

Lehninger

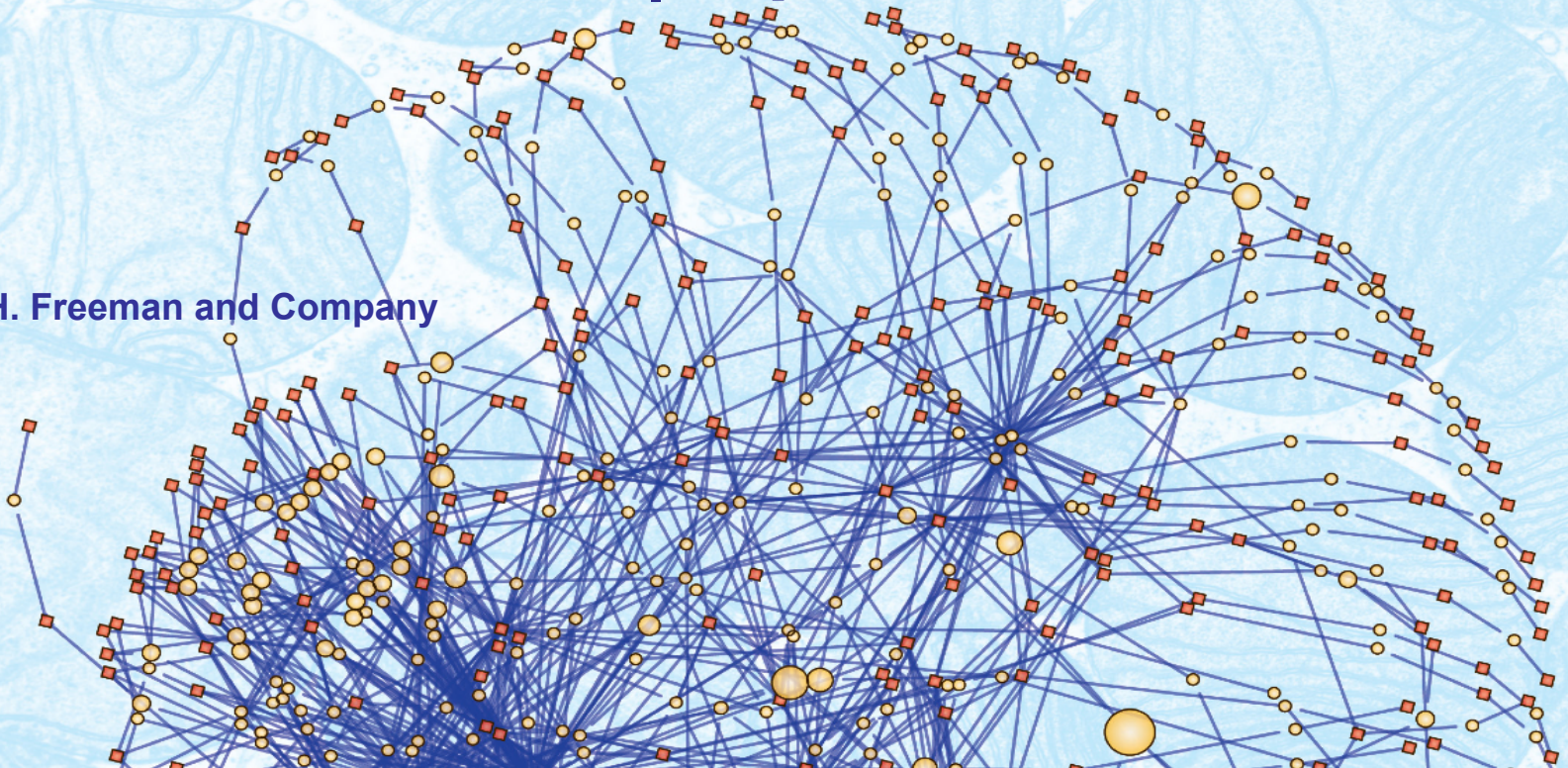
SIXTH EDITION

Principles of Biochemistry

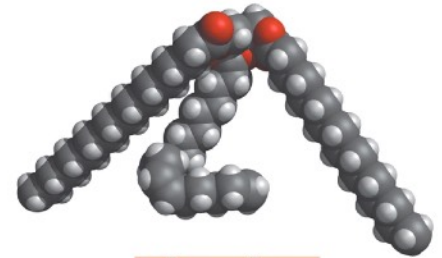
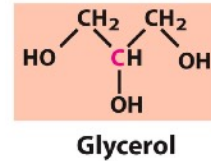
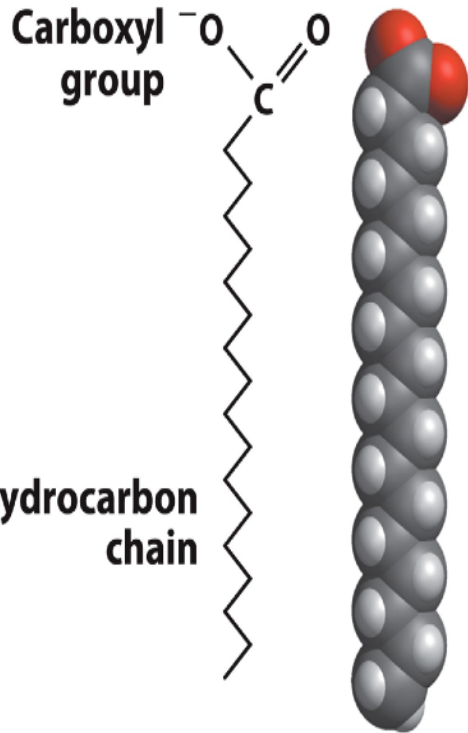
David L. Nelson | Michael M. Cox

10 | Lipids

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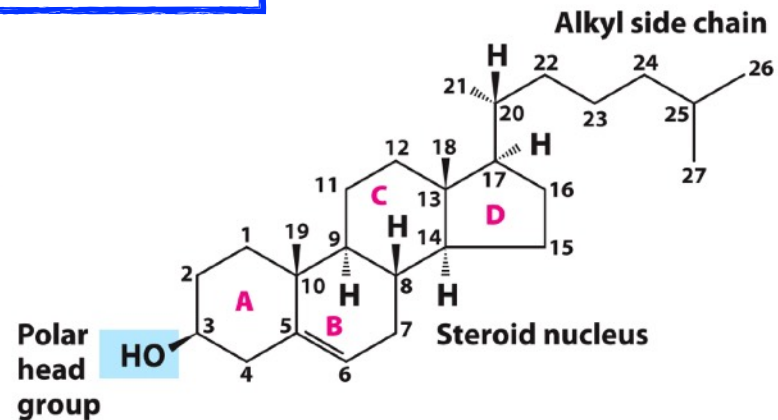
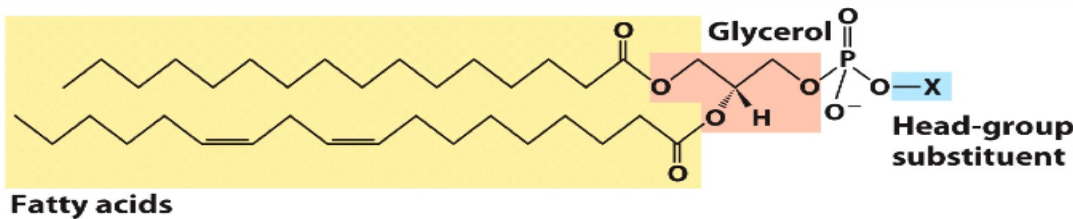
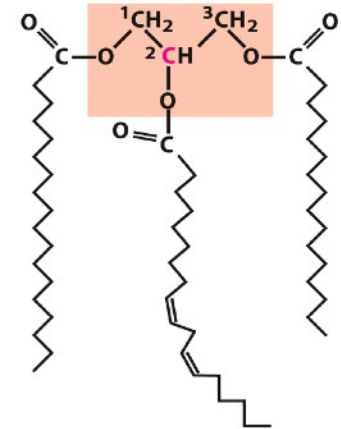


Lipids: A Structurally Diverse Class



Lipids are characterized by:

- Low solubility in water
- That means they are relatively **hydrophobic**



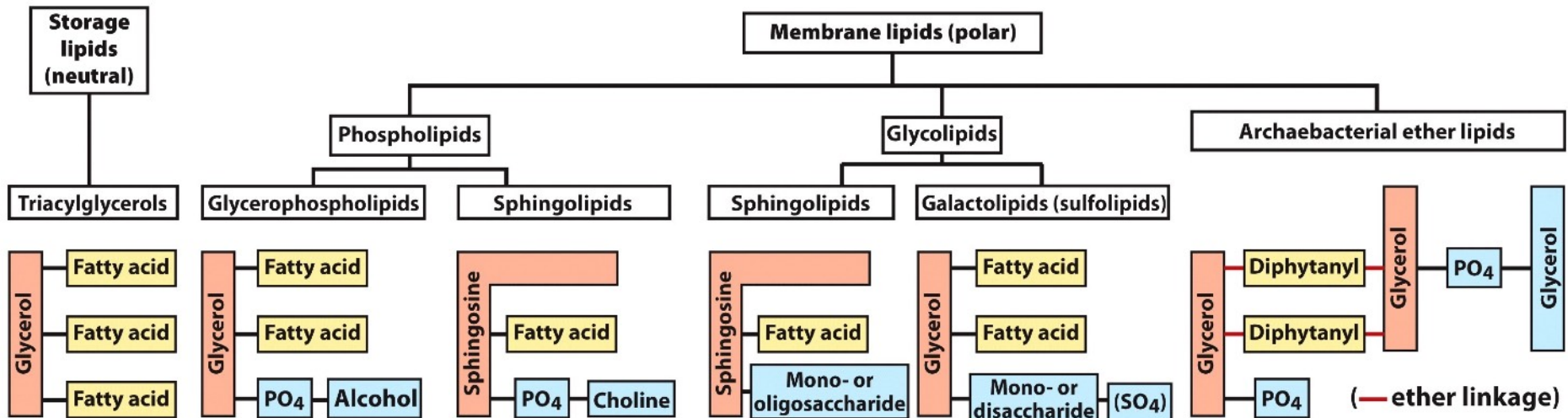
A Wide Variety of Biological Functions

- Storage of energy.
 - Reduced compounds: lots of available energy.
 - Hydrophobic nature: good packing.
- Insulation from environment.
 - Low thermal conductivity.
 - High heat capacity (can absorb heat).
 - Mechanical protection (can absorb shocks).
- Water repellent.
 - Hydrophobic nature prevents excessive wetting (birds).
 - Hydrophobic nature prevents loss of water via evaporation (plants).
- Membrane structure.
- Enzymes cofactors.
- Signaling molecules.
- **Pigments.**



Classification of Lipids

- Based on the structure and function.
 - Lipids that do NOT contain fatty acids such as cholesterol.
 - Lipids that contain fatty acids.
 - ▶ Storage lipids.
 - ▶ Membrane lipids.



Week 9 Chapter 10 Lipids

10.1 Storage lipids

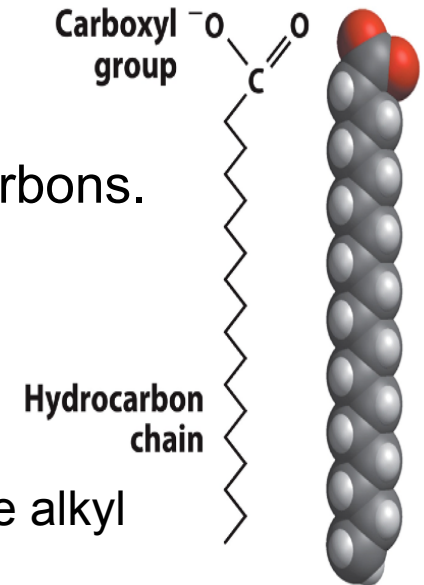
10.2 Structural lipids in membranes

10.3 Lipids as signals, cofactors and pigments

10.4 Working with lipids

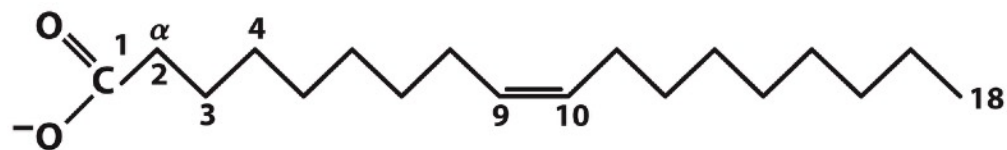
Fatty Acids

- Carboxylic acids with hydrocarbon chains containing from 4 to 36 carbons (C₄ to C₃₆).
 - Oxidation to CO₂ and H₂O is highly **exergonic**.
- Almost all natural fatty acids have an **even** number of carbons.
 - Two-carbon units are added each time during synthesis.
- Most natural fatty acids are unbranched.
 - **Saturated**: no double bonds between carbons in the chain.
 - **Monounsaturated**: one double bond between carbons in the alkyl chain.
 - **Polyunsaturated**: more than one double bond in the alkyl chain.

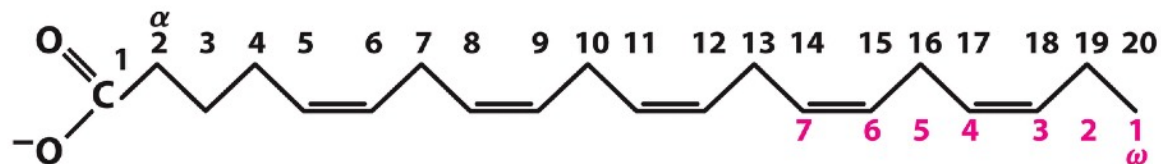


Fatty Acid Nomenclature

- Chain length : Number of double bonds.
 - 16:0 is a 16-carbon saturated fatty acid with no double bond.
- Positions of double bonds specified relative to carboxyl carbon (C-1).
 - 20:2($\Delta^{9,12}$) is a 20-carbon unsaturated fatty acid with two double bonds.
 - One double bond between C-9 and C-10.
 - The other double bond is between C-12 and C-13.
- Almost **never conjugated**. Almost always in **cis configuration**.
 - Conjugated double bonds: $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$.



(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid



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

Nomenclature of Saturated Fatty Acids

Carbon skeleton	Structure*	Systematic name [†]	Common name (derivation)	
12:0	$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$	<i>n</i> - <u>Dodecanoic acid</u>	Lauric acid (Latin <i>laurus</i> , "laurel plant")	十二烷酸, 月桂酸
14:0	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$	<i>n</i> - <u>Tetradecanoic acid</u>	Myristic acid (Latin <i>Myristica</i> , nutmeg genus)	十四烷酸, 肉豆蔻酸
16:0	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$	<i>n</i> - <u>Hexadecanoic acid</u>	Palmitic acid (Latin <i>palma</i> , "palm tree")	十六烷酸, 棕榈酸
18:0	$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$	<i>n</i> - <u>Octadecanoic acid</u>	Stearic acid (Greek <i>stear</i> , "hard fat")	十八烷酸, 硬脂酸
20:0	$\text{CH}_3(\text{CH}_2)_{18}\text{COOH}$	<i>n</i> - <u>Eicosanoic acid</u>	Arachidic acid (Latin <i>Arachis</i> , legume genus)	二十烷酸, 花生酸
24:0	$\text{CH}_3(\text{CH}_2)_{22}\text{COOH}$	<i>n</i> - <u>Tetracosanoic acid</u>	Lignoceric acid (Latin <i>lignum</i> , "wood" + <i>cera</i> , "wax")	二十四烷酸, 木蜡酸

- *n*- indicates "normal" unbranched structure.
- Prefix **deca-** means "ten".
- Prefix **eicosa-** means "twenty".

Nomenclature of Unsaturated Fatty Acids

16:1(Δ^9)	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	<i>cis</i> -9-Hexadecenoic acid	Palmitoleic acid	棕榈油酸
18:1(Δ^9)	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	<i>cis</i> -9-Octadecenoic acid	Oleic acid (Latin <i>oleum</i> , "oil")	油酸
18:2($\Delta^{9,12}$)	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	<i>cis</i> -, <i>cis</i> -9,12-Octadecadienoic acid	Linoleic acid (Greek <i>linon</i> , "flax")	亚油酸
18:3($\Delta^{9,12,15}$)	$\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	<i>cis</i> -, <i>cis</i> -, <i>cis</i> -9,12,15-Octadecatrienoic acid	α -Linolenic acid	亚麻酸
20:4($\Delta^{5,8,11,14}$)	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_3\text{COOH}$	<i>cis</i> -, <i>cis</i> -, <i>cis</i> -, <i>cis</i> -5,8,11,14-Icosatetraenoic acid	Arachidonic acid	花生四烯酸

- In biological fatty acids, the double bond configuration is almost *cis*.

