Binding of a substrate to an enzyme catalytic site brings about conformational changes in the enzyme with multiple weak interactions being formed with the substrate molecule. The amino acid side chains of the enzyme aid in cleavage and formation of bonds thereby providing a variety of mechanisms for catalysis to occur.

**Learning Objective**

After interacting with this Learning Object, the learner will be able to,

- Define Fatty acids.
- Describe the membrane lipids.
- Recall proteins in membrane structure,
- List out the properties of cell membranes.
Fatty acids are long hydrophobic chains of carbon atoms having different lengths and a carboxylate group at one end. Fatty acids that do not contain any double bonds are said to be saturated while those possessing one or more double bonds in their structure are unsaturated. Most naturally occurring fatty acids have an even number of carbon atoms with varying degrees of unsaturation. The carboxylate group is numbered as one and the last carbon atom that is furthest away from the carboxylate group is known as the omega carbon.
Fatty acids

The fatty acid names are derived from their corresponding parent hydrocarbons by replacing the ‘e’ at the end with ‘oic’ or ‘oate’. A saturated fatty acid with 16 carbon atoms, for instance, is known as hexadecanoate. If there is one double bond, then it becomes decenoate with the position of the double bond being indicated as a superscript after a delta symbol. For instance, a 18 carbon fatty acid with one double bond is known as ocatadecenoate while with two double bonds, it is known as octadecadienoate.
Membrane lipids

Phospholipids are composed of four components - fatty acids, a platform to which the fatty acid is attached, phosphate residue and an alcohol attached to the phosphate. The platform to which the fatty acids are linked may be glycerol or sphingosine. Phospholipids containing glycerol are known as phosphoglycerides, with two OH groups of glycerol being esterified with the carboxylate groups of fatty acids. The simplest phospholipid, phosphatidate, is made up of only the phosphate group and fatty acids attached to the glycerol backbone.
Membrane lipids

The important phosphoglycerides found in membranes are derived from phosphatidate by esterification of the phosphate group with the hydroxyl group of various alcohols. The most commonly observed phosphoglycerides include phosphatidyl serine, choline, ethanolamine, inositol and diphosphatidyl glycerol, also known as cardiolipin.
Membrane lipids
Sphingosine is another amino alcohol backbone that serves as a platform for attachment of fatty acids and alcohols. Sphingomyelin, derived from sphingosine, consists of a fatty acid linked to the amino group via an amide bond and a choline moiety attached to the primary hydroxyl group via a phosphate group.
Lipids that have a sugar component in them are known as glycolipids. They are made up of a sphingosine backbone with the amino group acylated by a fatty acid and one or more sugar residues attached to the primary hydroxyl group. The simplest glycolipid is known as cerebroside which contains either glucose or galactose as its sugar residue.
Membrane lipids
Another group of structural membrane lipids is the sterols, found in most eukaryotic cells. The steroid nucleus consists of four fused rings that are oriented in a planar manner. Cholesterol is an amphipathic molecule with a polar hydroxyl head group and a non-polar steroid nucleus and hydrocarbon side chain. In addition to having a structural role in membranes, sterols are precursors for several products such as steroid hormones and bile acids.
Membrane lipids
The amphipathic nature of the phosphoglyceride molecules consisting of a polar head group and a hydrophobic tail enables them to rearrange themselves in an aqueous environment. When they come in contact with aqueous surroundings, they can either reorient to form a micellar structure or a bilayer arrangement. In these arrangements, the polar head groups are in contact with water by means of hydrogen bonding while the hydrophobic tails interact with each other through hydrophobic and Van der Waals interactions. The lipid bilayer arrangement is more favoured for phospholipids and glycolipids.
Bacteriorhodopsin is an archaeal integral membrane protein that plays a role in energy transduction, using light energy for the transport of protons from inside to outside the cell. It is made of seven membrane-spanning alpha helices that are oriented perpendicular to the plane of the membrane. Determination of the amino acid sequence of this protein revealed that most of the residues within the membrane are non-polar, thereby allowing favorable interactions with the lipid hydrocarbon chains. Very few charged residues were found in the structure.
Porins are another class of integral membrane proteins that form channels within the membrane. They are composed entirely of β-strands with essentially no alpha helices in their structure. These beta strands are hydrogen bonded to each other to form a beta sheet which folds to form a hollow cylindrical structure. The folding occurs such that the polar amino acid residues line the inside of the cylinder, thereby making it hydrophilic. This allows the channel to be filled with water and also allows passage of small ions and charged molecules. The non-polar residues facing outside interact hydrophobically with the lipid chains of the membrane.
Peripheral membrane proteins are attached to either the outside or inside surface of the membrane via electrostatic and hydrogen bond interactions with either the lipid heads of the membrane or with other integral proteins. These polar interactions can be easily disrupted by addition of acids or alkali which modify the pH or by addition of salts.
It is possible to predict transmembrane helix regions of a protein by calculating the free energy changes associated with the transfer of residues from a hydrophobic to aqueous environment. The width of a membrane is typically around 30 Å, which can fit approximately 20 amino acid residues. Therefore the free energy change for hypothetical alpha helices formed every 20 residues, from residue1 to 20, 2 to 21, 3 to 22 and so on are calculated until the end of the sequence is reached. These free energy changes are plotted against the first amino acid residue of every 20-residue window to obtain a hydropathy plot. A peak above 84 kJ/mol is indicative of a likely membrane spanning helix. This, however, does not detect membrane spanning β-sheets.
Lateral diffusion of membrane components can be proved using fluorescence recovery after photobleaching technique. A cell surface component is first labelled by means of a fluorescent molecule and a small region of the cell surface is viewed by means of fluorescence microscopy. The fluorescent molecules in the region being viewed are destroyed by a laser pulse, a process known as bleaching. Fluorescence however reappears in the region after a certain time that is dependent on the diffusion coefficient of the molecules.
Properties of cell membranes

