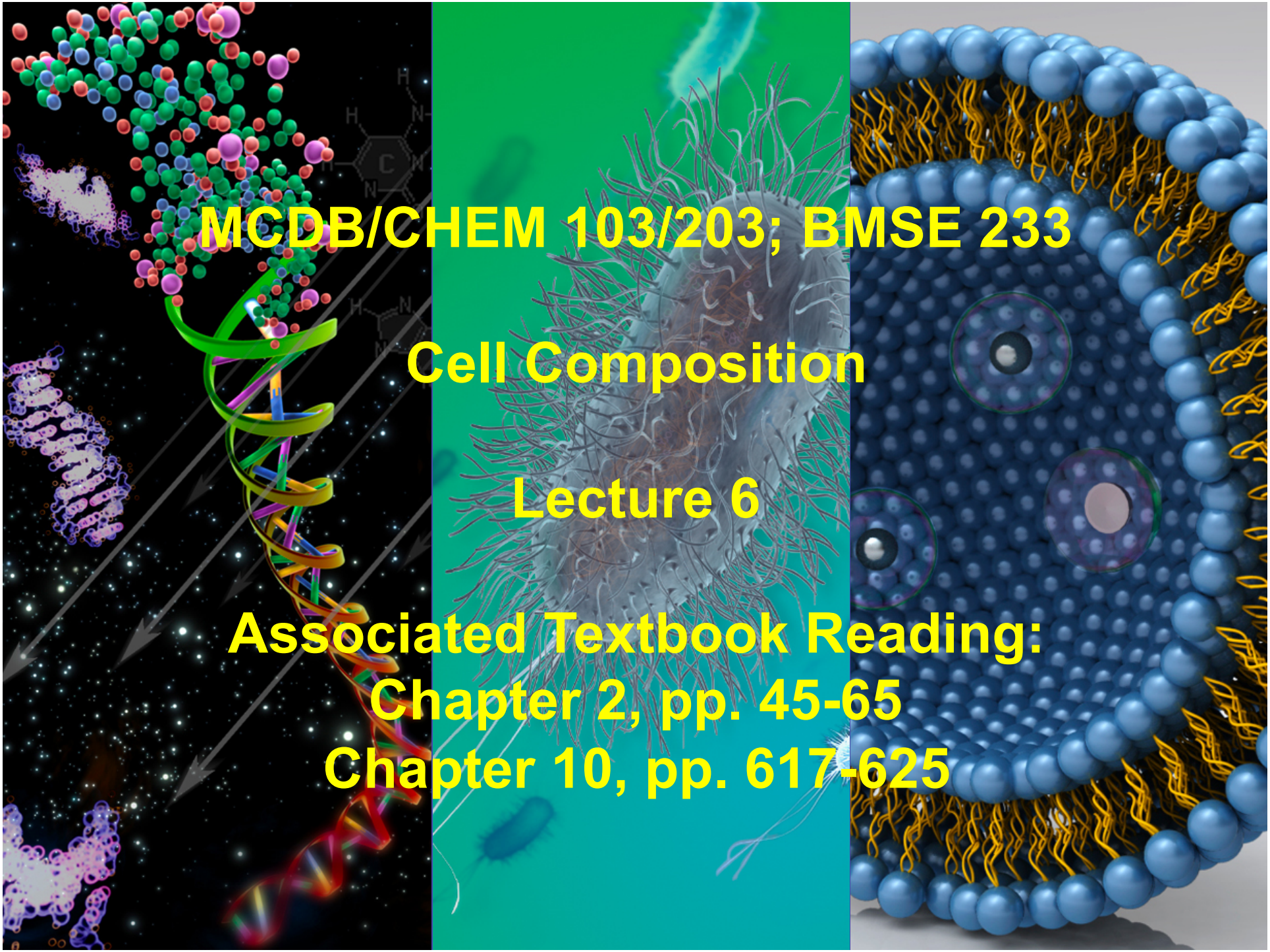


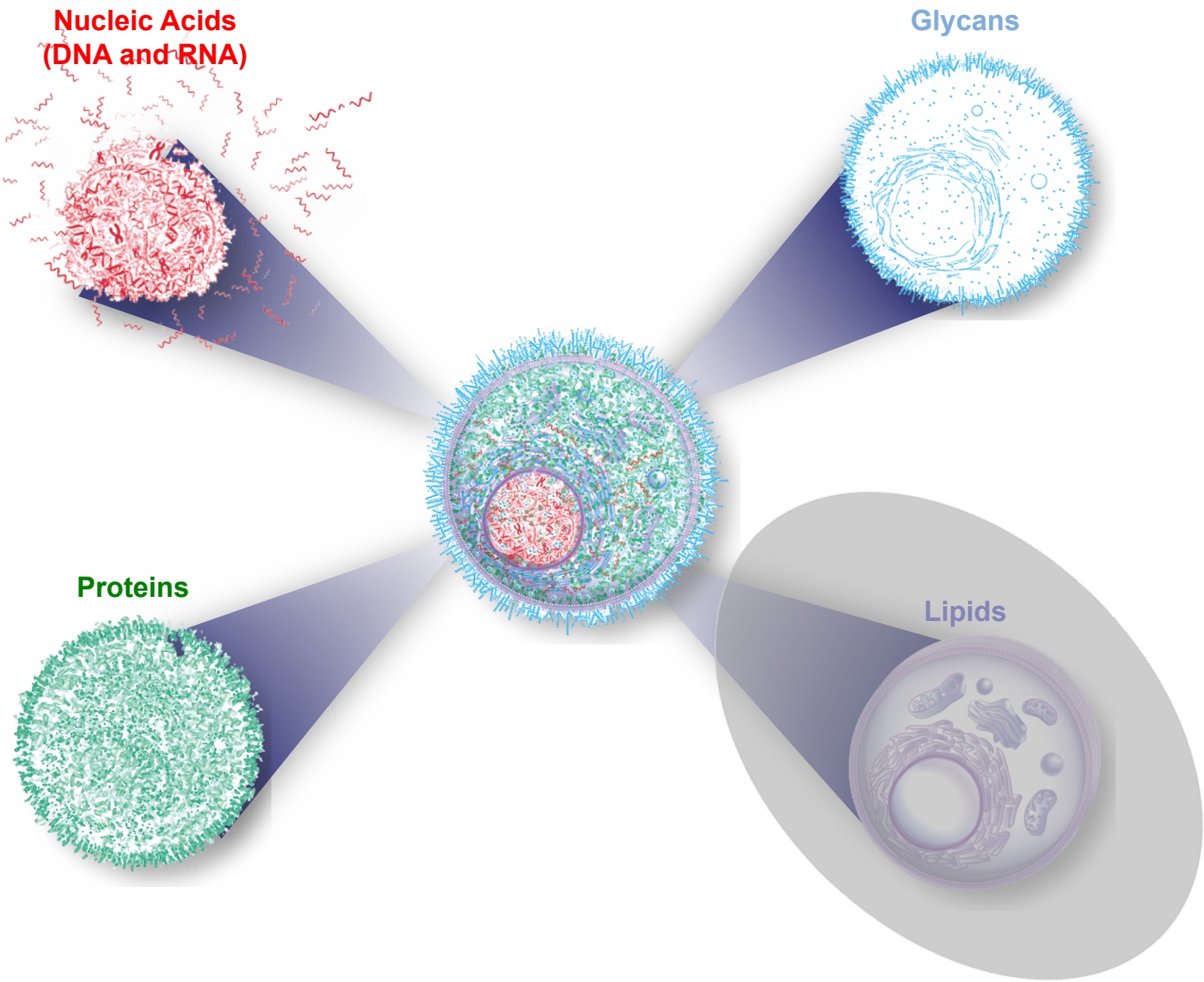
MCDB/CHEM 103/203; BMSE 233

Cell Composition

Lecture 6

Associated Textbook Reading:
Chapter 2, pp. 45-65
Chapter 10, pp. 617-625

Cells are Composed of Four Types of Molecular Components



THE CLASSIFICATION OF LIPIDS

Eight (8) Lipid Categories:

Fatty acyls
Glycerolipids
Glycerophospholipids
Sphingolipids
Sterol lipids
Prenol lipids
Saccharolipids
Polyketides

It is more important to understand the general properties of lipids than to memorize their specific structures.

LIPIDS

Fatty acyls: a generic term for describing conjugates and derivatives of a diverse group of molecules synthesized by chain-elongation of an acetyl-CoA primer with malonyl-CoA or methylmalonyl-CoA groups in a process called fatty acid synthesis.

Glycerolipids: Composed mainly of mono-, di- and tri-substituted glycerols, most well-known being the fatty acid esters of glycerol (triacylglycerols), also known as triglycerides.

Glycerophospholipids: also referred to as phospholipids, are ubiquitous in nature and are key components of the lipid bilayer of cells, as well as being involved in metabolism and cell signaling.

LIPIDS

Sphingolipids: a complex family of compounds that share a common structural feature, a sphingoid base backbone that is synthesized de novo from the amino acid serine and a long-chain fatty acyl CoA, then converted into ceramides, phosphosphingolipids, glycosphingolipids and other compounds.

Sterol lipids: such as cholesterol and its derivatives, are an important component of membrane lipids

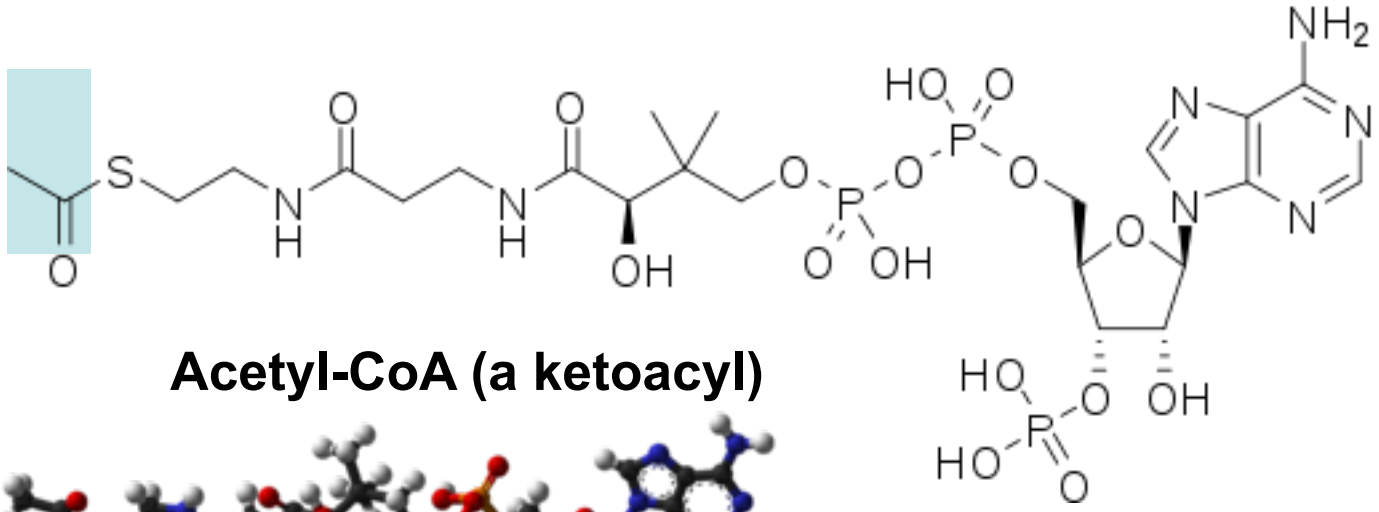
Prenol lipids: are synthesized from the 5-carbon precursors isopentenyl diphosphate and dimethylallyl diphosphate that are produced mainly via the mevalonic acid (MVA) pathway.

Saccharolipids: compounds in which fatty acids are linked directly to a sugar backbone, forming structures that are compatible with membrane bilayers.

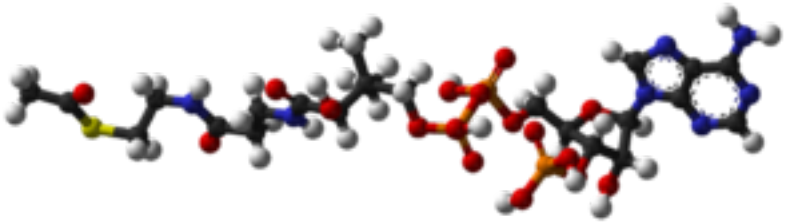
Polyketides: synthesized by polymerization of acetyl and propionyl subunits by classic enzymes as well as iterative and multimodular enzymes that share mechanistic features with the fatty acid synthases.

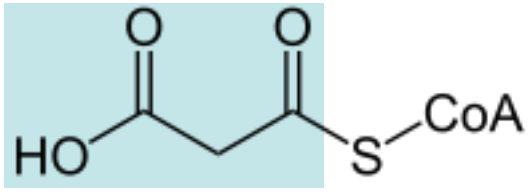
LIPID SYNTHESIS

Most lipids originate entirely or in part from two distinct types of biochemical subunits or "building blocks": ketoacyls and isoprenes.

