10 Lipids

P1 Principle 1 (1 of 4)

Fatty acids are water-insoluble hydrocarbons used for cellular energy storage. Fatty acids are highly reduced and thus provide a rich source of stored chemical energy for cells. Storage of hydrophobic fats as triacylglycerols is also highly efficient because water is not needed to hydrate the stored fats.

P2 Principle 2 (1 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

P3 Principle 3 (1 of 7)

Lipids have uses in the cell beyond energy storage and membranes construction. Many lipids are present in the cell at smaller amounts than those making up membranes or being stored as fat. These lipids can function as cellular messengers, hormones, electron carriers, or pigments.

P4 Principle 4 (1 of 6)

The chemical properties of lipids are related to their structure and composition. As in studies of other biomolecules, methods such as enzymatic, chromatographic, and mass spectrometry can all be used to identify lipids and determine their atomic structure.

10.1 Storage Lipids

P1 Principle 1 (2 of 4)

Fatty acids are water-insoluble hydrocarbons used for cellular energy storage. Fatty acids are highly reduced and thus provide a rich source of stored chemical energy for cells. Storage of hydrophobic fats as triacylglycerols is also highly efficient because water is not needed to hydrate the stored fats.

Fats and Oils Used as Stored Energy Are Derivatives of Fatty Acids

- **fatty acids** = hydrocarbon derivatives
- oxidation of fatty acids (to CO_2 and H_2O) is highly exergonic

Fatty Acids Are Hydrocarbon Derivatives

- fatty acids = carboxylic acids with hydrocarbon tails ranging from 4 to 36 carbons long (C_4 to C_{36})
  - can be saturated or unsaturated
  - can be branched or unbranched

Naturally Occurring Fatty Acids

TABLE 10-1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

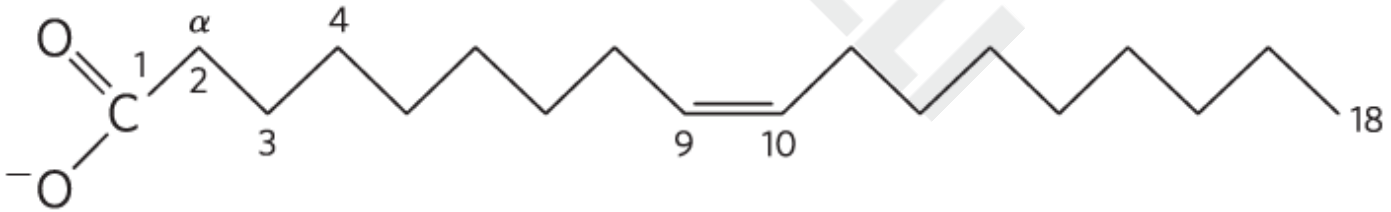
Carbon skeleton	Structure[a]	Systematic name[b]	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma* "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(^{9})	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1 to –0.5		
18:1(^{9})	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2(^{9,12})	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	–5		
18:3(^{9,12,15})	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	–11		
20:4(^{5,8,11,14})	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	–49.5		

[a] All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

[b] The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanic" specifies the linear unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Nomenclature for Unbranched Fatty Acids

- the chain length and number of bonds, separated by a colon
- numbering begins at the carboxyl carbon
- positions of double bonds are indicated by Δ and a superscript number



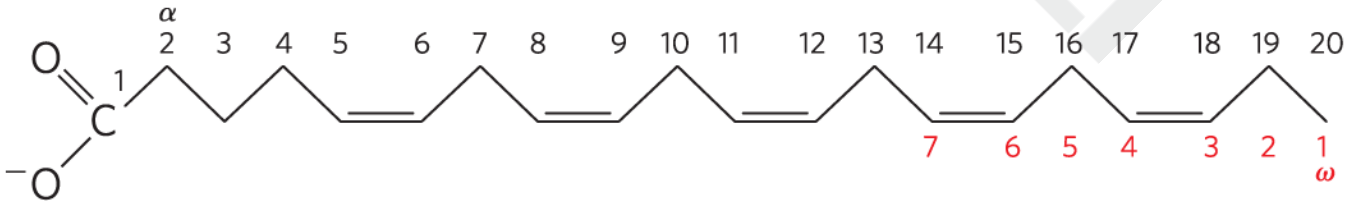
18:1(Δ^9) *cis*-9-Octadecenoic acid

Common Patterns in Fatty Acids

- most common fatty acids have even numbers of carbon atoms in an unbranched chain of 12 to 24 carbons
- in monounsaturated fatty acids, the double bond is usually between C-9 and C-10 (Δ^9)
- in polyunsaturated fatty acids:
  - the double bonds are usually Δ^{12} and Δ^{15}
  - double bonds are usually separated by a methylene group
- double bonds are usually in the cis configuration

Polyunsaturated Fatty Acids (PUFAs)

- **polyunsaturated fatty acids (PUFAs)** = contain more than one double bond in their backbone
  - **omega-3 (*ω*-3) fatty acids** = double bond between C-3 and C-4 relative to the most distant carbon (*ω*)
  - **omega-6 (*ω*-6) fatty acids** = double bond between C-6 and C-7 relative to *ω*



20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA)

omega-3 (ω-3) fatty acid

PUFAs and Human Nutrition

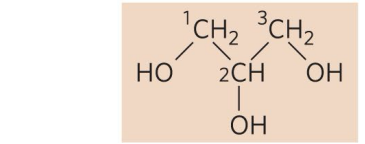
- humans must obtain the omega-3 PUFA α-linolenic acid (ALA; 18:3($\Delta^{9,12,15}$)) from their diet

- humans use ALA to synthesize:
  - eicosapentaenoic acid (EPA; 20:5($\Delta^{5,8,11,14,17}$))
  - docosahexaenoic acid (DHA; 22:6($\Delta^{4,7,10,13,16,19}$))

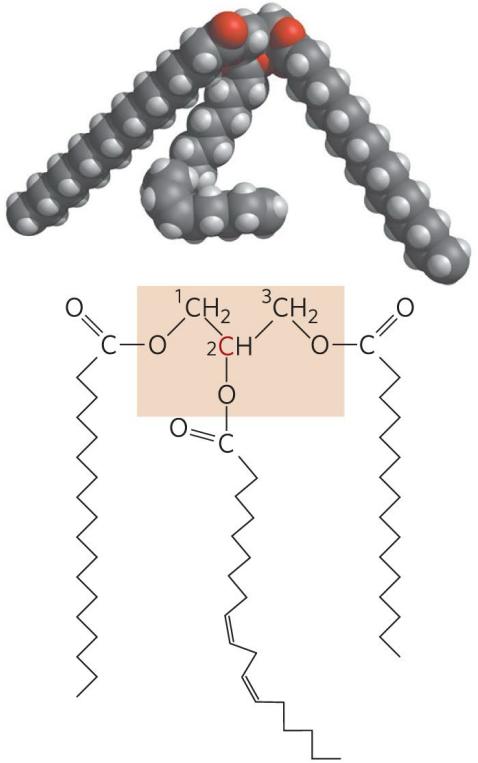
- the optimal dietary ratio of omega-6 to omega-3 PUFAs is between 1:1 and 4:1

Triacylglycerols Are Fatty Acid Esters of Glycerol

- **triacylglycerols** = simplest lipids constructed from fatty acids
  - composed of three fatty acids, each in ester linkage with a single glycerol
  - can be simple (one kind of fatty acid) or mixed (two or three different fatty acids)
  - non-polar, hydrophobic



Glycerol


1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

P1 Principle 1 (3 of 4)

Fatty acids are water-insoluble hydrocarbons used for cellular energy storage. Fatty acids are highly reduced and thus provide a rich source of stored chemical energy for cells. Storage of hydrophobic fats as triacylglycerols is also highly efficient because water is not needed to hydrate the stored fats.

