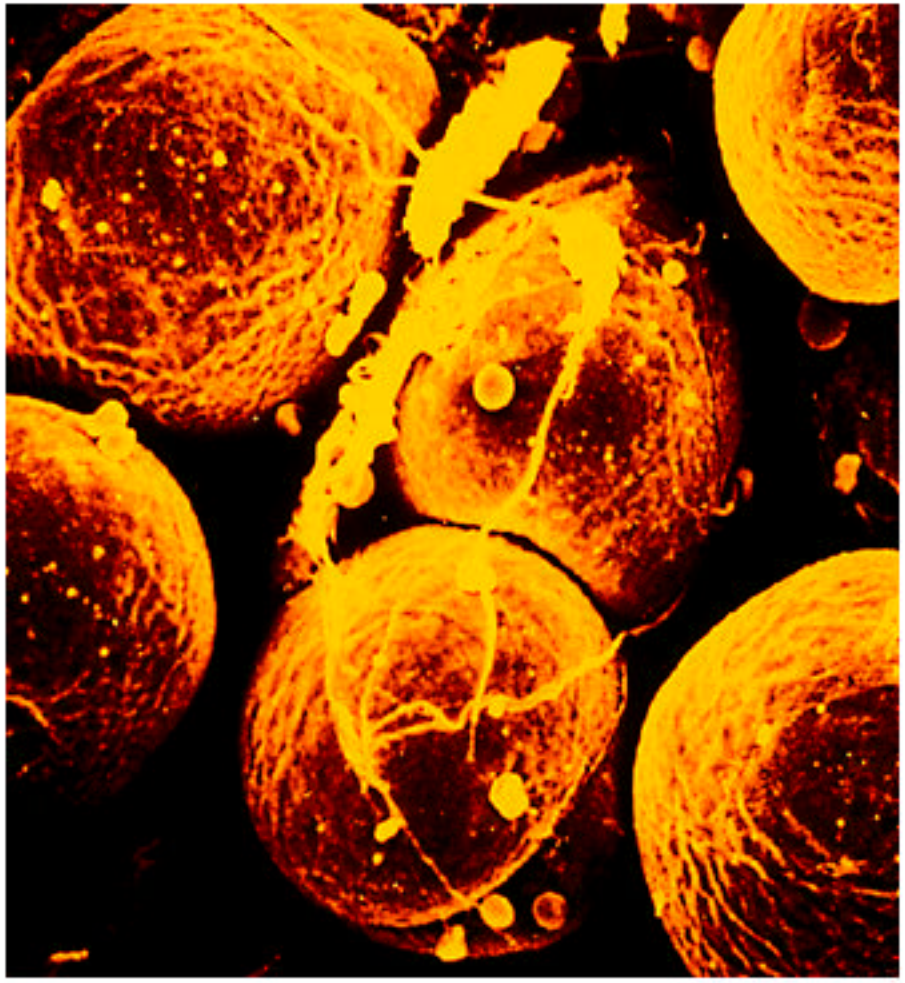
Lecture 4:
Review of Lipids (Ch. 9)



Fred E. Hossler/Visuals Unlimited.

Adipocytes or fat cells

LIPIDS

- A class of biological molecules (***i.e.***, are of biological origin) defined by low solubility in water and high solubility in non-polar solvents (such as chloroform)
- They are largely hydrocarbon in composition, thus
    - represent highly reduced forms of carbon, and
    - upon oxidation in metabolism, yield large amounts of energy.

Examples of LIPIDS:

- FATS and OILS,
- certain VITAMINS & HORMONES, and
- most NON-PROTEIN MEMBRANE COMPONENTS.

Lipids, ***per se***, are not bad; they are indispensable to metabolism & cell structure.

Section 9.1: Lipid Classification

*A. **Fatty acids** - get the picture & know some examples

*B. **Triacylglycerols** (see figures on p. 222)

C. **Glycerophospholipids** (= phosphoglycerides) — the major lipid component of membranes (see Fig. 9-3)

D. **Sphingolipids** — major membrane C18 amino alcohol

E. **Steroids** — three 6-membered rings + one 5-membered ring fused together---rigid; esp.important in diet/health:

*__Cholesterol__ (Fig. 9.10)

F. **'Other'** — Waxes, terpenes, *__Eicosanoids__

*Know best: are health- and diet-related.

FATTY ACIDS (see TABLE 9-1 and Fig. 9-1)

(Get the big picture, and KNOW the ones presented in class. You do not need to memorize all of them.)