Fatty Acid Nomenclature

- An alternative nomenclature for polyunsaturated fatty acids (PUFAs).
 - Start from the methyl end (most distant from carboxyl group).
 - Carbon of methyl group is called ω (omega) carbon and C-1.
 - **Physiological role** related more to position of the first double bond **near methyl end** than to carboxyl end.
- Omega-3 fatty acids have a double bond between C-3 and C-4.
- Omega-6 fatty acids have a double bonds between C-6 and C-7.



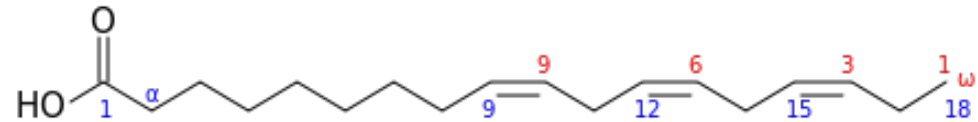
**(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), 二十碳五烯酸
an omega-3 fatty acid**



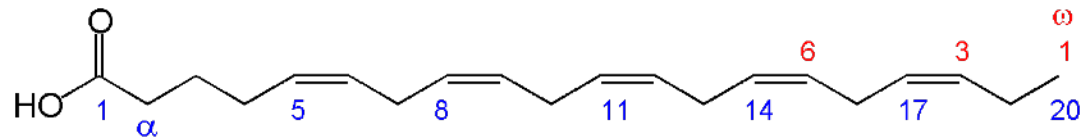
PUFAs and Cardiovascular Disease

- Omega-3 fatty acids are essential nutrients.
 - Human need them but cannot synthesize them.
 - Includes ALA, EPA and DHA.
 - ▶ ALA is 18:3($\Delta^{9,12,15}$).
 - ▶ EPA is 20:5($\Delta^{5,8,11,14,17}$).
 - ▶ DHA is 22:6($\Delta^{4,7,10,13,16,19}$).
- Human can synthesize EPA and DHA from ALA.
 - Efficiency of conversion much lower than adsorption from food.
- Imbalance of ω -6 and ω -3 PUFAs associated with increased risk of cardiovascular disease.
 - Optimal ratio between 1:1 and 4:1.
 - North American diet: 10:1 to 30:1.
 - Mediterranean diet: rich in ω -3 PUFAs, and lower cardiovascular risk.

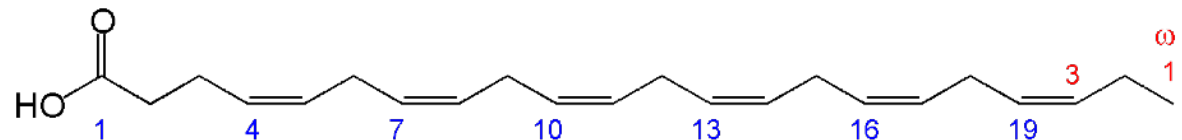
α -Linolenic acid



Eicosapentaenoic acid



Docosahexaenoic acid



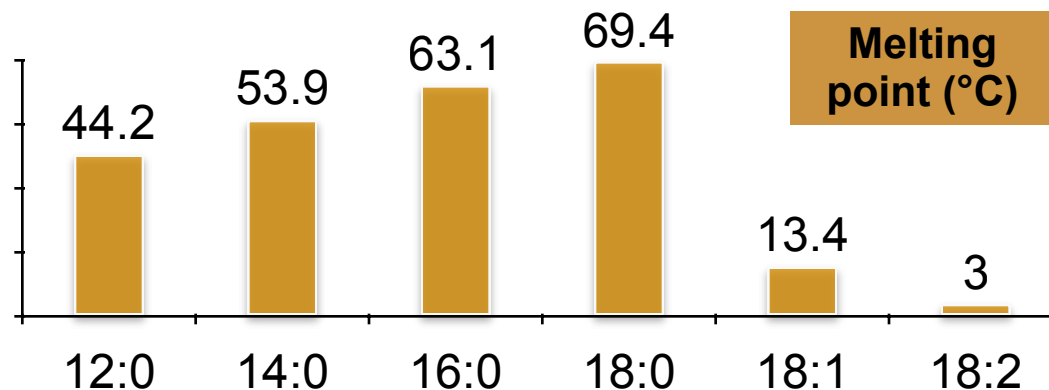
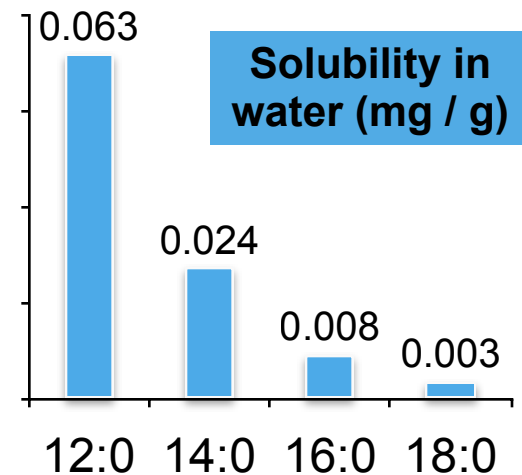
Solubility and Melting Point

- Solubility.

- Poor solubility in water due to nonpolar hydrocarbon chain.
- Fatty Acid 12:0 -> 0.06 mg/g; glucose -> 1100 mg/g.
- **Decrease as chain length increases.**

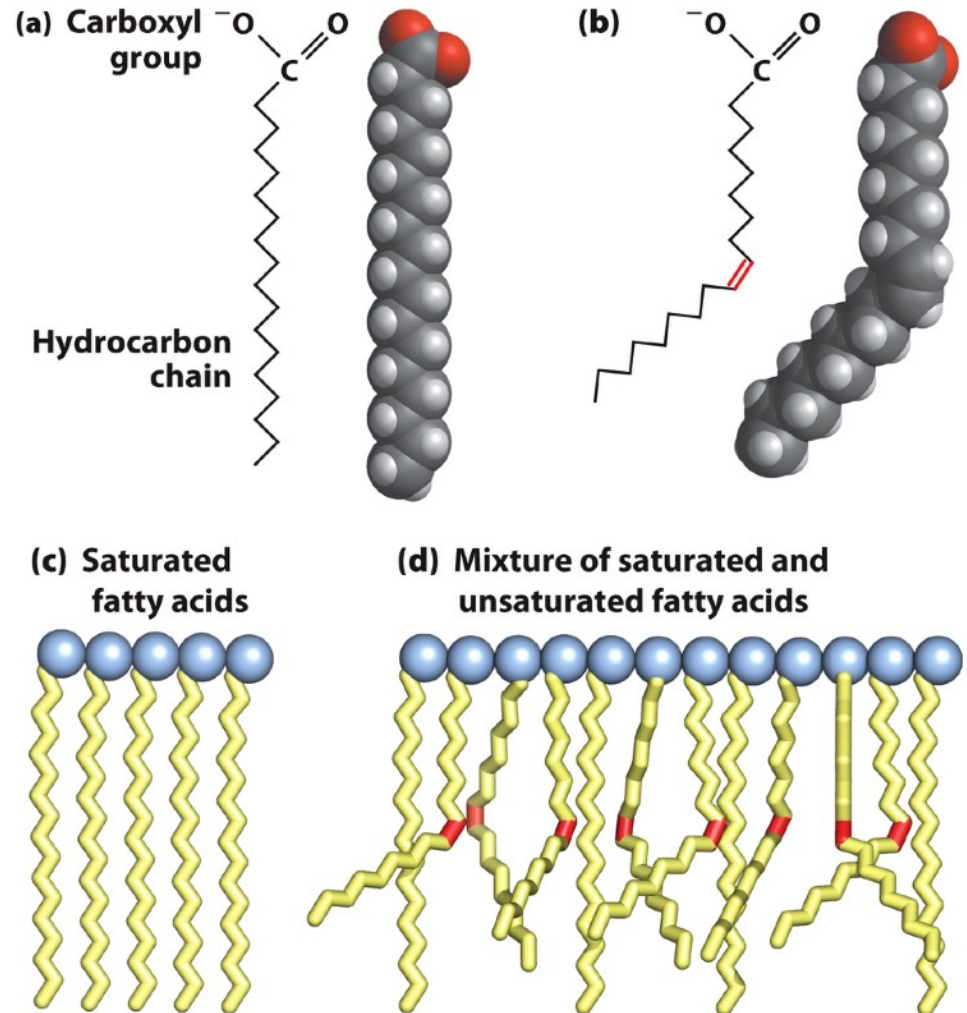
- Melting Point

- **Increase as chain length increases.**
- **Decrease as number of double bonds increases.**
 - ▶ Saturated FAs from 12:0 to 24:0 -> wax.
 - ▶ Unsaturated FAs from 12-carbon to 24-carbon -> oil.



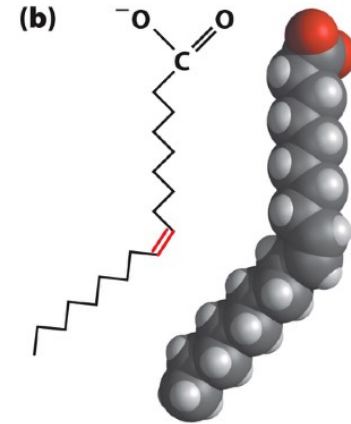
Melting Point and Packing

- Difference in melting points due to different degrees of **packing**.
- **Fully saturated** FAs in fully extended form.
 - **Pack tightly**.
- Cis double bond in **unsaturated** FAs forces a turn.
 - Cannot pack as tightly, and interactions are **weaker**.



Trans Fatty Acids

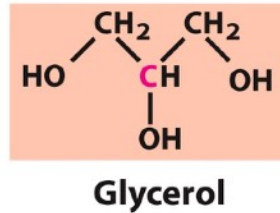
- Lipid-rich food may spoil and become rancid.
 - Oxidative cleavage of double bonds in unsaturated FAs.
 - Vegetable oils -> triacylglycerols with unsaturated FAs.
 - Beef fat -> triacylglycerols with saturated FAs.
- Partial hydrogenation.
 - Aims to convert double bonds to single bonds.
 - Improve shelf life and increase stability in high-temperature cooking.
 - Undesirable effect: some *cis* double bonds converted to **trans double bonds**.
- Consuming trans fats increases risk of cardiovascular disease.
 - Avoid deep-frying vegetable oils.
 - Deleterious effects occur at intakes of 2 to 7 g/day.



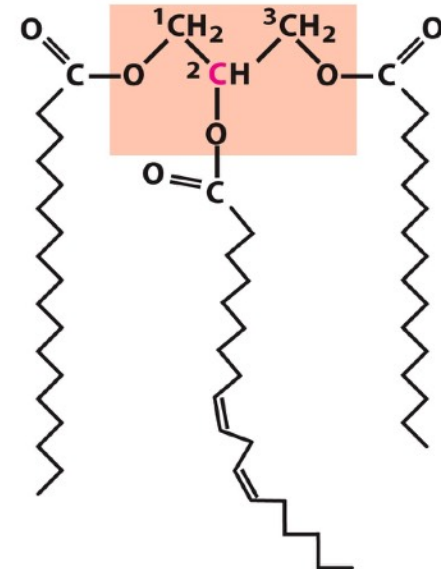
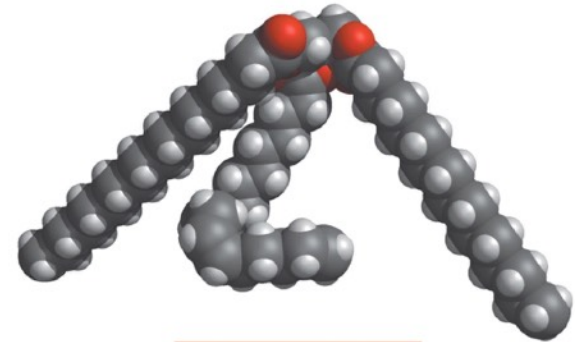
	In a typical serving (g)
French fries	4.7–6.1
Breaded fish burger	5.6
Breaded chicken nuggets	5.0
Pizza	1.1
Corn tortilla chips	1.6
Doughnut	2.7
Muffin	0.7
Chocolate bar	0.2

Triacylglycerols Are Esters of Glycerol

- 三酰甘油
- 甘油三酯



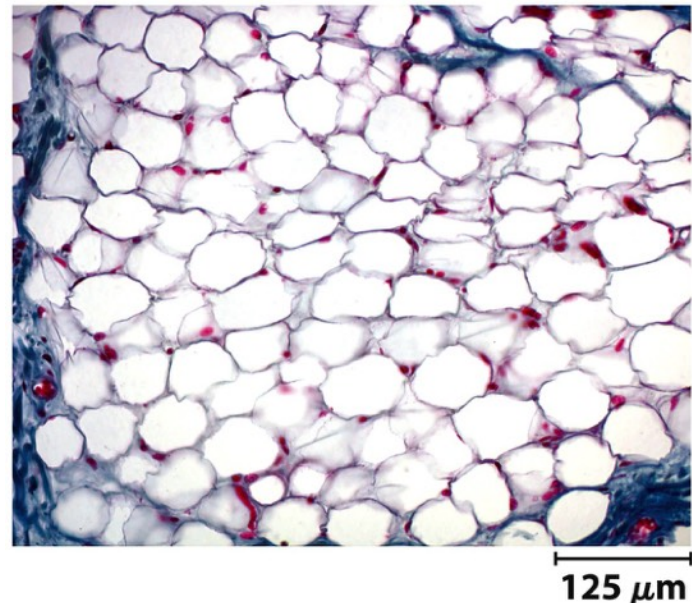
- Majority of fatty acids in biological systems are found in the form of triacylglycerols (TAG, or triglycerides).
 - Three fatty acids each in **ester linkage** with a single glycerol.
- Triacylglycerols are **nonpolar**, **hydrophobic** molecules.
 - Less soluble in water than fatty acids due to the lack of charged carboxylate group.



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

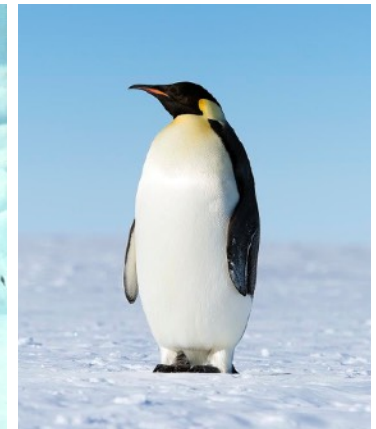
Triacylglycerols Provide Energy

- Adipocytes, fat cells, store large amount of triacylglycerols as fat droplets.
 - Fat droplets nearly fill the cell.
 - Nucleus squeezed against plasma membrane.
- **Why use triacylglycerols instead of polysaccharide to store energy?**
 - Triacylglycerols yield more energy (carbon atoms more reduced).
 - Triacylglycerols are hydrophobic and carry no extra water.
- Triacylglycerols in human body meet energy needs for **months**.
- Glycogen in human body stores less than a **day**'s energy supply.
- Carbohydrates are **quick** sources of energy (soluble in water).



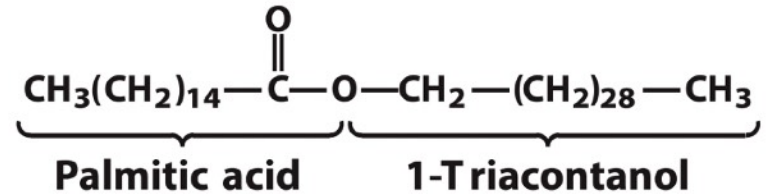
Triacylglycerols Provide Insulation

- Triacylglycerols serve as **energy stores** and also **insulation** against low temperatures.
 - Seals, walruses, penguins, and other warm-blooded polar animals.
 - Hibernating animals such as bears.
 - ▶ Not eat, drink, urinate or defecate for months.
 - ▶ Fat oxidation yields energy.
 - ▶ Glycerol is converted to blood glucose.



Waxes: Energy Stores & Water Repellents

- **Esters** of long-chain FAs with long-chain alcohols.
- High melting points and insoluble in water.
- A variety of functions.
 - Storage of metabolic fuel in plankton.
 - Waterproofing of feathers in birds.
 - Protection from evaporation in tropical plants and ivy.



Summary 10.1 Storage Lipids

- Lipids are water-insoluble. Almost all biological fatty acids have an even number of carbon atoms. They are either saturated or unsaturated, with double bonds almost always in *cis* configuration.
- Triacylglycerols contain three fatty acid molecules esterified to three hydroxyl groups of glycerol. Triacylglycerols are primarily storage fats.
- Partial hydrogenation converts some *cis* double bonds to *trans* configuration. *Trans* fats are an important risk factor for cardiovascular disease.