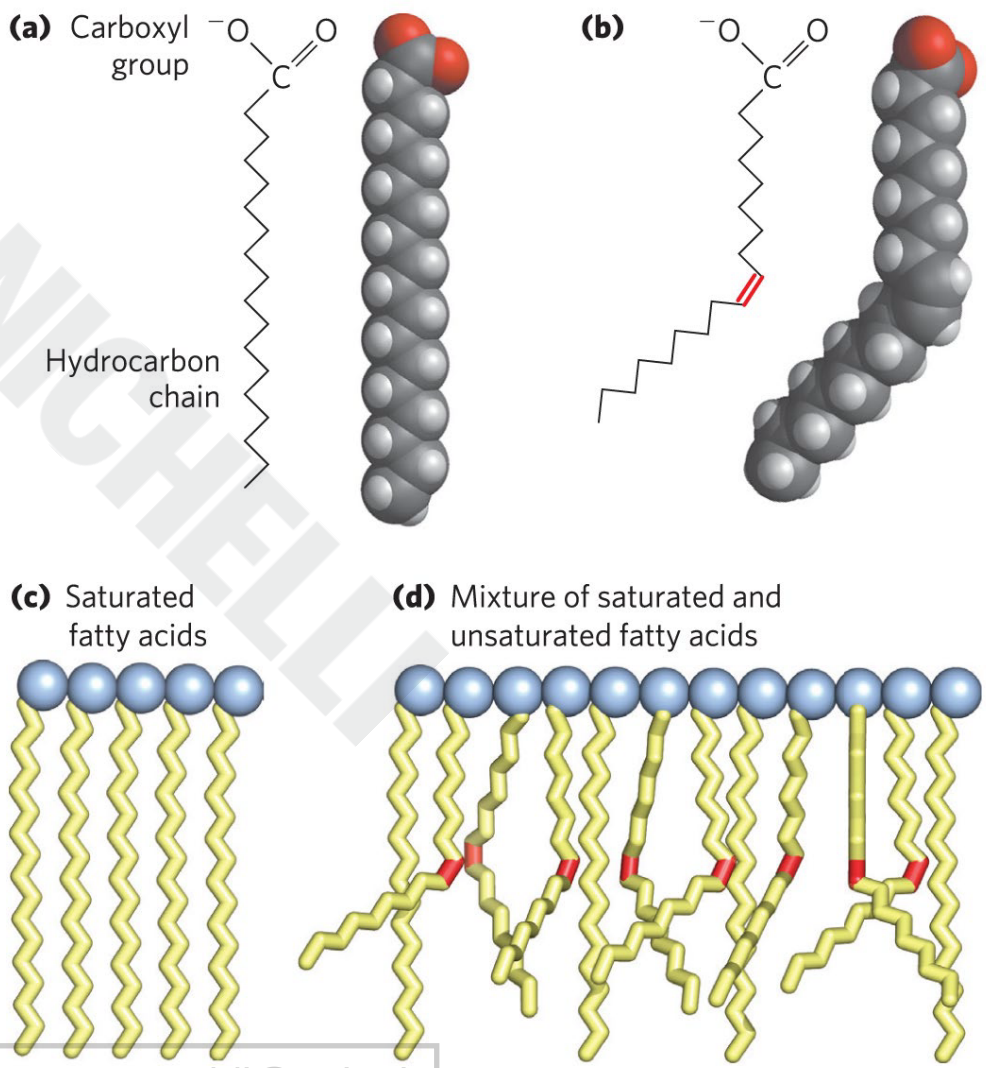
Solubility of Fatty Acids

- poor solubility in water due to the nonpolar hydrocarbon chain
  - increased chain length decreases solubility
  - decreased double bond number decreases solubility

- carboxylic acid group is polar and ionized at neutral pH

Melting Points of Fatty Acids

- at room temperature:
  - saturated fatty acids have a waxy consistency
  - unsaturated fatty acids are oily liquids
- extent of packing depends on degree of saturation



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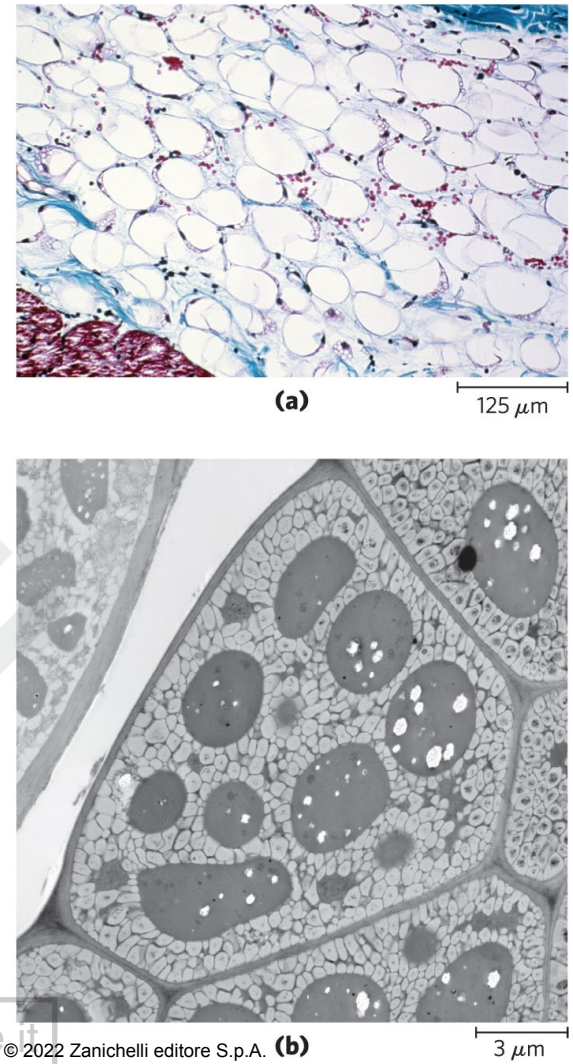
Triacylglycerols Provide Stored Energy and Insulation

- vertebrates store triacylglycerols as lipid droplets in adipocytes (fat cells)
- plants store triacylglycerols in the seeds



[(a) Biophoto Associates/Science Source. (b) Courtesy Howard Goodman, Department of Genetics, Harvard Medical School.