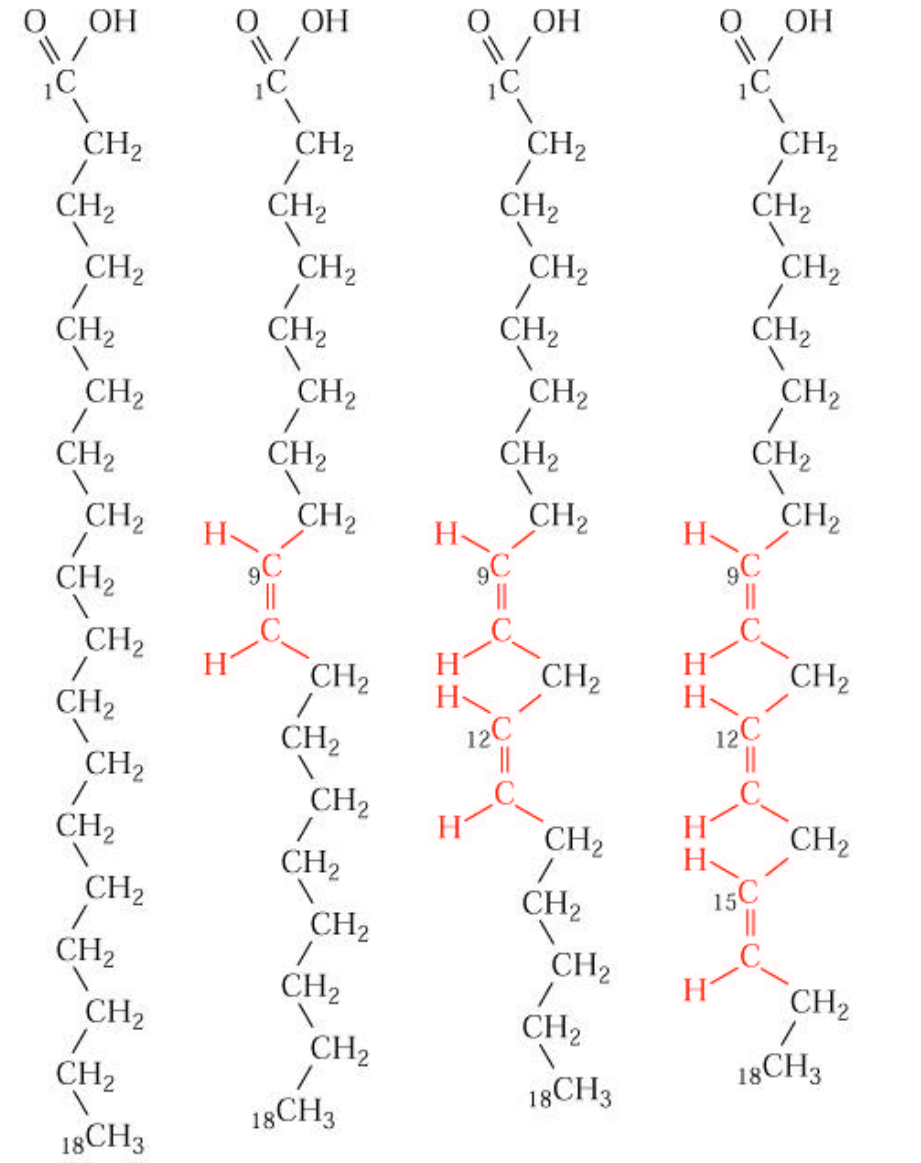
- are **carboxylic acids with long-chain hydrocarbon chains**
- are **rarely 'free' (uncomplexed) in nature** [except **arachidonic acid**]
- are **usually in esterified form** as major components of other lipids...
- are **often complexed in triacylglycerols** (TAGs)
- most have an **even number of carbon atoms (usually 14 to 24)**
- are **synthesized by concatenation of C_2 units.**
- **C_{16} & C_{18}** FAs are the most common FAs in higher plants and animals

- Are either:
  - —**saturated** (all C-C bonds are single bonds) or
  - —**unsaturated** (with one or more **double bonds** in the chain)
    - —**monounsaturated** (a single double bond)
    - —**polyunsaturated** (more then one double bond)
- the number of double bonds in FAs varies from 1 to 4 (usually), but in most bacteria it is rarely more than 1

Fig. 9-1:
C_{18} Fatty Acids

carboxylic acids with long-chain hydrocarbon chains

rarely 'free' in nature (as shown here)



Stearic acid **Oleic acid** **Linoleic acid** **α-Linolenic acid**

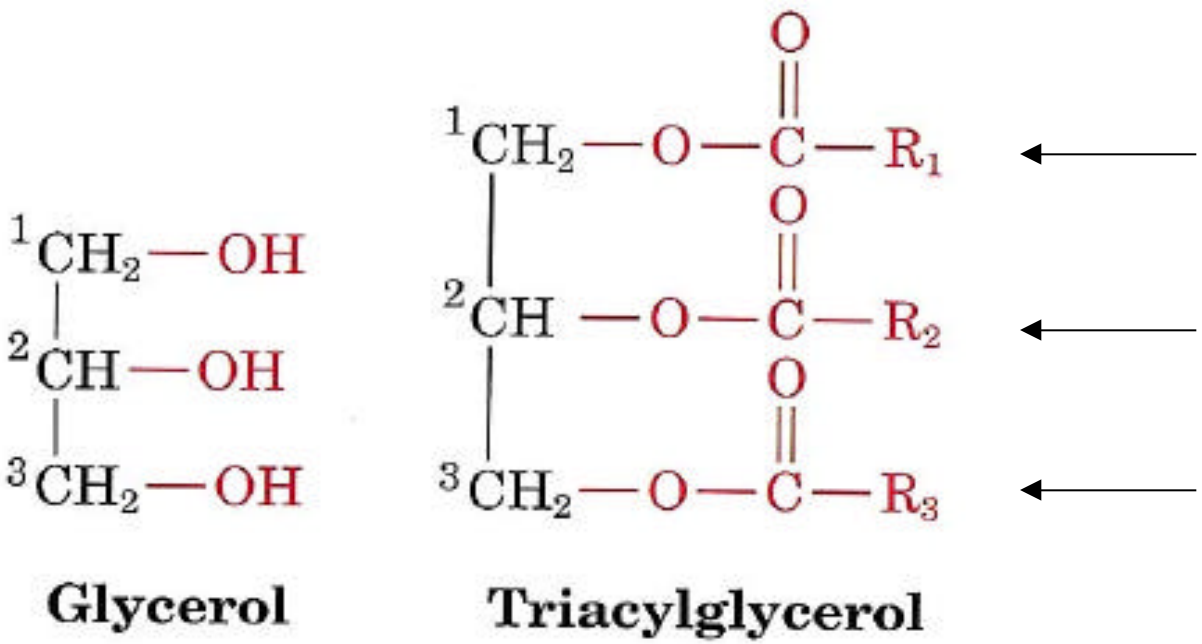
Figure 9-1. The structural formulas of some C_{18} fatty acids.

