CORE IDEA 1: THE CELL AND BIOMOLECULES OF LIFE
TOPIC 1.2: BIOMOLECULES

Learning Outcomes

You should be able to:

(g) describe the structure and properties of the following monomers:
- i. α-glucose and β-glucose (in carbohydrates)
- ii. glycerol and fatty acids (in lipids)
- iii. amino acids (in proteins) (knowledge of chemical formulae of specific R-groups of different amino acids is not required)

(h) describe the formation and breakage of the following bonds:
- i. glycosidic bond
- ii. ester bond
- iii. peptide bond

(i) describe the structures and properties of the following biomolecules and explain how these are related to their roles in living organisms:
- i. starch (including amylose and amylopectin)
- ii. cellulose
- iii. glycogen
- iv. triglyceride
- v. phospholipid

(m) explain primary structure, secondary structure, tertiary structure and quaternary structure of proteins, and describe the types of bonds that hold the molecule in shape (hydrogen, ionic and disulfide bonds, and hydrophobic interactions)

(n) explain the effects of temperature and pH on protein structure

(o) describe the molecular structure of the following proteins and explain how the structure of each protein relates to the function it plays:
- i. haemoglobin (transport)
- ii. collagen (structural)
- iii. *G-protein linked receptor (signalling) (knowledge of details of the number of amino acids and types of secondary structures present is not required**)***

Textbooks and References

Raven, P H, Johnson, G B, Mason, K A, Losos, J and Singer, S (2013) **Biology (10th Edition)** (McGraw-Hill) ISBN 007338307

Reece, J B, Urry, L A, Cain, M L, Wasserman, S A, Minorsky, P V and Jackson, R B (2011) **Campbell Biology (10th Edition)** (Pearson Higher Education) ISBN 0321739752

1 INTRODUCTION

Biomolecules are important components of cell structures, including membranes which are made up of phospholipids, cholesterol, carbohydrates and proteins. The different classes of biomolecules (carbohydrates, lipids, proteins and nucleic acids) function as molecular building blocks for macromolecules to be assembled.

Prior Knowledge

You should be able to:

A. *[syllabus 6093]* list the chemical elements which make up
   - carbohydrates
   - fats
   - proteins

B. describe and carry out tests for
   - starch (iodine in potassium iodide solution)
   - reducing sugars (Benedict's solution)
   - protein (biuret test)
   - fats (ethanol emulsion)

C. state that large molecules are synthesised from smaller basic units
   - glycogen from glucose
   - polypeptides and proteins from amino acids
   - lipids such as fats from glycerol and fatty acids

- In living organisms, large biological molecules can be classified into four major classes based on molecular structure:
  - Carbohydrates
  - Lipids
  - Proteins
  - Nucleic Acids *(covered in Core Idea 2: Topic 2.1)*

- Carbohydrates, proteins and nucleic acids are polymers (*polys* = many). Polymers are long molecules made from smaller repeating units called monomers (*monos* = single) in a process known as condensation.

2 CARBOHYDRATES

- Carbohydrates are generally known as ‘sugars” and are the main substrate used for cellular respiration to synthesise ATPs (which can be hydrolysed to release energy).

- They are a group of organic compounds consisting mainly of carbon (C), hydrogen (H) and oxygen (O). The general formula for carbohydrates is $C_x(H_2O)_y$.

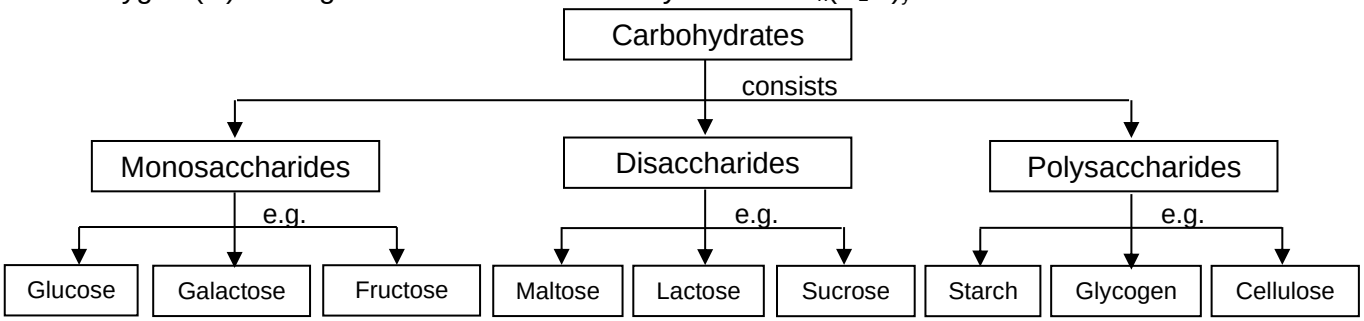


Fig. 2 Classification of carbohydrates

2.1 MONOSACCHARIDES

Learning Outcome (g)(i):
Describe the structure and properties of α-glucose and β-glucose (in carbohydrates).

- Monosaccharides are simple sugars (monomers) that cannot be further hydrolysed. They have a general formula of $(CH_2O)_n$, where n = 3 to 7.

- Monosaccharides can exist as linear chains or cyclic structures. When linear glucose cyclizes, it may form 2 different isomers:
  - α-glucose: the hydroxyl group (-OH) on C_1 is on the different plane as C_6.
  - β-glucose: the hydroxyl group (-OH) on C_1 is on the same plane as its C_6.

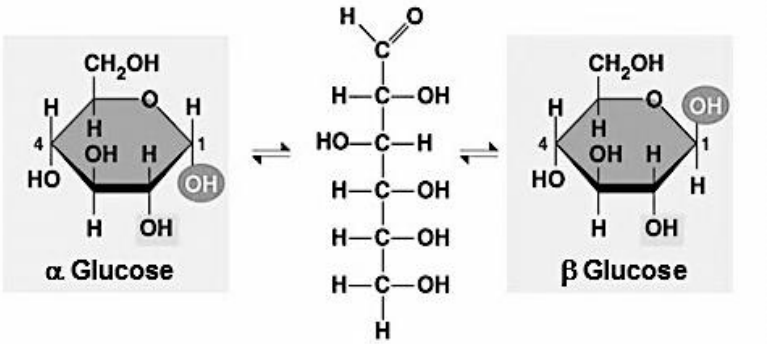


Fig. 2.1.1 Linear and ring forms of glucose

2.2 DISACCHARIDES

Learning Outcome (h)(i):
Describe the formation and breakage of the glycosidic bond.