Lipases

- **lipases** = enzymes that catalyze the hydrolysis of stored triacylglycerols, releasing fatty acids for export to sites where they are required as fuel
  - adipocytes and germinating seeds contain lipases

P1 Principle 1 (4 of 4)

Fatty acids are water-insoluble hydrocarbons used for cellular energy storage. Fatty acids are highly reduced and thus provide a rich source of stored chemical energy for cells. Storage of hydrophobic fats as triacylglycerols is also highly efficient because water is not needed to hydrate the stored fats.

Advantages to Using Triacylglycerols as Stored Fuels

- two significant advantages:
  - because carbon atoms of fatty acids are more reduced than those of sugars, oxidation of fatty acids yields more energy
  - because triacylglycerols are hydrophobic and unhydrated, the organism does not have to carry the extra weight of water hydration that is associated with stored polysaccharides

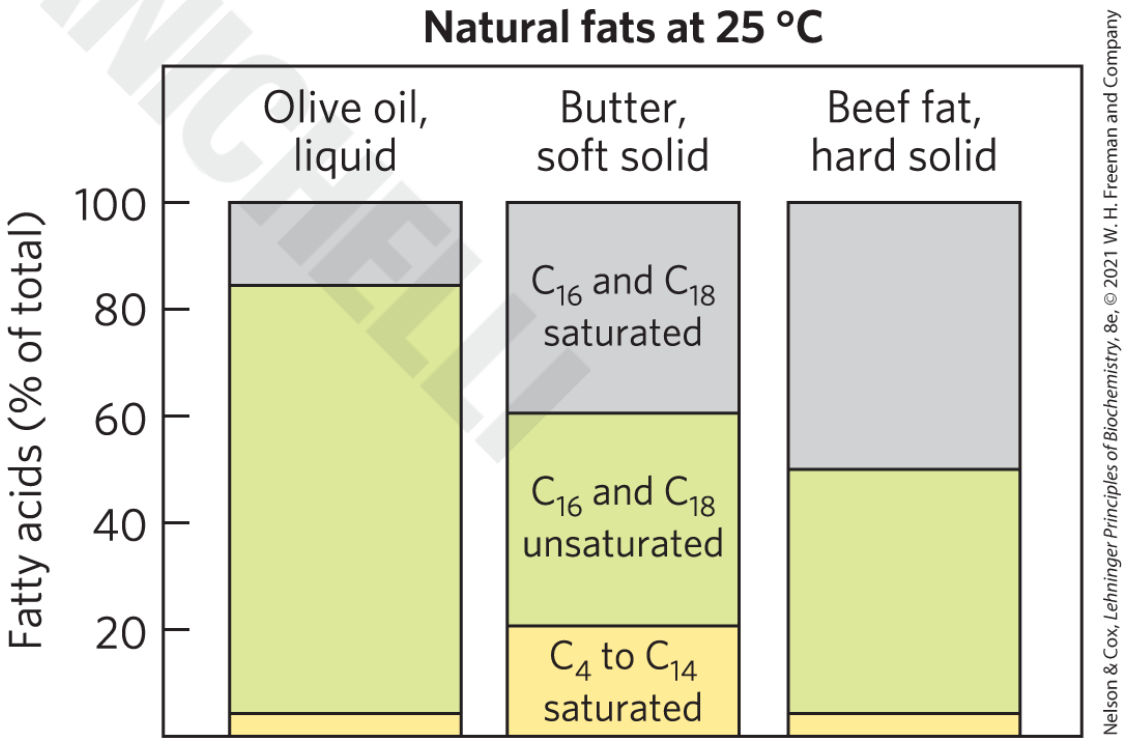
Triacylglycerols Provide Insulation

- seals, walruses, penguins, and other warm-blooded polar animals are amply padded with triacylglycerols
  - provides insulation against low temperatures

- hibernating animals (e.g. bears) accumulate huge fat reserves before hibernation
  - provides insulation and energy storage

Partial Hydrogenation of Cooking Oils Improves Their Stability but Creates Fatty Acids with Harmful Health Effects

- natural fats are complex mixtures of simple and mixed triacylglycerols



Partial Hydrogenation

- oxidative cleavage of double bonds in unsaturated fatty acids to aldehydes and carboxylic acids causes lipid-rich food to become rancid

- partial hydrogenation = process that converts many of the cis double bonds in the fatty acids to single bonds
  - improves shelf life and increases stability
  - increases the melting temperature
  - converts some cis double bonds to trans double bonds

Trans Fatty Acids ("Trans Fats")

- dietary intake of trans fatty acids is linked to a higher incidence of cardiovascular disease

- trans fatty acids:
  - raise the level of triacylglycerols in the blood
  - raise the level of LDL ("bad") cholesterol in the blood
  - lower the level of HDL ("good") cholesterol
  - increase the body's inflammatory response