FATTY ACIDS (see TABLE 9-1 and Fig. 9-1)

- are **carboxylic acids with long-chain hydrocarbon chains**
- are **rarely 'free' (uncomplexed) in nature** [except **arachidonic acid**]
- are **usually in esterified form** as major components of other lipids
- are **often complexed in triacylglycerols** (TAGs)
- most have an **even number of carbon atoms (usually 14 to 24)**
- are **synthesized by concatenation of C_2 units.**
- **C_{16} & C_{18}** FAs are the most common FAs in higher plants and animals

- Are either:
  - —**saturated** (all C-C bonds are single bonds) or
  - —**unsaturated** (with one or more **double bonds** in the chain)
    - —**monounsaturated** (a single double bond)
    - —**polyunsaturated** (more then one double bond)
- the number of double bonds in FAs varies from 1 to 4 (usually), but in most bacteria it is rarely more than 1

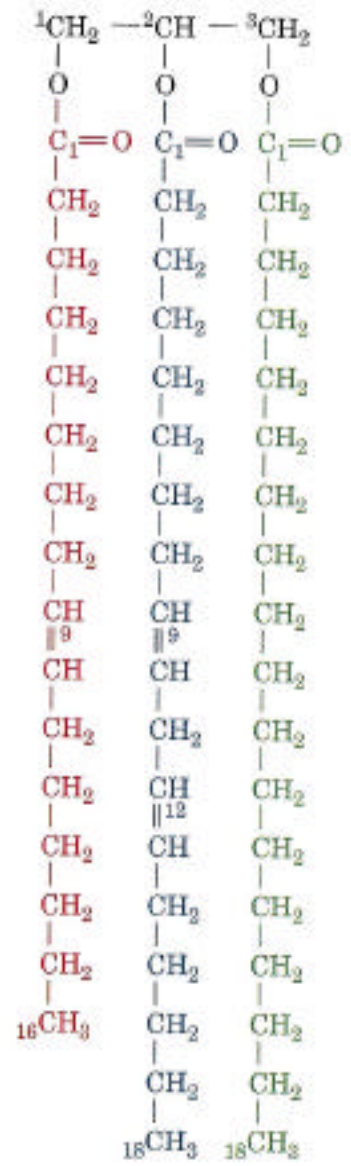
Triacylglycerol (TAG)



Fatty acids are esterified to glycerol to form TAGs

R1, **R2**, and **R3** can either be identical (simple TAG) or non-identical (mixed TAG)

A mixed TAG (p. 222)



1-Palmitoleoyl-2-linoleoyl-
3-stearoyl-glycerol

FATTY ACIDS (see Fig. 9-1 and TABLE 9-1)

(Get the big picture, and KNOW the ones presented in class. You do not need to memorize all of them.)

- are **carboxylic acids with long-chain hydrocarbon chains**
- are **rarely 'free' (uncomplexed) in nature** [except **arachidonic acid**]
- are **usually in esterified form** as major components of other lipids
- are **often complexed in triacylglycerols** (TAGs)
- most have an **even number of carbon atoms (usually 14 to 24)**
- **C_{16} & C_{18}** FAs are the **most common** FAs in higher plants and animals
- are **synthesized by concatenation of C_2 units.**

- Are either:
  - —**saturated** (all C-C bonds are single bonds) or
  - —**unsaturated** (with one or more **double bonds** in the chain)
    - —**monounsaturated** (a single double bond)
    - —**polyunsaturated** (more then one double bond)
- the number of double bonds in FAs varies from 1 to 4 (usually), but in most bacteria it is rarely more than 1

Table 9-1:

Table 9-1. The Common Biological Fatty Acids

Symbol[a]	Common Name	Systematic Name	Structure	mp (°C)
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
24:1	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

[a]Number of carbon atoms: Number of double bonds.

Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), Chapter 8, Clarendon Press (1986).

FATTY ACIDS (see Fig. 9-1 and TABLE 9-1)

- are **carboxylic acids with long-chain hydrocarbon chains**
- are **rarely 'free' (uncomplexed) in nature** [except **arachidonic acid**]
- are **usually in esterified form** as major components of other lipids
- are **often complexed in triacylglycerols** (TAGs)
- most have an **even number of carbon atoms (usually 14 to 24)**
- are **synthesized by concatenation of C_2 units.**
- **C_{16} & C_{18}** FAs are the **most common** FAs in higher plants and animals.