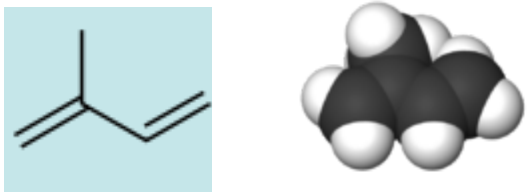


Acetyl-CoA (a ketoacyl)





Malonyl-CoA (a ketoacyl)



Isoprene

Functions of lipids

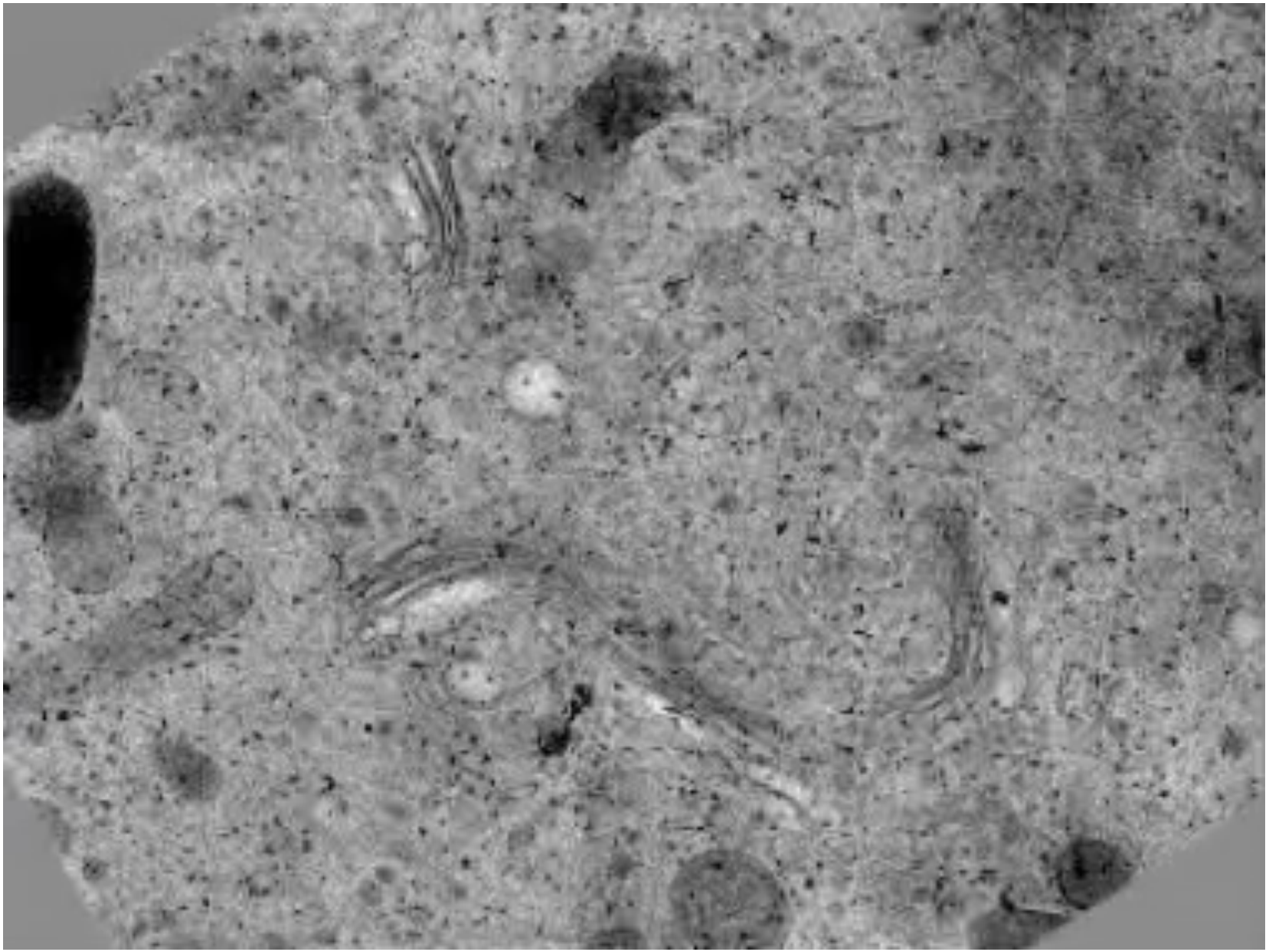
Structural:

Permeability barrier of a cell (plasma membrane) and cellular compartments (internal membranes)

Signaling:

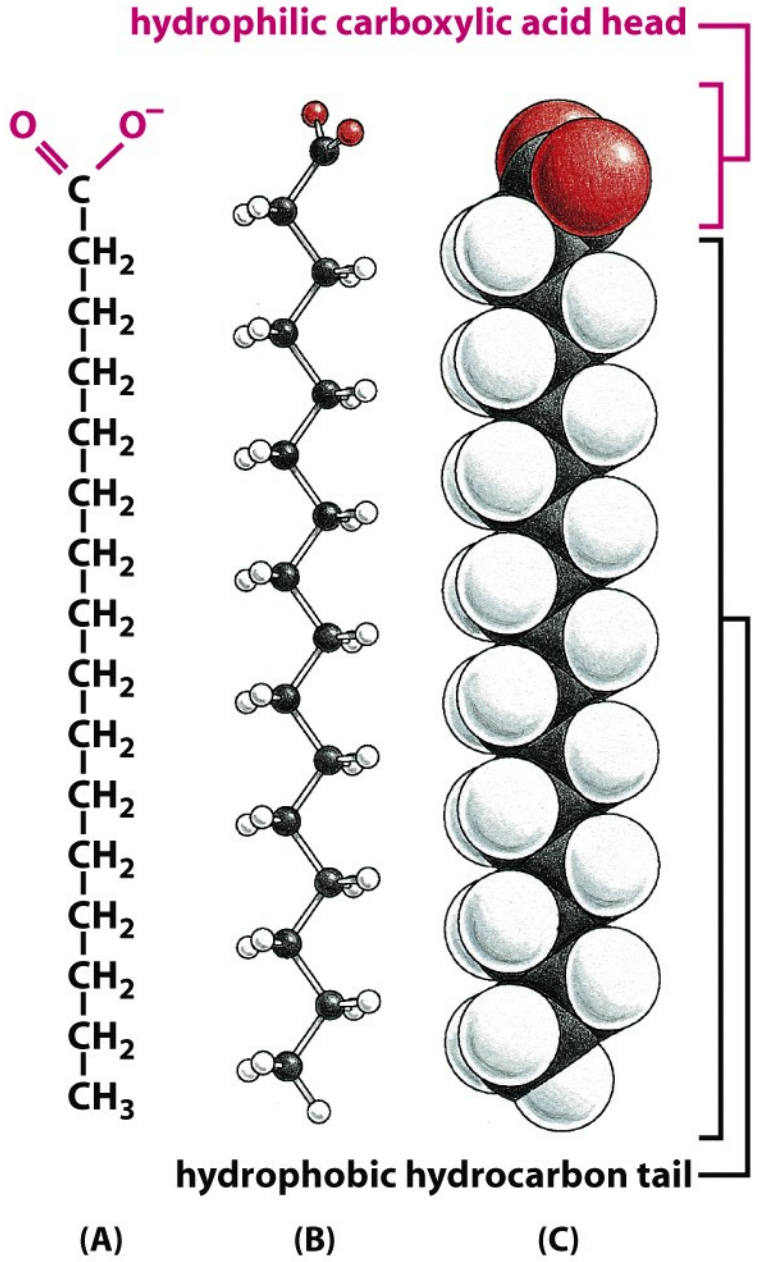
Energy storage, organization of cell signaling complexes & sources of signaling molecules

Membranes Define Cell Compartments (Movie)



Membrane Lipids:

Generic fatty acid



Most Lipids are Amphipathic Molecules

Definition of a hydrophilic molecules

Definition of a hydrophobic molecules

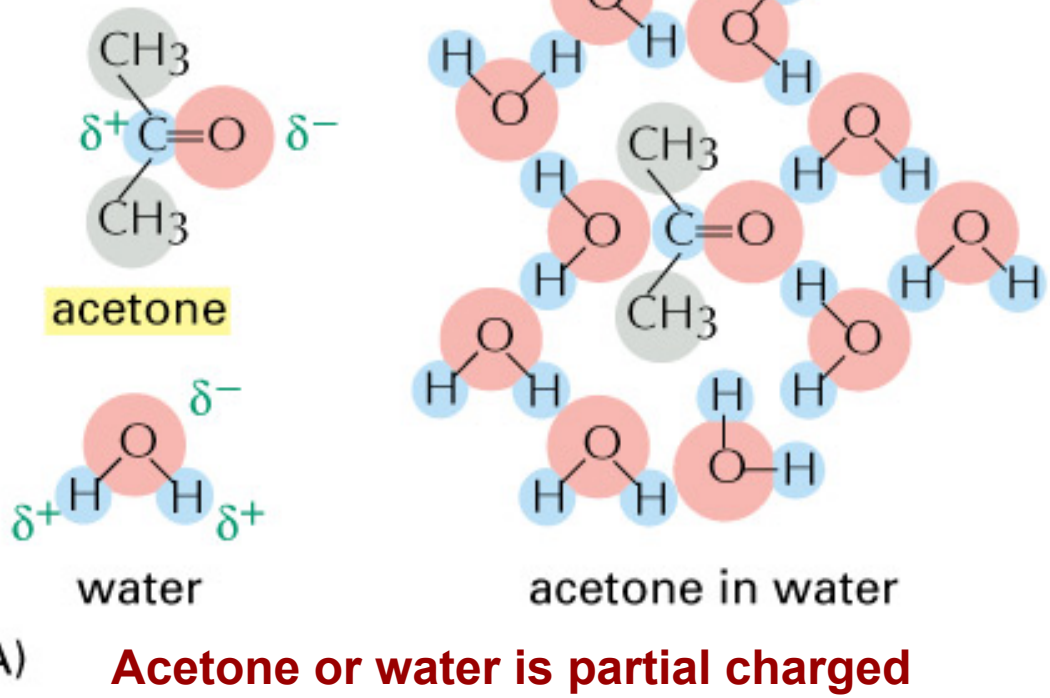
Definition of an amphipathic molecules

Hydrophilic (water-loving) molecules

A molecule is hydrophilic if it is charged or polar (partial charged)

Na+

Na+ is charged



(A) **Acetone or water is partial charged**

Na+, acetone and water are hydrophilic

What would happen if you mix acetone with water?

electrostatic interaction between acetone and surrounding water molecule

↓

energetically favorable

↓

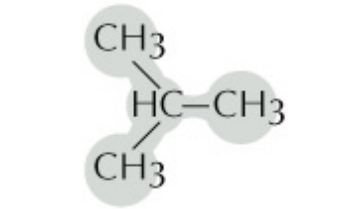
soluble in water

hydrophilic likes hydrophilic

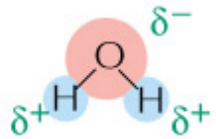
Hydrophobic (water-fearing) molecules

A molecule is hydrophobic if it is nonpolar (no charge or partial charge)

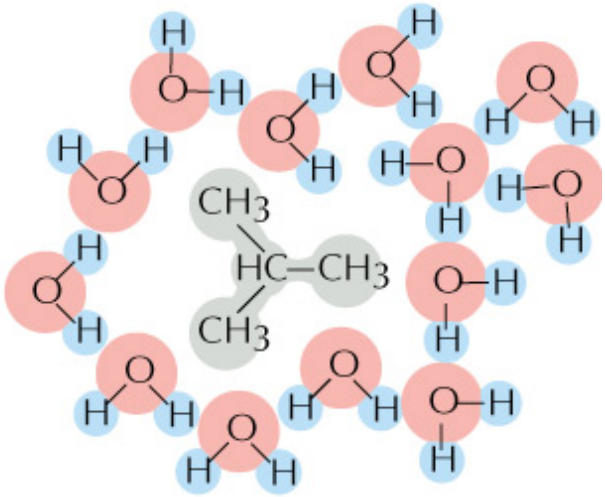
2-methyl propane is not charged



2-methyl propane



water



2-methyl propane in water

water is partially charged

2-methyl propane is hydrophobic

What would happen if you mix 2-methylpropane with water?

no electrostatic interaction between 2-methyl propane and surrounding water molecule

↓

energetically unfavorable

↓

insoluble in water

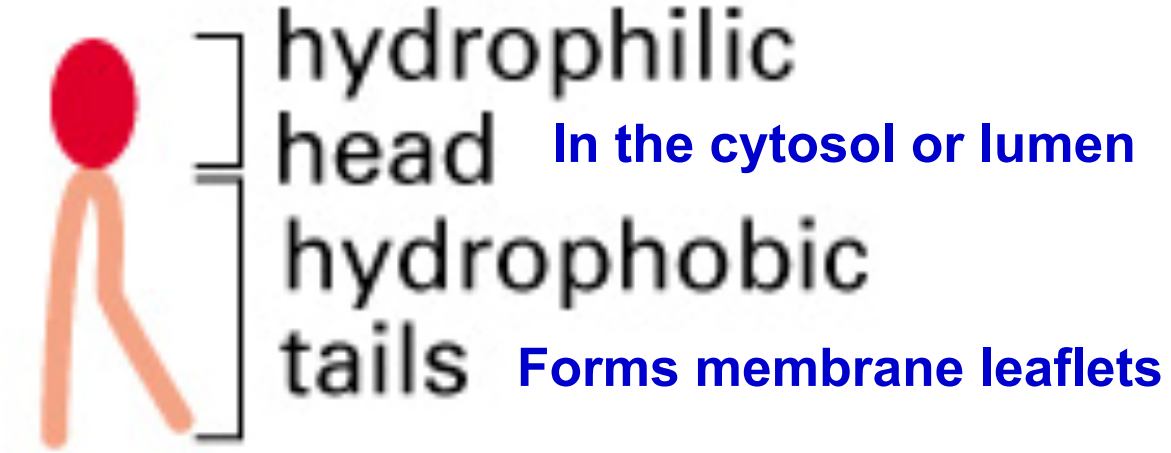
hydrophobic likes hydrophobic

Most Lipid Molecules are Amphipathic

Amphipathic molecules have both hydrophobic and hydrophilic properties.