Week 9 Chapter 10 Lipids

10.1 Storage lipids

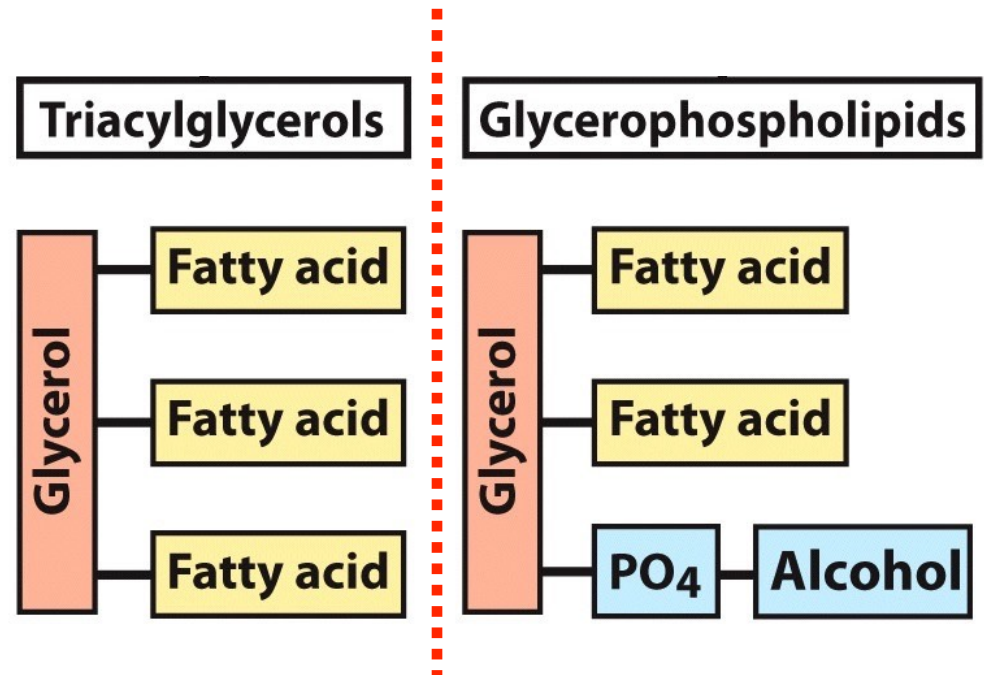
10.2 Structural lipids in membranes

10.3 Lipids as signals, cofactors and pigments

10.4 Working with lipids

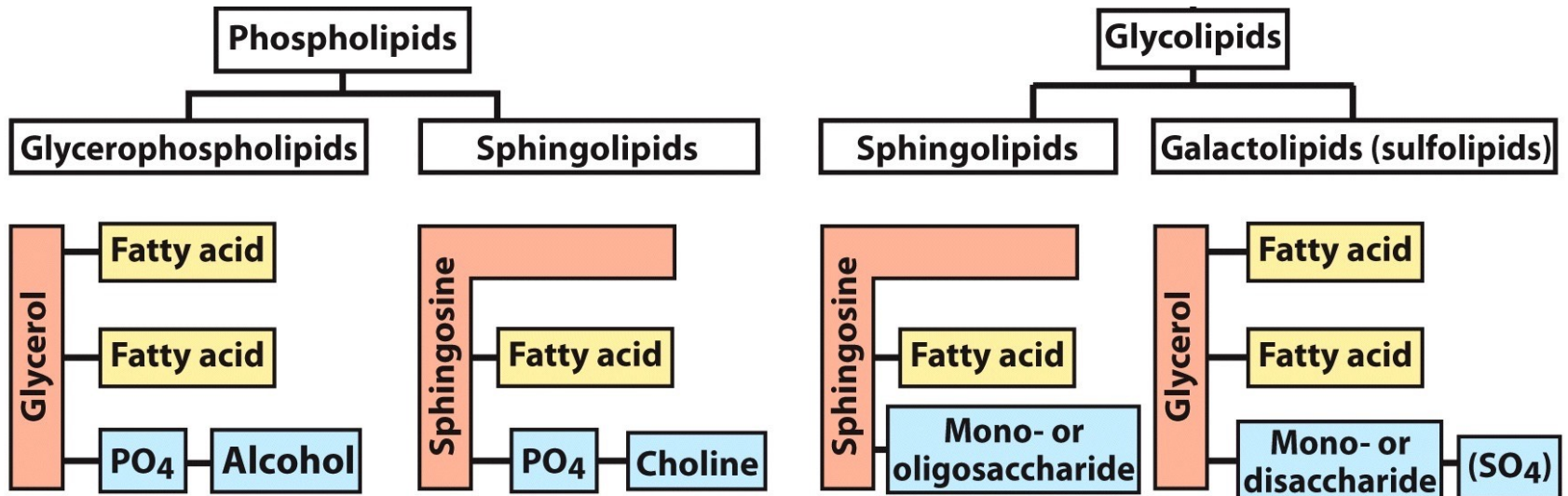
Lipids in Biological Membranes

- Biological membrane is a double layer of lipids (lipid bilayer).
 - Barrier to polar molecules and ions.
- **Membrane lipids are amphipathic.**
 - One end is hydrophobic, the other hydrophilic.
- Five types of membrane lipids.
 - Glycerophospholipids.
 - Galactolipids and sulfolipids.
 - Archaeal tetraether lipids.
 - Sphingolipids.
 - Sterols.



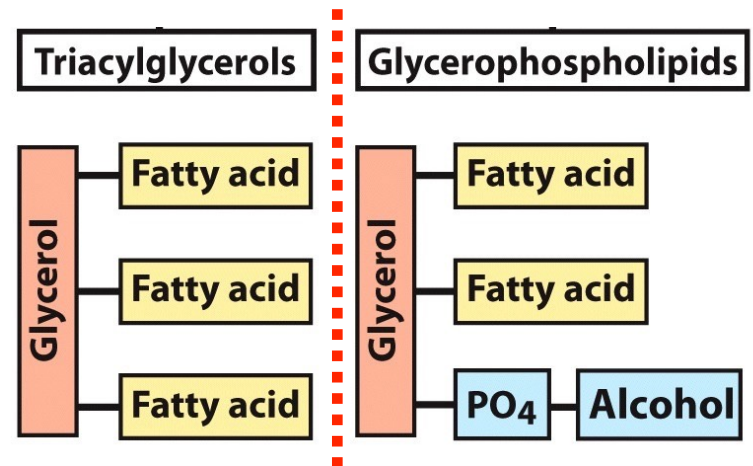
Amphipathic Molecules

- Possess **both hydrophilic and lipophilic** properties.
 - Hydrophilic (water-loving, polar) head.
 - Lipophilic (fat-loving, nonpolar) fatty acid tail.
- Linkage.
 - Phosphodiester bond (phospholipids).
 - Glycosidic bond (glycolipids).



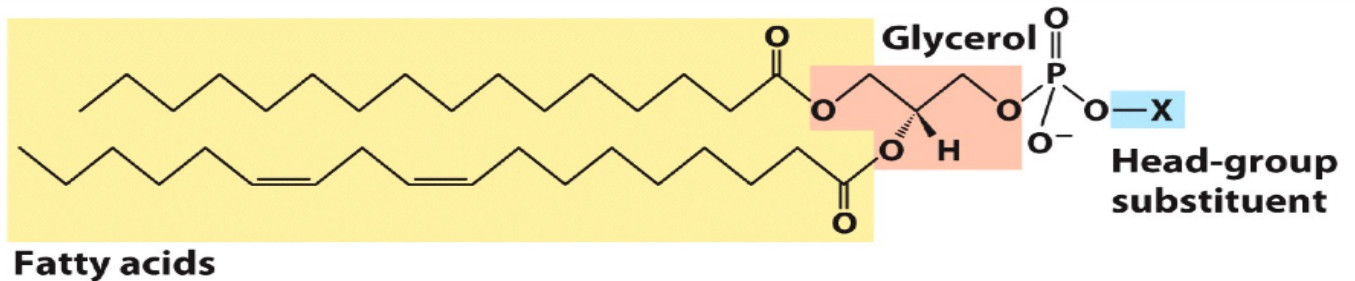
1. Glycerophospholipids

- Glycerophospholipids, or phosphoglycerides.
 - Glycerol backbone.
 - Two fatty acids attached in **ester** linkage (Diacylglycerols, DAG).
 - A polar or charged head group attached through a **phosphodiester** linkage.
- Glycerol is **prochiral**.
 - Contains no asymmetric carbon.
 - Attachment of phosphate converts it into a chiral molecule.



Saturated fatty acid
(e.g., palmitic acid)

Unsaturated fatty acid
(e.g., linoleic acid)



Glycerophospholipid Nomenclature

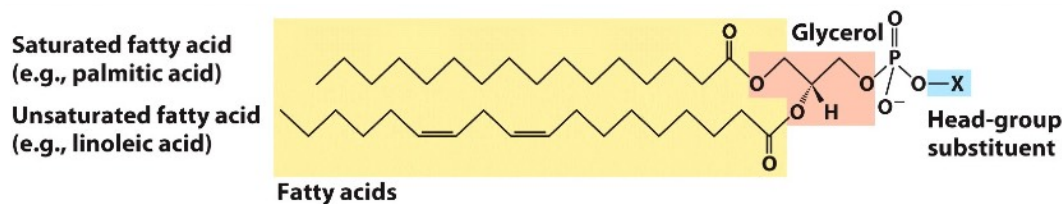
- Parent compound: phosphatidic acid (PA, phospho-mono-ester).

- Parent compound + polar head group.

- Phosphatidyl-choline has **choline** as polar head group.

- PIP₂ has **inositol 4,5-bisphosphate** as polar head group.

- 磷脂酸
- 胆碱
- 肌醇
- 磷脂酰甘油



- C-1:

- C₁₆ or C₁₈ saturated FA.

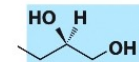
- C-2:

- C₁₈ or C₂₀ unsaturated FA.

Name of glycerophospholipid	Name of X—O	Formula of X
Phosphatidic acid	—	— H
Phosphatidylethanolamine	Ethanolamine	
Phosphatidylcholine	Choline	
Phosphatidylserine	Serine	

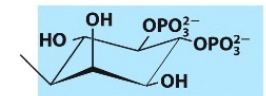
Phosphatidylglycerol

Glycerol



Phosphatidylinositol 4,5-bisphosphate

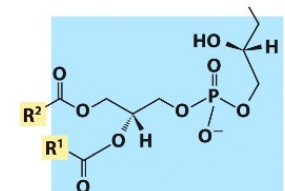
myo-Inositol 4,5-bisphosphate



PIP₂

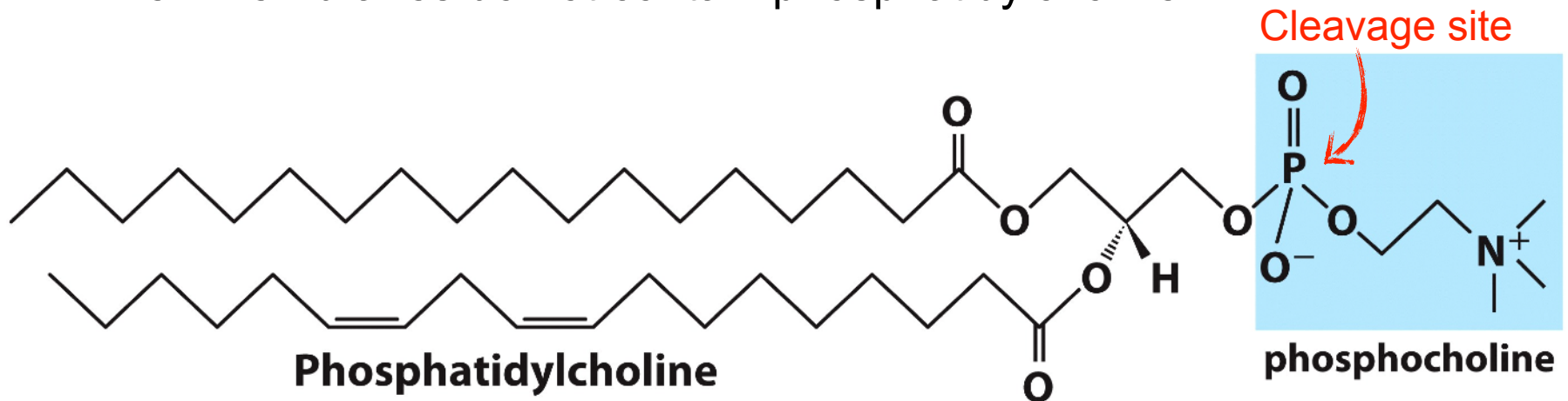
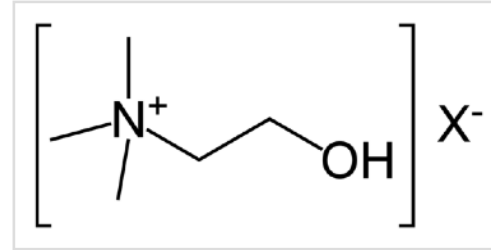
Cardiolipin

Phosphatidyl-glycerol



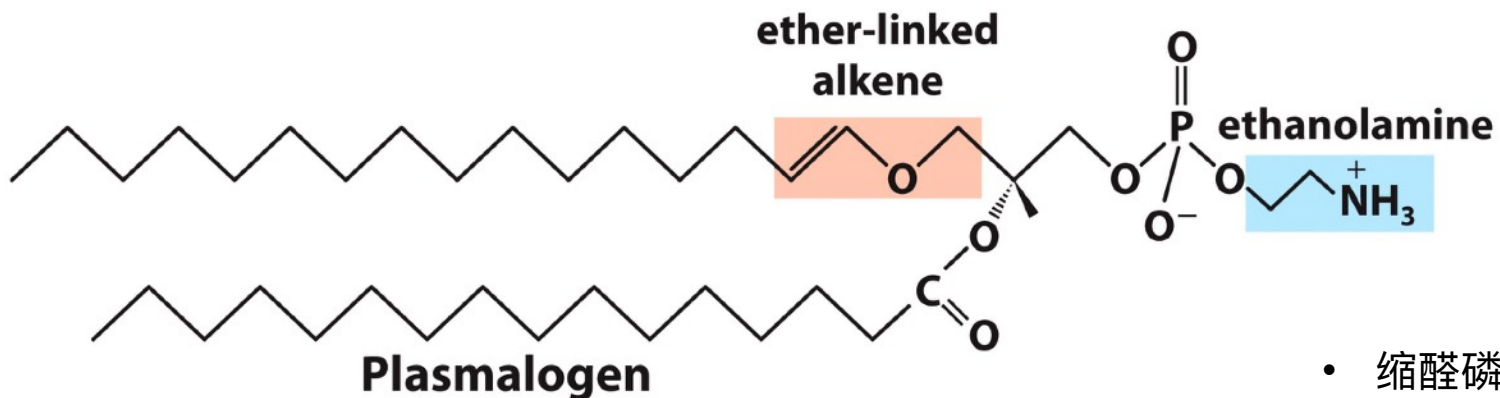
Phosphatidylcholine

- Phosphatidic acid derivative.
 - Choline as polar head group.
- Hydrolysis catalyzed by **phospholipase D** produces PA and choline.
- Major component of most **eukaryotic cell membranes**.
 - Many prokaryotes, including *E. coli*, cannot synthesize this lipid.
 - Their membranes do not contain phosphatidylcholine.

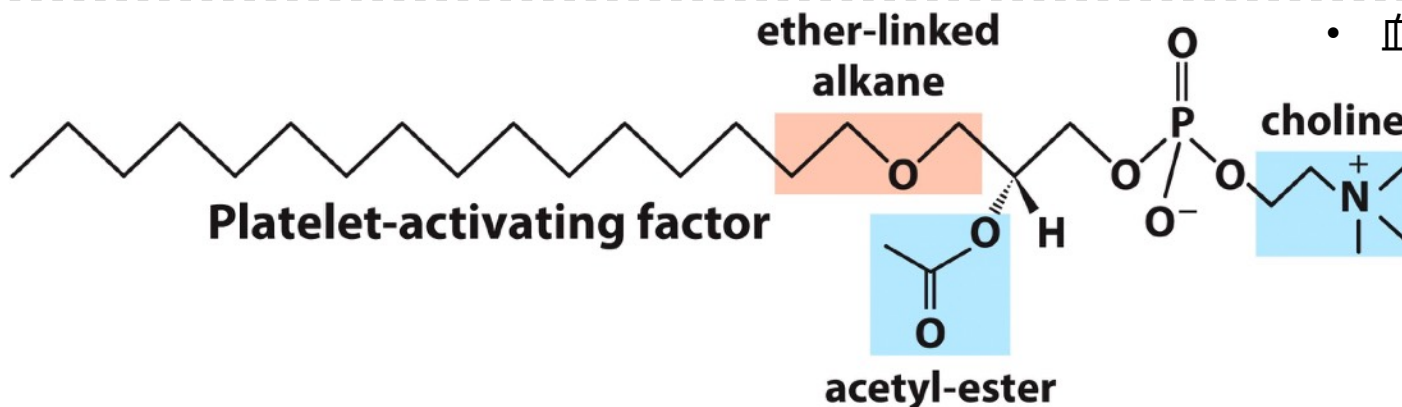


Ether-Linked Fatty Acids

- Some glycerophospholipids have **ether**-linked fatty acids.
 - One of two acyl chains attached to glycerol in ether (not ester) linkage.
 - Functional significance unknown.
 - **Resistance** to phospholipases that cleave ester-linked fatty acids.

