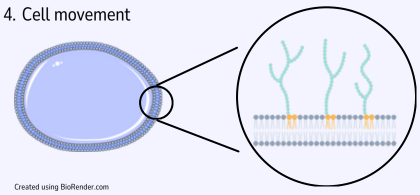
#6: Lipids and Biological Membranes BIOCHEM2280

Intro to Lipids & Membranes

- Cells are enclosed by a **membrane** made up of *lipids, proteins and carbohydrates*

<u>**The main functions of biological membranes are:**</u>

1. Separate cell or organelle contents from the environment
2. Control movement of molecules across the membrane through the use of proteins
3. Contain sensors and receptors which allow for communication with other cells and responses to external stimuli
4. Cell movement



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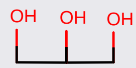
- Lipids have little to no solubility in water but will dissolve in **organic solvents**
- Lipids have the capacity to act as *energy storage molecules, enzymatic cofactors, signalling molecules, and pigments*

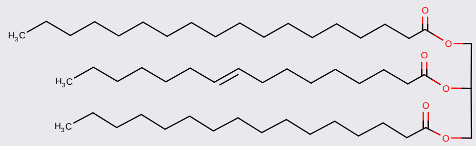
Triacylglycerols

- Synthesized through adding a fatty acid to each hydroxyl of glycerol (via *ester linkage*)
- **Glycerol** is a 3 carbon molecule with hydroxyl groups at each carbon



Glycerol

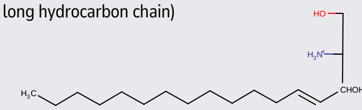
- Most contain 2 or 3 different types of fatty acids
- Used to store fatty acids as *energy* in fat cells (**adipocytes**)



Triacylglycerol (Triglyceride)

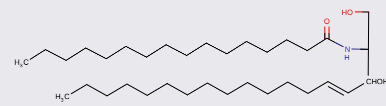
Sphingolipids

- Based on the molecule **sphingosine** (which contains a long hydrocarbon chain)



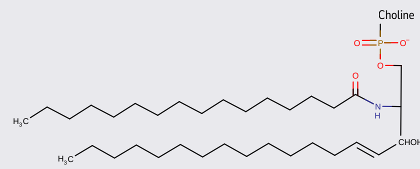
Sphingosine

- **Ceramides** can be formed by joining a fatty acid to sphingosine's amide group



Ceramide

- The terminal hydroxyl group of ceramides can be modified with **phosphoethanolamine** or **phosphocholine** to make **sphingomyelins** (found in the myelin sheath)

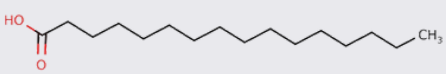


Sphingomyelin

- Can also have 1 or more monosaccharide groups added to make **glycosphingolipids**

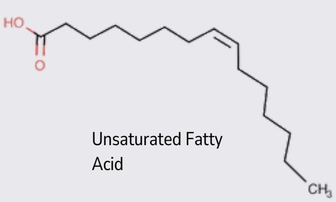
Fatty Acids

- Composed of a **hydrocarbon chain** that ends with a **carboxylic acid** group
- Usually contain an *even* number of carbons (range from 4 - 24)
  - If the hydrocarbon chains of the fatty acid have no double bonds, it is called a **saturated fatty acid**



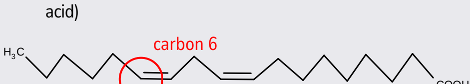
Saturated Fatty Acid

  - If the hydrocarbon chains of the fatty acid have double bonds, it is called an **unsaturated fatty acid (1 = monounsaturated, 2+ = polyunsaturated)**
    - The first carbon-carbon double bond is usually added between C-9 and C-10 and almost always is in **cis configuration (forms a kink in the chain)**
    - When additional carbon-carbon double bonds are added, they are usually added *every 3rd carbon*



Unsaturated Fatty Acid

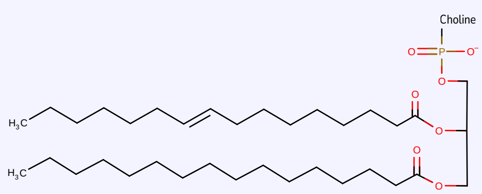
- In fatty acids, carbons are counted from the **methyl end (CH3)** by *nutritionists* while *organic chemists* count them from the **carboxyl end (COOH)**
- The terminal carbon is called the **omega carbon** and the distance from a double bond determines what type of omega fatty acid it is (Ex. If the double bond is 6 carbons away from terminal end, it will be called an omega-6 fatty acid)