- Are either:
  - —**saturated** (all C-C bonds are single bonds) or
  - —**unsaturated** (with one or more **double bonds** in the chain)
    - —**monounsaturated** (a single double bond)
    - —**polyunsaturated** (more then one double bond)
- the number of double bonds in FAs varies from 1 to 4 (usually), but in most bacteria it is rarely more than 1

Saturated FA:
Stearic Acid (18:0)

Monounsaturated FA:
Oleic Acid (18:1)

Polyunsaturated FAs:
Linoleic Acid (18:2) &
α-Linolenic Acid (18:3)

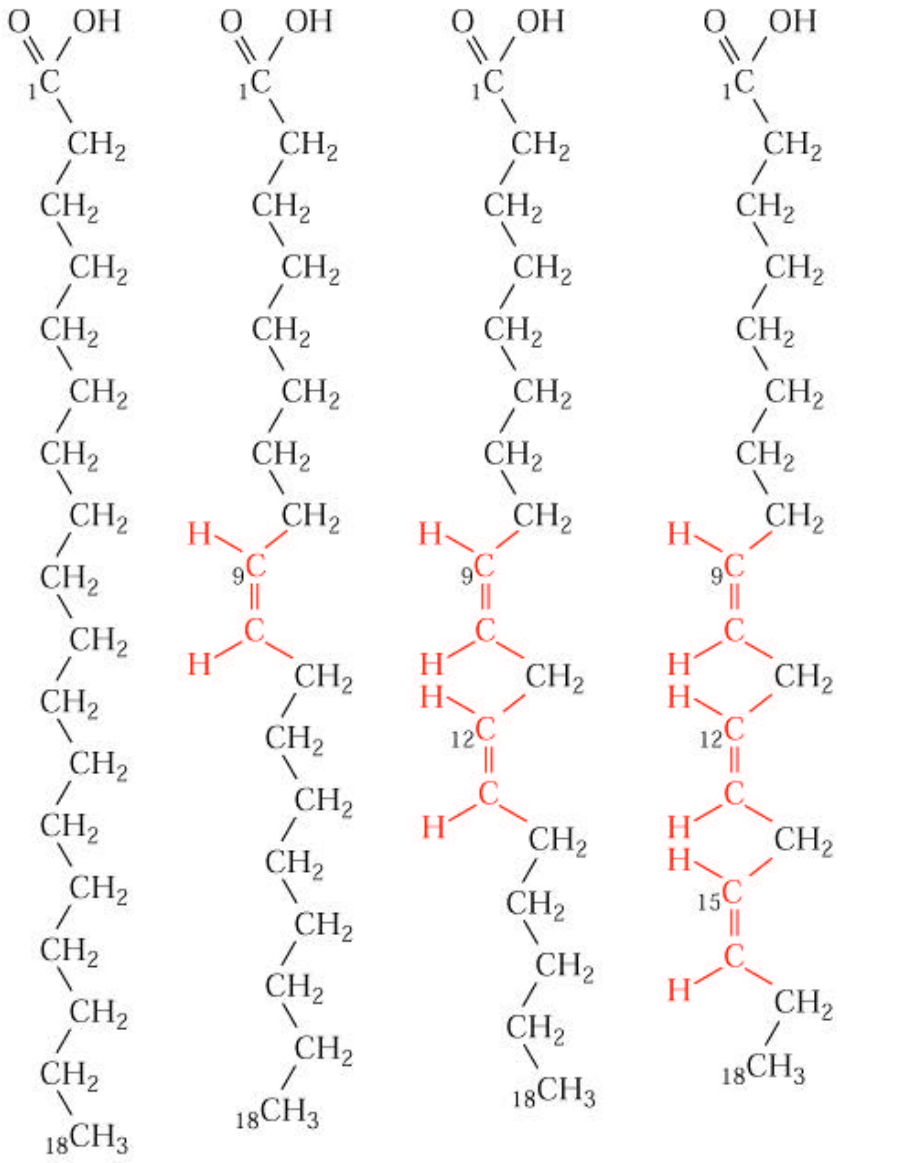


Figure 9-1. The structural formulas of some C_{18} fatty acids.

The first double bond in an <u>unsaturated</u> FA *usually* occurs between C(9) and C(10) counting from the carboxyl C atom (the -COOH at the end of the molecule).

Example of **<u>monoun</u>saturated FA**: **Oleic acid 18:1(9)**

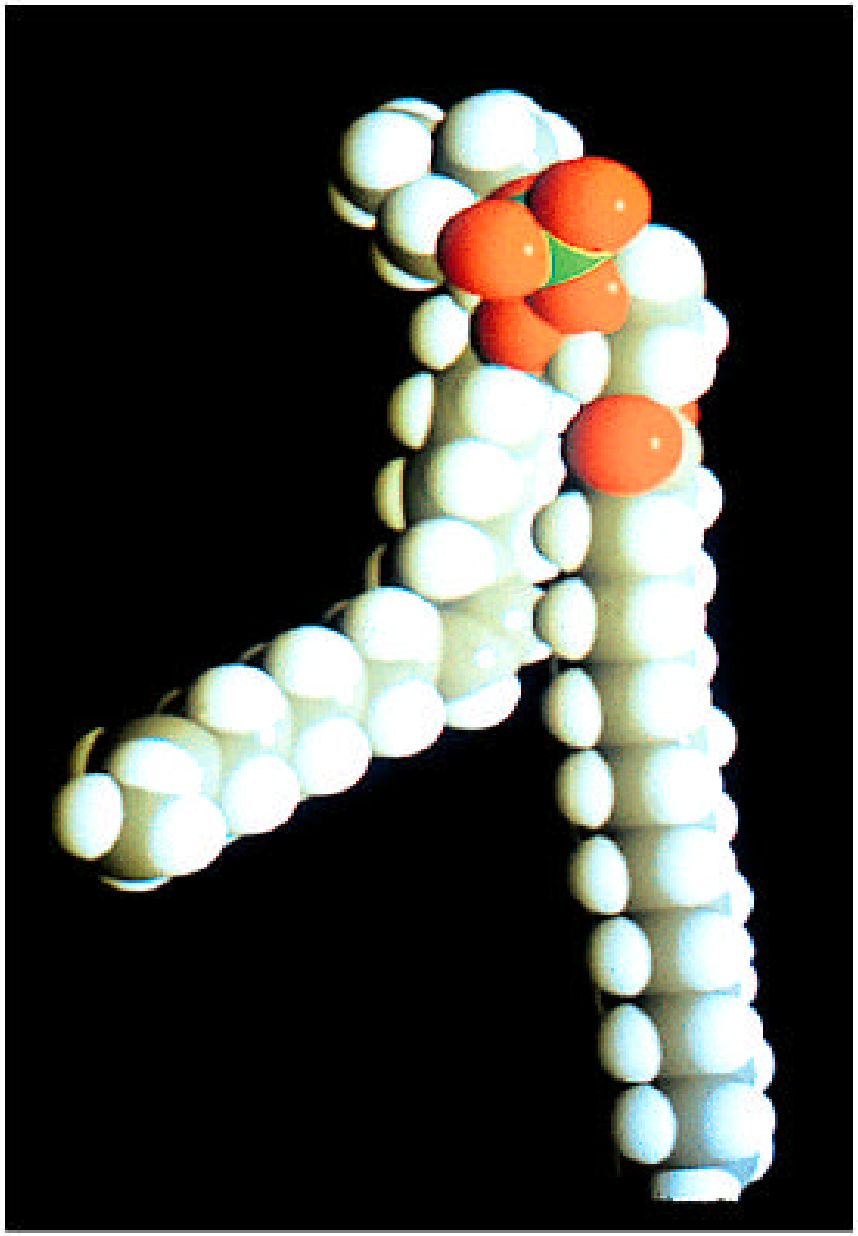
Oleic acid is the most common unsaturated FA

(the number in parentheses indicates that the double bond is between carbons 9 & 10)

$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$

Double bonds are almost all in the <u>*cis*</u> conformation (in FAs made by plants and animals)

Oleic acid
18:1(9) →



Courtesy of Richard Pastor, FCIA, Bethesda, Maryland.

As shown in Fig. 9.4, this *cis* bond causes a "kink" or bend in the FA chain. Because of these kinks, unsaturated FAs are unable to pack as closely together as can saturated FAs. (They are prevented from packing due to van der Waals radii.) This produces flexible, fluid membranes and aggregates.

← **Stearic acid**
18:0

Polyunsaturated fatty acids contain 2 or more double bonds. They usually occur at every third carbon atom towards the methyl terminus (-CH_3) of the molecule.

Example of polyunsaturated FA:

Linoleic acid **18:2(9,12)**

$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$

Table 9-1:

Table 9-1. The Common Biological Fatty Acids

Symbol[a]	Common Name	Systematic Name	Structure	mp (°C)
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
24:1	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

[a]Number of carbon atoms: Number of double bonds.

Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), Chapter 8, Clarendon Press (1986).

Saturated FAs are **highly flexible** molecules that can assume a **wide range of conformations** because there is relatively **free rotation about their C-C bonds**. Yet, their fully extended conformation is that of minimum energy because it has the least steric interference with neighboring methylene groups. Thus, saturated FAs can pack closely together to form ordered, rigid arrays under certain conditions (think of unbroken french fries packed tightly in a box---an appropriate analogy!) [Illustration in class with blue rods.] Saturated FAs pack tightly to form a **solid at room temperature**, such as butter.

The *cis* double bonds of unsaturated FAs put a rigid 30° bend in the hydrocarbon chain of unsaturated fatty acids that interferes with packing in space. This causes reduced **van der Waals interactions** which cause melting points to decrease –» lipid fluidity — like vegetable oil (and don't "clog your arteries")

Examples of melting points of fatty acids with the same number of carbon atoms, but different numbers of double bonds:

Formula	Name	Melting point (°C)
18:0	**Stearic acid**	**69.6**
18:1	**Oleic acid**	**13.4**
18:2	**Linoleic acid**	**-9.0**
18:3	**γ-Linolenic acid**	**-17.0**

 # carbon atoms

 # double bonds

NOTE: The lower the amount of saturation, the lower the melting point.

Table 9-1:

Note that the melting point also **increases** with increasing hydrocarbon **chain length.**

***Table 9-1.* The Common Biological Fatty Acids**

Symbol[a]	*Common Name*	*Systematic Name*	*Structure*	*mp (°C)*
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
24:1	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

[a]Number of carbon atoms: Number of double bonds.

Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), Chapter 8, Clarendon Press (1986).

FATS and **OILS** are both complex mixtures of triacylglycerols — they differ in that **fats are solid** and **oils are liquid** at room temperature (by definition).

Plant oils are usually richer in unsaturated fatty acids than are animal fats.

Melting point: Think about it!! It is intuitive. Think of butter ***vs*** vegetable oil at room temperature.

"Animal" fat usually means "cow fat" in the Western diet. The main "red meat" we eat is from ruminants (cows, sheep, deer, goats — all of which are foregut fermenters) and pigs (which is not a foregut-fermenter).

Is pork *really* "the other white meat"? Maybe.....foregut fermenters get many strange trans and single C-C bonded FAs from the bacteria in their foregut, so fat from them may be especially bad for us. ("You are what you eat" regarding FAs! Cows digest bacteria, we digest cows. FAs of the cow get incorporated into FA-containing compounds in our bodies.)

ESSENTIAL FATTY ACIDS (EFAs)

Polyunsaturated FAs,such as Linoleic acid and γ(gamma)-Linolenic acid, are ESSENTIAL FATTY ACIDS — we mammals cannot make them, and we need them, so we must get them in our diets (mostly from plant sources, many of which are rich in them). Arachidonic Acid — a very important C(20) compound that we will discuss — is not found in plants, and can only be synthesized by mammals from linoleic acid. One of the functions of the essential FAs is as precursors for the synthesis of eicosanoids (C20 compounds), such as prostaglandins, which are intracellular hormone-like substances (are usually made and used locally within cells, not transported in the bloodstream to other cells for action).

Essential Fatty Acids
(→)

Table 9-1. The Common Biological Fatty Acids

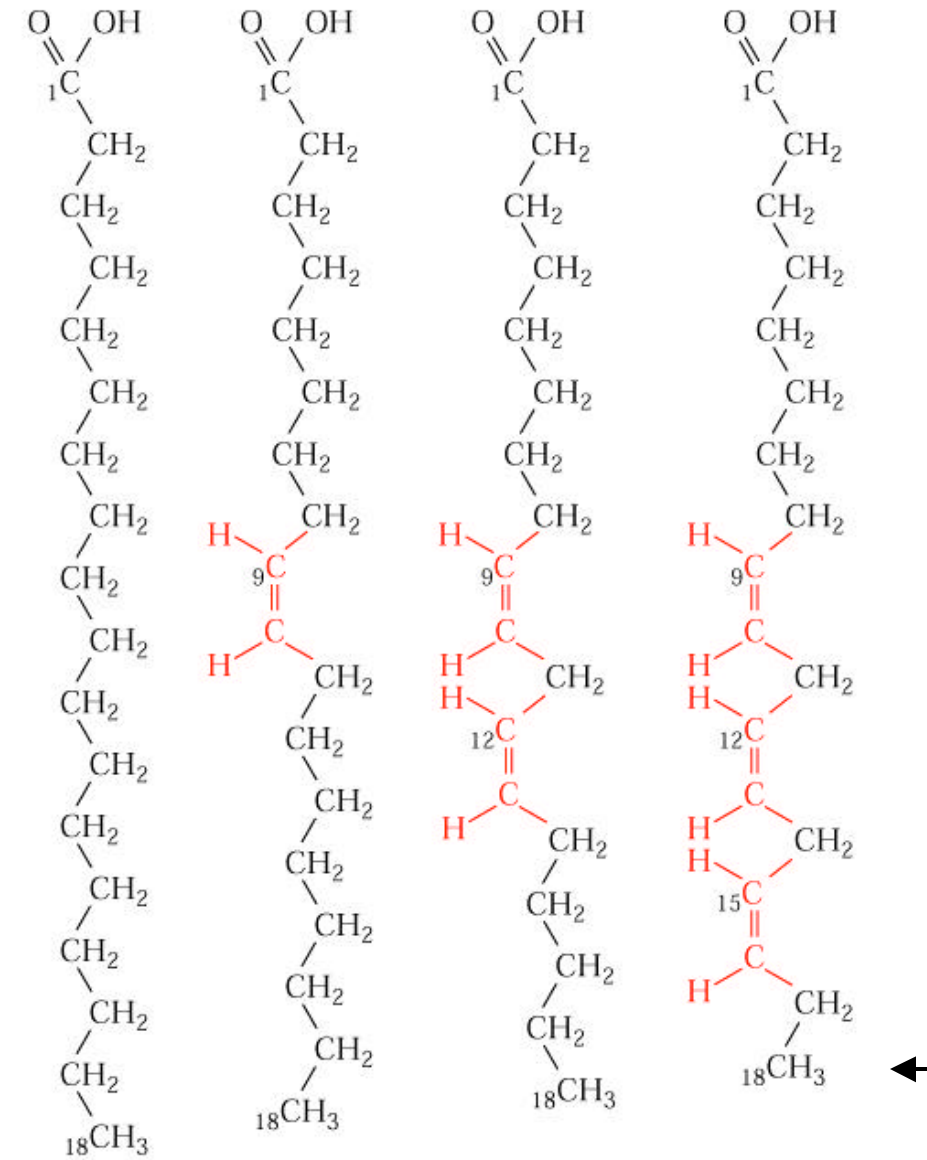
Symbol[a]	Common Name	Systematic Name	Structure	mp (°C)
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
24:1	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

[a]Number of carbon atoms: Number of double bonds.

Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), Chapter 8, Clarendon Press (1986).

"Essential Fatty Acids"

- eiscosanoid (C_{20}) precursors
- animals cannot synthesize EFAs, so must be supplied in diet
- are precursors for prostaglandins, thromboxanes, and leukotrienes, which are involved in intracellular communication



ω carbon

Figure 9-1. The structural formulas of some C_{18} fatty acids.

Linoleic acid 18:2 (9,12)

γ-linolenic acid, 18:3(6,9,12) = "GLA"

"Omega-6" – "ω-6" means the double bond is 6C from the terminal (or "ω") C.

α-Linolenic acid, 18:3(9,12,15)

Eicosapentaenoic acid ("EPA"), 20:5(5,8,11,14,17)

"Omega-3"

– found in marine animals, MP = -54°C!!!

	Omega-6	**Omega-3**
trans FA saturated → ↓ Alcohol cholesterol.	γ–linolenic GLA ↓ ↓ Arachidonic acid ↓ PGE_2	α-linolenic acid ↓ ↓ EPA ↓ PGE_3

We must get EFAs in our diets for good health. They are precursors for molecules such as:

- prostacyclins |
- prostaglandins | all C_{20} compounds (eicosanoids)
- thromboxanes |
- leukotrienes |

- These act at site they are made (intracellular) & are <u>not</u> transported in blood
- Are <u>like hormones</u>, in that...
    1) many effects mediated intracellularly by cAMP and
    2) they have profound physiological effects at <u>low concentrations</u>.
- They mediate (& regulate):
    1) Inflammatory response (joints, skin, eyes)
    2) Pain & fever
    3) Blood pressure regulation
    4) Blood clotting induction
    5) Many reproductive functions (***e.g.,*** labor induction) & menstrual cramps
    6) Sleep/wake cycle

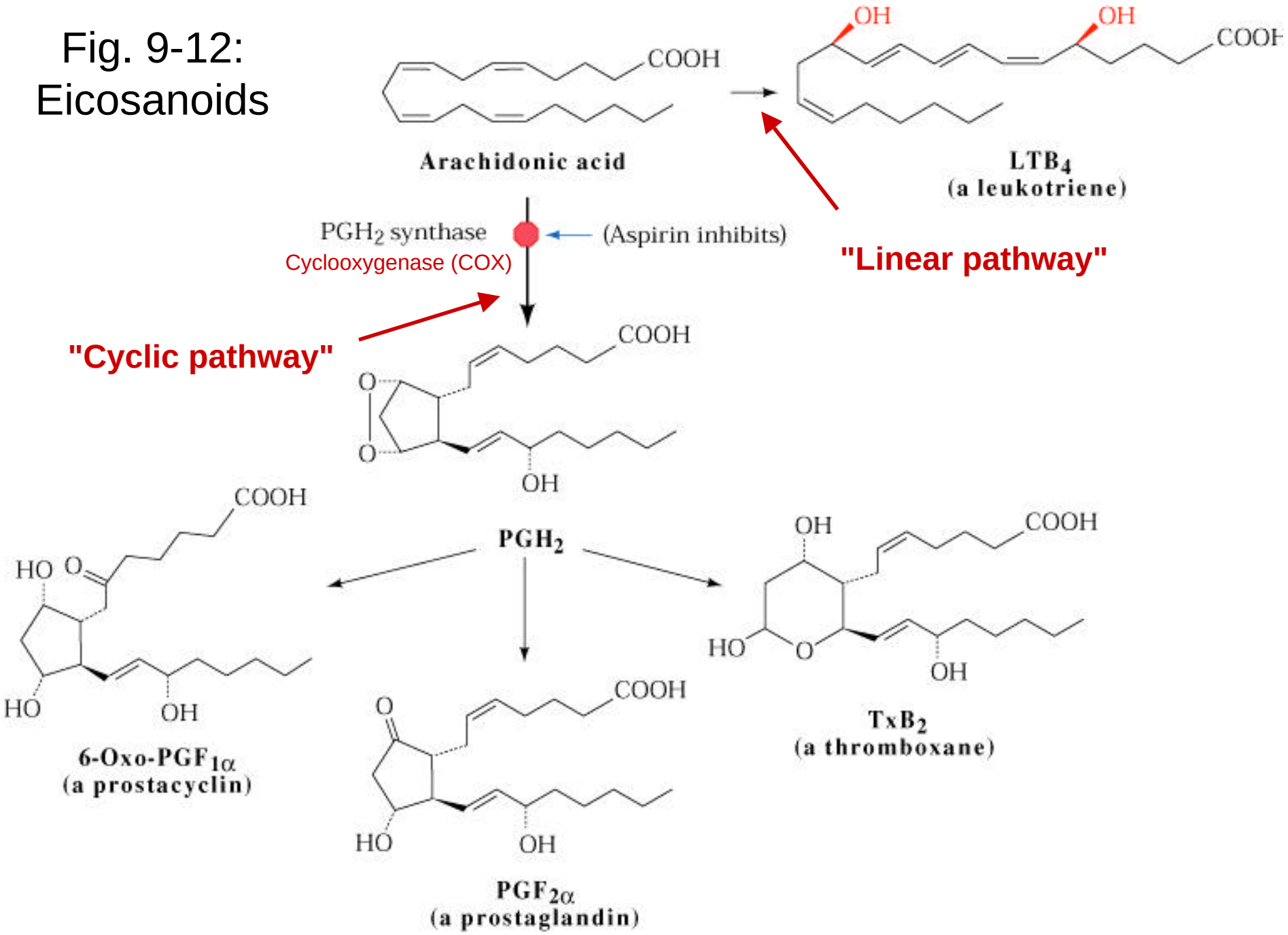
The enzymes that synthesize these C(20) compounds are major drug targets (lots of research going on right now in pharmaceutical companies).

Aspirin — discovered *many* years before we learned how it works.

- **"nonsteroidal anti-inflammatory drugs" (NSAIDs)** (aspirin, ibuprofen, acetaminophen)

- inhibit the synthesis of prostaglandins from **arachidonic acid**:

Fig. 9-12: Eicosanoids



Aspirin (acetylsalicylic acid) acetylates the enzyme. Low dose of aspirin (~1/2 per day) reported to reduce heart attacks & strokes. ***How?*** Aspirin inhibits platelet (blood cell) aggregation & thus blood clots do not form as well. Platelets lack nuclei (like all mammalian RBCs), and therefore these cells cannot resynthesize their inactivated enzymes.