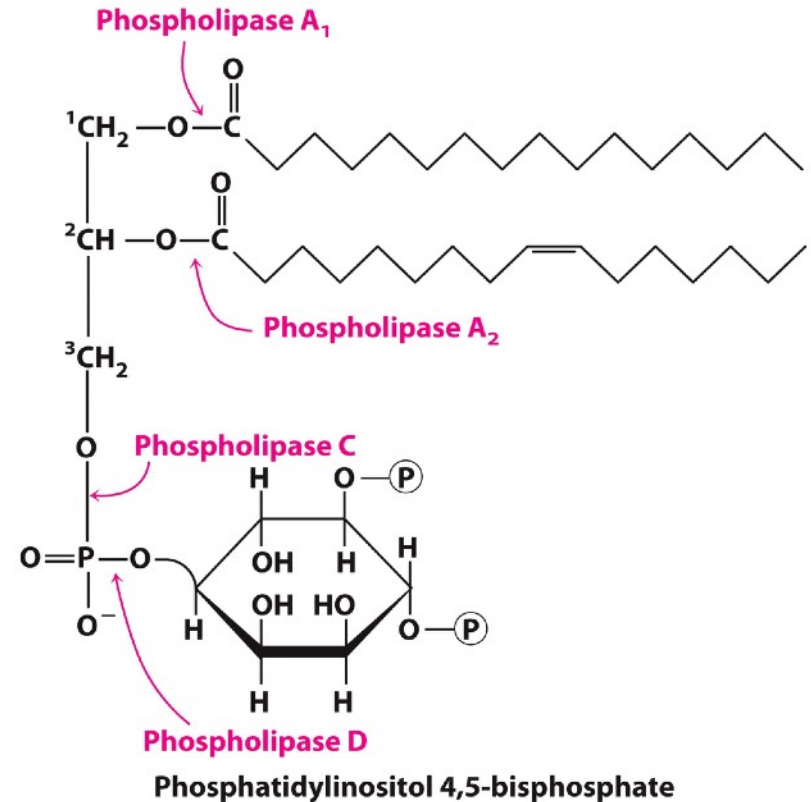


- 缩醛磷脂
- 血小板活化因子



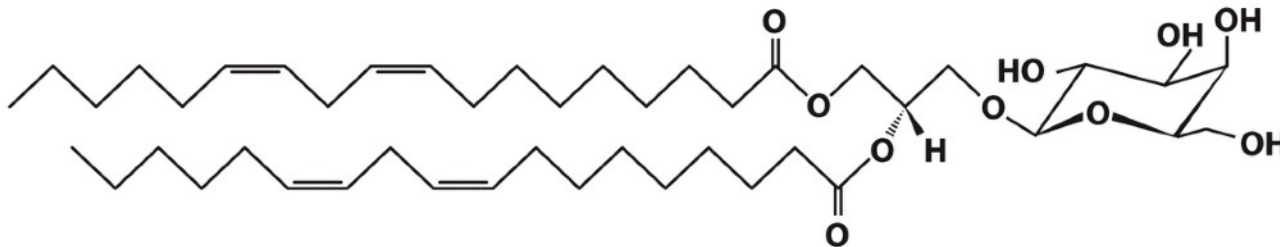
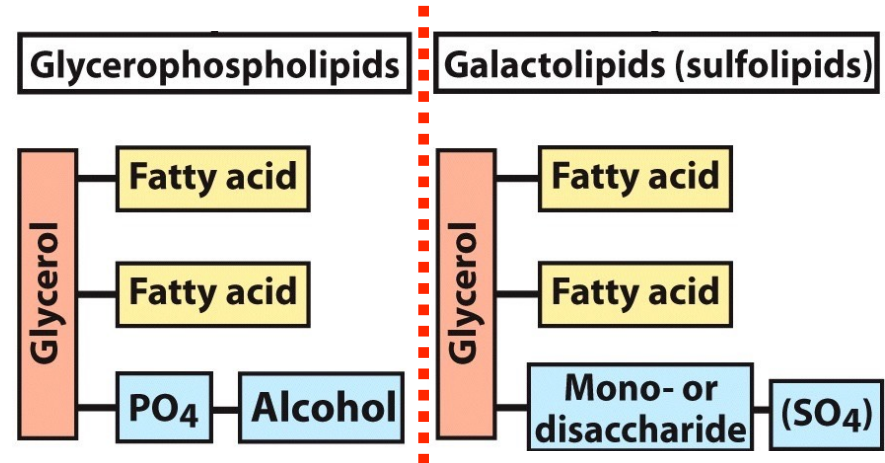
Phospholipids Degraded in Lysosomes

- Phospholipase A: hydrolysis of ester bond at C-1 and C-2.
 - NOT attack ether linkage in plasmalogen.
- Phospholipase C and D: hydrolysis of phosphodiester bond at C-3.
 - Enzyme: phospholipase C.
 - ▶ Substrate: PIP_2 .
 - ▶ Product: DAG and IP_3 .
 - Enzyme: phospholipase D.
 - ▶ Substrate: phosphatidylcholine.
 - ▶ Product: phosphatidic acid and choline.



2. Galactolipids and Sulfolipids

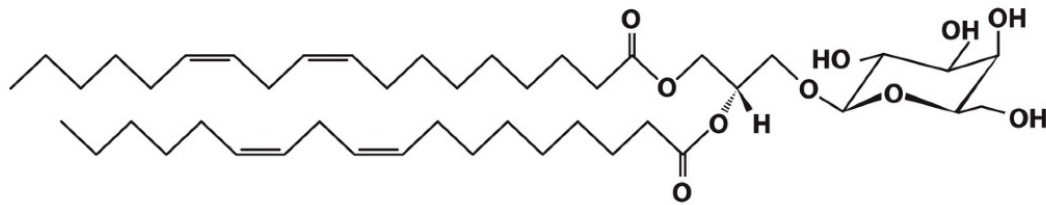
- Galactolipids.
 - One or two **galactose** residues connected to a diacylglycerol.
 - In **chloroplast**, 70 - 80% of total **membrane** lipids in a plant.
 - Phosphate-free lipids may be evolutionarily favorable.
- Sulfolipids.
 - Sulfonated glucose** residue.
 - Negative charge like phosphate group.



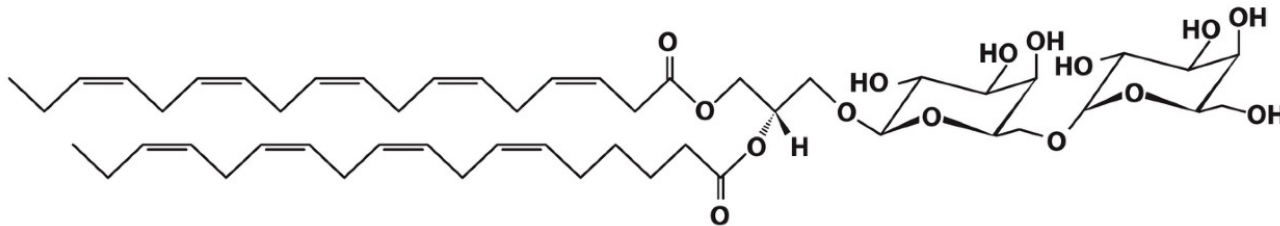
Monogalactosyldiacylglycerol (MGDG)

Linkage in Galactolipids and Sulfolipids

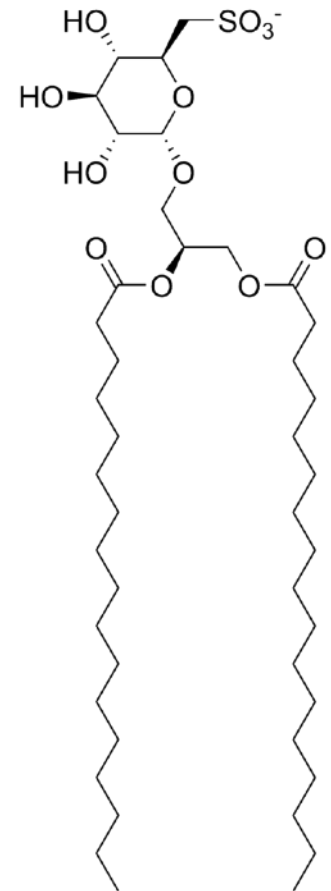
- Galactolipids.
 - One or two galactose residues connected to a diacylglycerol.
 - **Glycosidic** bond to C-3 of a 1,2-diacylglycerol.
- Sulfolipids.
 - Sulfonated glucose residue connected to a diacylglycerol.
 - **Glycosidic** bond to C-3 of a 1,2-diacylglycerol.



Monogalactosyldiacylglycerol (MGDG)



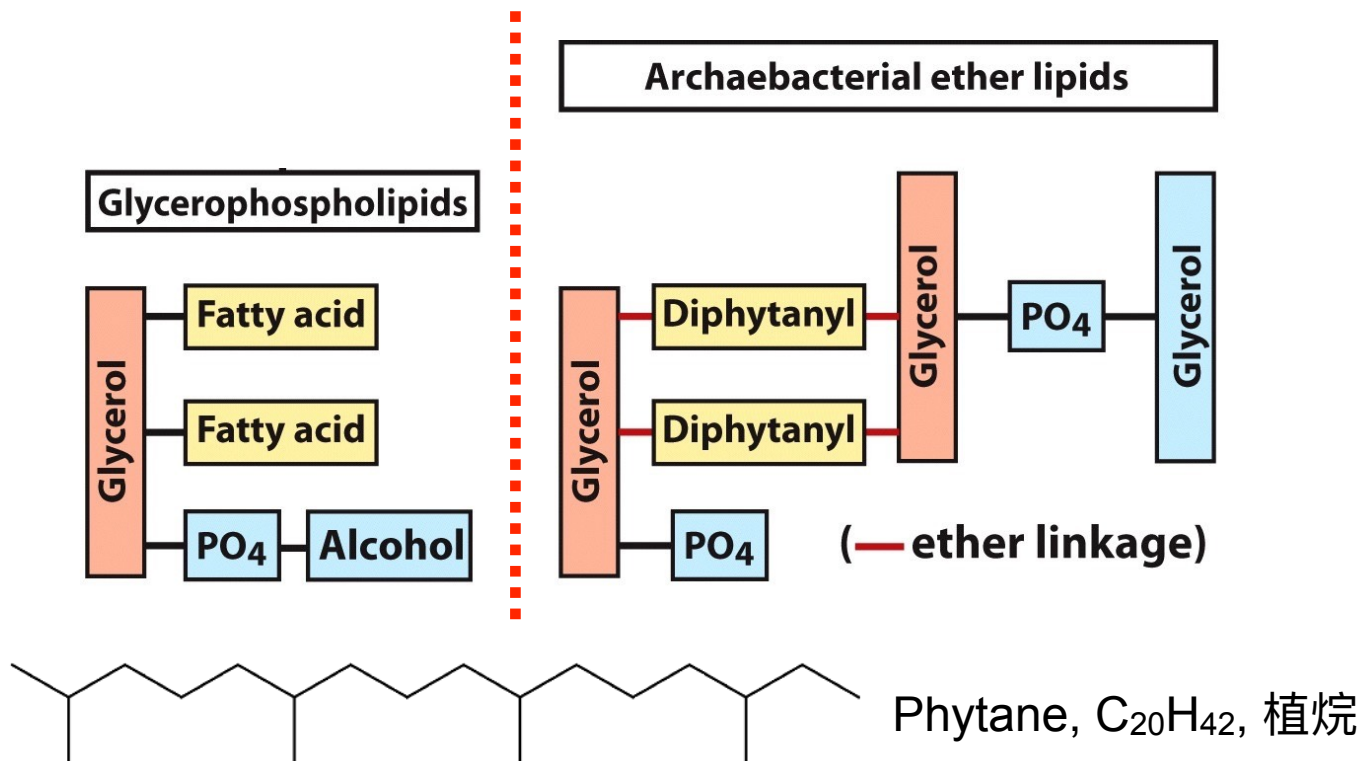
Digalactosyldiacylglycerol (DGDG)



Sulfoquinovosyldiacylglycerides (SQDG)

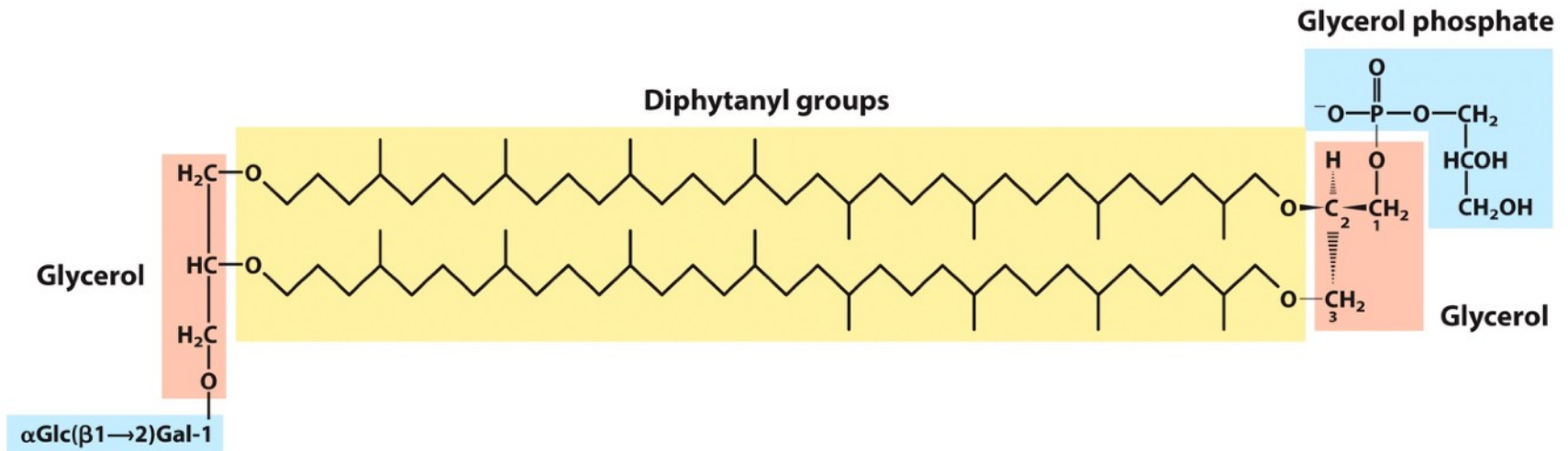
3. Archaeal Tetraether Lipids

- Some archaea live in extreme conditions.
 - High temperature, low pH, or high ionic strength.
 - Membrane lipids contain **very long (32 carbons)** hydrocarbon chains.
 - Twice the length of phospholipids.



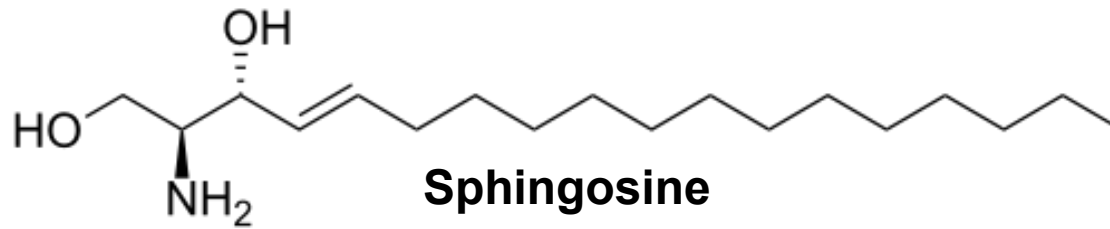
Linkage in Archaeal Tetraether Lipids

- **Ether** linkage between hydrocarbon chains and glycerols.
 - More **resistant** (than ester bond) to hydrolysis at low pH and high temp.
- Head polar group.
 - Glycerol linked to **either phosphate or sugar** residues.
 - General name: glycerol dialkyl glycerol tetraethers (GDGTs).