- Disaccharides are sugars made up of 2 monosaccharides. Commonly occurring disaccharides include maltose, lactose and sucrose.

- A disaccharide is formed when 2 monosaccharides are linked by a **glycosidic bond** that is formed via **condensation between OH groups**, with the **elimination of one water molecule**.

- The glycosidic bond formed will be named according to:
  - the glucose isomers used
  - the C atoms involved

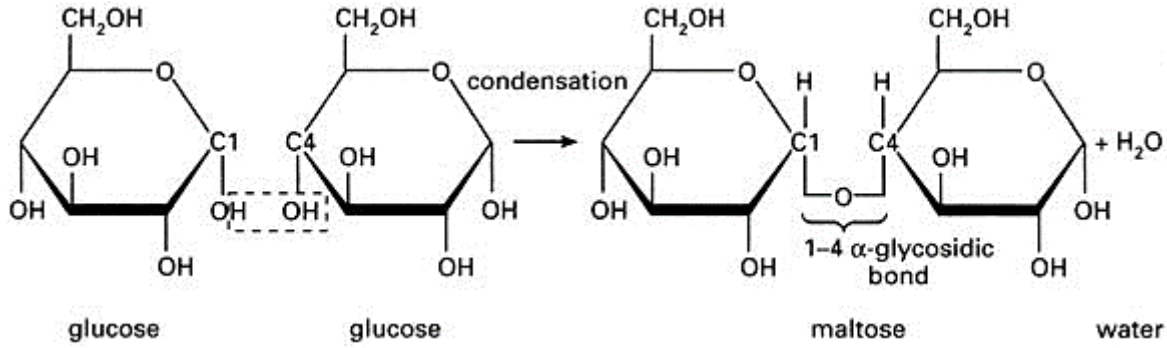


Fig. 2.2 Condensation reaction between 2 glucose monomers to form maltose and water

DID YOU KNOW?

What are the following disaccharides made up of?

1. Maltose (commonly known as malt) [ ] + [ ]
2. Sucrose (commonly known as table sugar) [ ] + [ ]
3. Lactose (commonly known as milk sugar) [ ] + [ ]

2.3 POLYSACCHARIDES

Learning Outcome (i):

Describe the structures and properties of the following biomolecules and explain how these are related to their roles in living organisms:

(i) starch (including amylose and amylopectin),
(ii) cellulose and
(iii) glycogen.

- Polysaccharides are polymers made up of hundreds to thousands of monosaccharides. The monosaccharides are connected through glycosidic bonds, formed through condensation reactions where multiple water molecules are eliminated.

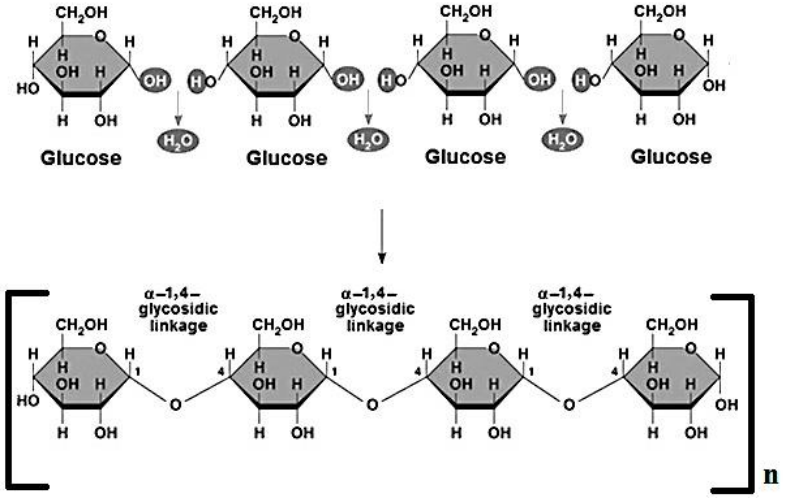


Fig. 2.3 Formation of a segment of a polysaccharide

- Polysaccharides can be divided into 2 groups based on function:
  - Storage polysaccharides (e.g. starch and glycogen)
  - Structural polysaccharides (e.g. cellulose)

2.3.1 STARCH

- **Starch** is a polysaccharide that serves a **storage function in plants**. It consists of thousands of **α-glucose monomers** and functions as a compact energy reserve formed from excess glucose synthesized during photosynthesis.

- Starch consists of **2 components**: **amylose** and **amylopectin**.

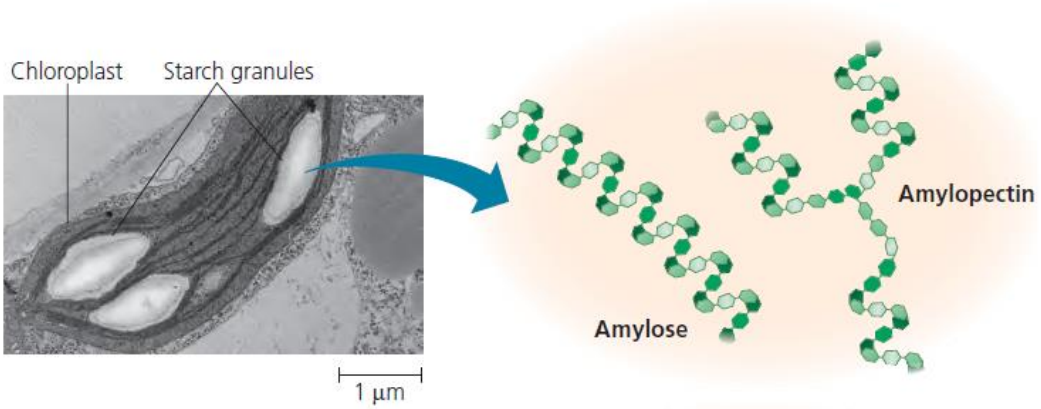
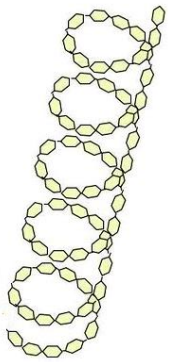


Fig. 2.3.1.1 Components of starch – amylose and amylopectin



- **Amylose** consists of thousands of α-glucose residues linked by **α-1,4-glycosidic bonds**.
- It is **helical** in shape. Its spiral configuration is stabilised by hydrogen bonds between hydroxyl (-OH) groups.