A lipid molecule is typically composed of a hydrophilic "head" and one or two hydrophobic "tails".

A common membrane lipid structure



Most lipids have two tails, while some have only one tail.

Head and tail domains of a lipid molecule interact with water differently.

.

What would happen if you put many lipid molecules together?

Major types of lipids in animal cells

Phospholipids

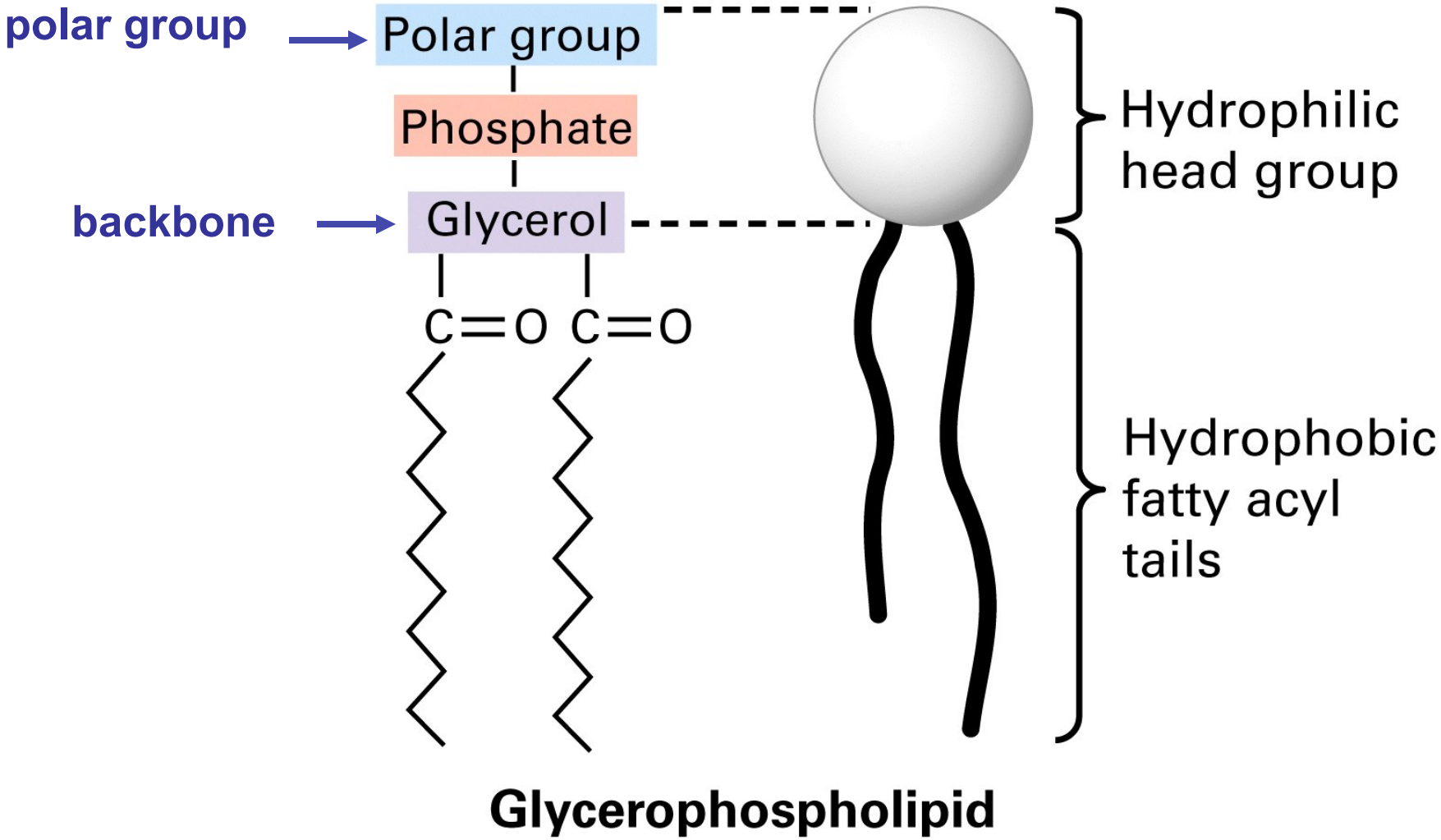
Glycolipids

Sterols

It is more important to understand the general properties of these lipids than to memorize their specific structures.

Phospholipids are the most abundant lipids

Glycerophospholipid is the most common type of phospholipid



Glycerophospholipid

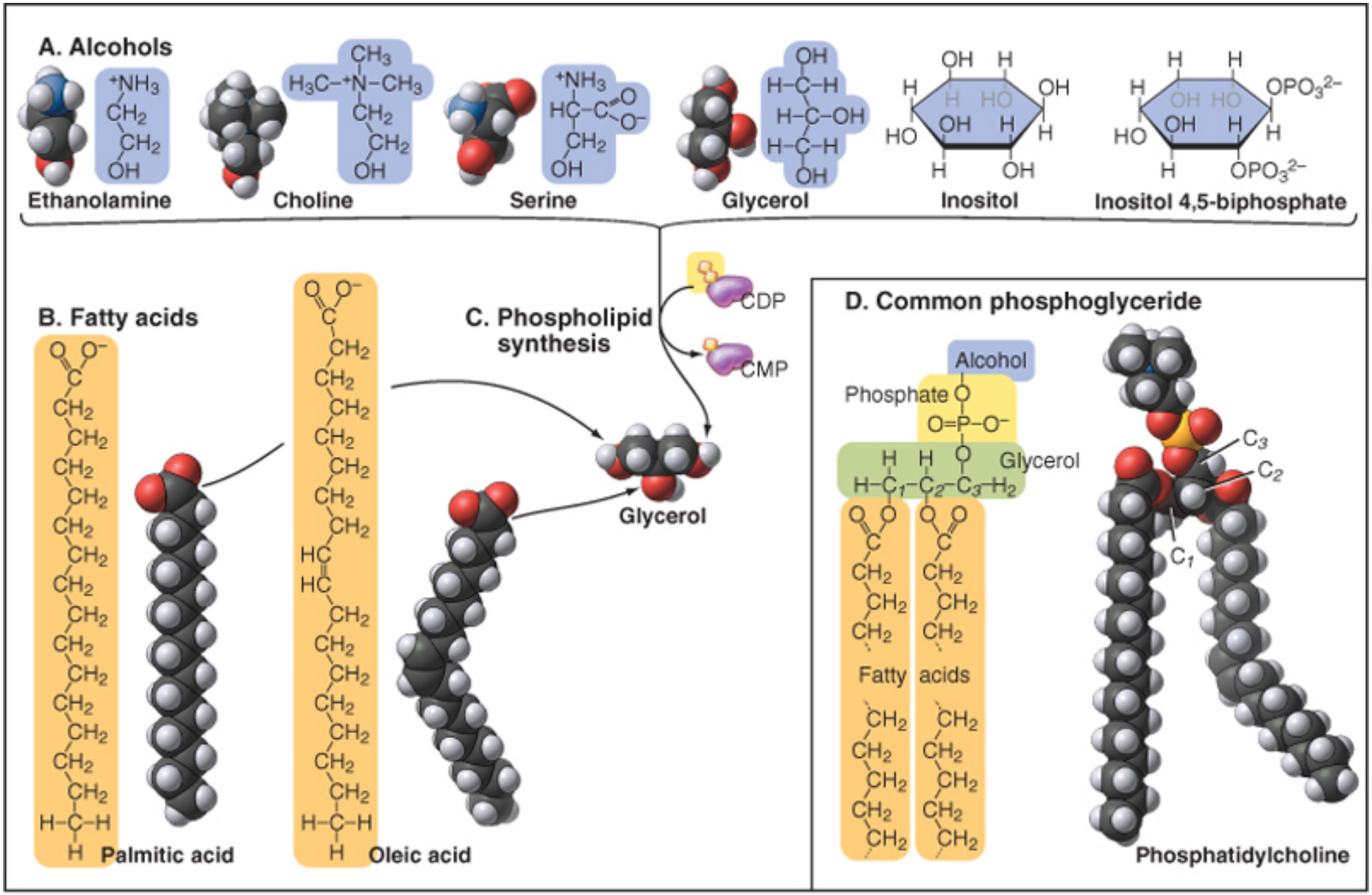
LIPIDS

TABLE 2-4 Fatty Acids That Predominate in Phospholipids

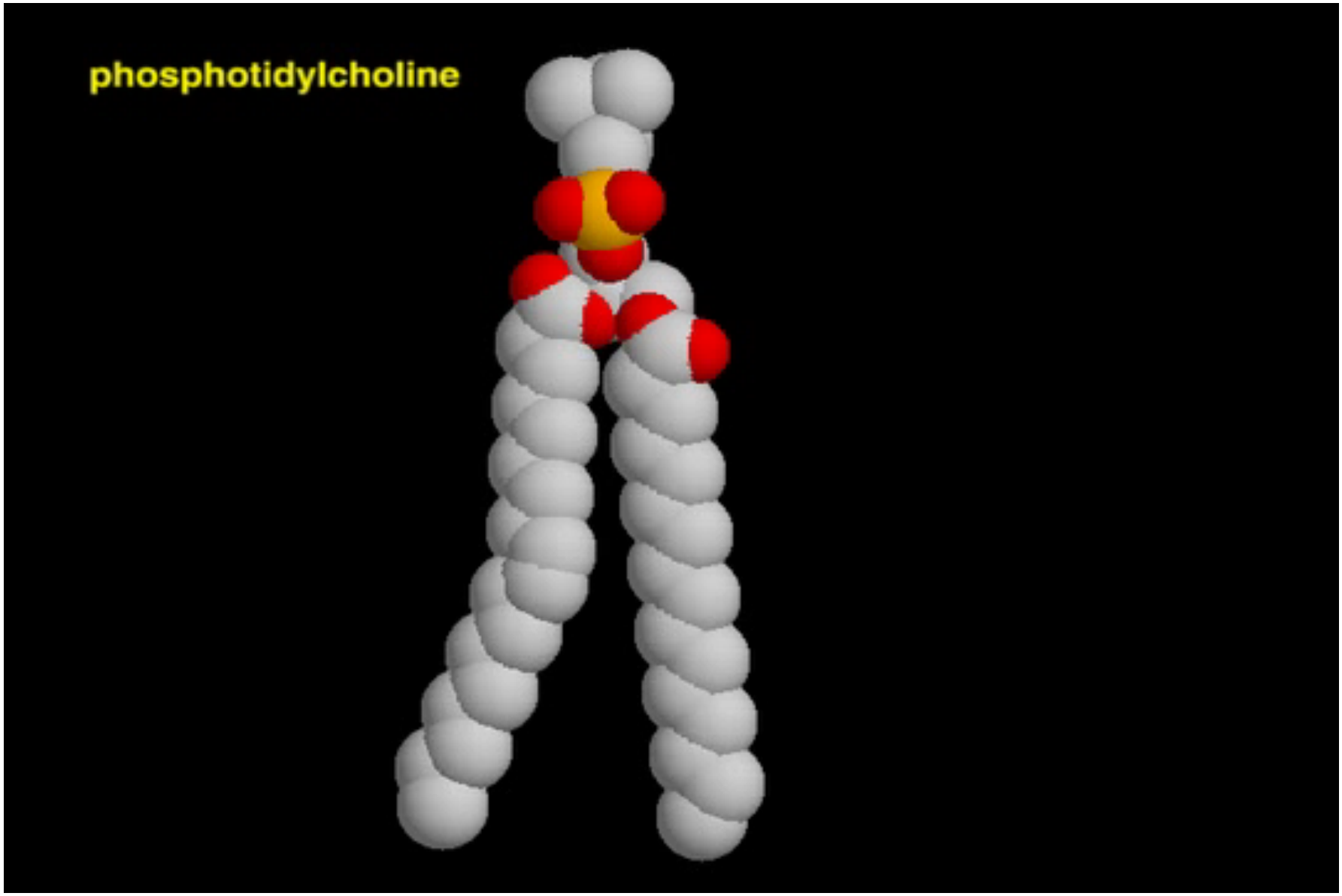
COMMON NAME OF ACID (IONIZED FORM IN PARENTHESES)	ABBREVIATION	CHEMICAL FORMULA
SATURATED FATTY ACIDS		
Myristic (myristate)	C14:0	$CH_3(CH_2)_{12}COOH$
Palmitic (palmitate)	C16:0	$CH_3(CH_2)_{14}COOH$
Stearic (stearate)	C18:0	$CH_3(CH_2)_{16}COOH$
UNSATURATED FATTY ACIDS		
Oleic (oleate)	C18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Linoleic (linoleate)	C18:2	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
Arachidonic (arachidonate)	C20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_3CH{=}CH(CH_2)_3COOH$