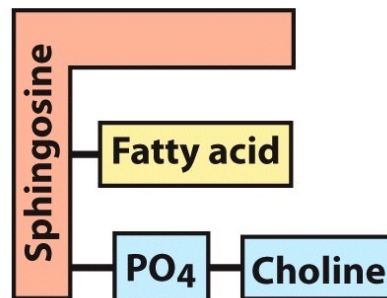
4. Sphingolipids

- Sphingolipids have a polar head and two nonpolar tails.
 - Contains no glycerol but **sphingosine** (long-chain amino alcohol).
 - One nonpolar tail from sphingosine, and the other from **fatty acid**.
 - **Polar head** is phosphate or sugar residues.

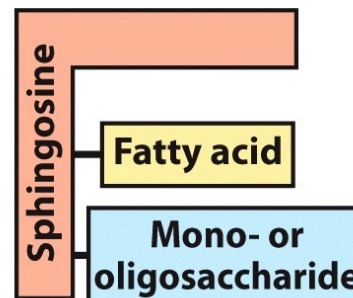


• 鞘氨醇

Sphingolipids

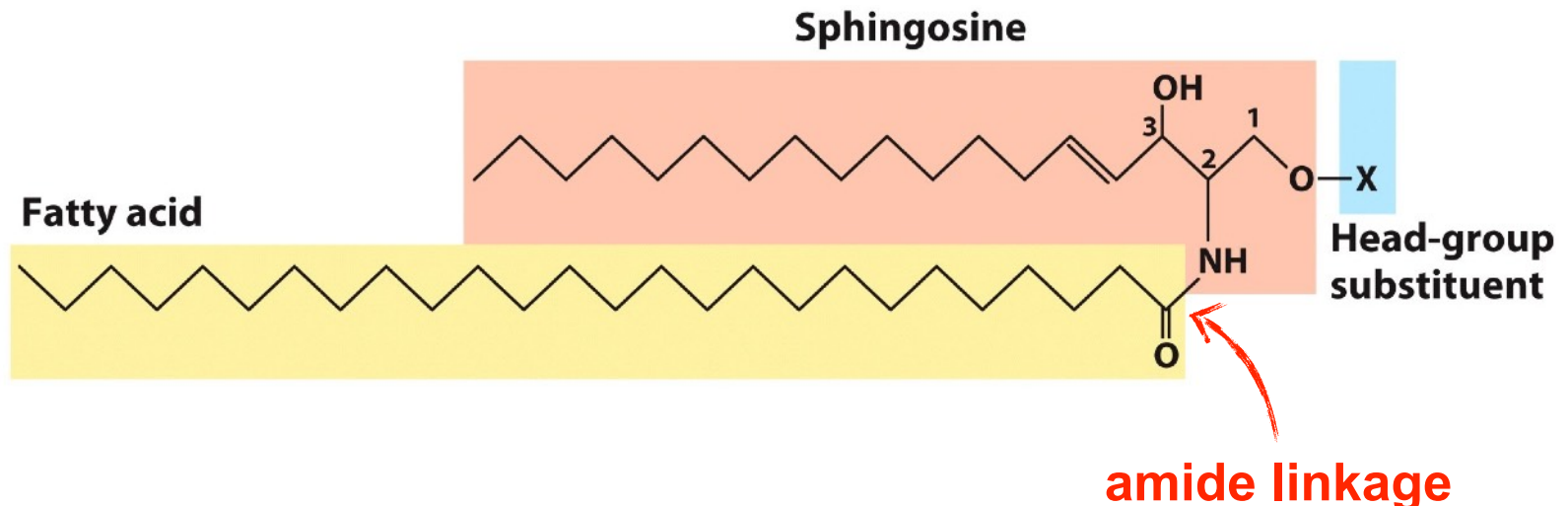


Sphingolipids



Ceramide is Structural Parent

- Ceramide is structurally similar to a diacylglycerol. • 神经酰胺
 - C-1, C-2 and C-3 of sphingosine analogous to three carbons in glycerol.
 - Ceramide: sphingosine with a fatty acid attached to amino group on C-2.
 - Polar head X.
 - ▶ X = H, ceramide;
 - ▶ X = phosphate or sugar, other sphingolipids.

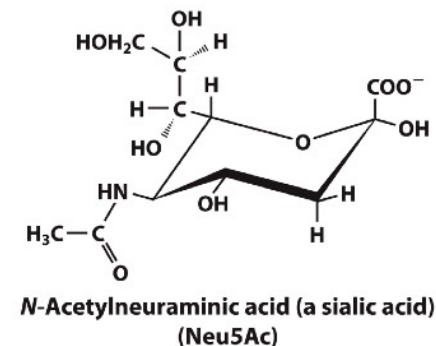


Three Subclasses of Sphingolipids

- Different head groups (phosphodiester or glycosidic bond).
 - **Sphingomyelins** contain phosphocholine or phosphoethanolamine.
 - **Neutral glycolipids** have one or more sugars.
 - **Gangliosides** have oligosaccharides as polar groups and sialic acid.

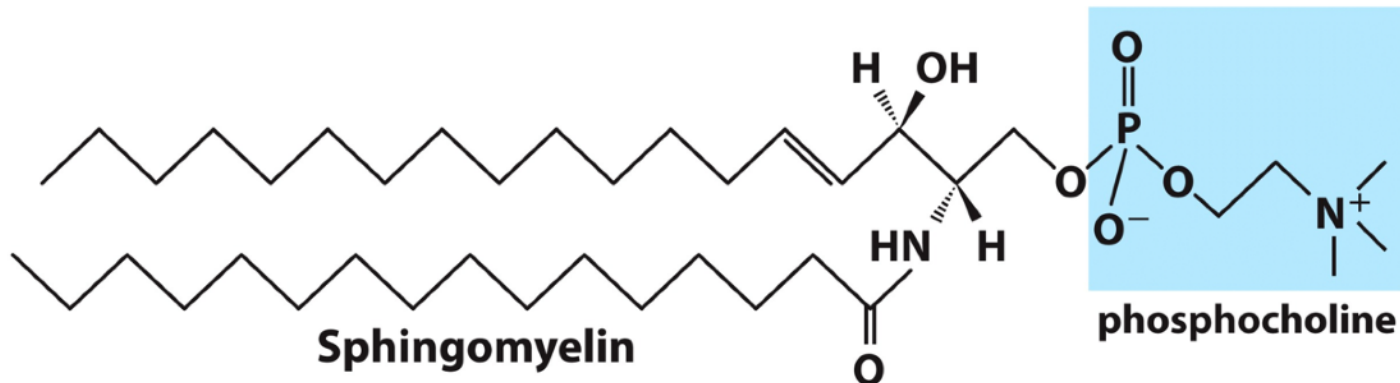
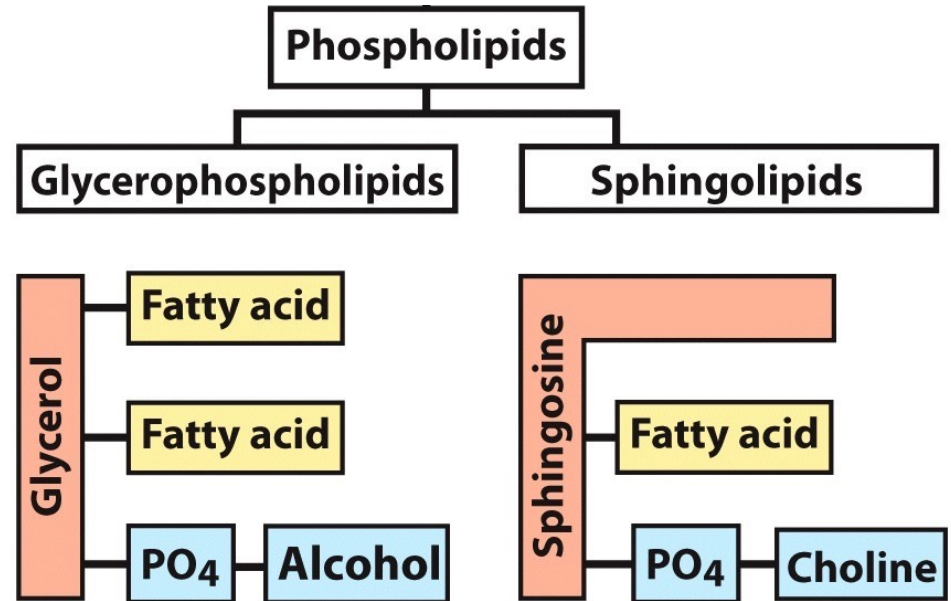
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

- 唾液酸
- 神经氨酸
- Galactose
- Glucose
- N-Acetylgalactosamine
- ◆ N-Acetylneuraminic acid



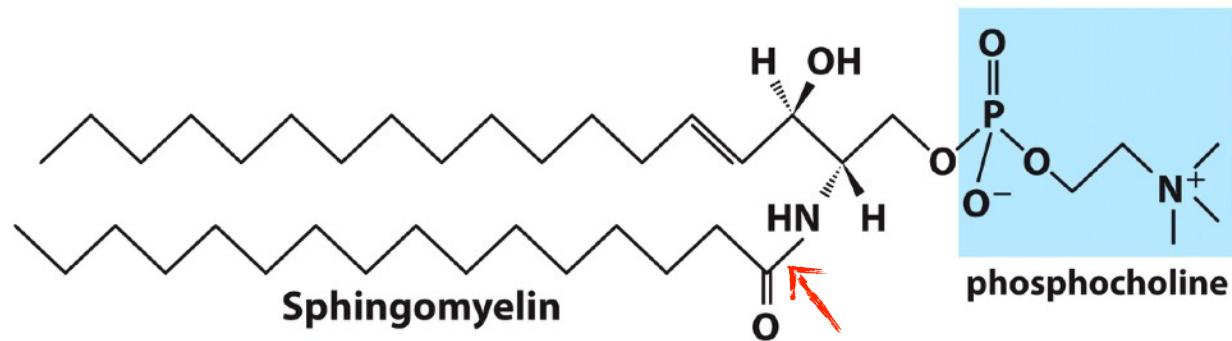
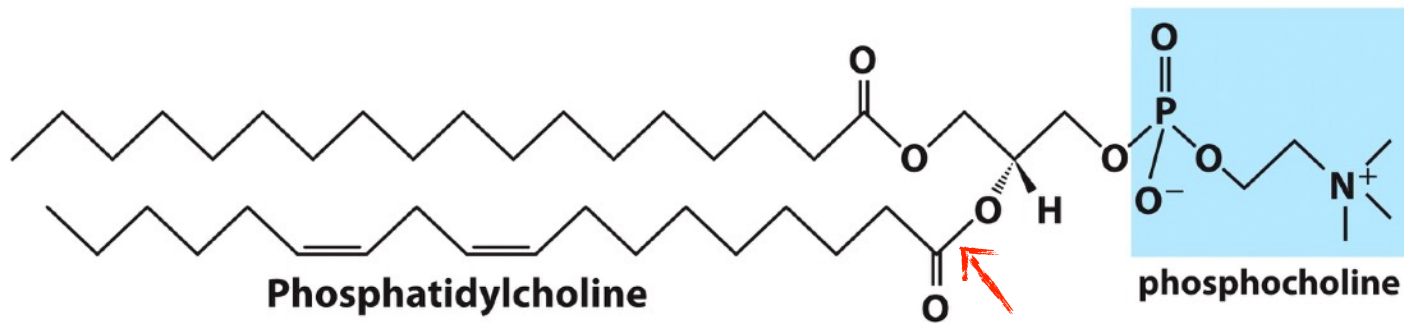
Sphingomyelins

- 鞘磷脂
- Sphingomyelins are classified as phospholipids.
 - Contain phosphocholine or phosphoethanolamine.
 - Present in plasma **membranes of animal cells.**



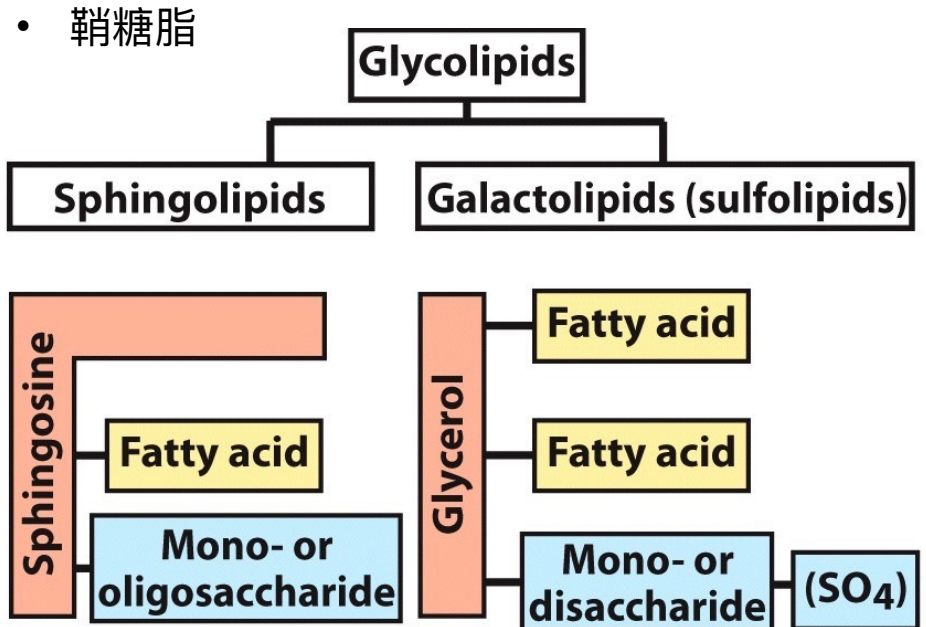
Sphingomyelins vs. Phosphatidylcholine

- Sphingomyelins are structurally similar to phosphatidylcholines.
 - Similar general properties and three-dimensional structure.
 - No net charge on head group.



Glycosphingolipids

- Glycosphingolipids are classified as glycolipids.
 - Cerebrosides have a single sugar (neutral). • 脑苷脂
 - Globosides have two or more sugars (neutral). • 红细胞糖苷脂
 - Gangliosides have oligosaccharides and Neu5Ac (negative charge). • 神经节苷脂



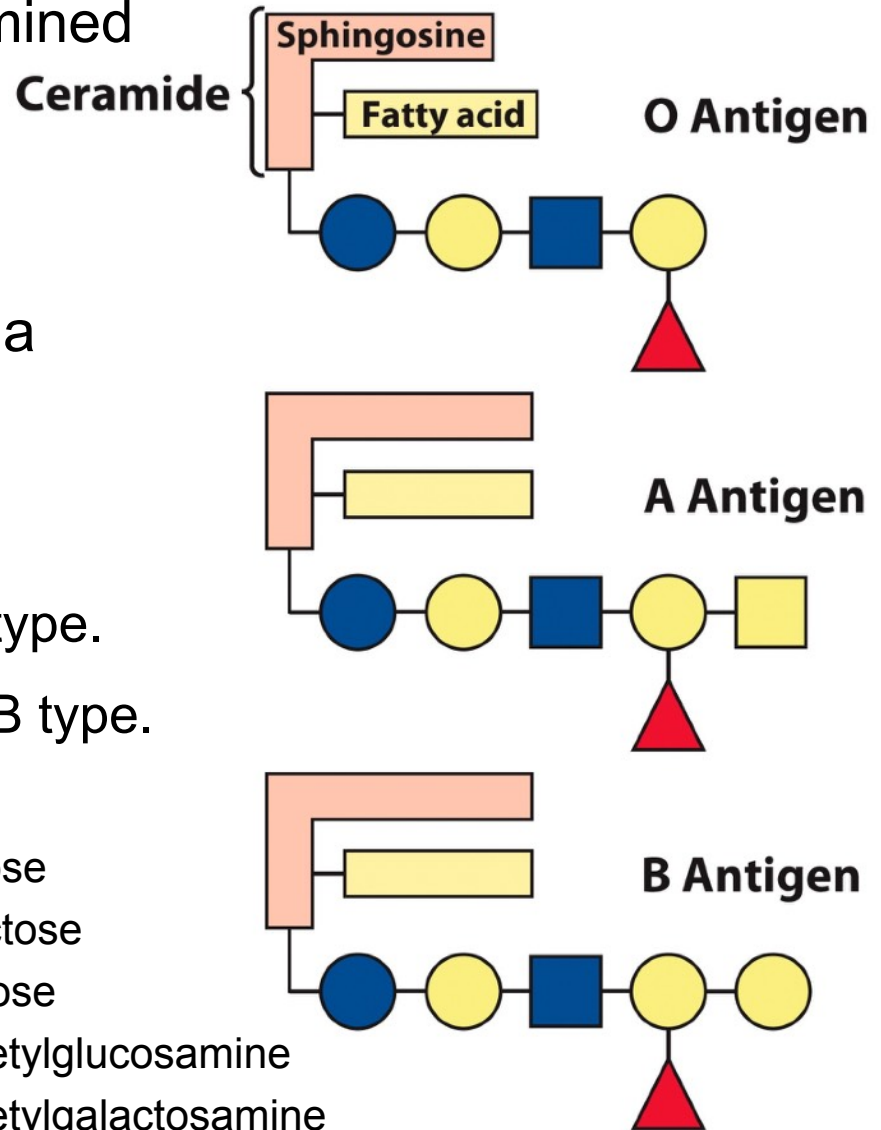
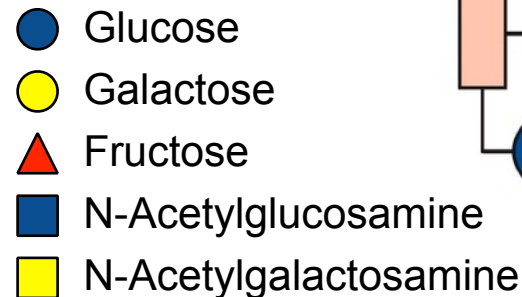
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

● Glucose
● Galactose
◆ N-Acetylneuraminic acid
■ N-Acetylgalactosamine

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

Glycosphingolipids and Blood Type

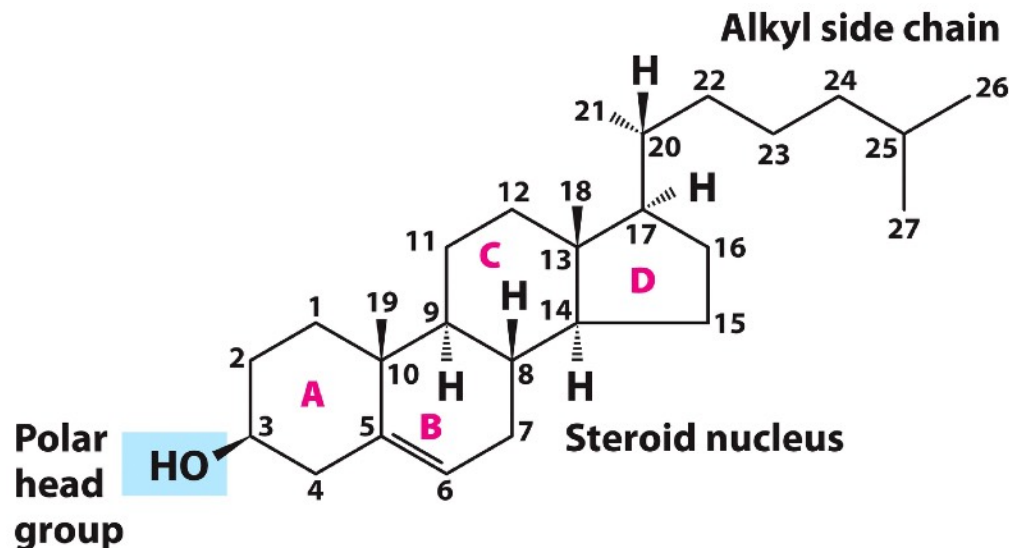
- Blood groups are in part determined by **sugar head** group in glycosphingolipids.
- Sugar structure determined by a **glycosyltransferase**.
 - No enzyme -> O type.
 - Enzyme transfers GalNAc -> A type.
 - Enzyme transfers galactose -> B type.



5. Sterols

- Sterols contain four fused rings (steroid nucleus).
 - Three with six carbons (A, B and C rings).
 - One with five carbons (D ring).
 - Almost planar and relatively rigid.
- Cholesterol is **amphipathic**.
 - Polar head group (OH group at C-3).
 - Nonpolar body (steroid nucleus and side chain at C-17).

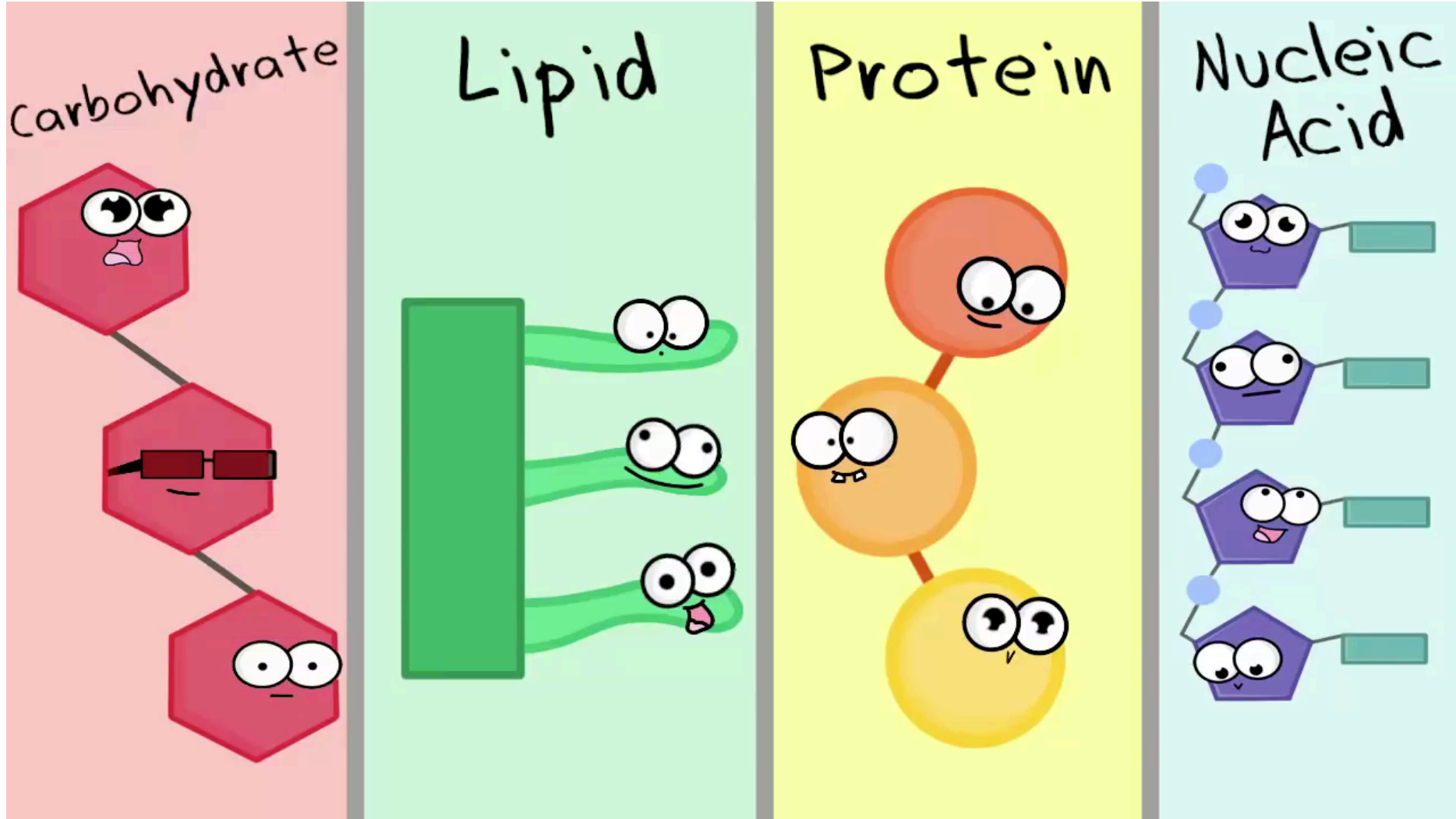
- 固醇
- 甾醇



Summary 10.2 Structural Lipids

- Polar lipids are major components of membranes. The most abundant are glycerophospholipids. It contains two fatty acids and one head group esterified to glycerol.
- Chloroplast membranes are rich in galactolipids (galactose-containing) and sulfolipids (sulfonated sugar-containing). Some archaea have long-chain alkyl groups ether-linked to glycerol at both ends.
- Sphingolipids contain sphingosine but no glycerol. Head group may include phosphate and sugar. Cholesterol has four fused rings and a hydroxyl group.

Biomolecules Review



Week 9 Chapter 10 Lipids

10.1 Storage lipids

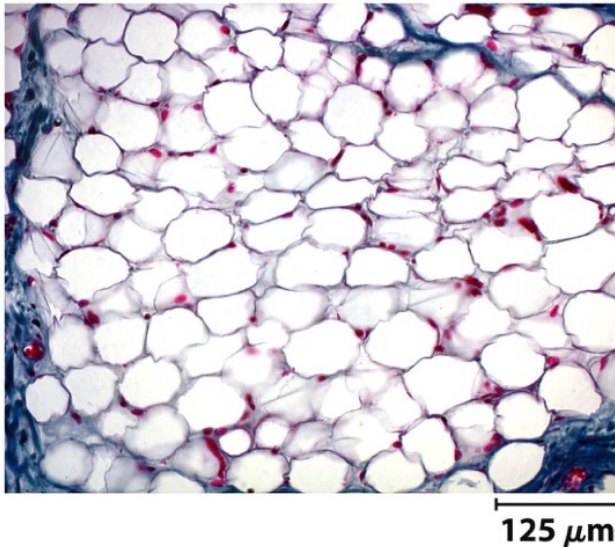
10.2 Structural lipids in membranes

10.3 Lipids as signals, cofactors and pigments

10.4 Working with lipids

Functions of Lipids

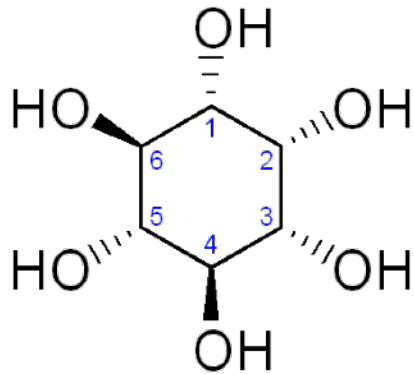
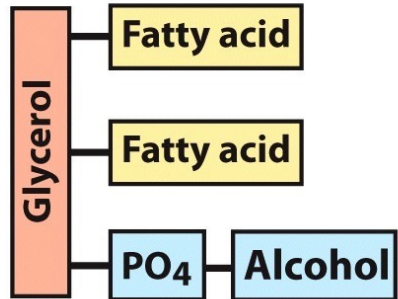
- Passive role.
 - Storage lipids, stored until oxidized by enzymes.
 - Structural lipids, impermeable barrier around a cell.
- Active role, present in much smaller amounts.
 - Signals such as hormones and intracellular messengers.
 - Enzyme cofactors.
 - Pigment molecules absorb light.



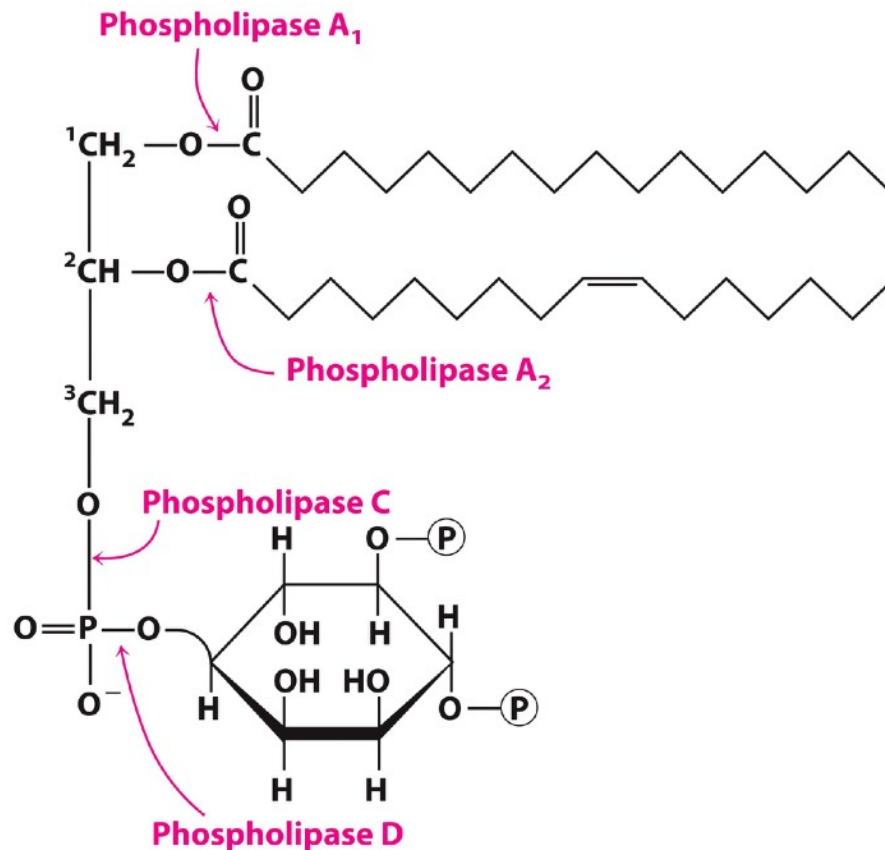
Intracellular Signal: Phosphatidylinositol

- Phosphatidylinositol and its phosphorylated derivatives.
 - Phosphatidylinositol 4,5-bisphosphate (PIP₂).

Glycerophospholipids



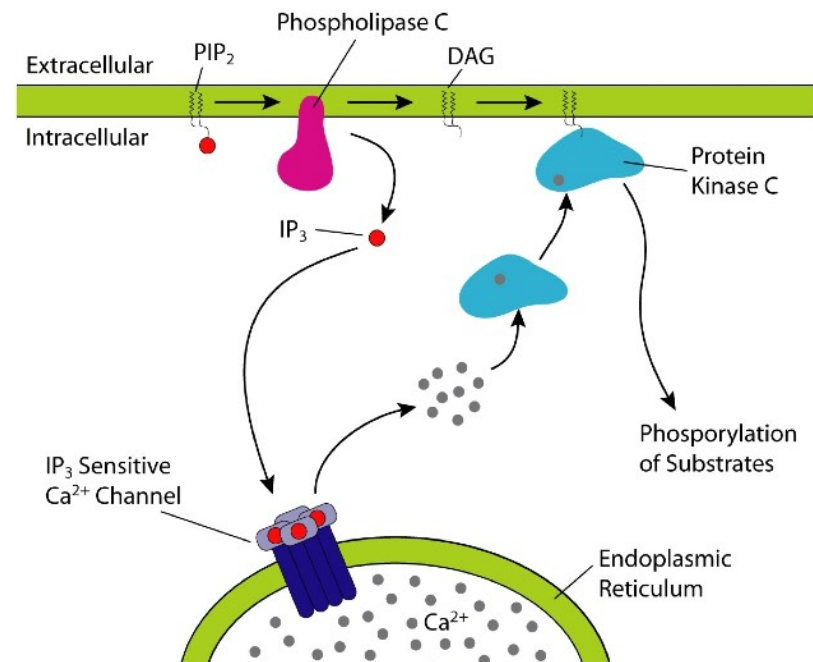
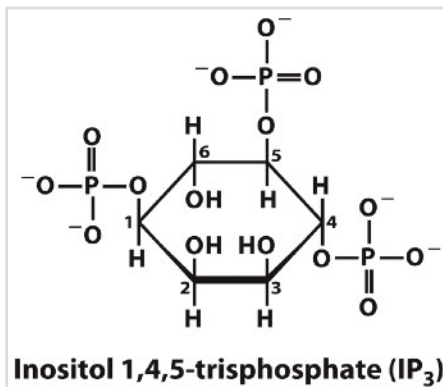
肌醇, 环己六醇 **Inositol**



Phosphatidylinositol 4,5-bisphosphate

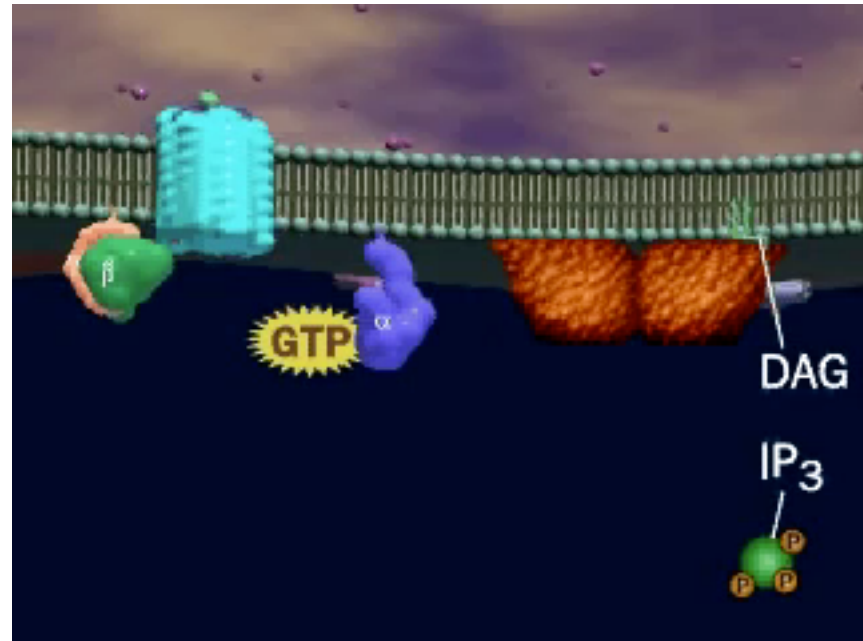
Intracellular Signal: Phosphatidylinositol

- Extracellular signals interact with surface receptors.
 - Extracellular signals activate phospholipase C in the membrane.
 - Phospholipase C hydrolyzes PIP₂.
- Two products act as intracellular messengers.
 - Inositol 1,4,5-trisphosphate (IP₃) is water-soluble and enters cytoplasm.
 - Diacylglycerol (DAG) remains associated with membrane.
- Messenger to response.
 - IP₃ triggers release of Ca²⁺.
 - DAG and Ca²⁺ activate PKC.
 - PKC elicits cell's response.