10.2 Structural Lipids in Membranes

P2 Principle 2 (2 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

Biological Membranes

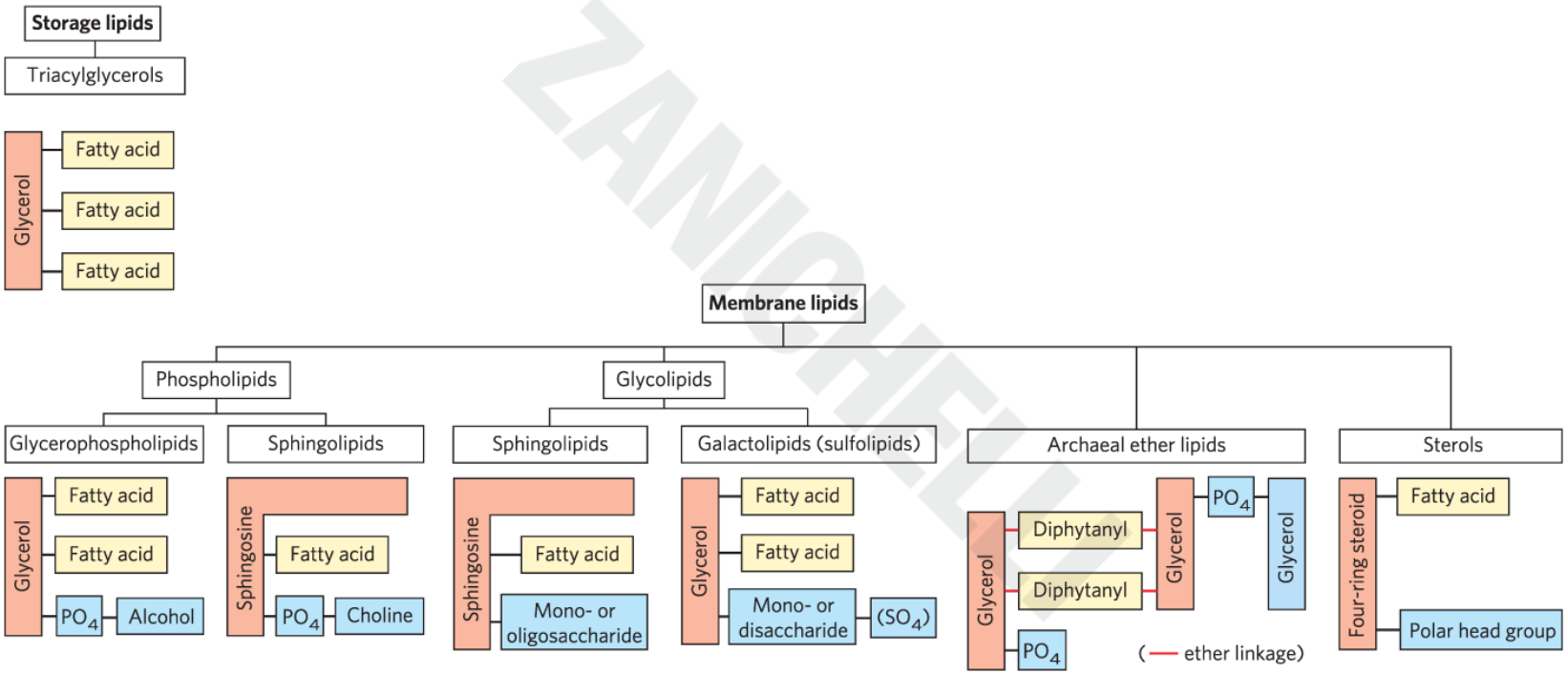
- biological membranes = double layer of lipids that acts as a barrier to polar molecules and ions

- membrane lipids:
  - amphipathic = one end of the molecule is hydrophobic, the other hydrophilic
  - hydrophobic regions associate with each other
  - hydrophilic regions associate with water

Four General Types of Membrane Lipids

- **phospholipids** = have hydrophobic regions composed of two fatty acids joined to glycerol or sphingosine
- **glycolipids** = contain a simple sugar or a complex oligosaccharide at the polar ends
- **archaeal tetraether lipids** = have two very long alkyl chains ether-linked to glycerol at both ends
- **sterols** = compounds characterized by a rigid system of four fused hydrocarbon rings

Some Common Types of Storage and Membrane Lipids



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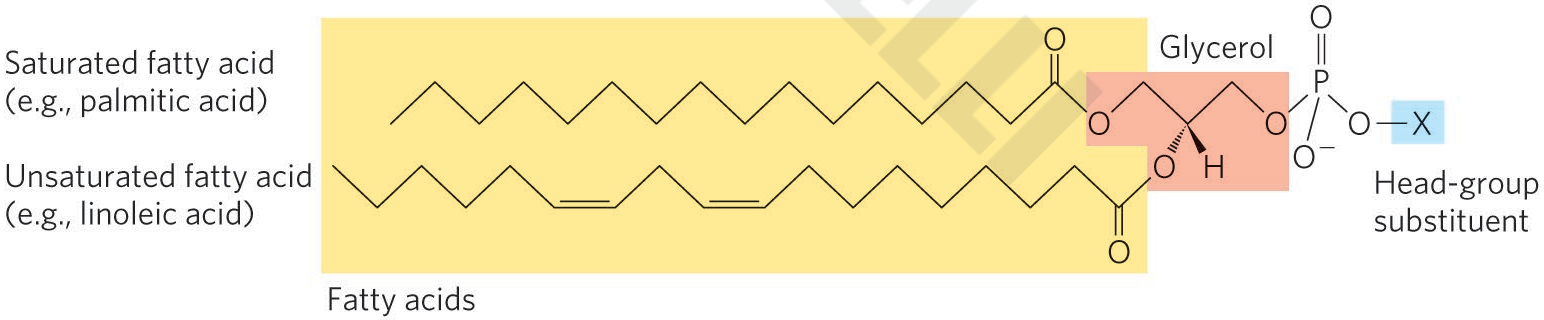
P2 Principle 2 (3 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

Glycerophospholipids Are Derivatives of Phosphatidic Acid

- **glycerophospholipids** (phosphoglycerides) = membrane lipids in which two fatty acids are attached in ester linkage to the first and second carbons of glycerol, and a highly polar or charged group is attached through a phosphodiester linkage to the third carbon



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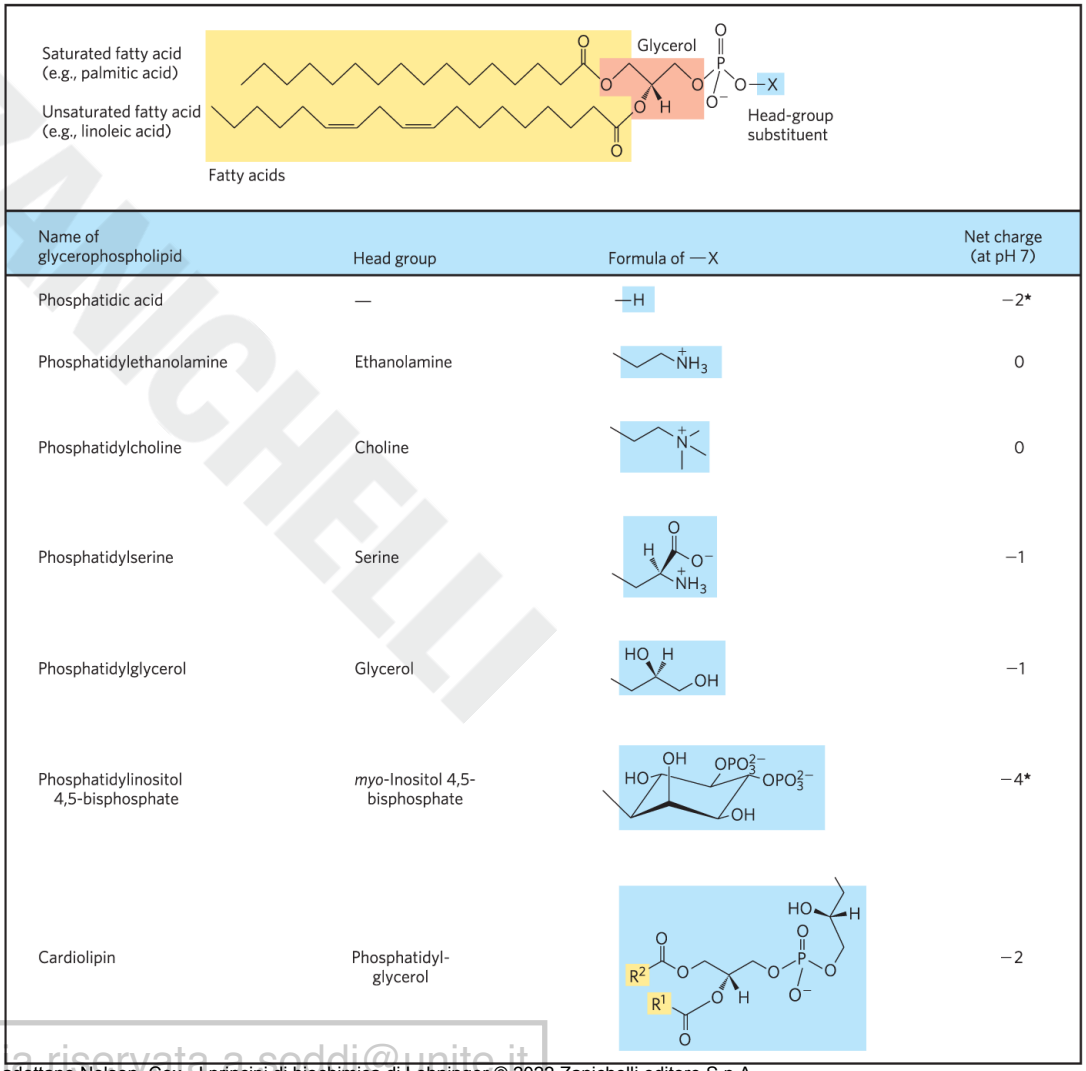
Glycerophospholipids Are Named as Derivatives of Phosphatidic Acid