Fig. 2.3.1.2 Structure of amylose

- **Amylopectin** consists of α-glucose residues linked by **α-1,4-glycosidic bonds and α-1,6-glycosidic bonds**. It has a **branched** structure. Branch points are due to the presence of α-1,6-glycosidic bonds.

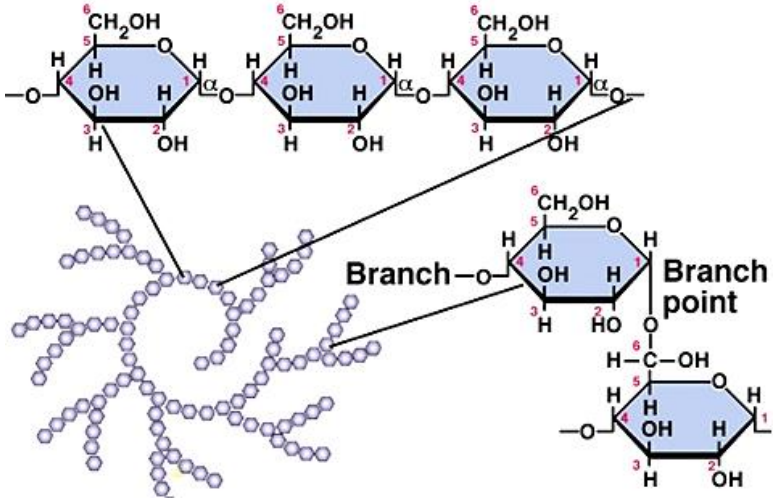


Fig. 2.3.1.3 Structure of amylopectin

Table 1: Structure to function adaptations of starch

Structural Features	Function Adaptation
• **Helical** structure of amylose and **branched** structure of amylopectin makes starch compact.	• Allows **efficient storage** of glucose molecules i.e. more molecules of starch can be stored within less space in plant cells.
• **α-glycosidic bonds** between glucose monomers.	• Can be **hydrolysed by amylase** to release glucose molecules for respiration.
• **Large** molecular weight. • Folding of the starch molecule such that the **hydroxyl groups (-OH)** are in the **interior** of the molecule, i.e. prevented from interacting with water.	• Makes starch **insoluble** (inability to form hydrogen bonds with water molecules), allowing it to be stored **without changing the osmotic potential** within the plant cell.
• **Branched** structure of amylopectin.	• Allows **multiple action sites** for amylase, increasing the rate of hydrolysis to release glucose monomers for respiration.
• Consists of **thousands of glucose** molecules.	• Allows **large amount of energy to be released** during hydrolysis as glucose is the main respiratory substrate.

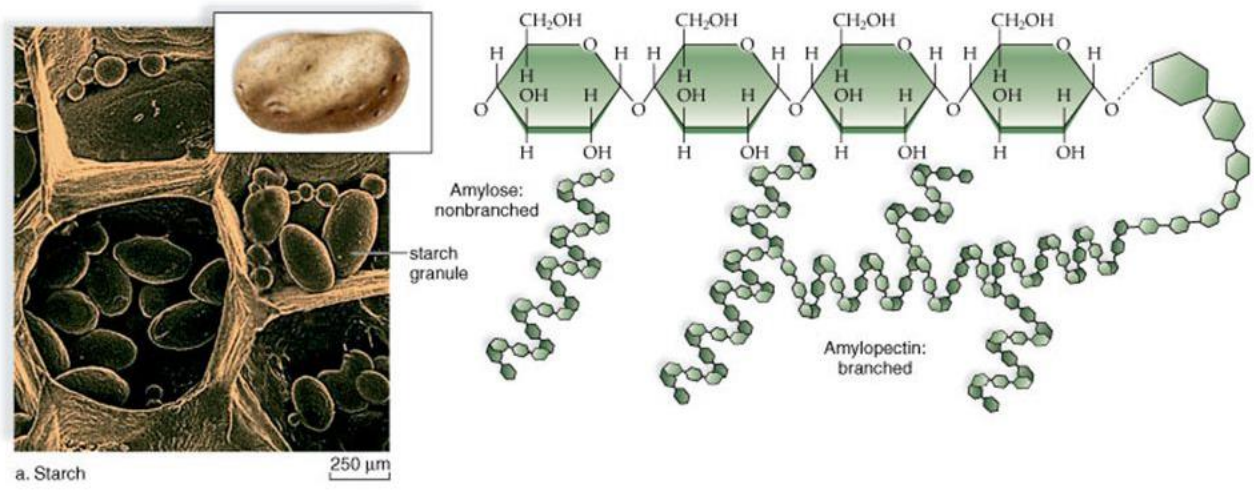


Fig. 2.3.1.4 Structure of starch

2.3.2 GLYCOGEN

- **Glycogen** is a polysaccharide that serves a **storage function in animals**. It consists of thousands of **α-glucose monomers** and functions as a compact energy reserve mainly in liver and skeleton muscle cells.

- Glycogen is similar in structure to amylopectin but is more **highly branched**.

- α-glucose monomers are linked by **α-1,4-glycosidic** and **α-1,6-glycosidic bonds**.