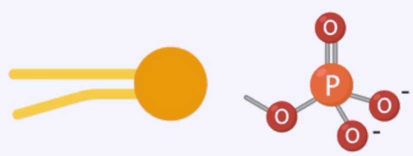
Linoleic Acid (An Omega-6 Fatty Acid)

Glycerophospholipids

- Similar to triglycerides, except the fatty acid on the end is replaced with a **phosphate group**
- The phosphate is often conjugated with either **serine (phosphatidylserine)** or **choline (phosphatidylcholine)**



Glycerophospholipid



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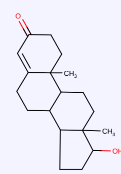
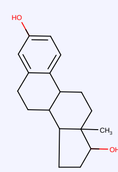
Steroids

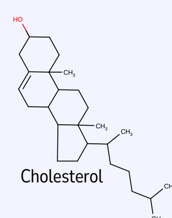
- The basis of a **steroids** are 4 fused planar rings (Three 6 carbon rings and one 5 carbon ring)
- Steroids with hydroxyl groups at carbon 3 are called **sterols**



Testosterone



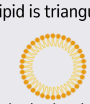
Estrogen



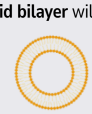
Cholesterol

Lipid Bilayers

- Some lipids, like fatty acids, glycerophospholipids, and sphingolipids, are **amphipathic**
  - Amphipathic means that one part of the molecule is <u>hydrophobic</u> and the other is <u>hydrophilic</u>
  - Amphipathic molecules in water will spontaneously arrange themselves so that the *hydrophilic regions* contact the water while the *hydrophobic regions* are tucked away
  - If the diameter of the hydrophilic groups > hydrophobic group diameter (lipid is triangular), a **micelle** will form:



  - If the diameter of the hydrophilic groups is approximately equal to hydrophobic group diameter (lipid is rectangular), a **lipid bilayer** will form:



<u>The fluidity of lipid bilayers changes depending on several factors:</u>

1. **Temperature:** High fluidity at high temperatures (vice versa at low temperatures)
2. **Proportion of Unsaturation:** The more unsaturated fatty acyl chains (specifically the more cis bonds there are in a chain), packing into bilayer is reduced so fluidity is increased
3. **Length of Fatty Acyl Chains:** Shorter the chains the more fluid the bilayer is (vice versa for longer chains)
4. **Cholesterol Content:** Because cholesterol is amphipathic, the more cholesterol the more fluid the bilayer is
   - <u>Note: Above 37 degrees Celsius, more cholesterol will reduce fluidity as it will pack between lipid molecules</u>

- Lipid bilayers are **asymmetrical** meaning the composition of one side of the bilayer is different than the other
- Asymmetry is regulated by **phospholipid translocases (flippase)**

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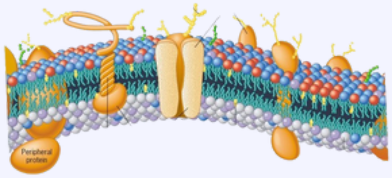
Biological Membranes

- Proteins make up about 50% of the mass of typical biological membranes
- Behaviour of proteins within the lipid bilayer is described by the **Fluid Mosaic Model**: Proteins are free to diffuse laterally within the bilayer, unless their movement is restricted by cellular components