- a phosphodiester bond joins the head group to glycerol
- the phosphate group can bear a negative, neutral, or positive charge



Name of glycerophospholipid	Head group	Formula of —X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−2*
Phosphatidylethanolamine	Ethanolamine		0
Phosphatidylcholine	Choline		0
Phosphatidylserine	Serine		−1
Phosphatidylglycerol	Glycerol		−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4*
Cardiolipin	Phosphatidyl-glycerol		−2

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The Fatty Acids in Glycerophospholipids

- can be any of a wide variety

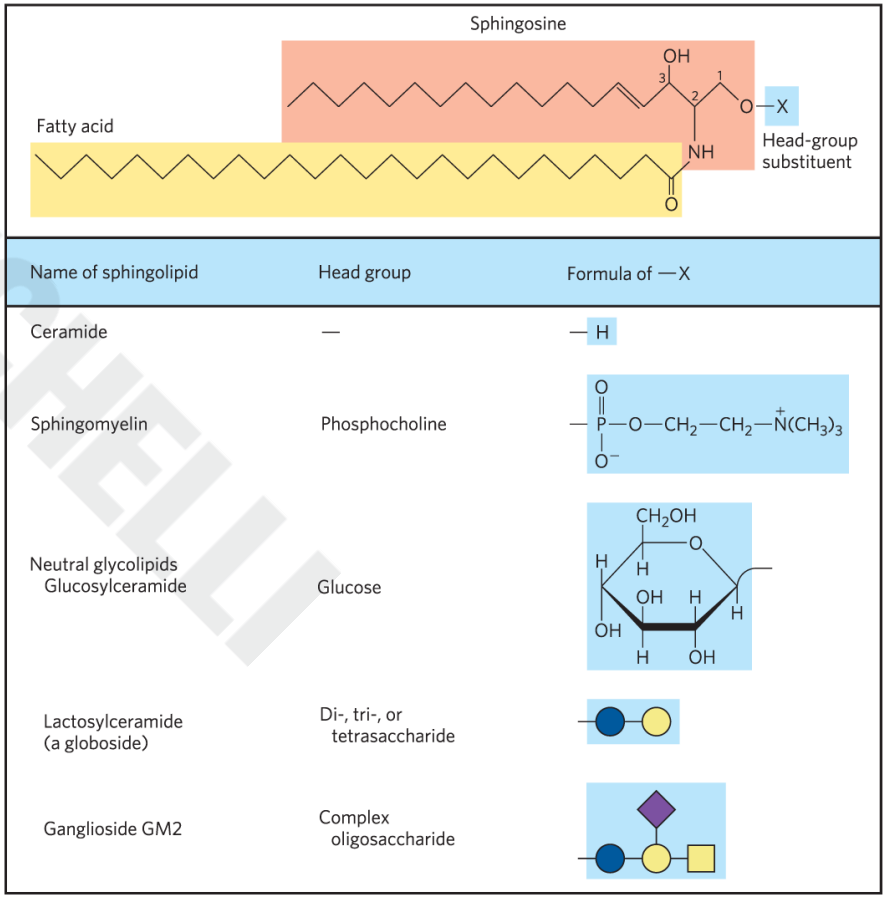
- in general, glycerophospholipids contain:
  - a C_{16} or C_{18} saturated fatty acid at C-1
  - a C_{18} or C_{20} unsaturated fatty acid at C-2

P2 Principle 2 (4 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

Sphingolipids Are Derivatives of Sphingosine

- **sphingolipids** = large class of membrane phospholipids and glycolipids
  - have a polar head group and two nonpolar tails
  - contain no glycerol
  - contain one molecule of the long-chain amino alcohol sphingosine or one of its derivatives