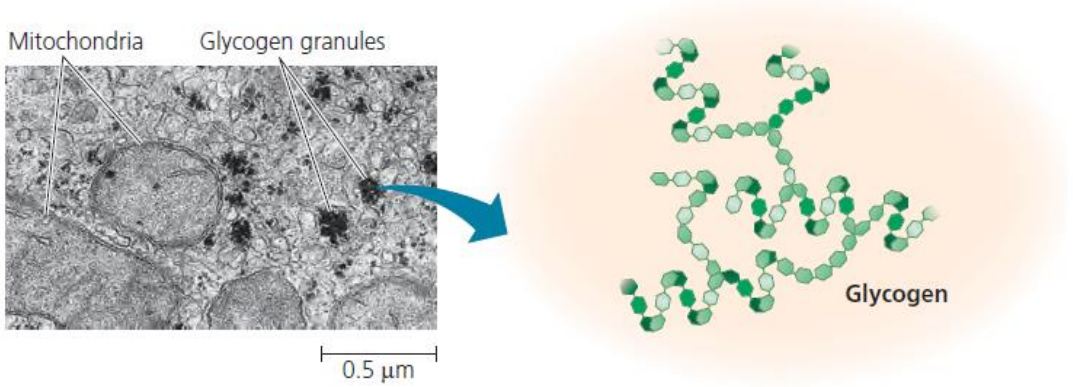
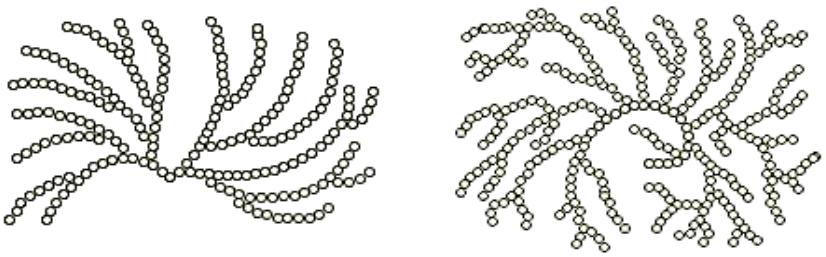


Fig. 2.3.2.1 Structure of glycogen



Amylopectin (component of starch)

Glycogen

Fig. 2.3.2.2 Branching structures in amylopectin vs glycogen

Table 2: Structure to function adaptations of glycogen

Structural Features	Function Adaptation
• **Branched** structure of glycogen makes it compact.	• Allows **efficient storage** of glucose molecules i.e. more molecules of glycogen can be stored within less space in animal cells.
• **Highly branched** structure of glycogen.	• Allows **multiple action sites** for glycogen phosphorylase, increasing rate of hydrolysis to release glucose monomers.
• **α-glycosidic bonds** between glucose monomers.	• Can be **hydrolysed by glycogen phosphorylase** to release glucose molecules for respiration.
• **Large** molecular weight of glycogen. • Folding of the glycogen molecule such that the **hydroxyl groups (-OH)** are in the **interior** of the molecule, i.e. prevented from interacting with water.	• Makes glycogen **insoluble**, allowing it to be stored **without changing the osmotic potential** within the animal cell.
• Consists of **thousands of glucose** molecules.	• Allows **large amount of energy to be released** during hydrolysis as glucose is the main respiratory substrate.

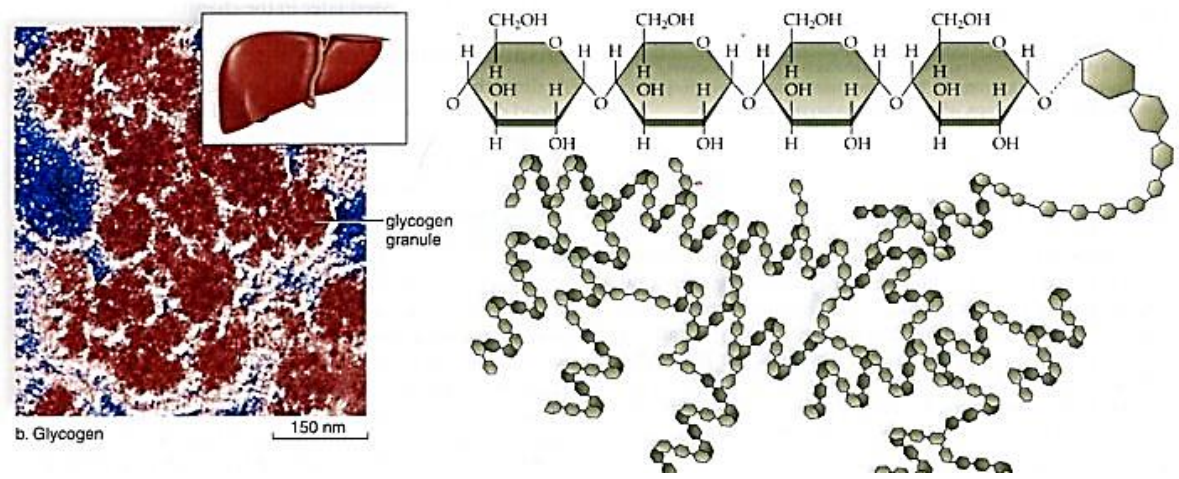


Fig. 2.3.2.3 Structure of glycogen

2.3.3 CELLULOSE

- **Cellulose** is a polysaccharide that serves a **structural function in plants**. It consists of **β-glucose monomers** linked by **β-1,4-glycosidic bonds**.

- Cellulose is a **major component of the plant cell wall**, which functions to

    - maintain the shape of the plant cell, preventing it from bursting and
    - protect the plant from mechanical injuries

- Every β-glucose unit is inverted 180° to the adjacent unit to bring the reacting OH groups into close proximity during condensation.