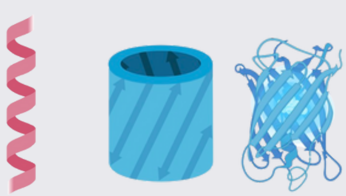


Sourced from: https://bookdown.org/jcog196013/BS2004/eukaryotic-organelles.html

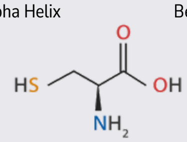
Membrane Proteins

<u>Proteins associate with the membrane in 4 different ways:</u>

1. **Integral Membrane Proteins**: A part of the polypeptide chain contacts the hydrophobic interior of the membrane
   - Some are embedded in the membrane but do not cross (more common to find transmembrane proteins though)
2. **Transmembrane Proteins:** Type of integral membrane protein in which the peptide chain(s) completely crosses the membrane and is exposed to the aqueous environment on both sides. Usually have *alpha helical secondary structure* (if only 1 polypeptide chain crosses the membrane, it will always be alpha helical)
   - Useful because alpha helix will maximize intramolecular bonding which minimizes interaction of protein with hydrophobic interior
   - Membrane spanning alpha helices typically are composed of <u>20 hydrophobic amino acids</u>
   - Removing an alpha helix from the membrane would cause exposure of hydrophobic regions to aqueous environments (not favorable)
   - Some alpha helices will have hydrophobic residues facing the lipids and polar groups in the middle (amphipathic). These can form **channels**
   - Some transmembrane proteins have β-strands that come together to make **β-barrel structures** that cross the membrane
     - The outside of the barrel is hydrophobic while the side chains inside of the barrel are often polar
3. **Peripheral Membrane Proteins:** Not anchored into the lipid bilayer but associate with integral membrane proteins or with the hydrophilic head groups of membrane lipids
4. **Lipid-Linked Proteins:** One or more lipid molecules are covalently attached to the end of the protein or to particular side chains, usually cysteine
   - Lipids are embedded in the membrane, but the protein side chains are not exposed to the bilayer hydrophobic interior



Alpha Helix Beta Barrels



Cysteine

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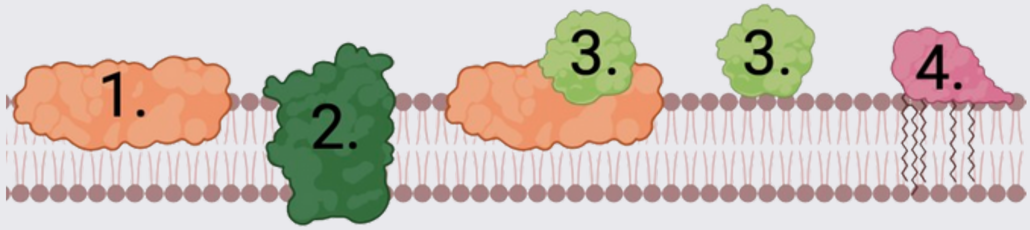
Membrane Proteins: A Closer Look



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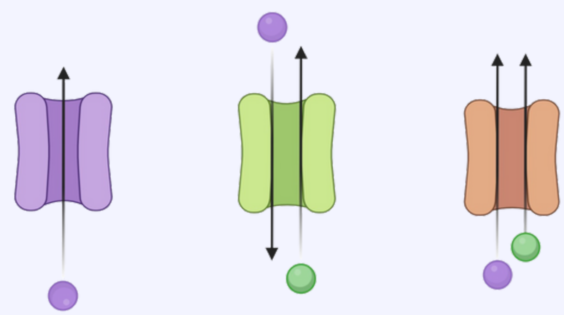
1. **Integral membrane protein**
2. **Transmembrane protein** (A type of integral membrane protein)
3. **Peripheral Membrane Protein**
4. **Lipid-Linked Protein** (See the darker coloured lipid anchor attaching it to the membrane)

Functions of Membrane Proteins

Membrane proteins have various functions:

- Can act as **transporters and channels**:
  - Help bring ions and polar molecules across the membrane (Facilitated transport)
    - **Uniporters**: Move one molecule across the membrane
    - **Symporters**: Move two molecules in the same direction across the membrane
    - **Antiporters**: Move two molecules in opposite directions across the membrane
  - Molecules move toward compartments with a favourable **electrical gradient** (positive to negative and vice versa) as well as a favourable **concentration gradient** (high to low) and this will form the basis of an **electrochemical gradient**
    - **Active transport:** requires ATP to move molecules against gradient
    - **Passive transport:** Molecules move spontaneously across membranes



Uniporter Antiporter Symporter

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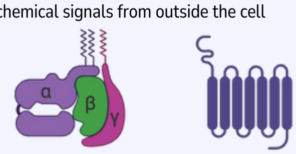
- Can act as **receptors** to sense and interpret chemical signals from outside the cell



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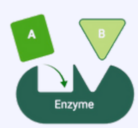
Ex. G-Protein Coupled Receptors (GPCRs)

- Can act as **enzymes** to catalyze chemical reactions



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- Can act as **anchors** to provide stability to the membrane and will bind to molecules on both sides

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Ex. CD90 (A cell-surface anchor protein)

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