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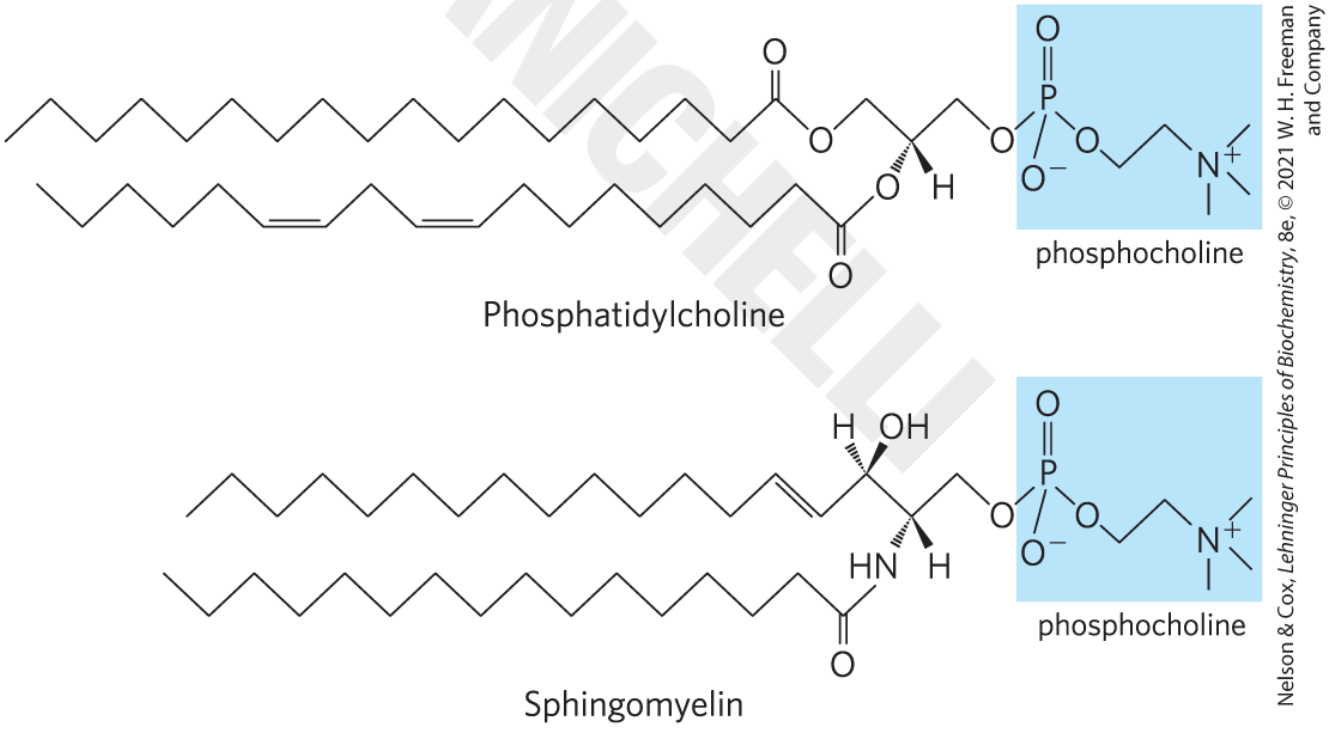
Ceramides Are The Structural Parent of All Sphingolipids

- C-1, C-2, and C-3 of sphingosine are structurally analogous of the three carbons of glycerol in glycerophospholipids

- **ceramide** = compound resulting when a fatty acid is attached in amide linkage to the $–NH_2$ on C-2
  - structurally similar to a diacylglycerol

Sphingomyelins

- **sphingomyelins** = subclass of sphingolipids that contains phosphocholine or phosphoethanolamine as their polar head group



Glycosphingolipids

- **glycosphingolipids** = have head groups with 1+ sugars connected directly to the –OH at C-1 of the ceramide moiety
  - do not contain phosphate
  - occur largely in the outer face of plasma membranes

Cerebrosides and Globosides

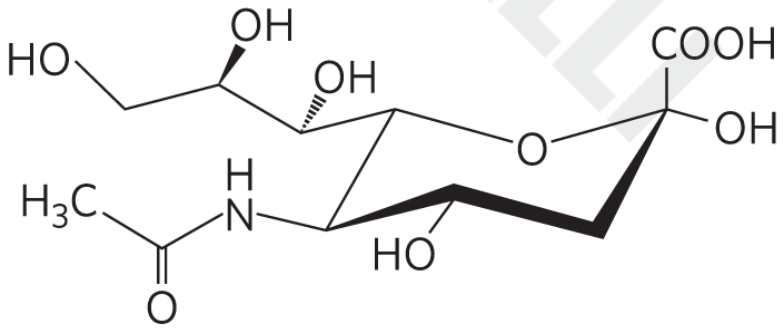
- **cerebrosides** = have a single sugar linked to ceramide
  - those with galactose are found in the plasma membranes of cells in neural tissue
  - those with glucose are found in the plasma membranes of cells in nonneural tissues

- **globosides** = glycosphingolipids with 2+ sugars, usually D-glucose, D-galactose, or *N*-acetyl-D-galactosamine

- sometimes called **neutral glycolipids**, as they have no charge at pH 7

Gangliosides

- **gangliosides** = have oligosaccharides as their polar head groups and 1+ residues of *N*-acetylneuraminic acid (Neu5Ac), a sialic acid, at the termini
  - 1 sialic acid residue = GM (*M* for mono-) series
  - 2 sialic acid residues = GD (*D* for di-) series
  - 3 sialic acid residues = GT (*T* for tri-) series (and so on)



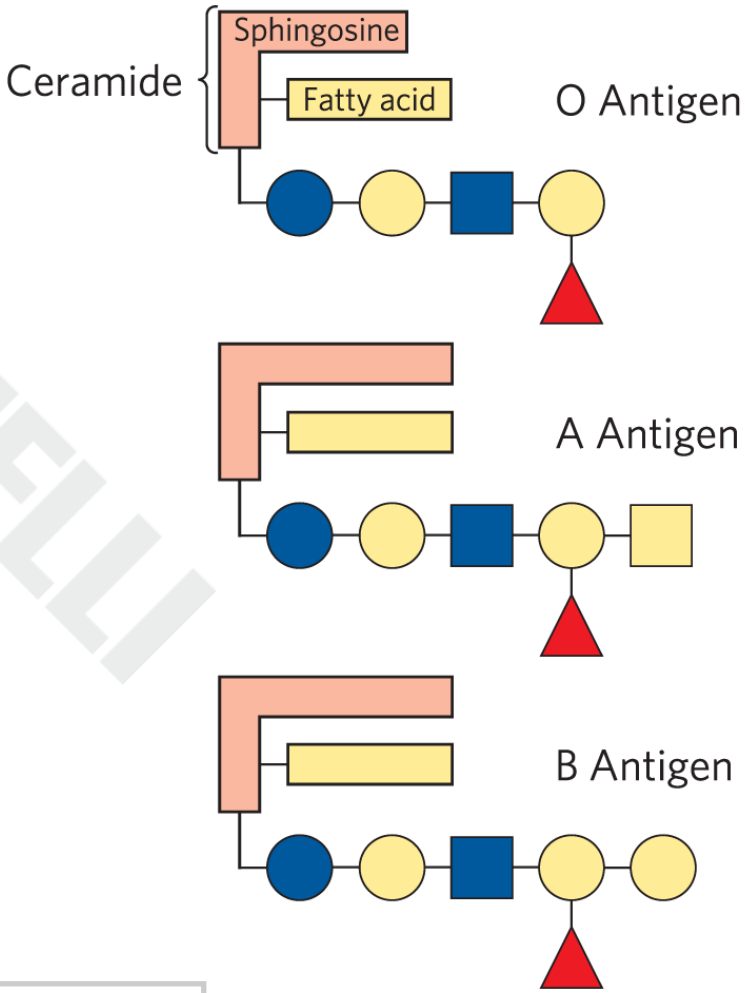
α-*N*-Acetylneuraminic acid (a sialic acid) (Neu5Ac)

P2 Principle 2 (5 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

Sphingolipids at Cell Surfaces Are Sites of Biological Recognition

- prominent in the plasma membranes of neurons
- human blood groups (O, A, B) are determined in part by the oligosaccharide head groups of these glycosphingolipids



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P2 Principle 2 (6 of 6)

Membrane lipids are composed of hydrophobic tails attached to polar head groups. Cellular membranes are composed of a variety of lipids, including glycerophospholipids and sterols. These lipids are used for structuring membranes as well as for displaying molecules on the membrane surfaces for signaling and molecular recognition.