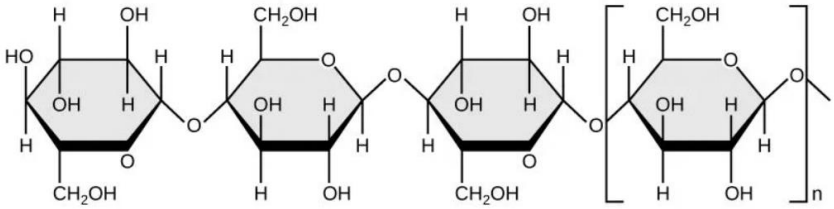


Fig. 2.3.3.1 Inversion of every alternate glucose unit

- This forms a linear, unbranched chain of cellulose with protruding OH groups. The linear chains bundle together to form microfibrils, stabilized by crosslinks of hydrogen bonds between protruding OH groups with their neighbouring chains.

- Microfibrils are further bundled to form macrofibrils. Macrofibrils are embedded in a matrix of pectin and hemicellulose in the cell wall.

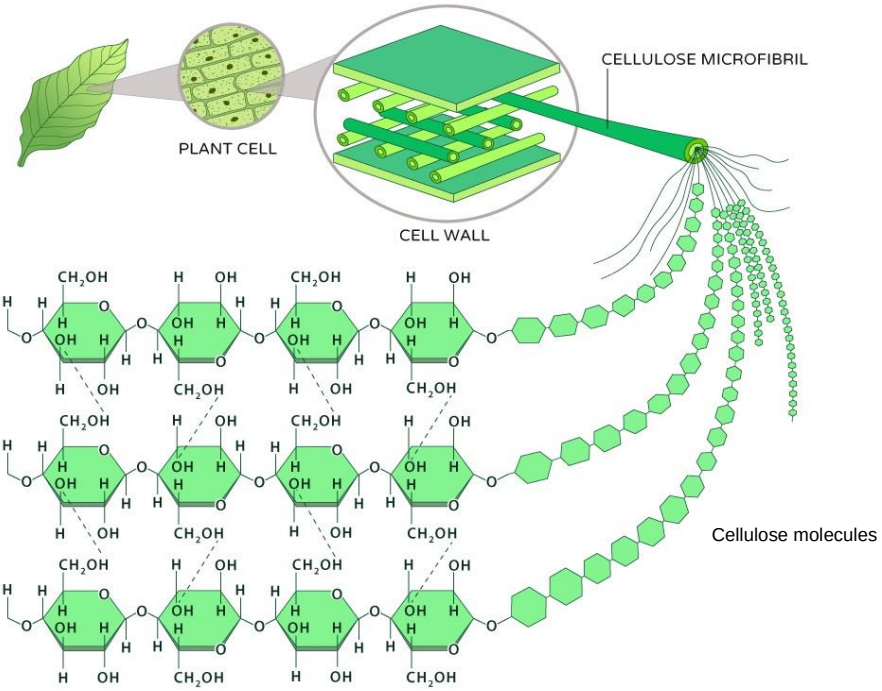


Fig. 2.3.3.2 Protruding OH groups and crosslinks of hydrogen bonds between cellulose molecules to form fibrils

Table 3 Structure to function adaptations of cellulose

Structural Features	Function Adaptation
• **Large** molecule consisting of **thousands of β glucose** monomers linked by β-1,4 glycosidic bonds.	• Allows **storage of large amount of energy** (for organisms, e.g. herbivores, termites, that are able to hydrolyse cellulose).
• **Alternate β-glucose is inverted**, resulting in formation of **linear** chains.	• Allows **bundling into microfibrils and macrofibrils** to increase tensile strength.
• **Hydroxyl groups (-OH) projecting out** of cellulose chains.	• Allow **hydrogen bond cross-linkages** to form between OH groups of neighbouring cellulose chains to increase **tensile strength**. • Allow full permeability to water and solutes (as cross links do not restrict movement of substances). Note: cross links here refer to the hydrogen bonds between cellulose chains.
• Cellulose is **embedded in hemicellulose and pectin** in cell wall.	• Increase **tensile strength** and **mechanical strength**.
• Cell wall allows for **lignin deposition**.	

Checkpoint 1

Complete the following table.

Polysaccharide	Starch	Glycogen	Cellulose
Sugar monomer			
Bond(s) present between monomers			
Appearance of molecule	Amylose: Amylopectin:	Similar to amylopectin but more highly branched	
Orientation of adjacent monomers	adjacent monomers in same orientation		
Location			
Function			

3 LIPIDS

- Lipids are a diverse group of hydrophobic molecules with no general formula, consisting mainly of the elements carbon (C) and hydrogen (H) in variable ratios, and may include other elements such as phosphorus (P) and nitrogen (N).

- All lipids have low solubility in polar solvents (e.g. water) but high solubility in organic solvents (e.g. acetone). This non-polar, hydrophobic property of lipids is due to the presence of long hydrocarbon chains.

- Lipids in liquid state are known as oils while in solid state are generally referred to as fats.

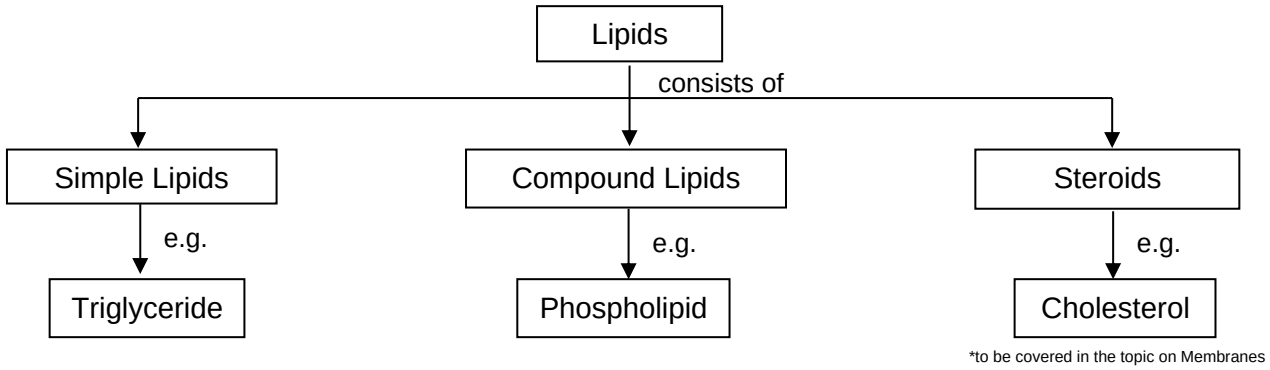


Fig. 3 Classification of lipids

3.1 COMPONENTS OF LIPIDS

Learning Outcome (g)(ii):
Describe the structure and properties of the following glycerol and fatty acids (in lipids).