Table 2-4
Molecular Cell Biology, Sixth Edition

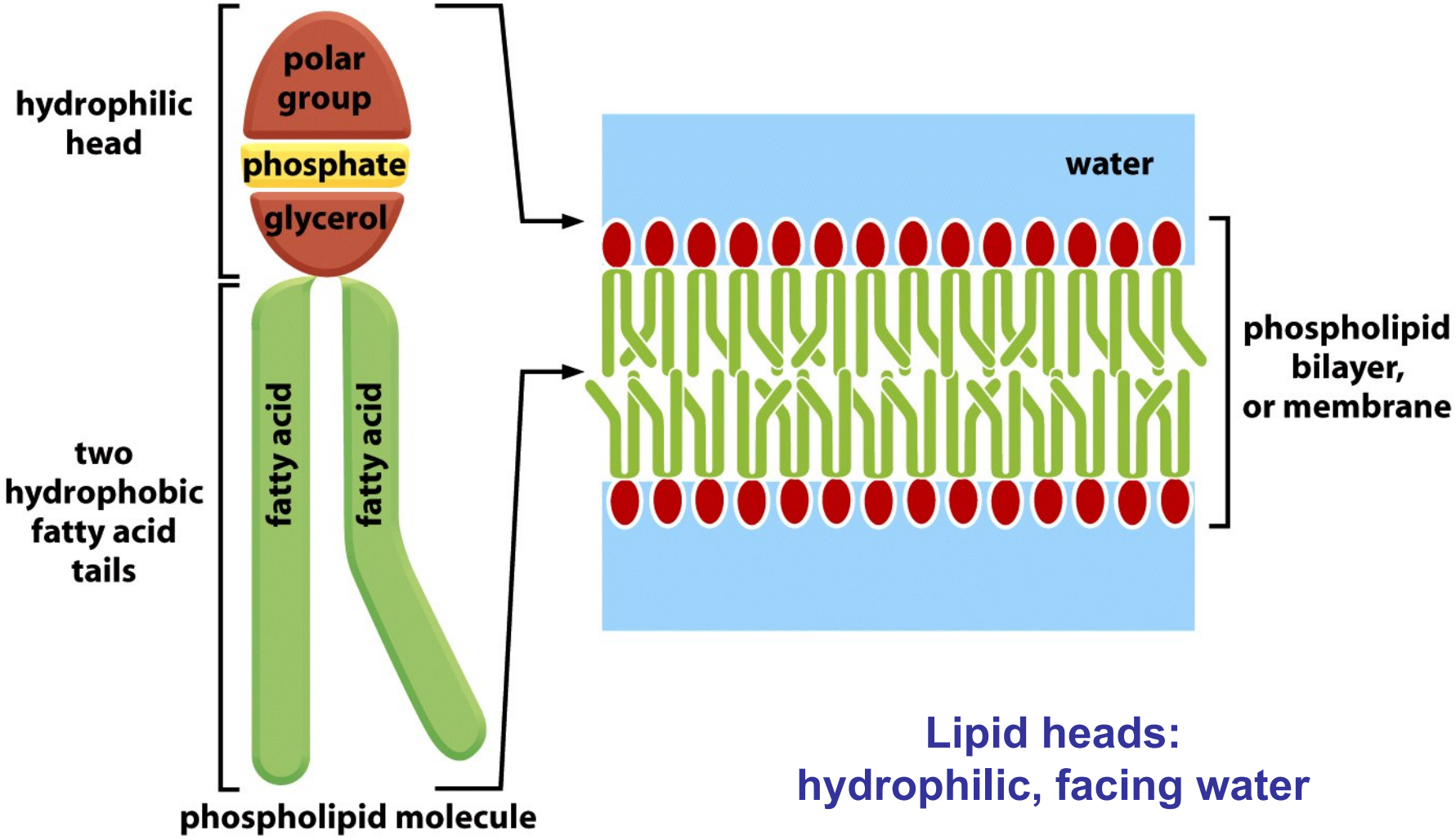
PHOSPHOLIPIDS



Fundamentals of Lipid and Membrane Structure-Movie



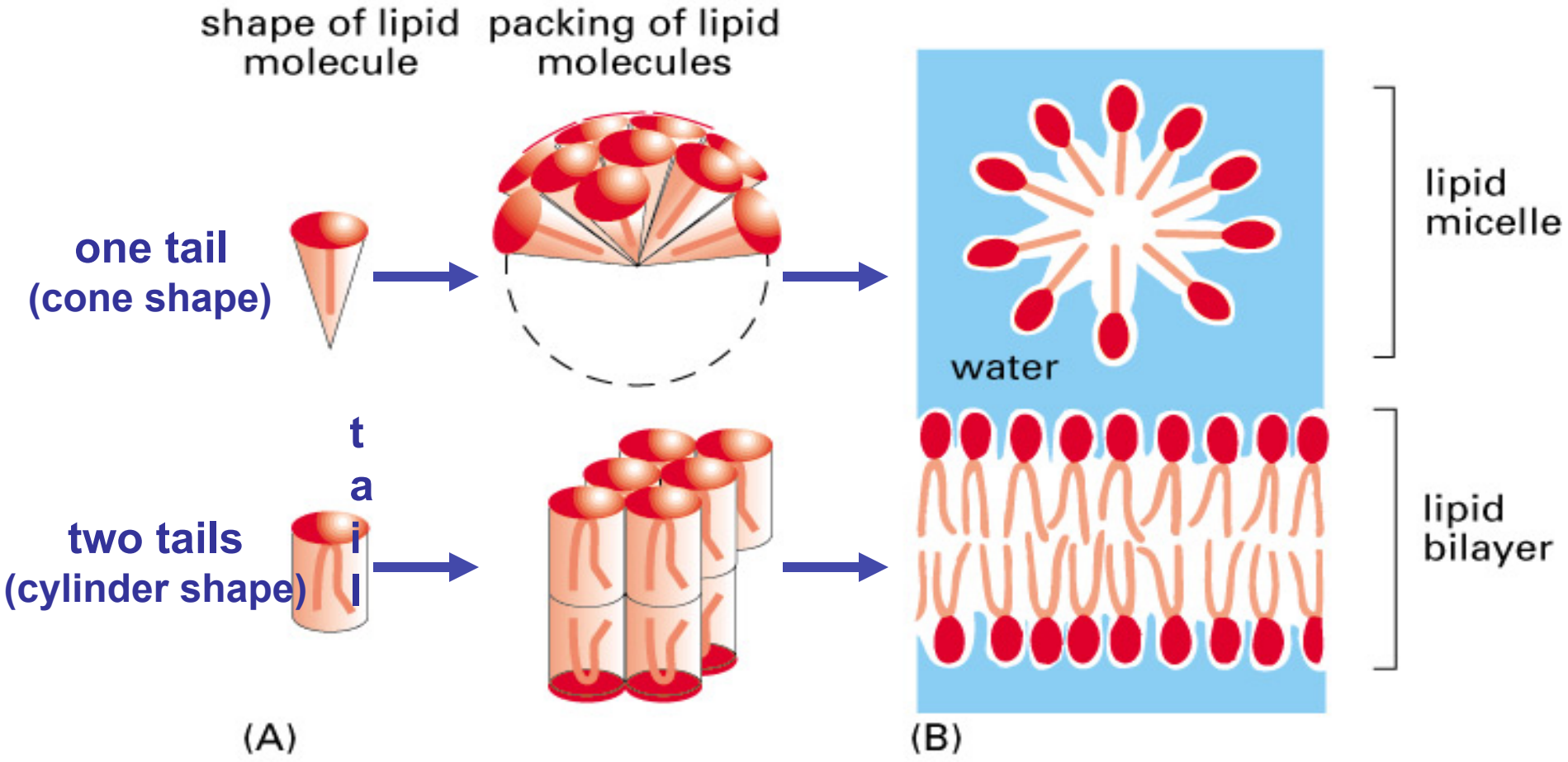
Lipids Form Membranes



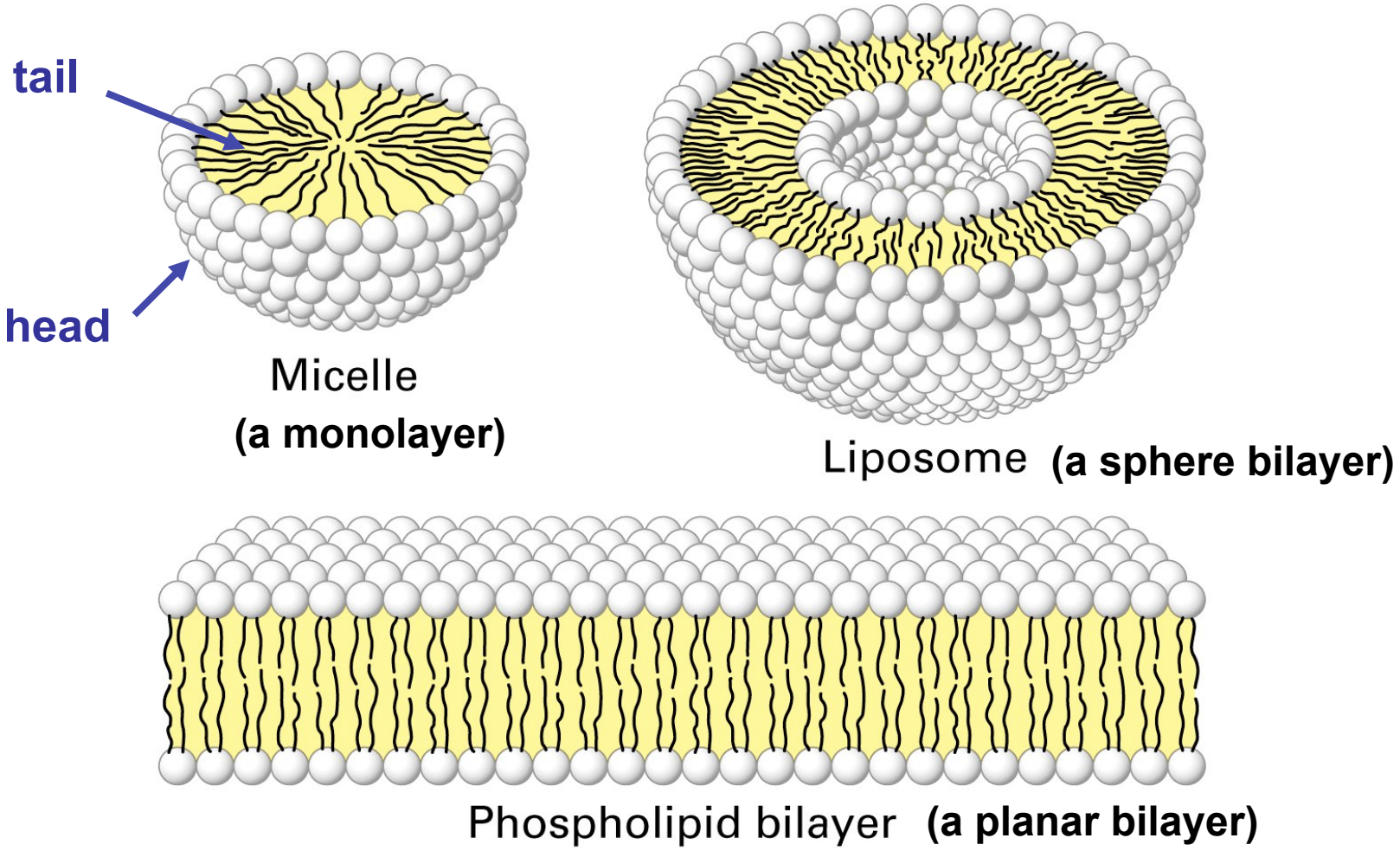
Lipid heads:
hydrophilic, facing water

Lipid tails:
hydrophobic, facing away from water

Steric Effects of Lipid Tail Number



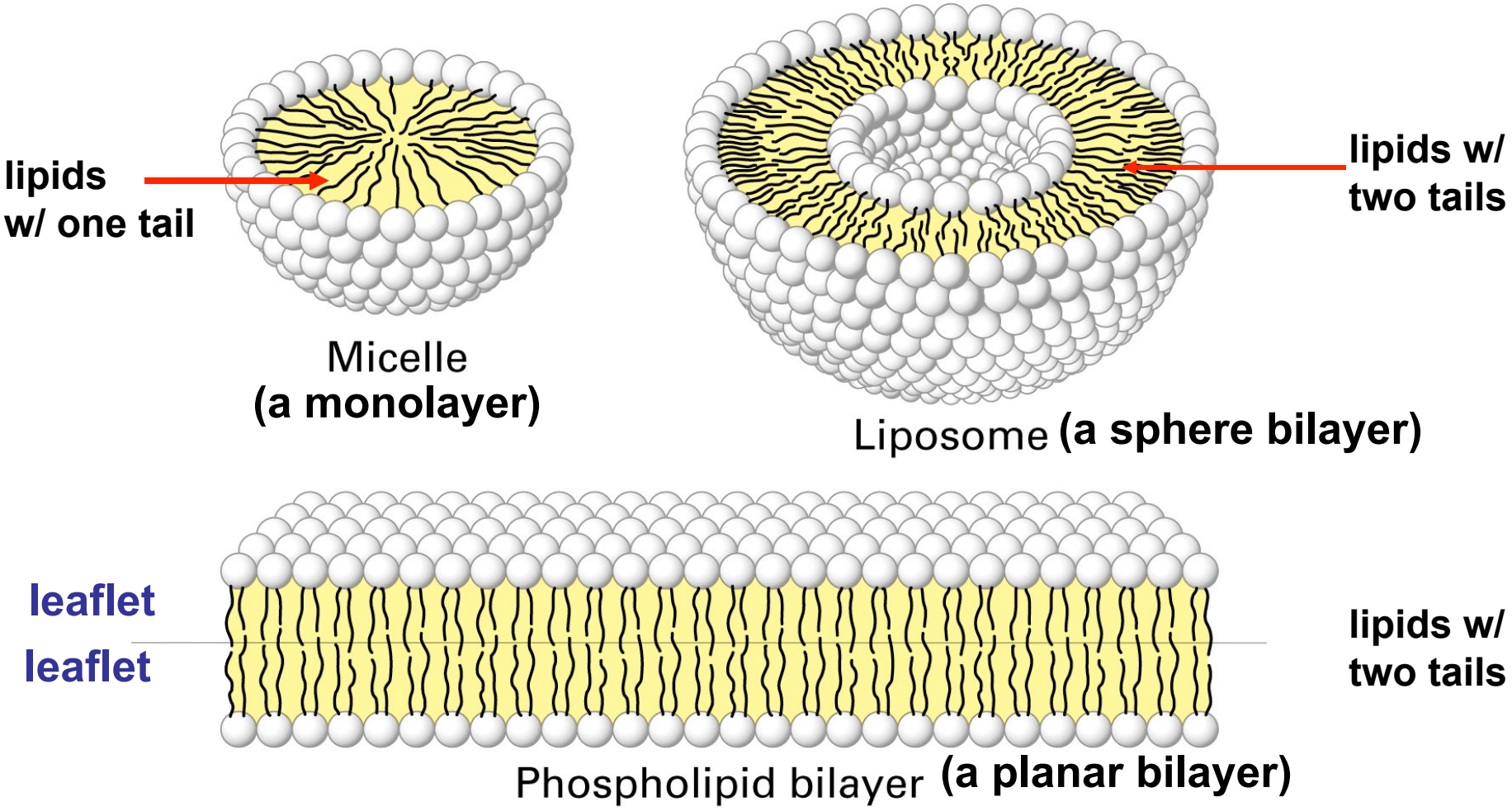
Because of the differential interaction between water and the head or tail part of a lipid, there are three possible packing forms of lipids



In every form, the lipid heads face aqueous environment, yet the lipid tails stay away from aqueous environment as seen in the cross sections of each packing form below.