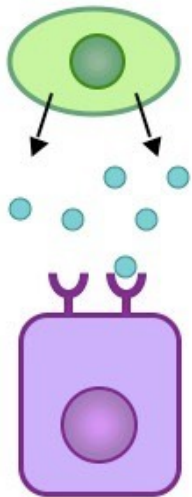
IP₃ Trigger Calcium Release

- Phospholipase C is activated.
 - Substrate: phosphatidylinositol 4,5-bisphosphate (PIP₂).
 - Phospholipase C hydrolyzes PIP₂.
- Two products act as intracellular messengers.
 - Inositol 1,4,5-trisphosphate (IP₃) and diacylglycerol (DAG).
- IP₃ binds to calcium channel on smooth endoplasmic reticulum.
 - Channel opens.
 - Ca²⁺ ions flood into cytosol.
 - Lead to cellular responses.

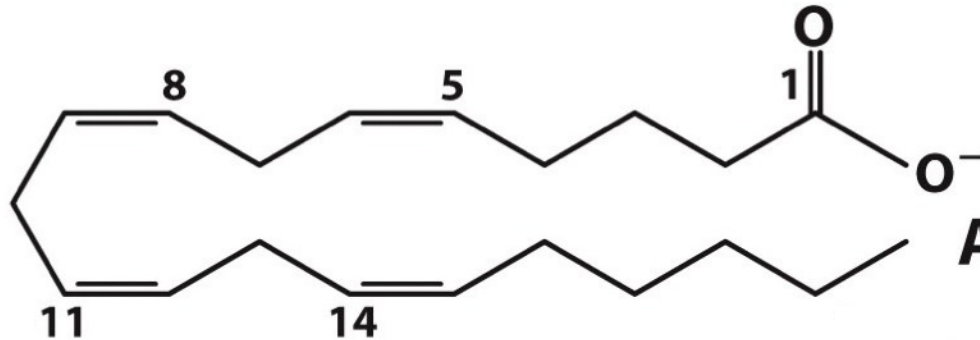


Paracrine Signaling

- Cell communication with nearby cells.
 - Paracrine factors secreted to **immediate** extracellular environment.
 - Signaling molecules diffuse over a relatively **short** distance.
- **Eicosanoids** are paracrine (local) hormones.
 - Act only on cells near point of hormone synthesis.
 - Derived from arachidonic acid 20:4($\Delta^{5,8,11,14}$).
 - Involved in fever, pain, blood clotting and other processes.



Paracrine

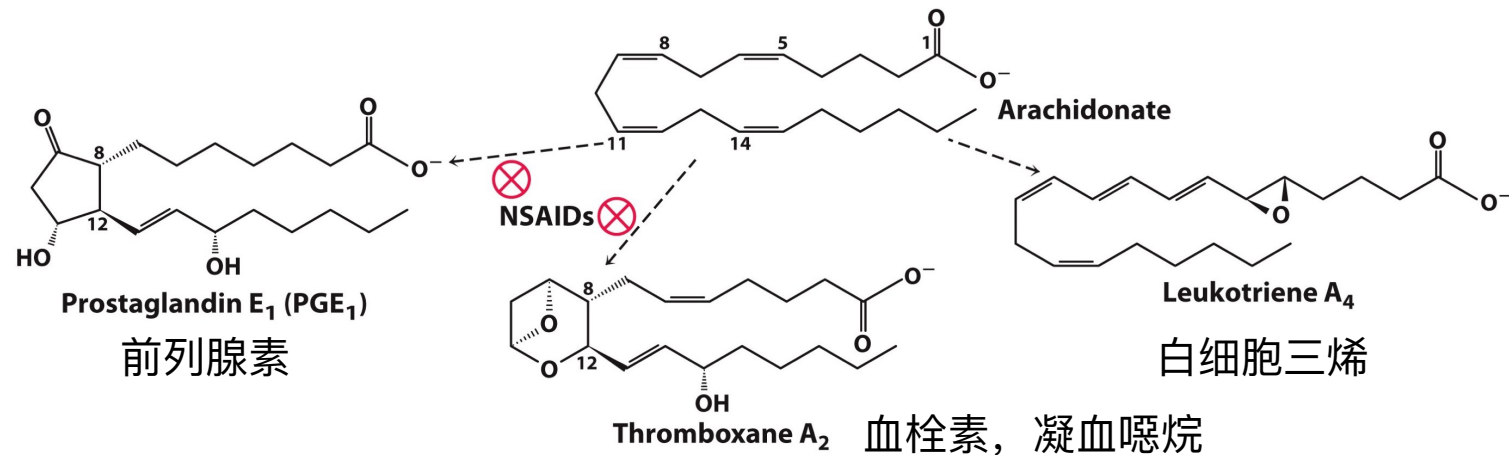


Arachidonate

- 类二十烷酸
- 旁泌性
- 花生四烯酸

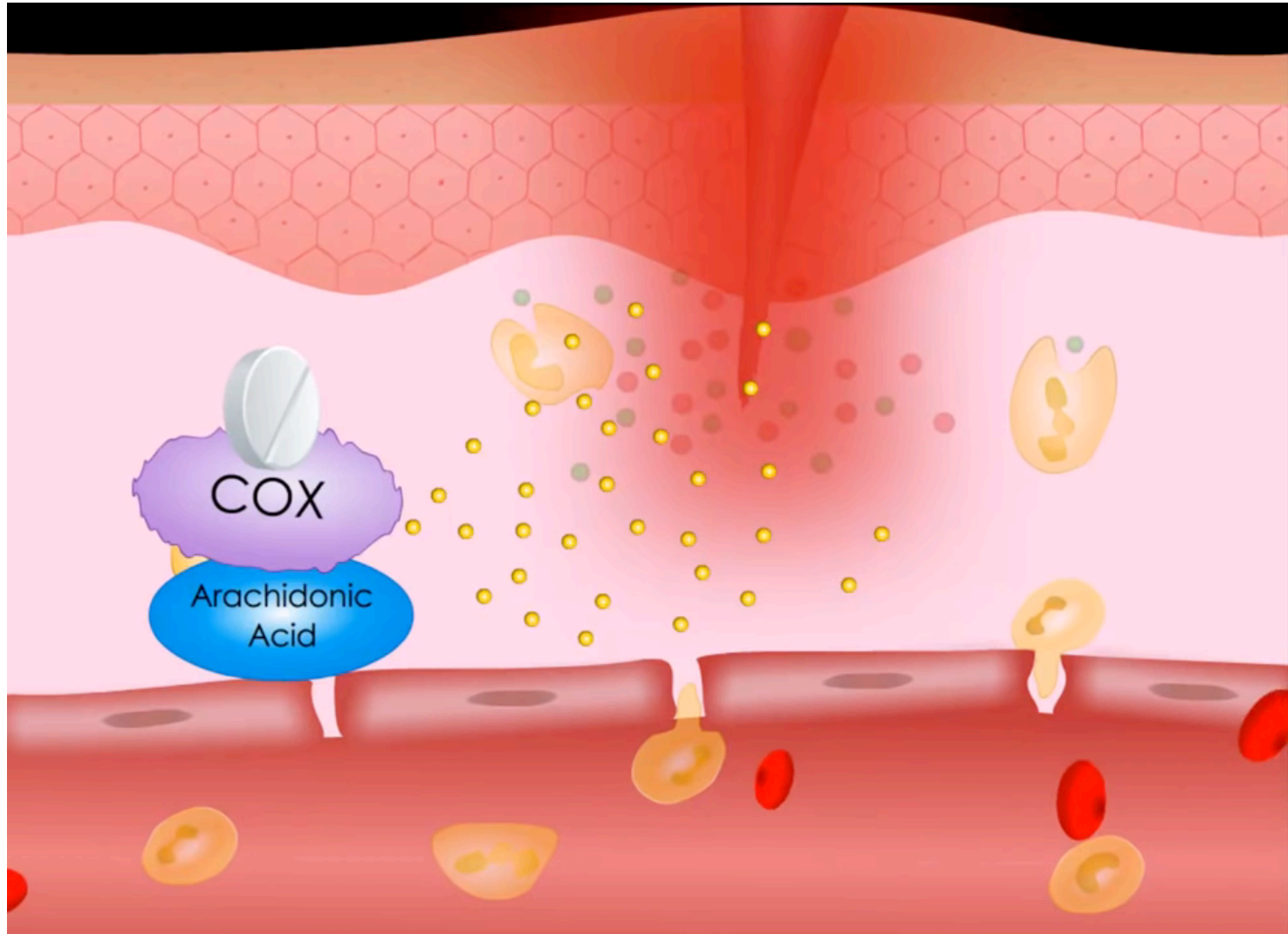
Three Classes of Eicosanoids

- Prostaglandins contain a five-carbon ring.
 - Elevate body temperature and cause inflammation and pain.
- Thromboxanes have a six-membered ring containing an ether.
 - Act in formation of blood clots.
- Leukotrienes contain three conjugated double bonds.
 - Overproduction causes asthmatic attacks.



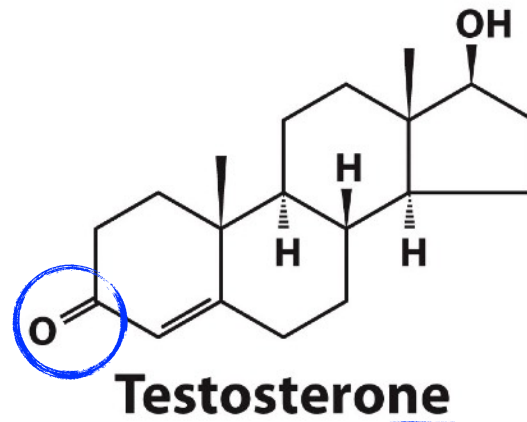
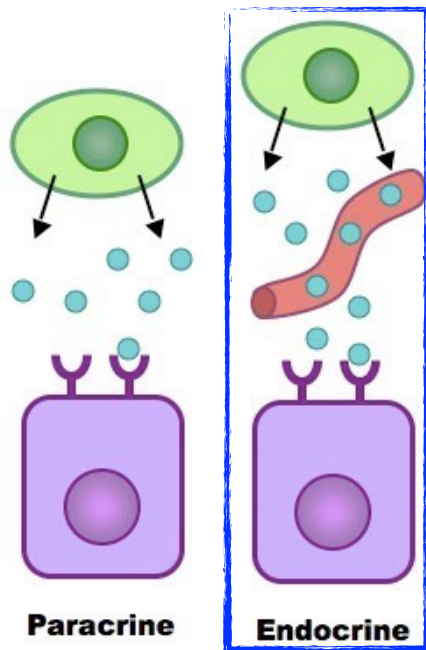
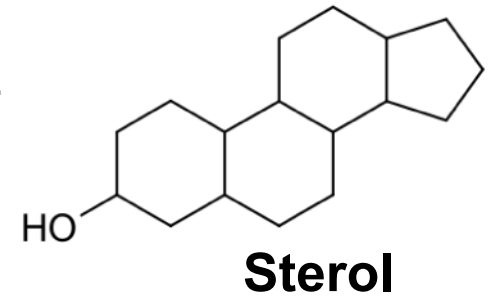
Nonsteroidal anti-inflammatory drugs (**NSAIDs**) such as **aspirin** and **ibuprofen** inhibit an enzyme involved in the conversion of arachidonate to prostaglandin and thromboxane.

How Does Aspirin Work?

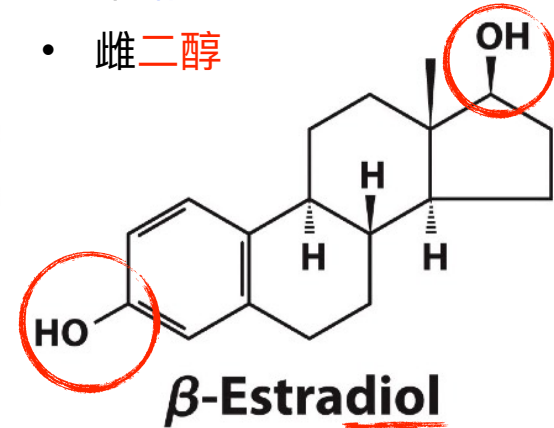


Messages Transmission between Tissues

- Steroid hormones carry messages between tissues.
 - Oxidized derivatives of sterols.
 - Have sterol nucleus but lack alkyl chain attached to D ring.
 - Move through **bloodstream** to target tissues.
- Male and female sex hormones.
 - Testosterone, male sex hormone, produced in testes.
 - Estradiol, one of female sex hormones, produced in ovaries and placenta.

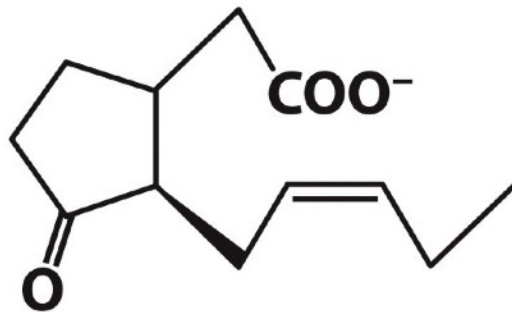


- 内分泌性
- 睾酮
- 雌二醇

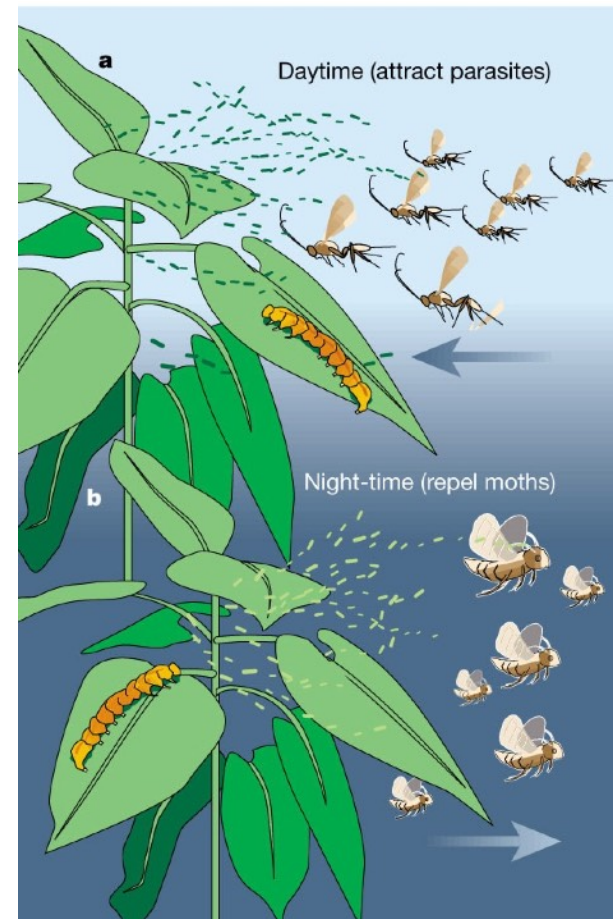


Volatile Signals for Other Organisms

- Plants produce and use volatile compounds to:
 - Attract pollinators such as bees, butterflies and beetles.
 - Repel herbivores (animals eating plants as food).
 - Communicate with other plants.
- Jasmonate is derived from fatty acid 18:3($\Delta^{9,12,15}$).
 - Triggers defense against insects.
 - **Inter-plant communication.**
 - Methyl ester of jasmonate -> fragrance of jasmine oil in perfume industry.