- Most lipids are made up of glycerol and fatty acids.

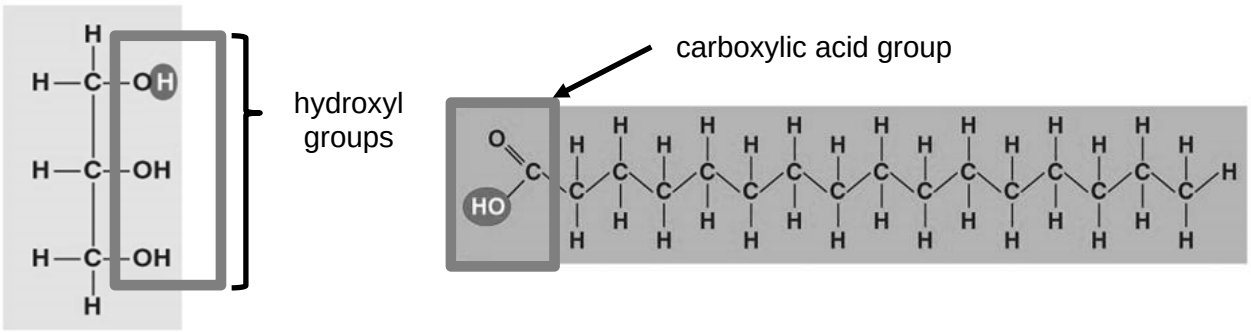


Fig. 3.1 Functional groups in glycerol (left) and a fatty acid (right)

3.1.1 GLYCEROL

- Glycerol is an alcohol with 3 carbon atoms, each bearing a hydroxyl group (-OH).
- The presence of the polar OH groups allows glycerol to interact with water molecules, making it soluble in water.

3.1.2 FATTY ACIDS

- Fatty acids are carboxylic acids with long-chain hydrocarbon side groups.
- A hydrocarbon chain (denoted as R in some instances) consists of a chain of carbon (C) atoms to which hydrogen (H) atoms are attached.
- Due to these nonpolar C-H bonds, fatty acids are not soluble in water and are known as hydrophobic (water-fearing).
- **Hydrocarbon chains** in fatty acids **differ by length and degree of saturation**, affecting their melting points

1. **<u>Length</u>**

   - The hydrocarbon chain of fatty acids may differ by length (normally between 14 - 20 carbon atoms).

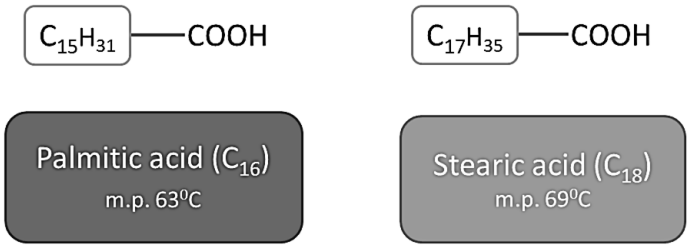


Fig. 3.1.2.1 differences in melting point due to length of carbon chain

   - Molecules of fatty acids are bonded to each other by hydrophobic interactions in the hydrocarbon chain. Melting involves breaking of these inter-molecular hydrophobic interactions.

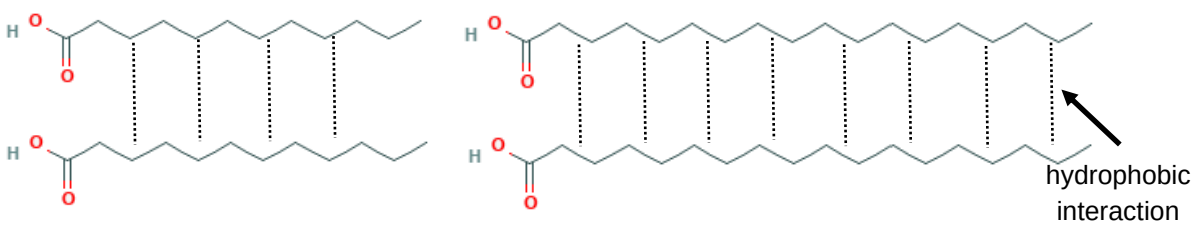


Fig. 3.1.2.2 Varying number of hydrophobic interactions between fatty acids with different chain length

- A longer hydrocarbon chain (i.e. more carbon atoms) increases the number of hydrophobic interactions.

- The more unsaturated the hydrocarbon chain (i.e. less C-C bonds or more C=C bonds) has more kinks thus less hydrophobic interactions between the fatty acid molecules of comparable length.

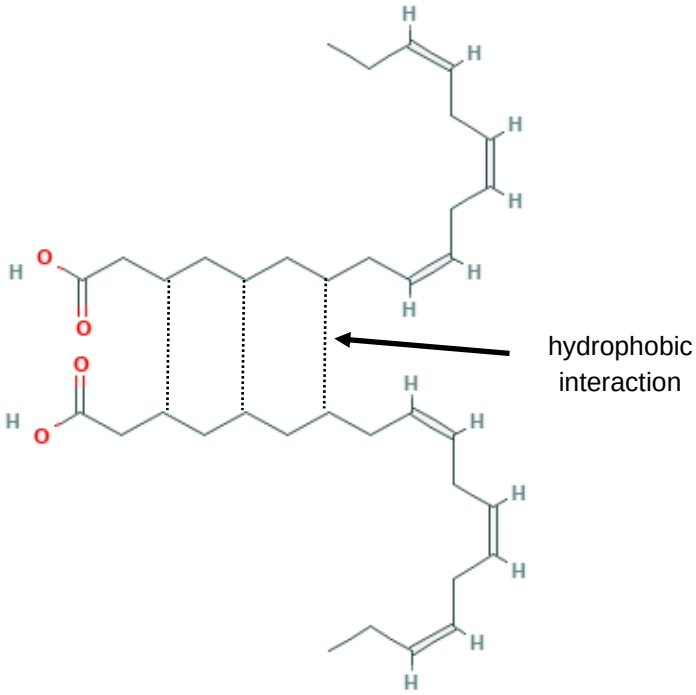


Fig. 3.1.2.3 Hydrophobic bonds between unsaturated fatty acids.

- Thus, fatty acids with longer chain length and/or more saturated would have a larger number of hydrophobic interactions, thus requiring a higher temperature to disrupt the weak hydrophobic interactions between fatty acid molecules to result in melting.

2. Degree of saturation

- Degree of saturation **refers to the number of carbon-carbon single bonds (C-C)** in a hydrocarbon chain.

- The hydrocarbon chain in saturated fatty acids does not contain carbon-carbon double bond (C=C) i.e. contains only C-C bonds.

- The hydrocarbon chain in unsaturated fatty acids contains C=C bonds which causes a kink in the molecule.

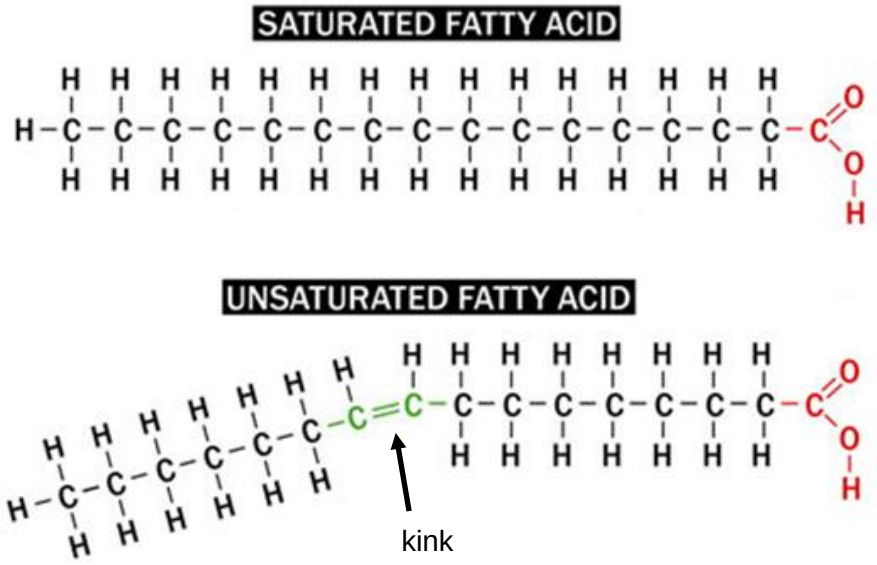
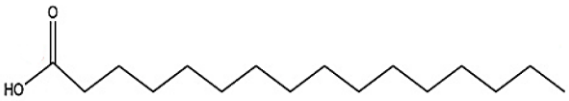
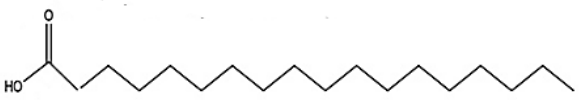
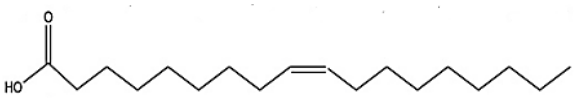
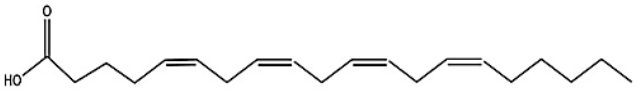
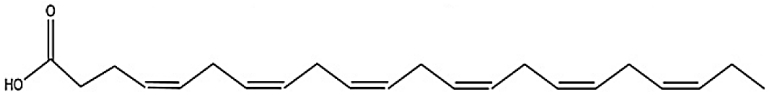


Fig. 3.1.2.4 Saturated fatty acid (top) and unsaturated fatty acid (bottom)

Checkpoint 2

Complete the following table.

Fatty Acid	No. of carbon	Degree of saturation	Number of C=C
 **Palmitic acid (PA)**			
 **Stearic acid (SA)**			
 **Oleic acid (OA)**			
 **Arachidonic acid (AA)**			
 **Docosahexaenoic (DHA)**			

You probably know that you should not consume too much fat. But is fat all bad? What else should you know about this nutrient?

Click on the link or scan the QR code to read on to find out

https://www.healthhub.sg/live-healthy/getting%20the%20fats%20right

SCAN ME

Learning Outcome (h)(ii):
Describe the formation and breakage of an ester bond.

Learning Outcome (i)(iv)&(v):
Describe the structures and properties of triglycerides and phospholipids, and explain how these are related to their roles in living organisms:

3.2 TRIGLYCERIDES

- Triglycerides are the most abundant and functionally important lipid in the biological system.

- A triglyceride is made of 1 glycerol and 3 fatty acid chains. The fatty acid chains are joined to the glycerol via condensation reactions, with the removal of 3 water molecules, resulting in the formation of an ester bond.

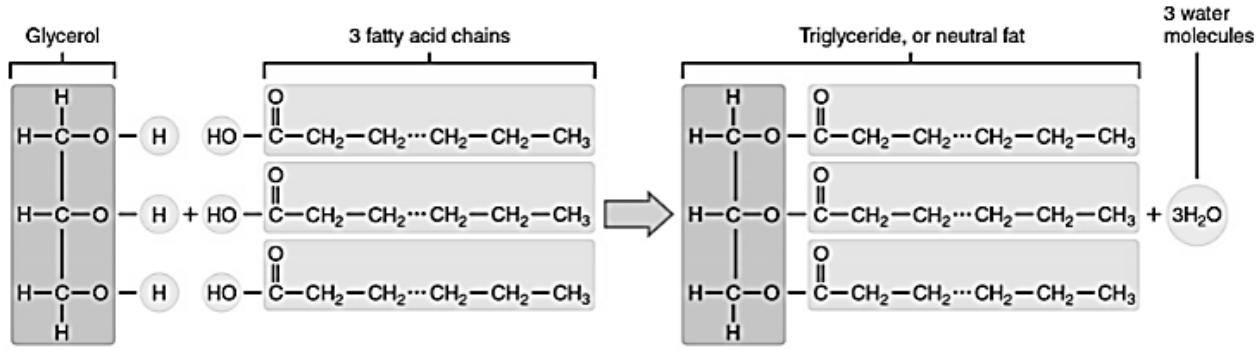


Fig. 3.2 Formation of ester bonds

- Due to the presence of 3 nonpolar fatty acid chains and the absence of polar OH groups, triglyceride is hydrophobic.