The Fluid Mosaic model explains the lateral diffusion of membrane components but not the transverse diffusion. Lateral diffusion is a rapid process taking place in the range of microseconds. However, transverse diffusion, also known as the ‘flip flop’ reaction takes place very slowly over a period of several hours. This reaction is facilitated by the enzyme flippase, which carries out transverse diffusion in the time range of few seconds.
Properties of cell membranes

The fluidity of any biological membrane is dependent on the properties of the fatty acid chains present in it. Transition of the membrane from a rigid state to a fluid state occurs abruptly as the temperature is increased and crosses the melting temperature, Tm. This melting temperature is a function of the length of fatty acyl chains present and their degree of unsaturation. Increase in length of fatty acyl chain increases the Tm while increase in the degree of unsaturation decreases the Tm. In other words, greater number of double bonds disrupts the packing order achieved by saturated fatty acids thereby decreasing the Tm. In animals, the cholesterol content is another regulator of fluidity. Greater the amount of the bulky steroid, higher is the Tm.
**Fatty acids**

1. **Fatty acid**: Fatty acids, more simply known as fats, are the key components of lipids that play an important role in signal transduction pathways and as structural elements of membranes. They are long hydrophobic chains of different lengths that possess a carboxylate group at one end. Most naturally occurring fatty acids have an even number of carbon atoms with varying degrees of unsaturation.

2. **Degree of unsaturation**: The number of double bonds present in a fatty acid chain defines its degree of unsaturation.

3. **Chain length**: The total number of carbon atoms present in a fatty acid chain is its chain length.

4. **ω carbon**: Fatty acids are numbered starting from their carboxyl group with the second and third carbon atoms being known as the α and β carbons. The carbon atom that is furthest away from the carboxylate group, at the distal end of the chain is known as the ω carbon.
1. Lipids: These are water insoluble biomolecules that readily dissolve in organic solvents like chloroform and have a wide range of biological functions. They are important components of membranes, serve as fuel reserves and signalling molecules. Three important membrane lipids include phospholipids, glycolipids and cholesterol.

2. Phospholipid: Phospholipids are composed of four components - fatty acids, a platform to which the fatty acid is attached, phosphate residue and an alcohol attached to the phosphate. The platform to which the fatty acids are linked is commonly glycerol but in some cases, a more complex alcohol known as sphingosine may also be present. Phospholipids containing glycerol are known as phosphoglycerides, with two OH groups of glycerol being esterified with the carboxylate groups of fatty acids. The fatty acid chains form the hydrophobic tail while the remaining components constitute the hydrophilic head group.