Linear pathway → leukotrienes (WBCs, lung, spleen, brain & heart).

Peptidoleukotrienes are components of slow-acting substances of anaphylaxis (violent/fatal? allergic reaction)

- ~ 10,000x more potent than histamine (stimulates allergic reactions)
- constrict the bronchi & increase mucus secretion
  → are mediators of asthma

A take-home message from this: FA-wise, "you are what you eat"!

What we eat has far-reaching effects on our health. Although they are highly involved in obesity and heart disease (as we will discuss next time), they have more far reaching effect in general health. While it is true that all fats (butter *vs* margarine *vs* oils) have the same # of calories per unit weight, not all fats in our diets have the same effects regarding health and weight loss.
Saturated fats (animal fats and butter) are worse for your health than mono- and polyunsaturated fats, both from the standpoint of weight loss and heart disease, but also because they are very low in C(20) precursors, which are needed for all sorts of health reasons.

Cholesterol:

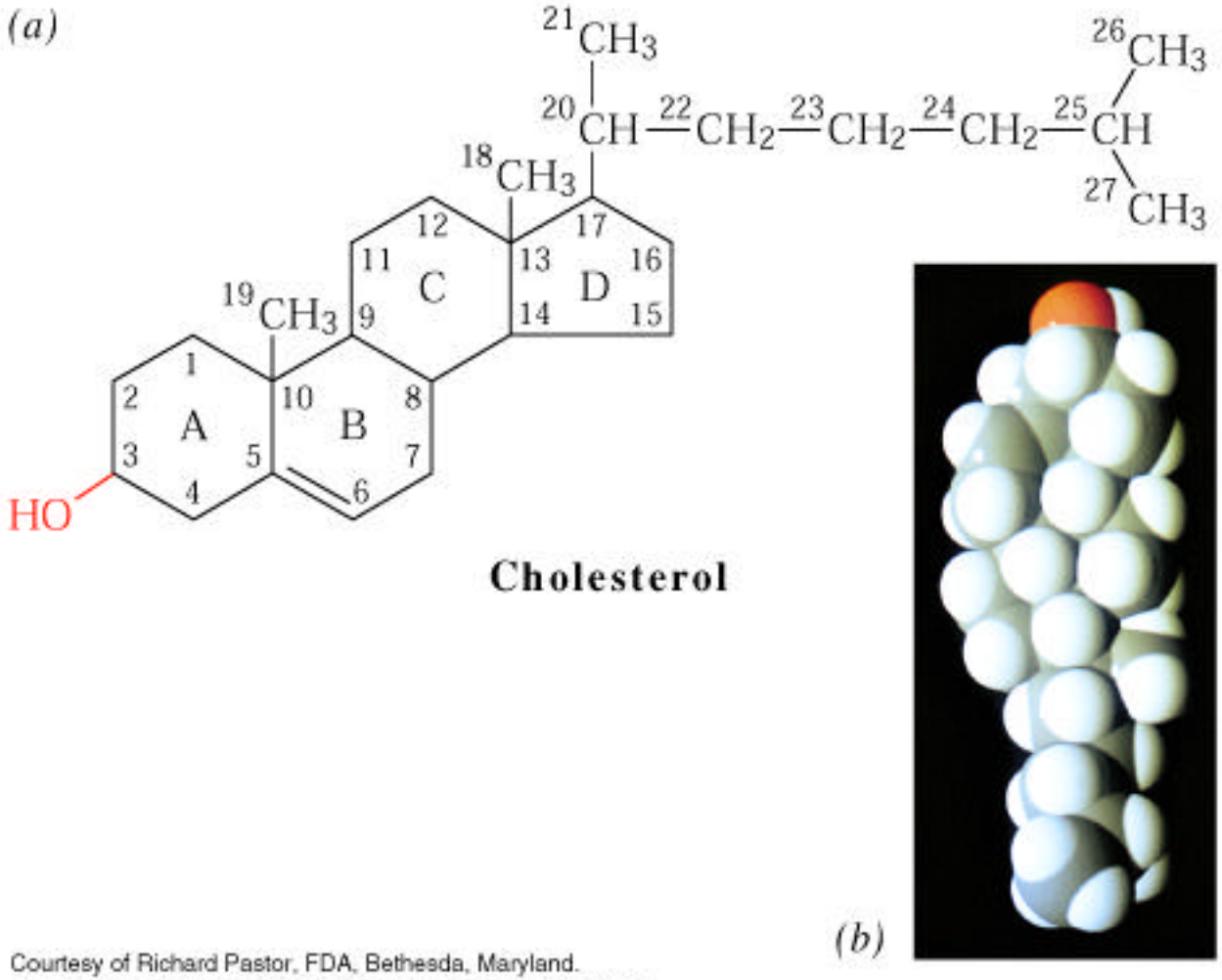
Many important steroids are derived from cholesterol in animals, including...

- several **HORMONES** (including androgens, estrogens, progestins, glucocorticoids, and mineralocorticoids)

and

- **BILE ACIDS (**which are detergent molecules secreted in bile from the gallbladder that assist in the absorption of dietary lipids in the intestine).

Fig. 9.10



Next:

Lipoproteins (Ch. 10 review?)

and Fattty Acid Catabolism (Ch. 19)