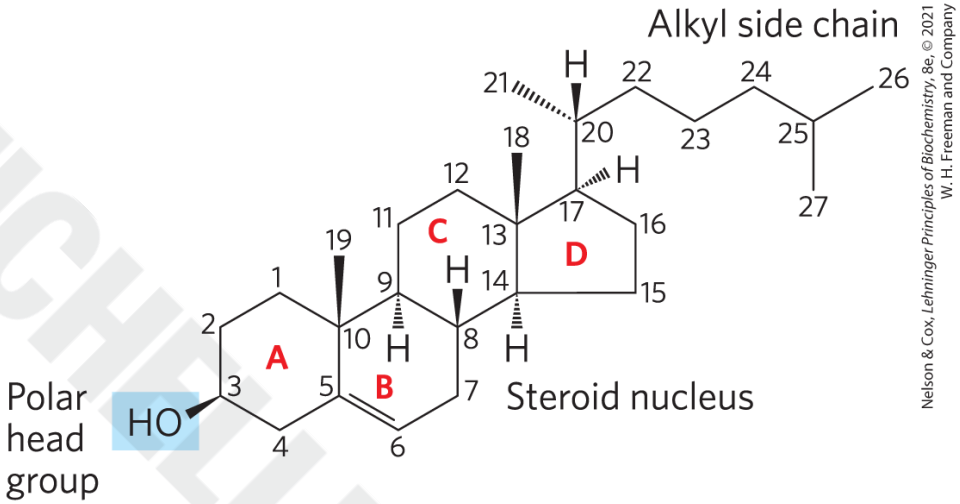
Sterols Have Four Fused Carbon Rings

- **sterols** = structural lipids present in the membranes of most eukaryotic cells

- steroid nucleus:
  - consists of four fused rings
  - almost planar
  - relatively rigid

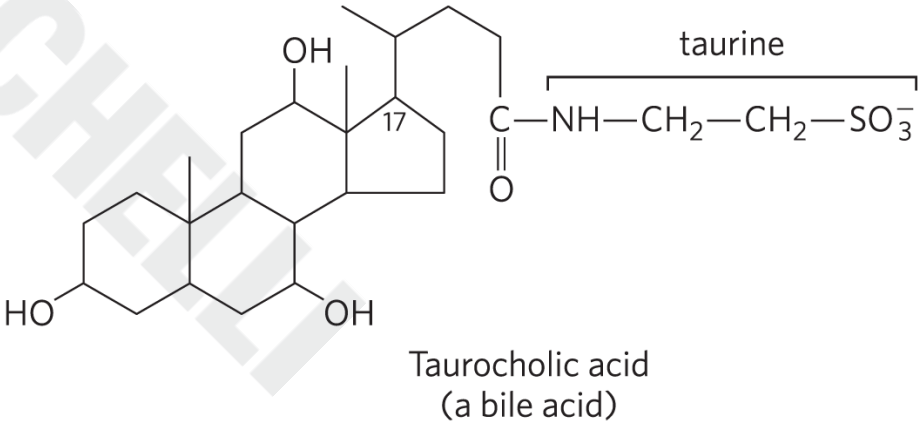
Cholesterol

- **cholesterol** = major sterol in animal tissues
  - amphipathic
  - polar head group
  - nonpolar hydrocarbon body
  - membrane constituents
  - similar to stigmasterol in plants and ergosterol in fungi



Sterols Serve as Precursors for Products with Specific Biological Activities

- steroid hormones regulate gene expression
- **bile acids** = polar derivatives of cholesterol that emulsify dietary fats in the intestine to make them more readily accessible to digestive lipases



Taurocholic acid
(a bile acid)

P3 Principle 3 (2 of 7)

Lipids have uses in the cell beyond energy storage and membranes construction. Many lipids are present in the cell at smaller amounts than those making up membranes or being stored as fat. These lipids can function as cellular messengers, hormones, electron carriers, or pigments.

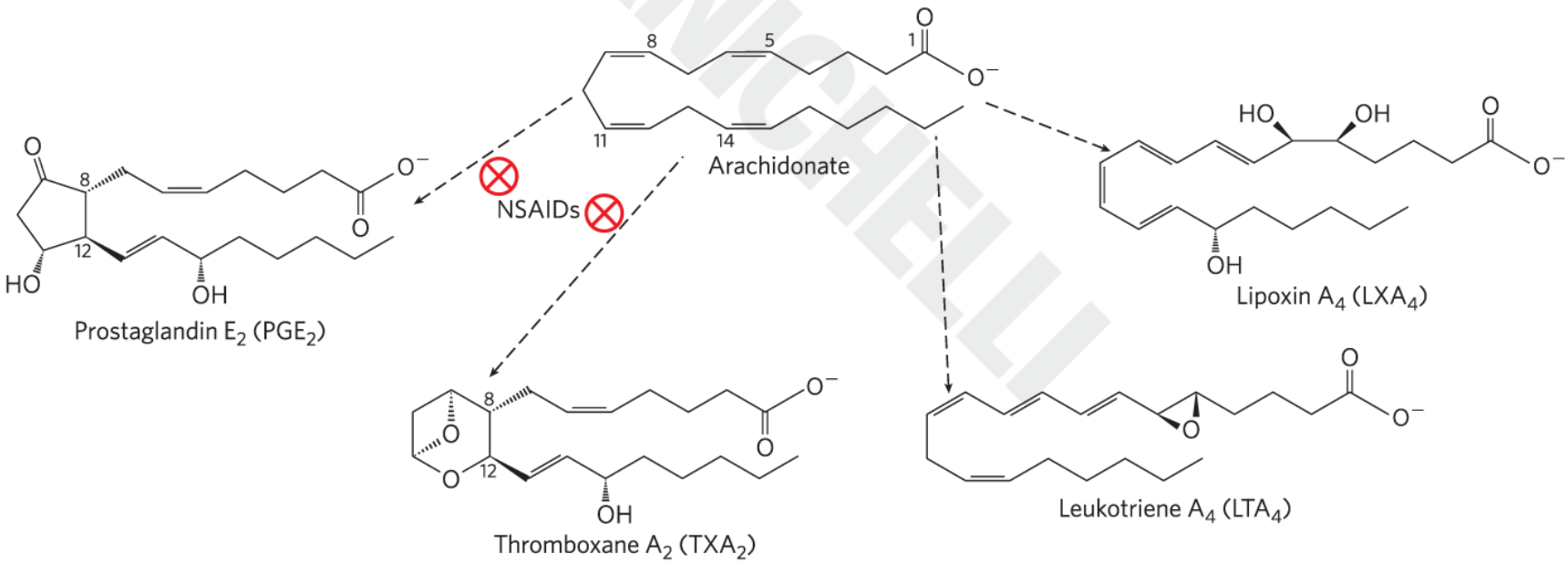
Eicosanoids Carry Messages to Nearby Cells