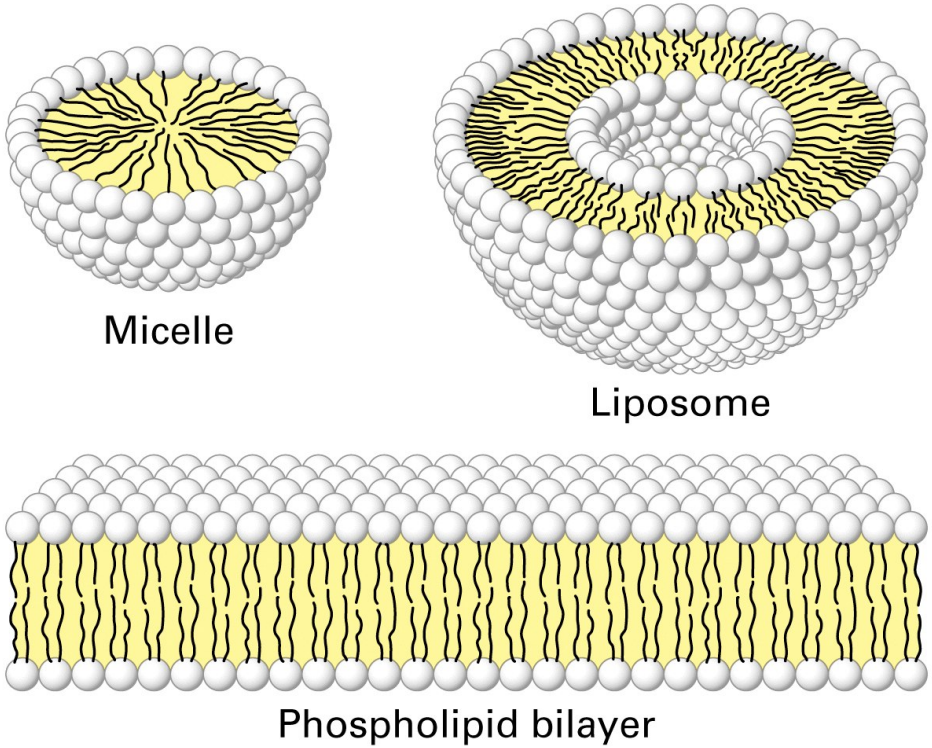
Three Possible Packing Forms of Lipids as a Consequence of its Differential Interaction w/ water

Note the different number of tails in a lipid molecule



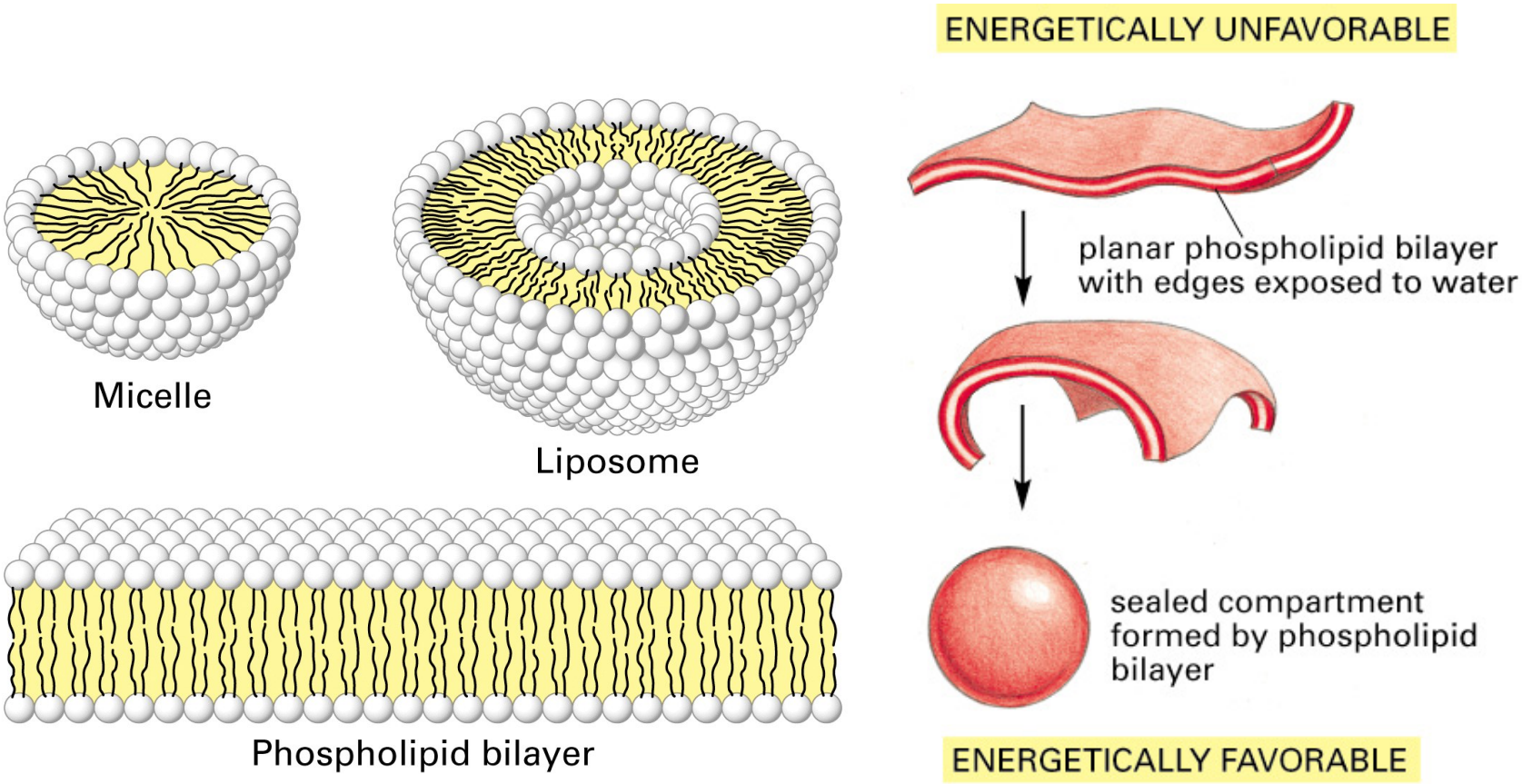
Lipids with two tails are most abundant

Which packing form does a biological membrane adopt (micelle-like, liposome-like or phospholipid bilayer –like)?



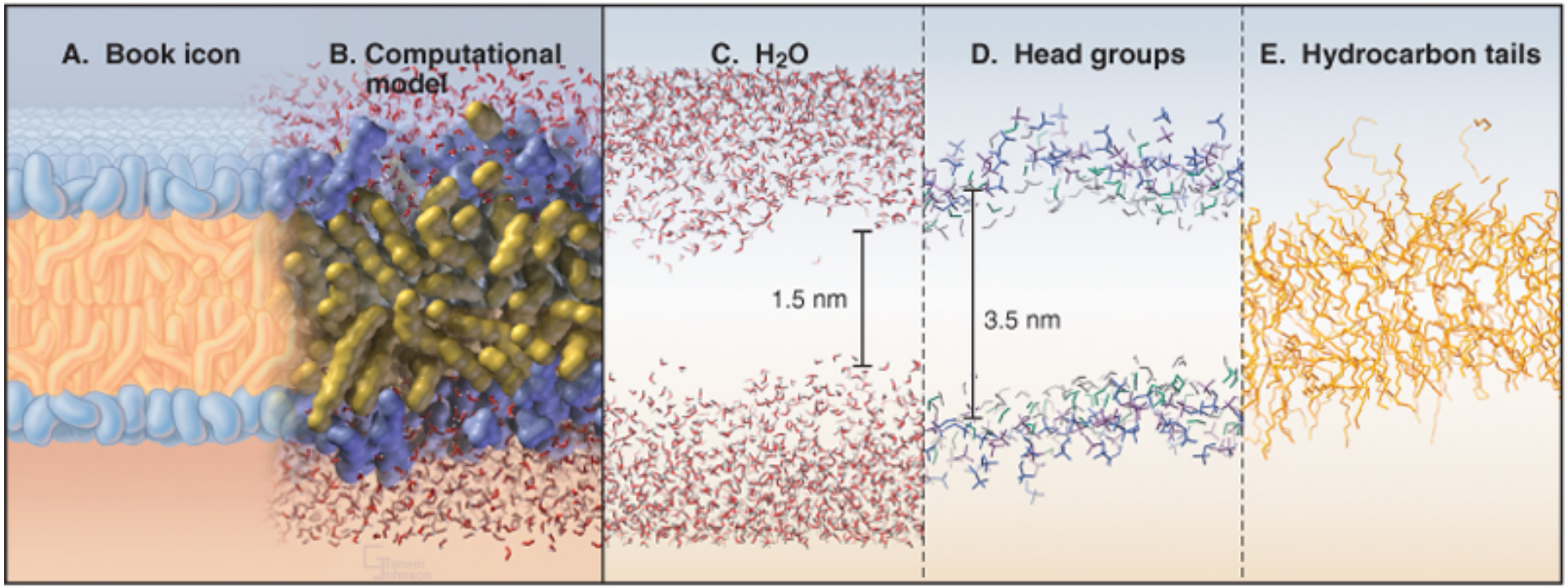
Biological membranes are of the bilayer type with two leaflets.

Which packing form does a biological membrane adopt?



Since phospholipids are most abundant, they play an important role in determining the packing of lipids (as a sealed planar bilayer) in a biological membrane.

Atomic Model of Phosphatidylcholine Bilayer

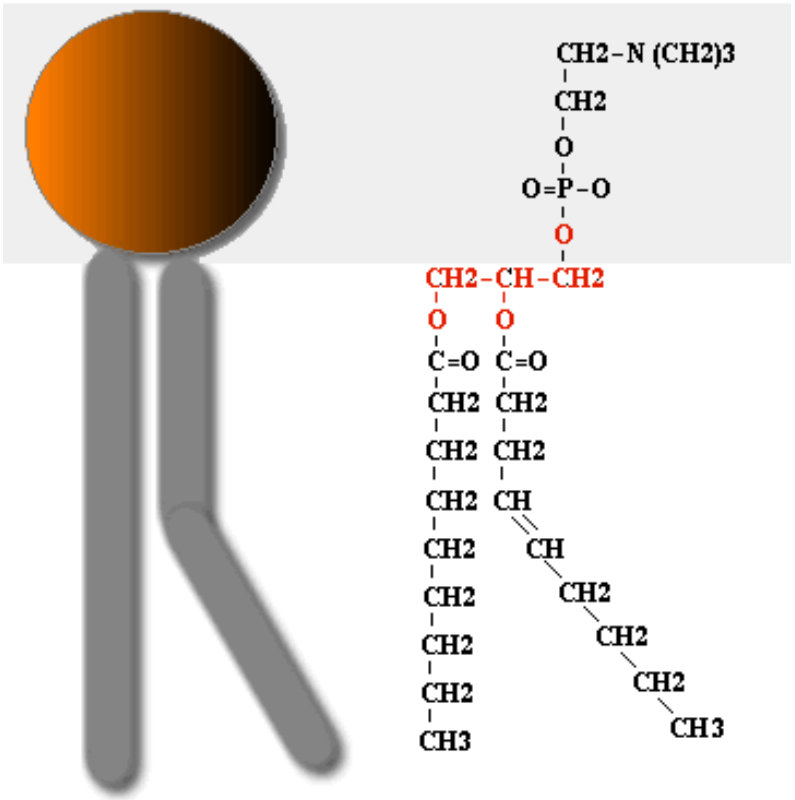


Detergents Disrupt Membranes

Effects of Lipid Tails and Their Composition

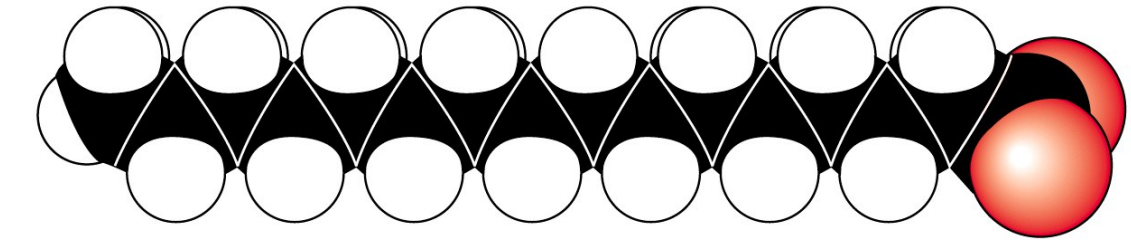
The fatty acyl hydrocarbon chain of a lipid tail can be either saturated (containing no C=C bond) or unsaturated (containing at least one C=C bond).