Jasmonate

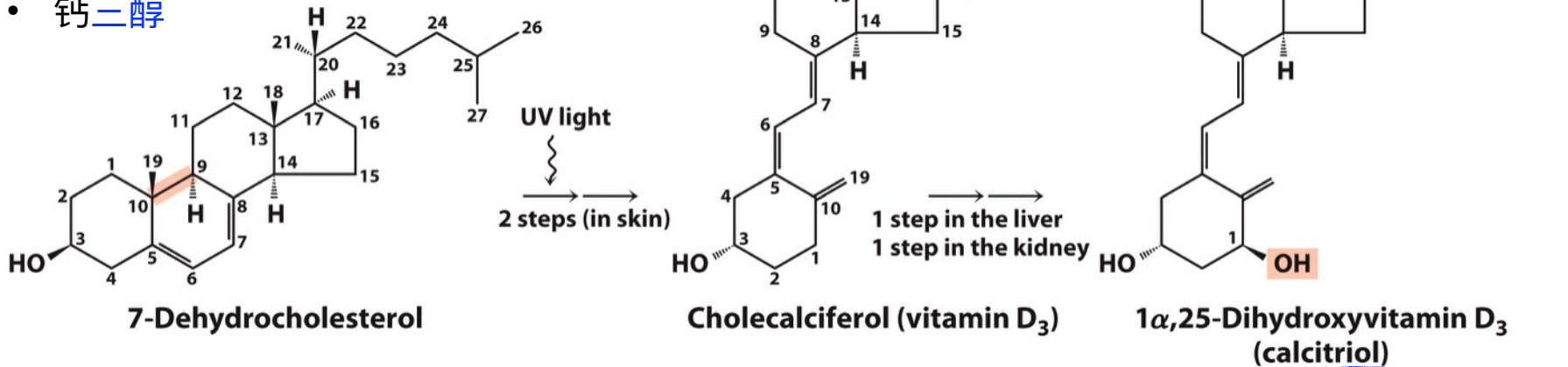


Vitamin D₃ is Hormone Precursor

- Vitamin D₃ is formed in a reaction driven by **UV light**.
 - Formed in skin from 7-dehydrocholesterol.
 - Vitamin D₃ itself is not biologically active.
 - 1 α ,25-dihydroxyvitamin D₃ regulates calcium uptake in intestine.
- Deficiency of vitamin D leads to disease **rickets**.
 - Due to inadequate calcium uptake.
 - Administration of vitamin D produces a dramatic cure.
 - Vitamin D₂ is similar to D₃, and added to milk as supplement.



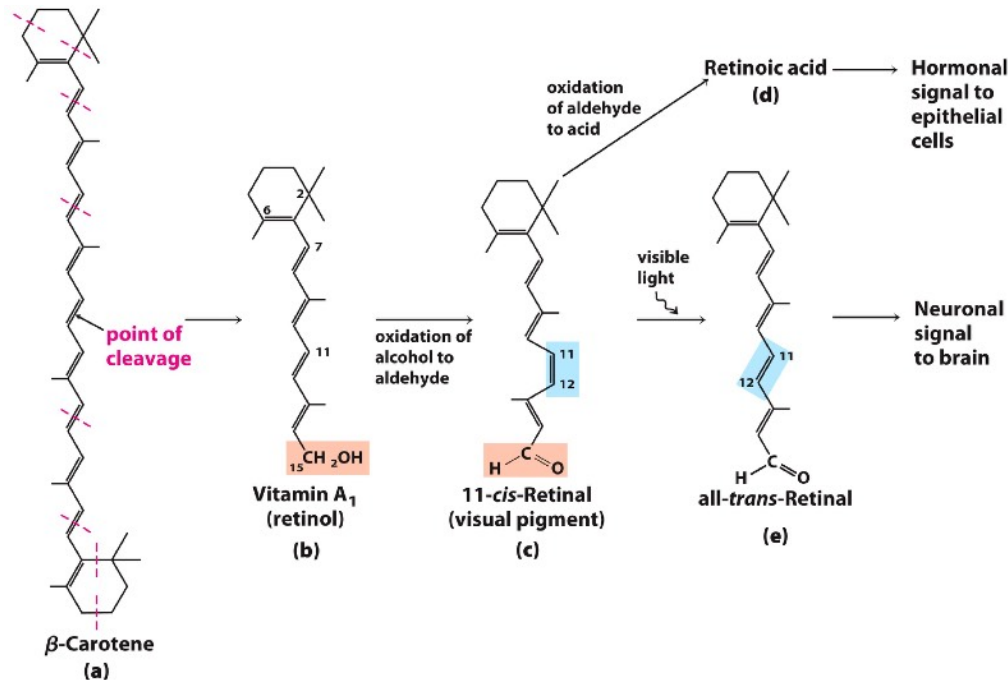
- 佝偻病, 软骨病
- 胆钙化醇
- 钙三醇



Vitamin A (Retinol) is Hormone Precursor

- Vitamin A functions as a hormone and as a visual pigment.
 - Derivative retinoic acid regulates development of epithelial tissues.
 - Derivative retinal initiates response of retina to light.
- Deficiency of vitamin A leads to night blindness.
 - Eggs and whole milk are good dietary sources.
 - β -carotene can be enzymatically converted to vitamin A in human.
 - β -carotene gives orange-yellow color to carrots and sweet potatoes.

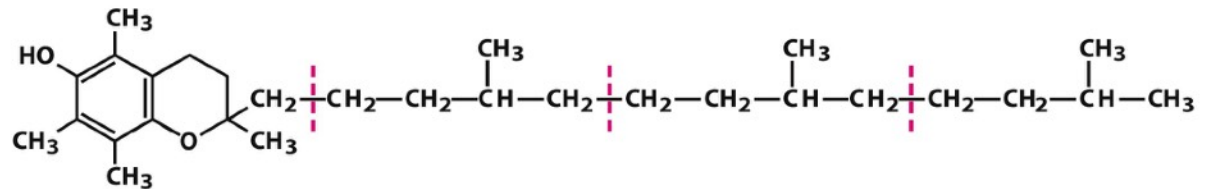
- 胡萝卜素
- 视黄醇
- 视黄醛
- 异戊二烯
- isoprene unit



Vitamin E and K are Redox Cofactors

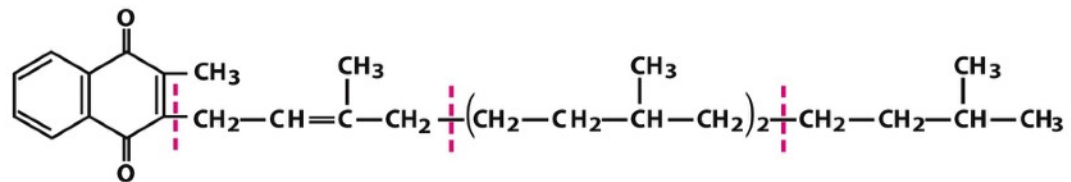
- Vitamin E functions as biological antioxidant.
 - Substituted aromatic ring and long alkyl chain (hydrophobic).
 - React with reactive oxygen radicals and **prevent oxidative damage**.
 - Vitamin E deficiency in humans is very rare.
- Vitamin K is also a redox cofactor.
 - Participates in formation of prothrombin.
 - Prothrombin is a proteolytic enzyme that converts fibrinogen to fibrin.
 - Fibrin is an insoluble protein that holds **blood clots** together.

(a)
Vitamin E: an antioxidant



- 凝血酶原
- 纤维蛋白原
- 叶绿醌

(b)
Vitamin K₁: a blood-clotting cofactor (phylloquinone)



Summary 10.3 Lipids as Signals and More

- PIP_2 is hydrolyzed to yield two intracellular messengers, DAG and IP_3 . Eicosanoids are paracrine hormones. Sex hormones are derived from sterols.
- Vitamins D, A, E and K are fat-soluble compounds.
 - Vitamin D -> calcium metabolism.
 - Vitamin A -> eye pigment.
 - Vitamin E -> oxidative damage.
 - Vitamin K -> blood clotting.
- Lipidic conjugated dienes serve as pigments in flowers and fruits, and give bird feathers their striking colors.

Week 9 Chapter 10 Lipids

10.1 Storage lipids

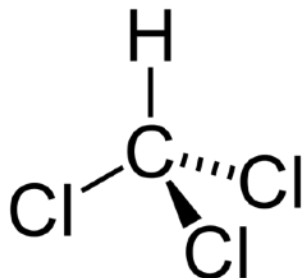
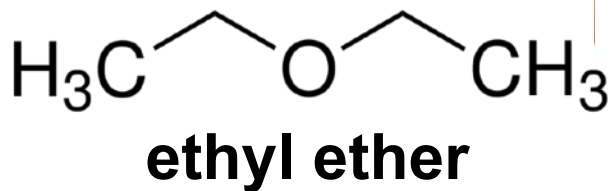
10.2 Structural lipids in membranes

10.3 Lipids as signals, cofactors and pigments

10.4 Working with lipids

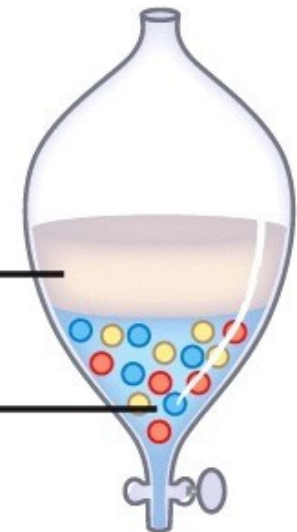
Lipid Extraction by Organic Solvents

- Lipids are **insoluble** in water.
 - Extraction and separation techniques different from purification of water-soluble molecules such as proteins, carbohydrates and nucleic acids.
 - In aqueous solution, hydrophobic interactions drive lipid clustering.
 - **Organic solvents**, such as ethyl ether and chloroform, are required.



chloroform

Methanol + water
Chloroform + lipids

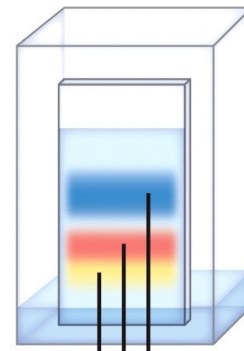


Separation due to Different Polarity

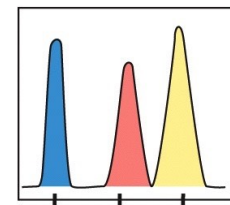
- Adsorption chromatography.
 - Polar materials such as silica gel $\text{Si}(\text{OH})_4$ packed into a glass column.
 - Neutral (nonpolar) lipids pass directly through column, and emerge first.
 - Polar lipids bind tightly to silica gel.
 - Polar lipids are eluted, in the order of increasing polarity.

- Thin-layer chromatography.
 - A thin layer of silica gel on a glass plate.
 - Lipid sample applied near bottom of plate.
 - Organic solvent rises by capillary action, and carries certain lipids with it.
 - ▶ Less polar lipids move farthest.

Thin-layer chromatography



Adsorption chromatography, gas chromatography, HPLC



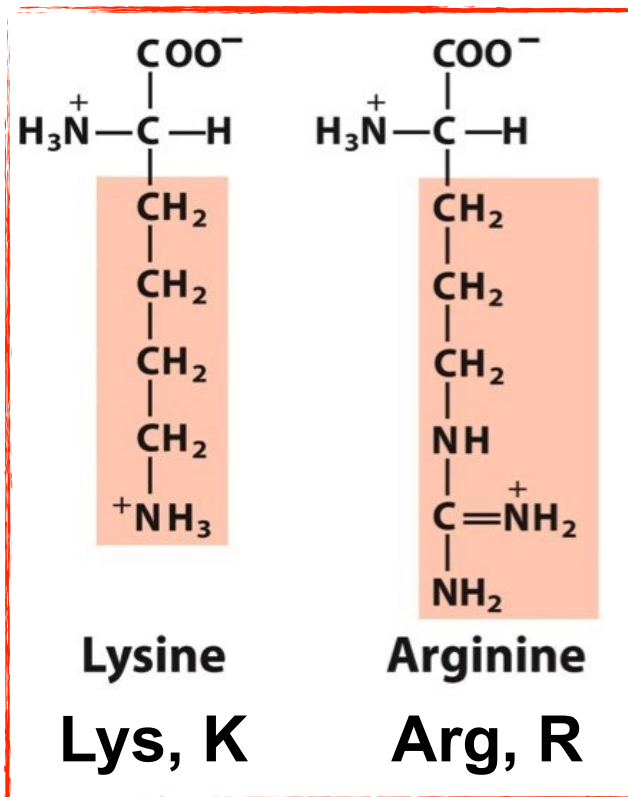
Neutral lipids (chloroform)

Polar but uncharged lipids such as cerebroside (acetone)

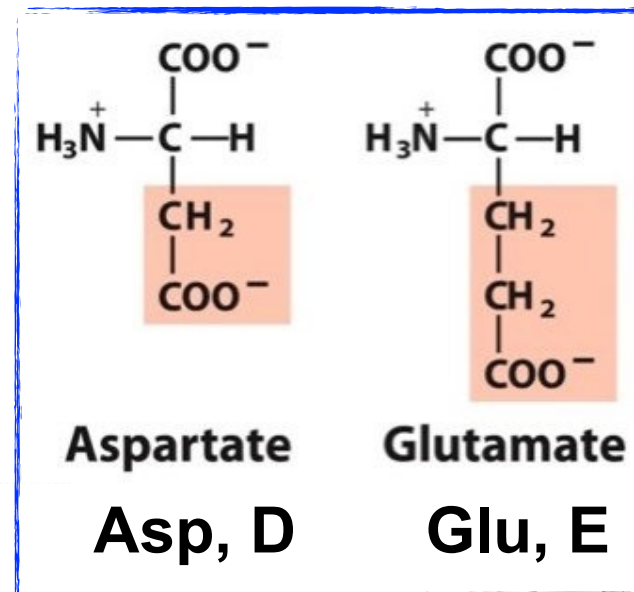
Very polar or charged lipids such as glycerophospholipids (methanol)

Summary 10.4 Working with Lipids

- Lipids are extracted from tissues with organic solvents and separated by adsorption chromatography, thin-layer chromatography or other techniques.



Amino acids
for 9th week



Example Question

Biological waxes are:

- A) diesters of glycerol and fatty acids.
- B) esters of single fatty acids with long-chain alcohols.
- C) triesters of glycerol and three long-chain fatty acids.
- D) sphingolipids.
- E) None of the above.

Example Question

Which of the following molecules or substances contain, or are derived from, fatty acids?

A) Triacylglycerols

B) Beeswax

C) Prostaglandins

D) Sphingolipids

E) All of the above contain or are derived from fatty acids.

Example Question

Fatty acids are a component of:

- A) β -carotenes.
- B) sterols.
- C) cerebrosides.
- D) vitamin E.
- E) vitamin K.

Example Question

Which of the following is *not* a consequence of partial hydrogenation of vegetable oils?

- A) Longer shelf life
- B) Reduction of some *cis* double bonds to single bonds
- C) Conversion of some *cis* double bonds to *trans* double bonds
- D) Increased risk of cardiovascular disease upon consumption by humans
- E) Lower melting temperature

Example Question

Which of the following is *not* true?

- A) Testosterone is an important male sex hormone.
- B) Lipids are more soluble in chloroform than in water.
- C) Lipids play only passive roles as energy-storage molecules.
- D) Sterols are precursors of steroid hormones.
- E) Sterols have a structure that includes four fused rings.

Example Question

Non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin and ibuprofen act by blocking production of:

- A) biological waxes
- B) prostaglandins**
- C) sphingolipids
- D) vitamin D
- E) none of the above

Example Question

Which of the following is *not* a fat-soluble vitamin?

A) A

B) D

C) C

D) E

E) K

Example Question

Identify the molecule(s) derived from sterols.

- A) Arachidonic acid
- B) Phosphatidylcholine
- C) Cerebroside
- D) Prostaglandins
- E) β -Estradiol

Example Question

What is the structural relationship between sphingosine and ceramide?

Example Question

Match the compounds on the left with the important roles they play listed on the right.

- | | | |
|--------------------|----------|--------------------------------|
| (a) prostaglandins | <u>d</u> | blood clotting |
| (b) vitamin E | <u>e</u> | intra-tissue messengers |
| (c) vitamin A | <u>c</u> | necessary for sight |
| (d) thromboxanes | <u>a</u> | mediates pain and inflammation |
| (e) steroids | <u>b</u> | reducing agent |

Example Question

Match each of these vitamins with its biological role: Vitamins A, D, E, K.

 K blood clotting

 A vision

 D Ca²⁺ metabolism

 E prevention of oxidative damage