- **eicosanoids** = paracrine hormones, substances that act only on cells near the point of hormone synthesis instead of being transported in the blood

- involved in:
  - reproductive function
  - inflammation, fever, and pain associated with injury or disease
  - formation of blood clots
  - regulation of blood pressure
  - gastric acid secretion

Eicosanoids Are Derived From Arachidonic Acid

- four major classes of eicosanoids = prostaglandins, thromboxanes, leukotrienes, and lipoxins



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Prostaglandins (PG)

- **prostaglandins (PG)** = class of eicosanoids that contain a five-carbon ring

- array of functions:
  - stimulate contraction of the smooth muscle of the uterus
  - affect blood flow to specific organs, the wake-sleep cycle, and the responsiveness of certain tissues to hormones
  - elevate body temperature and cause inflammation and pain

Thromboxanes (TX)

- **thromboxanes (TX)** = class of eicosanoids that have a six-membered ring containing an ether
- produced by platelets (also called thrombocytes)
- act in the formation of blood clots and reduction of blood flow to the site of a clot

Leukotrienes (LT)

- **leukotrienes (LT)** = class of eicosanoids that contain three conjugated double bonds

- powerful biological signals
  - leukotriene D_4 induces contraction of the smooth muscle lining the airways to the lung

Lipoxins (LX)

- **lipoxins (LX)** = class of eicosanoids that are linear and contain several hydroxyl groups along the chain

- potent anti-inflammatory agents

P3 Principle 3 (5 of 7)

Lipids have uses in the cell beyond energy storage and membranes construction. Many lipids are present in the cell at smaller amounts than those making up membranes or being stored as fat. These lipids can function as cellular messengers, hormones, electron carriers, or pigments.

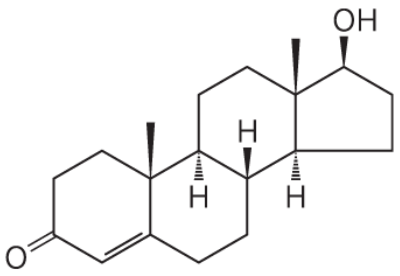
Steroid Hormones Carry Messages between Tissues

- steroids = oxidized derivates of sterols
  - lack the alkyl chain attached to ring D of cholesterol
  - more polar than cholesterol

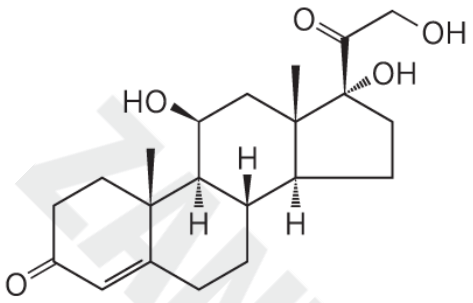
- steroid hormones move through the bloodstream (on protein carriers) to target tissues

- binding to highly specific receptor proteins in the nucleus triggers changes in gene expression

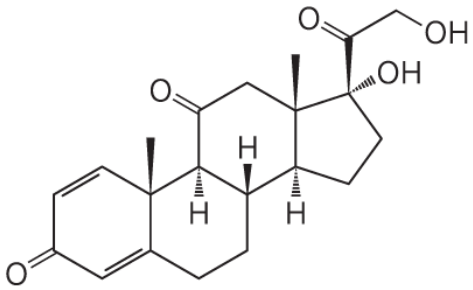
Steroids Derived From Cholesterol



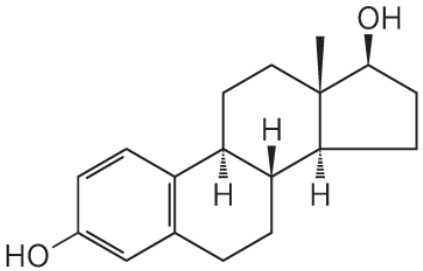
Testosterone
Male sex hormone
produced in the testes



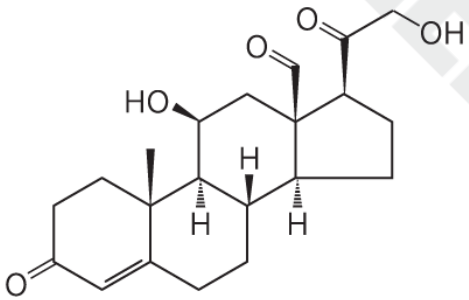
Cortisol
Hormone produced in the
adrenal cortex; regulates
glucose metabolism



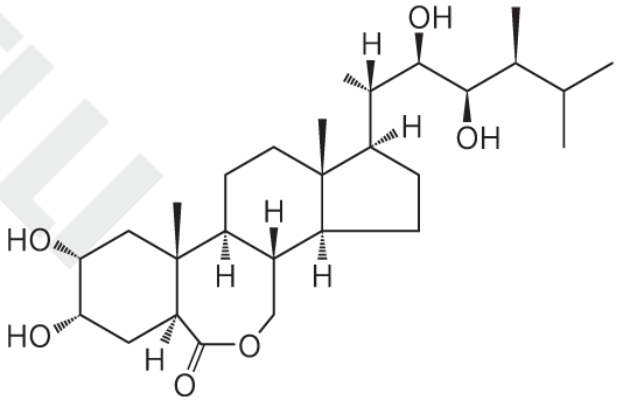
Prednisone
Synthetic steroid used as
an anti-inflammatory agent



β-Estradiol
Female sex hormone produced
in the ovaries and placenta



Aldosterone
Hormone produced in the
adrenal cortex; regulates
salt excretion



Brassinolide (a brassinosteroid)
Growth regulator found
in vascular plants

Nelson & Cox, *Lehninger Principles of Biochemistry*, 8e, © 2021 W. H. Freeman and Company

P3 Principle 3 (6 of 7)

Lipids have uses in the cell beyond energy storage and membranes construction. Many lipids are present in the cell at smaller amounts than those making up membranes or being stored as fat. These lipids can function as cellular messengers, hormones, electron carriers, or pigments.

P3 Principle 3 (7 of 7)

Lipids have uses in the cell beyond energy storage and membranes construction. Many lipids are present in the cell at smaller amounts than those making up membranes or being stored as fat. These lipids can function as cellular messengers, hormones, electron carriers, or pigments.

Vitamins A and D Are Hormone Precursors

- **vitamins** = compounds that are essential to the health of humans and other vertebrates but cannot be synthesized

- fat-soluble vitamins include the groups A, D, E, and K

The Lipidome

- **lipidome** = the full complement of lipids present in a specific cell type under particular conditions