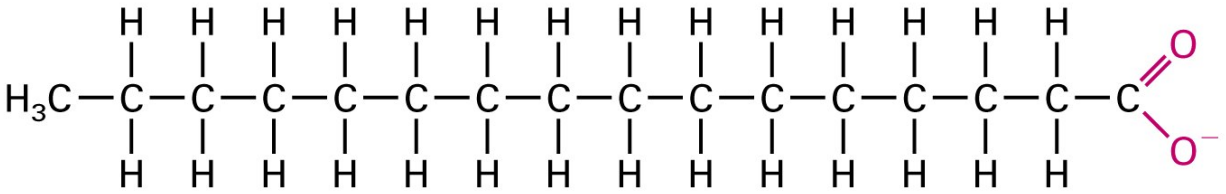
Membrane lipids typically have one saturated and one unsaturated tail.



C=C double bond causes a 'kink' in the lipid tail.

Shape of Saturated Fatty Acids





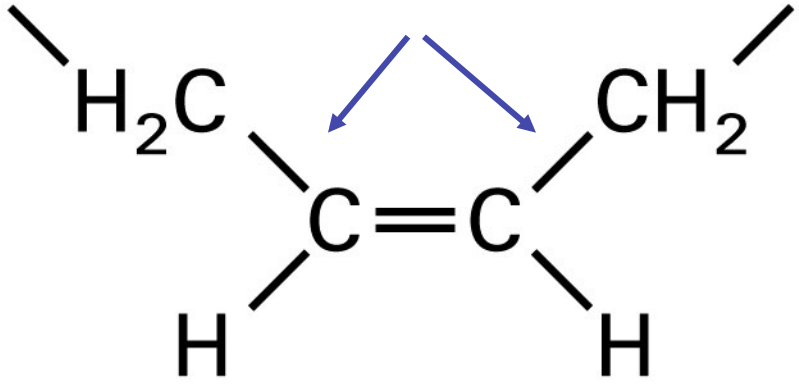
Palmitate
(ionized form of palmitic acid)

A linear carbon backbone leads to a linear fatty acid molecule that takes up less space.

Shapes of Unsaturated Fatty Acids

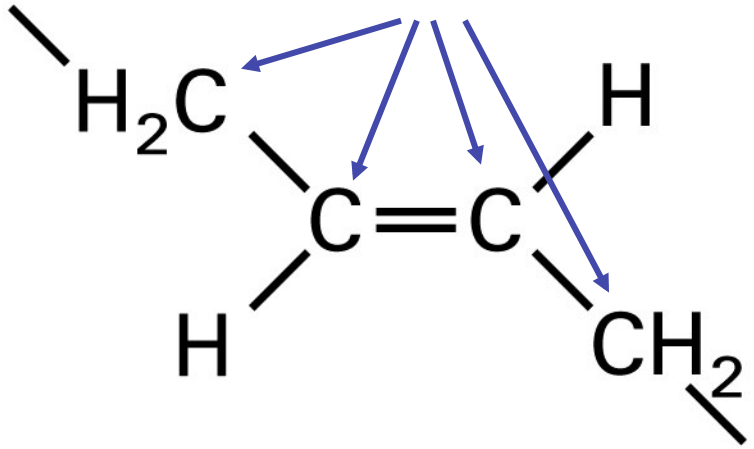
Two possible configurations of a C=C bond: Cis and Trans

non-linear carbon backbone



Cis

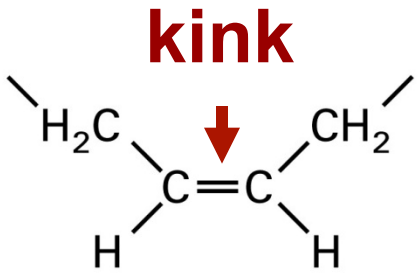
more linear carbon backbone



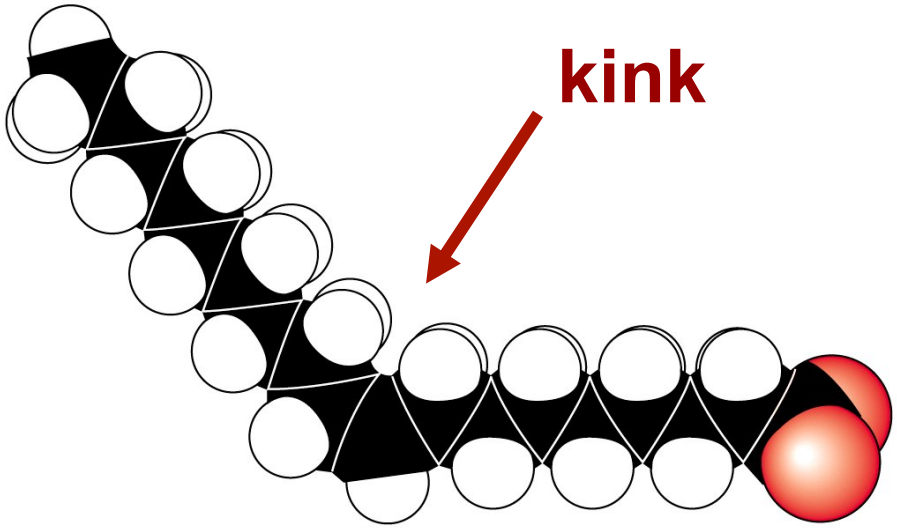
Trans

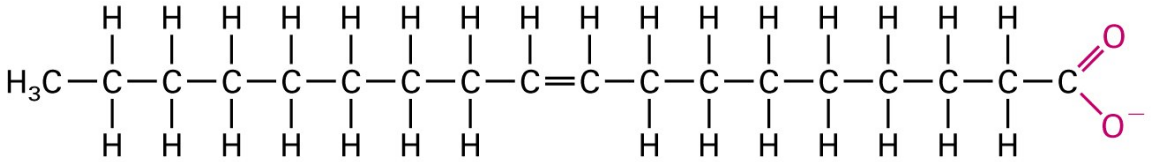
The Cis configuration is by far the dominant biological form of the C=C bonds found in unsaturated fatty acids of lipids in biological membranes.

Shape of Unsaturated Fatty Acid Oleate



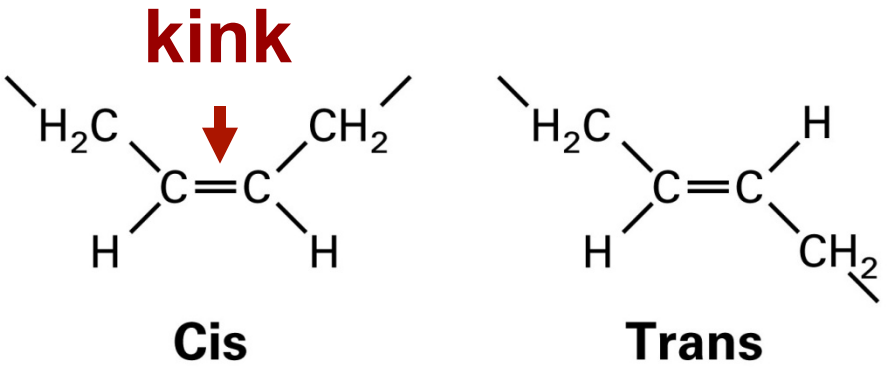
Cis

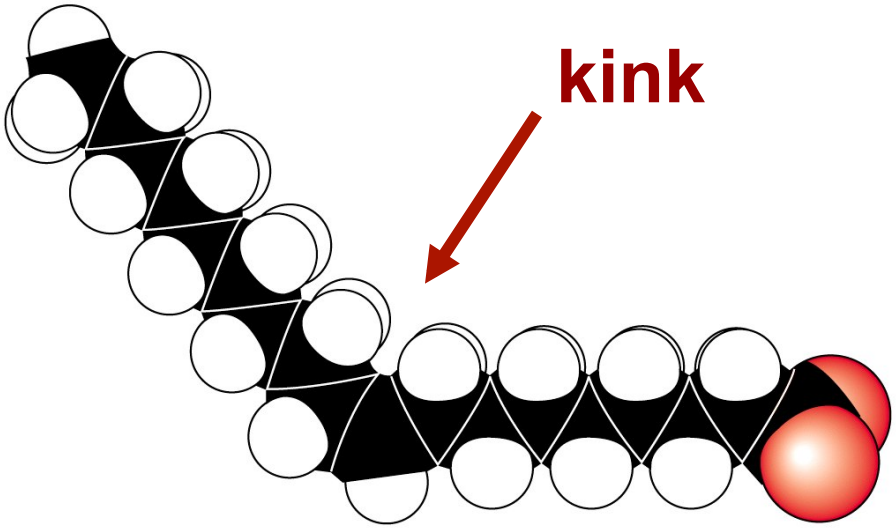


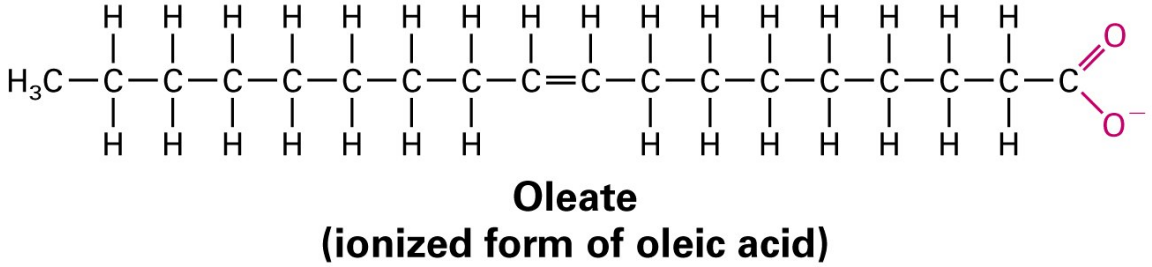


Oleate
(ionized form of oleic acid)

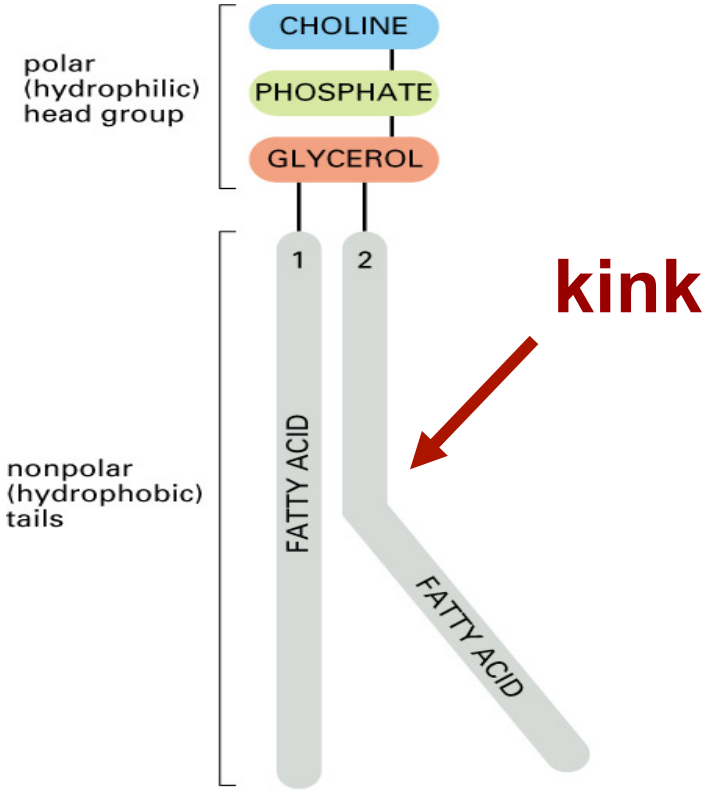
Effect of Unsaturated Fatty Acids on Lipid Structure





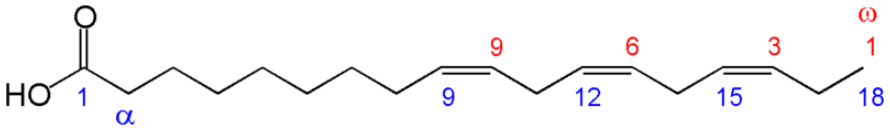


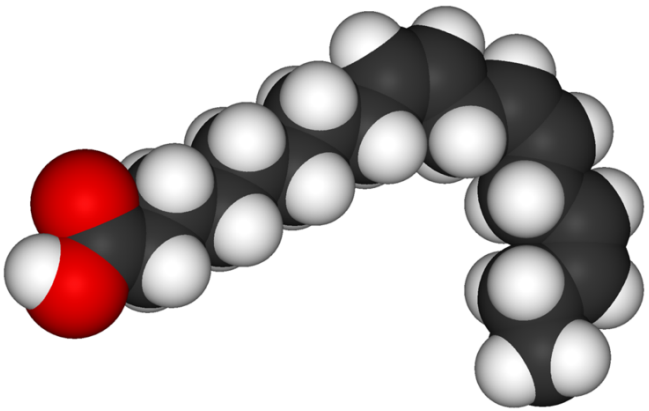
Oleate
(ionized form of oleic acid)



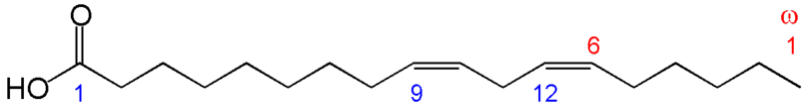
ESSENTIAL LIPIDS: Two are Required from Diet

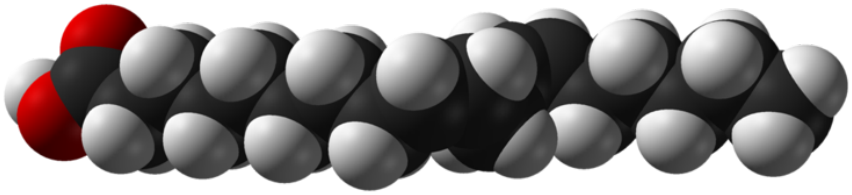
alpha-linolenic acid



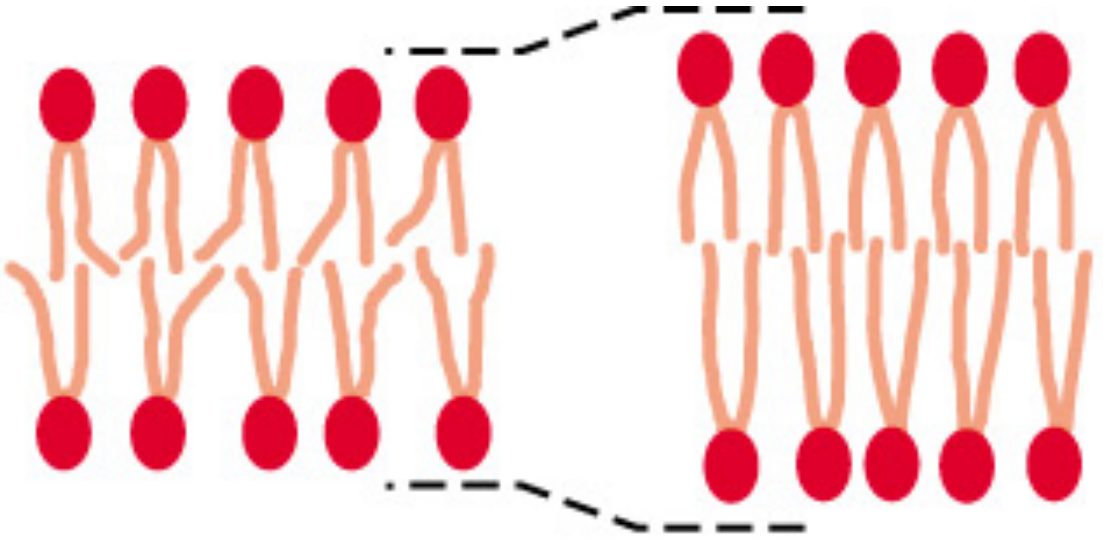


linoleic acid





Effects of Unsaturated Fatty Acids



unsaturated hydrocarbon chains with *cis*-double bonds

saturated hydrocarbon chains

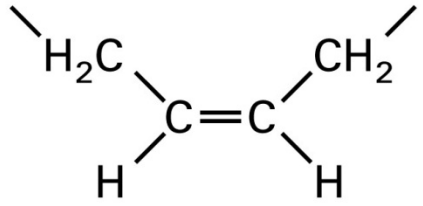
more spread apart and thinner

more compact and thicker

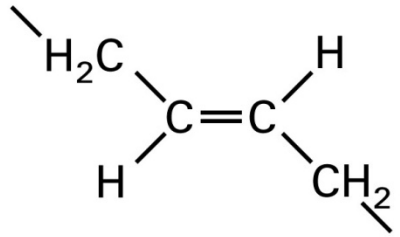
more fluidity

less fluidity

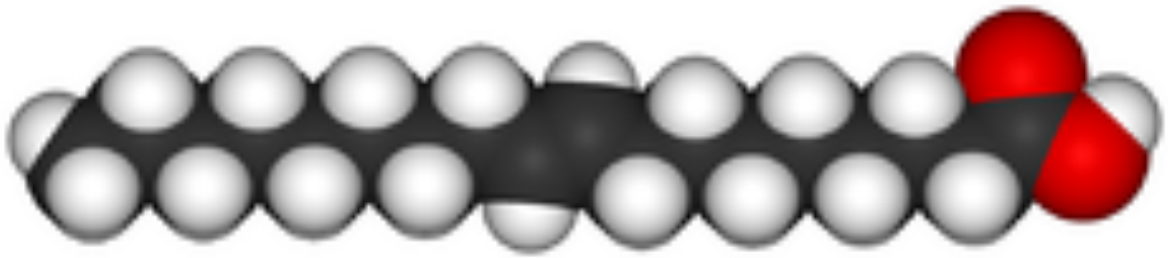
A Trans Fat - Elaidic Acid



Cis



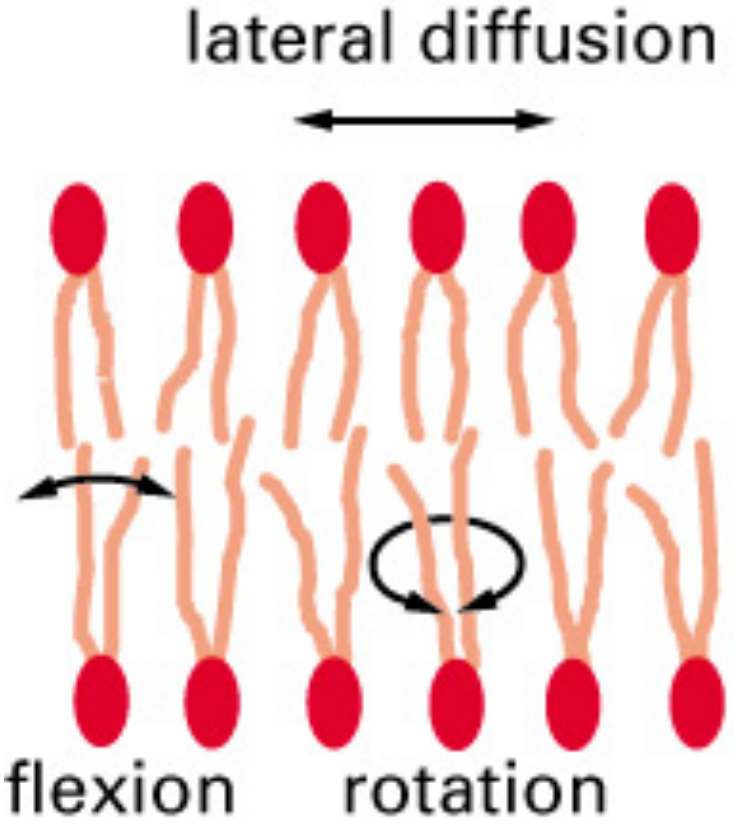
Trans



Membrane fluidity-Movie

The lipid bilayer of a biological membrane is fluid

Different types of movement of a lipid molecule in a bilayer



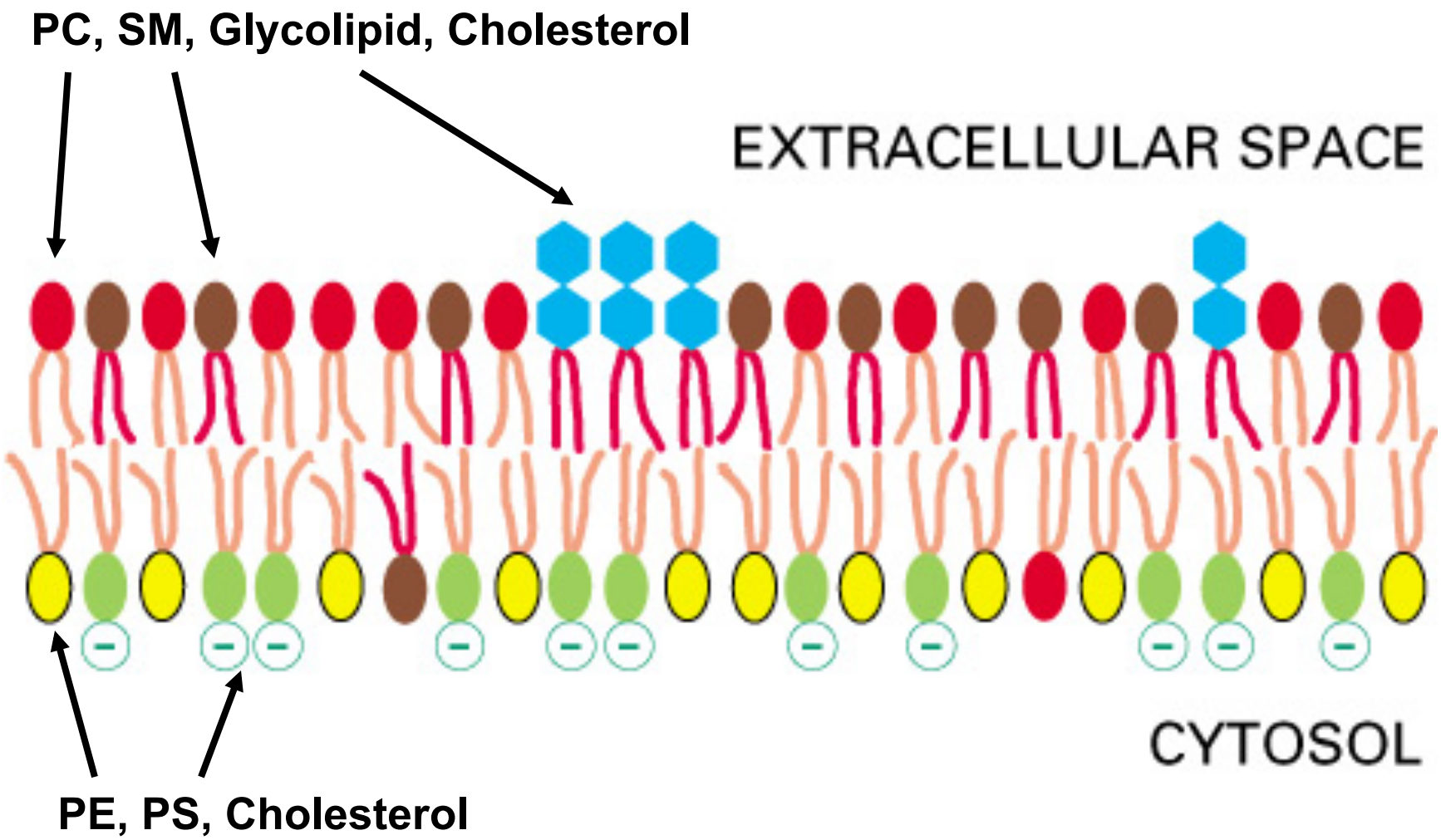
(within one leaflet, a frequent event)

(between two leaflets, a rare event)
(required to maintain asymmetry)

(within one leaflet, a frequent event)

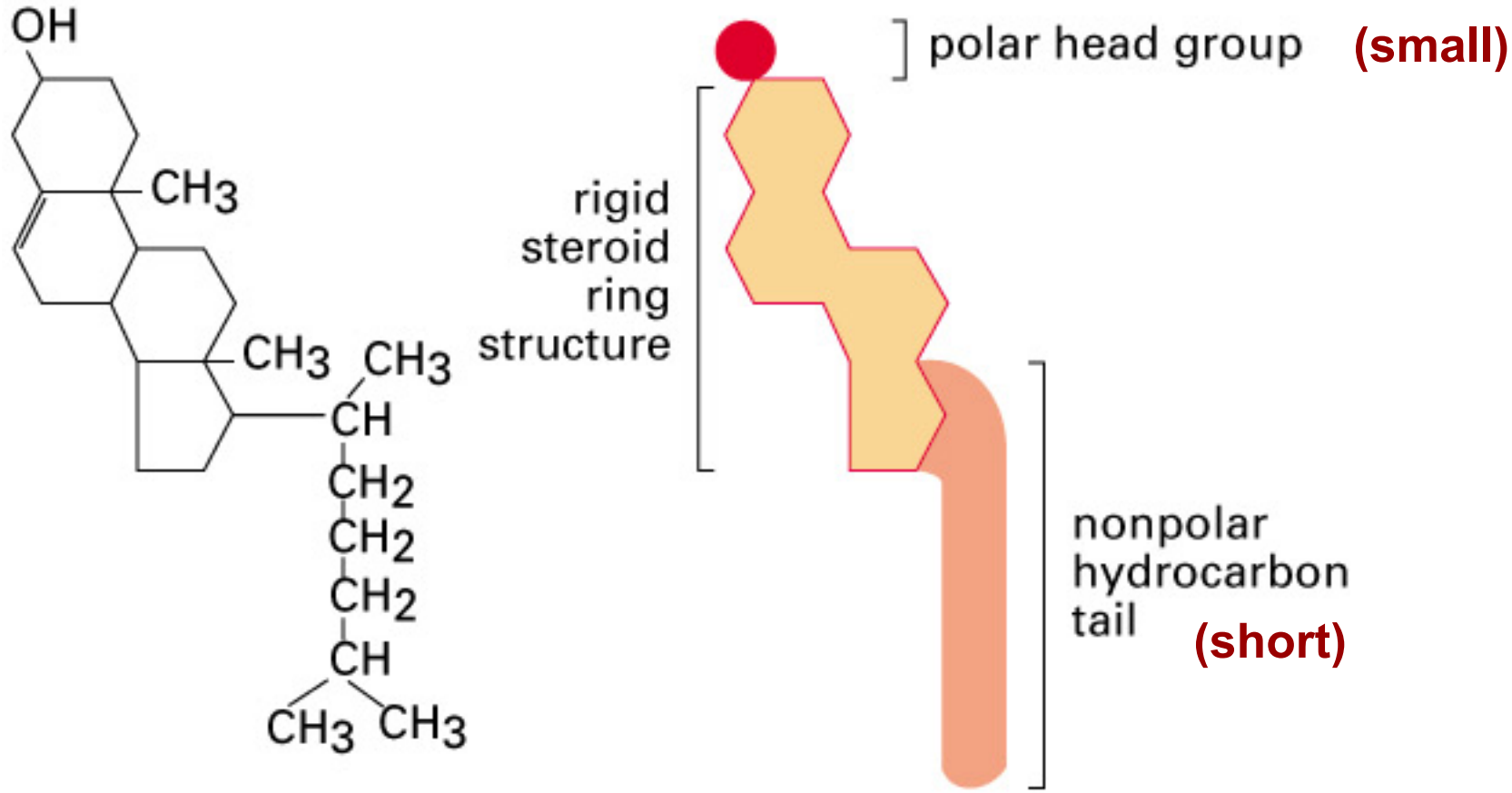
Lateral diffusion, flexion, and rotation contribute to the fluidity

Biological Membranes are Complex and Asymmetric

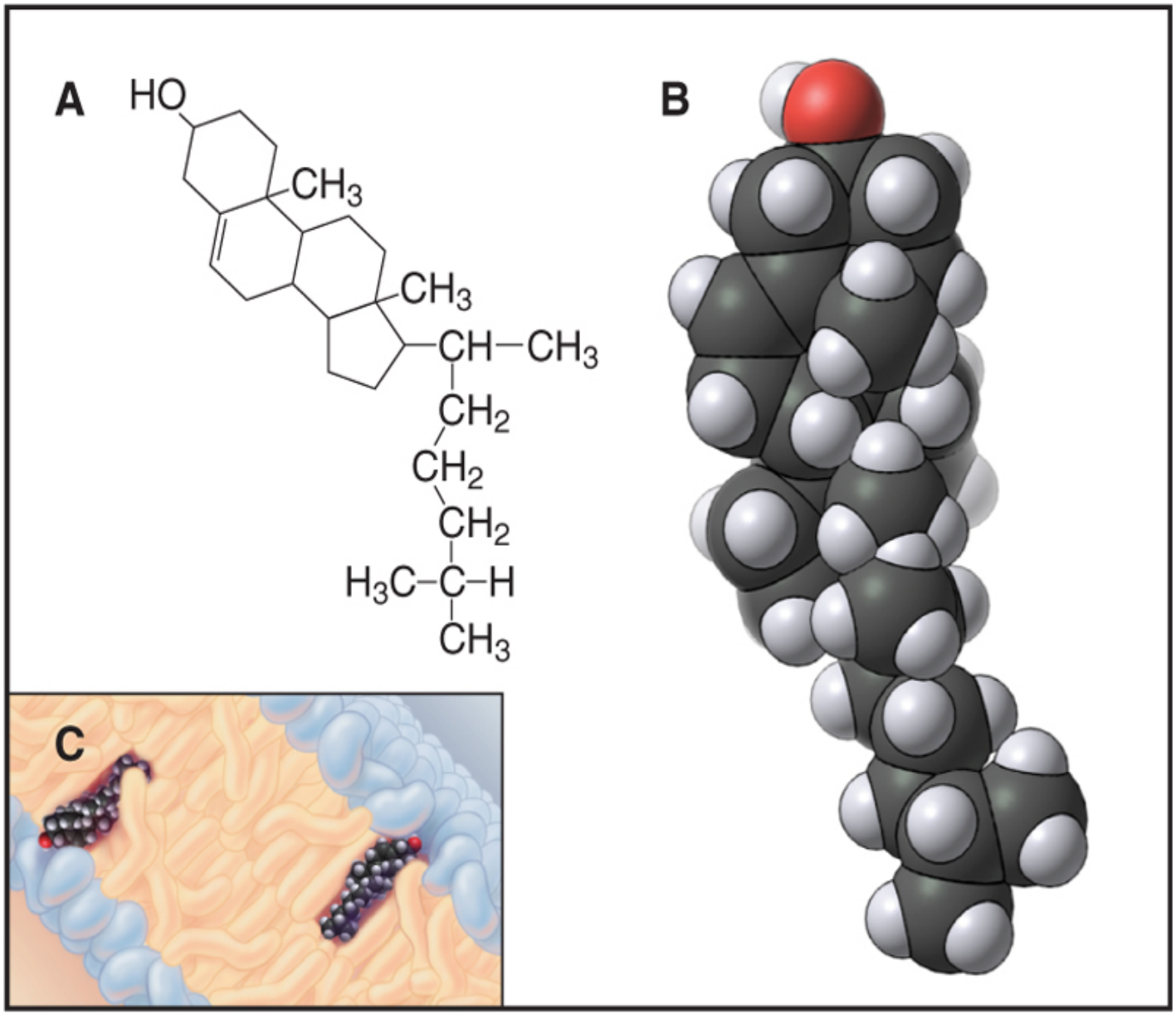


How is the lipid composition asymmetry maintained?

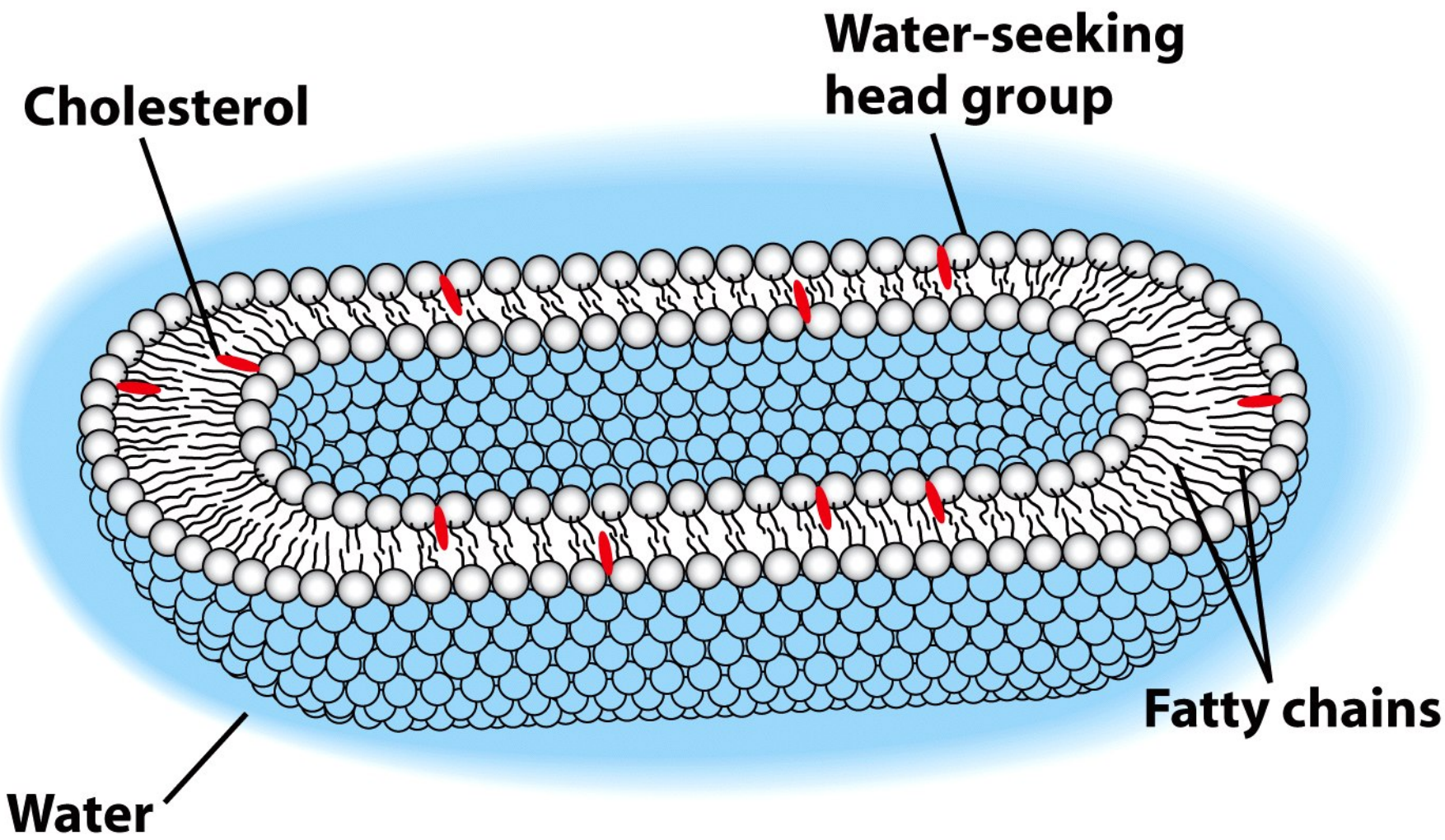
Cholesterol is a Major Form of Sterol Lipid in Animals



Cholesterol Intercalates into the Plasma Membrane



Cholesterol in a Membrane Bilayer



Lipid Breakdown is termed Lipolysis and is a Catabolic Process that Creates Energy

Lipolysis occurs by lipases, enzymes that break down lipids to their constituents.

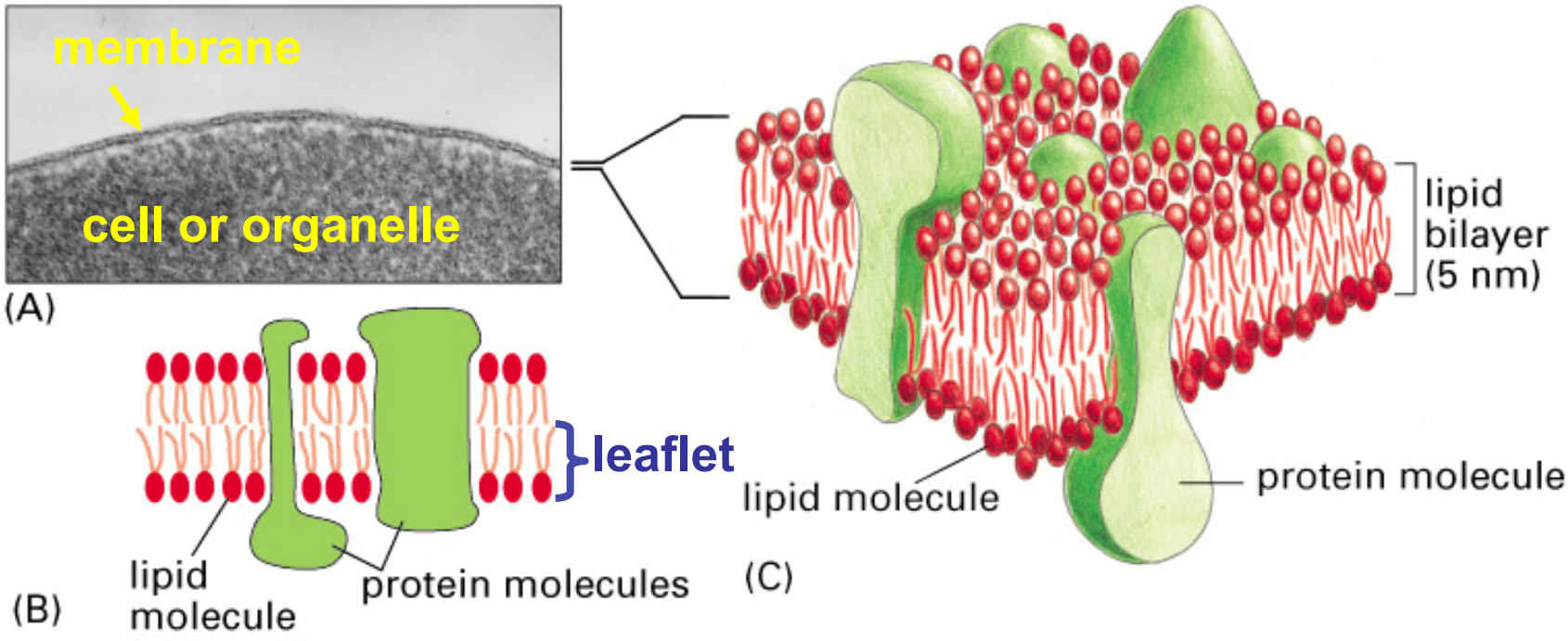
Lipids as energy stores (typically triglyceridese) are broken down to Acetyl Co-A and other energy-rich molecules for biologic and anabolic processes.

Defects in plasma lipid catabolism are the bases of several severe diseases.

Some forms of lipid breakdown also produce signaling molecules.

We will review more about lipid breakdown later and once we begin to address specific sub-cellular organelle structure and function.

Biological Membranes Include Proteins



A membrane has two major components: proteins and lipids

For most membranes:	50% protein content
For myelin membrane:	25% protein content
For mitochondrial inner membrane:	75% protein content