picture is trying to understand the agricultural practices of people long ago -- several millennia ago. The approach is to analyze residues found on archeological materials, such as pottery vessels. The chemistry is analyzing the isotopes in fats in those residues, and trying to identify the source.

B A S Van Mooy et al, Phytoplankton in the ocean use non-phosphorus lipids in response to phosphorus scarcity. Nature 458:69, 3/5/09. Some organisms respond to phosphate limitation by making lipids with reduced P content. They may replace phospholipids by structurally similar lipids containing N or S. This spares the P supply, which is essential for nucleotides and nucleic acids. The substitution helps to emphasize the functional nature of lipids.

S Nagahuedi et al, Mimicking the natural doping of migrant sandpipers in sedentary quails: effects of dietary n-3 fatty acids on muscle membranes and PPAR expression. Journal of Experimental Biology 212:1106-1114, 4/15/09. (There is also a related “Commentary” by one of the authors: J-M Weber, The physiology of long-distance migration: extending the limits of endurance metabolism. Journal of Experimental Biology 212:593-597, 3/1/09.) (“n-3” means the same as “ω-3”, used elsewhere in this handout.) A fascinating biology story. Certain birds change their diet prior to a long migration. The key dietary change is to eat very high levels of n-3 fatty acids; this leads to metabolic changes that prepare them for the endurance flight. The paper tests their ideas with another bird, one that is normally non-migratory. The paper integrates organismal behavior with physiological and biochemical explanations.

R N Collins & J Zimmerberg, Cell biology: A score for membrane fusion. Nature 459:1065, 6/25/09. News. We have noted how the physical properties of lipids can lead to spontaneous formation of bilayers, as found in biological membranes. But real membranes are more complex. For one thing, they are dynamic; membrane fusion and budding are important parts of biological processes. This news story describes recent work in developing an in vitro system for studying membrane fusion. It includes 17 purified proteins.

D Lingwood & K Simons, Lipid rafts as a membrane-organizing principle. Science 327:46, 1/1/10. Review. Biological membranes are non-uniform, with regard to both lipid and protein content. Some regions, called rafts, are relatively rigid. They develop due to interactions among the lipids and proteins. Since rafts have special composition, it should not be surprising that they may have special functions. Studying both the composition and function of rafts is an active field.

M M Kozlov, Biophysics: Joint effort bends membrane. Nature 463:439, 1/28/10. News. “The curvature of cellular membranes is generated by proteins and lipids. A synthetic experimental system allows the interplay between protein- and lipid-generated bending mechanisms to be studied directly.”

G A M Cross, Drug discovery: Fat-free proteins kill parasites. Nature 464:689, 4/1/10. News. Some proteins (Ch 15) are modified by attaching a fatty acid; this provides a nice hydrophobic group on the protein, and is sometimes used for membrane attachment. The work reported here shows that the lipid-adding enzyme used by the trypanosome that causes sleeping sickness is distinct enough from the mammalian enzyme that it might be a suitable drug target.

Computer resources (See web page for details and links.)

Adipose Tissue. One of the important general findings of recent years is the active role of fat tissue. Leptin is but one example of a hormone made by such tissue.

I have listed three sites that have good discussions of the role of **cholesterol** in membranes. In fact, each site can be pursued further, for more about membranes, and more cell biology.

The web page includes a link to an FDA site on **COX-2 inhibitors**. Also see Chandrasekharan et al (2002) and Egan et al (2004), above. There is more on this topic on my “Further reading: Medical topics” page.

There are a couple of sites about TFA (trans fatty acids). One is an FDA site on **Questions and Answers about Trans Fat Nutrition Labeling**. The other is a site to help restaurants eliminate the use of TFA in cooking. Also see Segura et al (2005).

The 2003 Nobel prize in chemistry was awarded to two scientists for their work on **transport channels,** for water and ions, in biological membranes.

The 1982 Nobel prize in medicine was awarded to three scientists "for their discoveries concerning **prostaglandins** and related biologically active substances."

Environmental estrogens and other hormones. The general theme is hormone mimics: chemicals that are not a normal part of the human body but which may behave like hormones in the body. These include chemicals found in nature either naturally (e.g., the so-called phytoestrogens in plants) or derived from pesticides etc. The site is from the Center for Bioenvironmental Research, at Tulane and Xavier Universities, in New Orleans.

ChemCases (from Kennesaw State Univ, Georgia) develops 12 "case studies" of chemistry. Each analyzes the development of a product, and includes economic and safety issues, as well as the underlying chemistry. Among the case studies, for this Ch, is the fat substitute Olestra. (Also see Redgrave et al, 2005, above.) (There is a lot to explore here… The complete set of cases is listed on the web page.)

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