3. Glycolipid: Lipids that have a sugar component in them are known as glycolipids. They are made up of a sphingosine backbone with the amino group acylated by a fatty acid and one or more sugar residues attached to the primary hydroxyl group. The simplest glycolipid is known as cerebroside which contains either glucose or galactose as its sugar residue.
4. **Cholesterol**: Cholesterol is a steroid molecule whose structure is significantly different from that of phospholipids and glycolipids. Cholesterol is found in varying quantities in animal membranes but is not present in prokaryotes. It is composed of a hydrocarbon chain linked to one end and a hydroxyl group at the other end.
1. Lipid bilayer: The flat membrane sheets that form a barrier around cells consisting of two layers of lipid molecules is known as the lipid bilayer. The hydrophobic tail regions are sequestered within the bilayer, away from the aqueous environment while the polar heads face outward and interact with the surrounding molecules. The bilayer is also embedded with proteins that perform specific functions for the cell.

2. Integral proteins: Those proteins that span the membrane and are embedded within the lipid bilayer are known as integral proteins. They interact extensively with the hydrophobic chains of lipids and cannot be easily dissociated from the membrane.

3. Peripheral proteins: Peripheral membrane proteins, however, are only bound to the membrane surfaces by means of electrostatic and hydrogen bond interactions with the polar head groups of the lipids. They can be easily dissociated from the membrane with mild agents such as salts, acids or alkali since they are not embedded within it.

4. Glycoprotein: Carbohydrate groups are often covalently attached to proteins to form glycoproteins. The sugar residues are typically attached to the amide nitrogen atom of the aspargine side chain or to the oxygen atom of the serine or threonine side chain. These glycoproteins are components of cell membranes and have a variety of functions in cell adhesion processes.
1. **Fluorescence Recovery After Photobleaching (FRAP):** This is a technique by which a cell surface component is first labelled by means of a fluorescent molecule and a small region of the cell surface is viewed by means of fluorescence microscopy. The fluorescent molecules in the region being viewed are destroyed by a laser pulse, a process known as bleaching. Once this occurs, the time required for fluorescence to reappear in this region is plotted against the fluorescence intensity. This helps in understanding the movement of molecules across the cell surface.

2. **Lateral diffusion:** The process by which membrane components move laterally from one region to another in the same plane. This is a quick process and takes place in a matter of microseconds. Proteins exhibit varying degrees of lateral mobility, with some being as mobile as lipids and others being almost immobile.

3. **Transverse diffusion (flip-flop):** This is a process by which molecules in the membrane transition from one surface of the membrane to the other. The time required for transverse diffusion is significantly more than that for lateral diffusion and can be measured by electron spin resonance techniques. This process is made quicker by the enzyme 'flippase'.
4. Fluid Mosaic Model: The overall organization and properties of biological membranes were proposed by Jonathan Singer and Garth Nicolson in 1972 as the Fluid Mosaic Model. They proposed that membranes are two-dimensional solutions of oriented lipids and globular proteins, with the lipids serving as a “solvent” for integral membrane proteins and functioning as a permeability barrier. They also hypothesized that membrane proteins undergo lateral diffusion freely but not transverse diffusion.
1. How many double bonds would be present in a fatty acid having the systematic name “all-cis-Δ⁹, Δ¹₂, Δ¹⁵-Octadecatrienoate”?

- 1
- 2
- 3
- 4

Congratulations, you have chosen the correct answer.
Which of the following is a saturated fatty acid with 18 carbon atoms?

- cis-Δ⁹-Octadecenoate
- Octadecanoate
- Eicosanoate
- Tetradecanoate

Congratulations, you have chosen the correct answer.
Which of the following components is not present in Phosphatidyl inositol?

- Sphingosine
- Glycerol
- Phosphate
- Inositol

Congratulations, you have chosen the correct answer.
If the degree of unsaturation of fatty acyl chains increases, what happens to the $T_m$?

- $T_m$ increases
- $T_m$ remains same
- $T_m$ decreases
- None of the above

Congratulations, you have chosen the correct answer.
The threshold value of hydropathy index for detection of alpha helices is:

-22 kJ/mol
+22 kJ/mol
+67 kJ/mol
+84 kJ/mol

Congratulations, you have chosen the correct answer.
Books:

1) Biochemistry by Stryer et al., 6th edition
2) Biochemistry by A.L. Lehninger et al., 4th edition
3) Biochemistry by Voet & Voet, 3rd edition

Research papers: