Quiz
Chapter 8

Lipids

What is the structure, chemistry, and biological function of lipids?
Lipids - outline

• Structure and Chemistry of Fatty Acids
• Structure and Chemistry of Triacylglycerols
• Structure and Chemistry of Glycerophospholipids
• Sphingolipids, and Their Importance for Higher Animals
• Steroids and Their Cellular Functions
Classes of Lipids

*All biological lipids are amphipathic*

- Fatty acids
- Triacylglycerols
- Glycerophospholipids
- Sphingolipids
- Waxes
- Isoprene-based lipids (including steroids)
Fatty Acids

- Composed of a long hydrophobic chain (tail) and a carboxyl group (head)
- Two types depending on “tail”
  - Saturated (all single bond)
  - Unsaturated (one or more double bonds)
    - Monounsaturated – single double bond
    - Polyunsaturated – more than one double bond
# Fatty acids

<table>
<thead>
<tr>
<th>Number of Carbons</th>
<th>Common Name</th>
<th>Systematic Name</th>
<th>Symbol</th>
<th>Structure</th>
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<tbody>
<tr>
<td>Saturated fatty acids</td>
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<tr>
<td>12</td>
<td>Lauric acid</td>
<td>Dodecanoic acid</td>
<td>12:0</td>
<td>CH₈(CH₂)₁₀COOH</td>
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<tr>
<td>14</td>
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<tr>
<td>Unsaturated fatty acids (all double bonds are cis)</td>
<td></td>
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Numbering & notation of fatty acid carbons

\[ \text{cis-}\Delta^9 \ \text{means cis double bond between C-9 & C-10} \]
\[ \text{trans-}\Delta^2 \ \text{means trans double bond between C-2 & C-3} \]
Omega-3 fatty acid

An ω-3 fatty acid
### Fatty acids

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**cis-Δ⁹-octadecanoic acid**

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The structures of some typical fatty acids

Note that the double bonds are nearly always cis and rarely conjugated.

Essential fatty acid not synthesized acquired from diet

18:1 (9)
Structures of unusual fatty acids (modified)

lactobacillic acid, a fatty acid containing a cyclopropane ring

tuberculostearic acid, a branched-chain fatty acid
Triacylglycerols

*Also called triglycerides*

Formed by glycerol and three fatty acids

A major energy source for many organisms

- Yields large amounts of energy in the metabolic oxidative reactions
- No solvation needed
- Efficient packing
Triacylglycerols

Other advantages accrue to users of triacylglycerols

• Insulation
• Energy without nitrogen
• Metabolic water (oxidation of fatty acid yields carbon dioxide and water)

• Read about Polar Bears in “A Deeper Look”
Glycerophospholipids
Members of the class of lipids known as phospholipids

1, 2 - diaclyglycerol

Phosphoester on 3rd carbon of the glycerol backbone

Phosphatidic acid, the parent compound for glycerophospholipids.
Structures of several glycerophospholipids
phosphatidylcholine, phosphatidylglycerol, and phosphatidylinositol.
Ether Glycerophospholipids

An ether instead of an acyl group at C-1

Plasmalogens are ether glycerophospholipids in which the alkyl chain is unsaturated

A 1-alkyl 2-acyl-phosphatidylethanolamine (an ether glycerophospholipid).
Ether Glycerophospholipids

- Platelet activating factor (PAF) is an ether glycerophospholipid
- PAF is a potent biochemical signal molecule
- Note the short (acetate) fatty acyl chain at the C-2 position in PAF

The structure of 1-alkyl 2-acetyl-phosphatidylcholine, also known as platelet activating factor or PAF.
Ether Glycerophospholipids

choline plasmalogen.

cis-α,β-unsaturated
Sphingolipids

*Base structure is sphingosine*
- Sphingosine is an 18-carbon amino alcohol

- Ceramides are amide linkages of fatty acids to the nitrogen of sphingosine

- Glycosphingolipids are ceramides with one or more sugars in beta-glycosidic linkage at the 1-hydroxyl group
Formation of an amide linkage between a fatty acid and sphingosine produces a ceramide.
choline sphingomyelin formed from stearic acid

Choline sphingomyelin with stearic acid
Sphingolipids

- Glycosphingolipids with one sugar are cerebrosides
Gangliosides - ceramides with 3 or more sugars, one of which is a sialic acid.

The structures of several important gangliosides. Also shown is a space-filling model of ganglioside GM1.
Biological functions of glycosphingophospholipids

• Although present in relatively small amounts – GSP play important biological roles

• Appear at cell surface and mediate cell-cell recognition and tissue specificity

• Important in nerve pulse propagation
Steroids
terpene-based lipids

• Based on a core structure consisting of three 6-membered rings and one 5-membered ring, all fused together
• Cholesterol is the most common steroid in animals and precursor for all other steroids in animals
• Steroid hormones serve many functions in animals - including salt balance, metabolic function and sexual function
The structures of several important sterols derived from cholesterol.
Chapter 9

Membranes

What are the properties and characteristics of biological membranes that account for their broad influence on cellular processes and transport?
Outline

• The Chemical and Physical Properties of Membranes

• The Structure and Chemistry of Membrane Proteins
The Chemical and Physical Properties of Membranes

*Structures with many cell functions*

- Barrier to toxic molecules
- Help accumulate nutrients
- Carry out energy transduction
- Facilitate cell motion
- Assist in reproduction
- Modulate signal transduction
- Mediate cell-cell interactions
Common Features of Biological Membranes

Membranes are noncovalent assemblies. Constituent protein & lipid molecules are held together by noncovalent interactions, which are cooperative.

Membranes are asymmetric. The two faces always differ from each other.

Membranes are fluid structures. Lipid molecules diffuse rapidly in the membrane plane, as do proteins, unless they are anchored by specific interactions. In contrast, these molecules do not readily rotate across the membrane. Membranes are regarded as two-dimensional solutions of oriented proteins & lipids.

Most cell membranes are electrically polarized, the inside is negative, typically - 60 mV. Membrane potential plays a key role in transport, energy conversion, and excitability.

Three major types of membrane lipids: phospholipids, glycolipids, cholesterol.
Lipids Form Ordered Structures Spontaneously in Water

Hydrophobic interactions

- Very few lipids exist as monomers
- Monolayers arrange lipid tails in the air
- Micelles bury the nonpolar tails in the center of a spherical structure
- Micelles reverse in nonpolar solvents
Lipids Form Ordered Structures Spontaneously in Water

- Lipid bilayers can form in several ways
  - unilamellar vesicles (liposomes)
  - multilamellar vesicles (Alex Bangham)
The Fluid Mosaic Model Describes Membrane Dynamics

S. J. Singer and G. L. Nicolson

- The phospholipid bilayer is a *fluid matrix*
- The bilayer is a two-dimensional solvent
- Lipids and proteins can undergo rotational and lateral movement
- Two classes of proteins:
  - peripheral proteins (extrinsic proteins)
  - integral proteins (intrinsic proteins)
Motion in the Bilayer

Lipid chains can bend, tilt and rotate

- Lipids and proteins can migrate ("diffuse") in the bilayer
- Frye and Edidin proved this (for proteins), using fluorescent-labelled antibodies
- Lipid diffusion has been demonstrated by NMR and EPR (electron paramagnetic resonance) and also by fluorescence measurements
Lateral movement

Rapid

Lateral diffusion
Human cells with membrane antigens for red fluorescent antibodies were mixed and fused with mouse cells having membrane antigens for green fluorescent antibodies. Treatment of the resulting composite cells with red- and green-fluorescent – labeled antibodies revealed a rapid mixing of the membrane antigens in the composite membrane. This experiment demonstrated the lateral mobility of membrane proteins.
Membranes are Asymmetric Structures

• Lateral Asymmetry of Proteins:
  • Proteins can associate and cluster in the plane of the membrane - they are not uniformly distributed in many cases

• Lateral Asymmetry of Lipids: Lipids can cluster in the plane of the membrane - they are not uniformly distributed

Phase separations of phosphatidylserine (green circles) can be induced by divalent cations such as Ca2+. 
Transverse movement

Very slow

Tranverse diffusion
(flip-flop)
Membranes are Asymmetric Structures

- Transverse asymmetry of proteins
  - e.g. N-terminus of glycophorin is extracellular whereas C-terminus is intracellular
- Transverse asymmetry of lipids
  - In most cell membranes, the composition of the outer monolayer is quite different from that of the inner monolayer
Flippases
• Lipids can be moved from one monolayer to the other by flippase proteins
• Some flippases operate passively and do not require an energy source
• Other flippases appear to operate actively and require the energy of hydrolysis of ATP
• Active flippases can generate membrane asymmetries
Phospholipids are arranged asymmetrically in most membranes.
Membranes Undergo Phase Transitions

• Below a certain transition temperature, membrane lipids are rigid and tightly packed.

• Above the transition temperature, lipids are more flexible and mobile.

• The transition temperature is characteristic of the lipids in the membrane.

• Only pure lipid systems give sharp, well-defined transition temperatures.

A decrease in bilayer thickness is observed.
Melting temp \((T_m)\) for a phospholipid membrane
Some \( (T_m) \) examples

<table>
<thead>
<tr>
<th>Number of carbon</th>
<th>Number of double bonds</th>
<th>Fatty acid</th>
<th>Common name</th>
<th>Systematic name</th>
<th>( T_m ) ( (^\circ \text{C}) )</th>
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<td>(-22)</td>
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</tbody>
</table>
Packing of fatty acid chains in a membrane

(A) Stearate (C-18, saturated)

(B) 2 stearate & 1 oleate (C18, unsaturated)
Packing of cholesterol in a membrane
An archaeon membrane

Archaeal membranes: ether lipids with branched chains – which have the same membrane structural consequence as the double bond

Volcanic vent

Archaea, orange mat

Sulfurous deposits on edge, yellow
Question

A decrease in the concentration of cholesterol in the membrane would have which of the following effects on a rigid membrane?

a. Increased fluidity  
b. Decreased fluidity  
c. Increased electrostatic interactions  
d. Decreased protein content
Cells adjust lipid composition of membranes to maintain proper fluidity as the environment changes
The Structure and Chemistry of Membrane Proteins

- Integral (intrinsic) proteins
- Peripheral (extrinsic) proteins
- lipid-anchored proteins
An example of a peripheral membrane protein

prostaglandin H2

Alpha helix embedded in the membrane
Integral Membrane Proteins are Imbedded in the Membrane

- Transmembrane region hydrophobic – does not fold similarly to soluble proteins because of the hydrophobic lipids
- They can only be removed from the membrane by denaturing the membrane (organic solvents, or strong detergents)
- α-helical bundles found in plasma membrane of eukaryotes and inner membrane of bacteria, mitochondria, and chloroplasts
- β-barrel (even number of β-strands) located in outer membrane
- Glycophorin, bacteriorhodopsin are examples
Glyophorin

A single-transmembrane-segment protein

One transmembrane segment with globular domains on either end

Transmembrane segment is alpha helical and consists of 19 hydrophobic amino acids

Extracellular portion contains oligosaccharides and these constitute the ABO and MN blood group determinants
Bacteriorhodopsin

**A 7-transmembrane-segment (7-TMS) protein**

- Found in purple patches of *Halobacterium halobium*

- Consists of 7 transmembrane helical segments with short loops that interconnect the helices

- bR is a light-driven proton pump!

- Transmembrane alpha-helix requires 21-25 residues
Porins

*Found both in Gram-negative bacteria and in mitochondrial outer membrane*

- Porins are pore-forming proteins - 30-50 kD

- General or specific

- Porin from *Rhodobacter capsulatus* has 16-stranded beta barrel that traverses the membrane to form the pore
Structure of maltoporin from *E. coli*.

Beta-strand requires only 9-11 residues per transmembrane strand.
The arrangement of the peptide chain in maltoporin from *E. coli*
Lipid-Anchored Membrane Proteins

• Four types have been found:
  – Amide-linked myristoyl anchors
  – Thioester-linked fatty acyl anchors
  – Thioether-linked prenyl anchors
  – Glycosyl phosphatidylinositol anchors
Amide-Linked Myristoyl Anchors

- Always myristic acid
- Always N-terminal
- Always a Gly residue modification
- Examples: cAMP-dependent protein kinase, pp60^{src} tyrosine kinase, calcineurin B, alpha subunits of G proteins, gag protein of HIV-1
Thioester-linked Acyl Anchors

- Broader specificity for lipids - myristate, palmitate, stearate, oleate all found
- Broader specificity for amino acid links - Cys, Ser, Thr all found
- Examples: G-protein-coupled receptors, surface glycoproteins of some viruses, transferrin receptor triggers and signals
Thioether-linked Prenyl Anchors

- Prenylation refers to linking of "isoprene"-based groups

- Always Cys of CAAX (C=Cys, A=Aliphatic, X=any residue)

- Isoprene groups include farnesyl (15-carbon, three double bond) and geranylgeranyl (20-carbon, four double bond) groups

- Examples: yeast mating factors, p21\textsuperscript{ras} and nuclear lamins
Glycosyl Phosphatidylinositol Anchors

- Always attached to a C-terminal residue
- Ethanolamine link to an oligosaccharide linked in turn to inositol of PI