3.2.1 FUNCTIONS OF TRIGLYCERIDES

1) Energy Storage

Property	Function adaptations
• Fats have **high calorific value**. One gram of fat stores twice as much energy as one gram of carbohydrate.	• Upon oxidation (respiration), triglycerides can yield twice as much energy per unit mass than carbohydrates due to **higher proportion of C-H bonds**, making it a more compact energy reserve than carbohydrates (i.e. less mass of fat for the same amount of energy stored).
• Fats are **insoluble** in water.	• Lipids are stored in adipose tissue as anhydrous oil droplets (without water). Thus, more fats can be stored for a given weight. This is useful in animals and plant seeds where movement and mobility are important as their mass is kept to a minimum. • Lipids are not easily leached from cells. Thus, lipids can be stored in large amounts without affecting the water potential of cells.

2) Heat Insulation

Property	Functions
• Fats are **poor conductors of heat**.	• Fats are stored in adipocytes (fat cells), specialised for the synthesis and storage of fats. They act as **heat insulators**, preventing excessive heat loss. This is important for hibernating animals living in cold climates (e.g. polar bears) and aquatic animals (e.g. whales), which store up large amount of subcutaneous fat.

3) Buoyancy

Property	Functions
• Fats is **less dense than water**.	• Fats **increase buoyancy** in marine animals as it is less dense than water (e.g. blubber in whales). This is important for aquatic animals that breathe atmospheric air as they need to swim to the surface regularly.

4) Source of Water

Property	Functions
• Complete **oxidation of fats produces metabolic water**	• **Fats can serve as a source of water** as complete oxidation of fats produces metabolic water. This is important for desert animals (e.g. camel and kangaroo rat).

5) Mechanical Protection

Property	Functions
• Fats acts as a **shock absorber**	• Fats provide **protection against mechanical damage**. Fat is often found under the skin and around delicate organs such as kidneys

3.3 PHOSPHOLIPIDS

3.3.1 STRUCTURE OF PHOSPHOLIPIDS

- Phospholipids are the main component of the cell membranes.
- Phospholipids are made of 1 glycerol, 2 fatty acid chains and 1 phosphoric acid (H_3PO_4).
- The fatty acid chains are joined to glycerol via condensation reactions, with the removal of 2 water molecules, resulting in the formation of ester bonds.

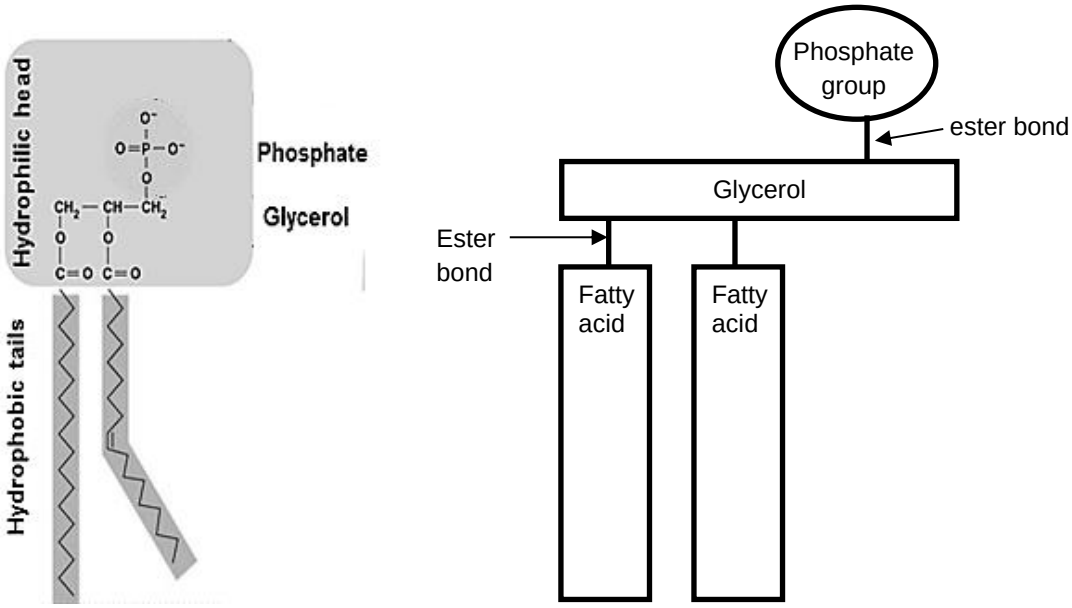


Fig. 3.3.1 Structure of phospholipid

- Phospholipids are amphipathic (i.e. have both a hydrophobic and hydrophilic region).
    - The phosphate group is negatively charged, forming the hydrophilic head.
    - The two fatty acid chains made of nonpolar hydrocarbons, forming the hydrophobic tails.
- Due to the amphipathic nature of phospholipids, they self-assemble in aqueous medium (e.g. water) to form structure such as a lipid bilayer, a micelle, or a liposome. The hydrophilic head faces the aqueous medium while the hydrophobic tails are face the interior, shielding the hydrophobic portion from water.

3.3.2 FUNCTION OF PHOSPHOLIPIDS

- Phospholipids are a major component of the cell surface membrane. Fatty acid tails of phospholipids help in regulation of membrane fluidity and permeability.

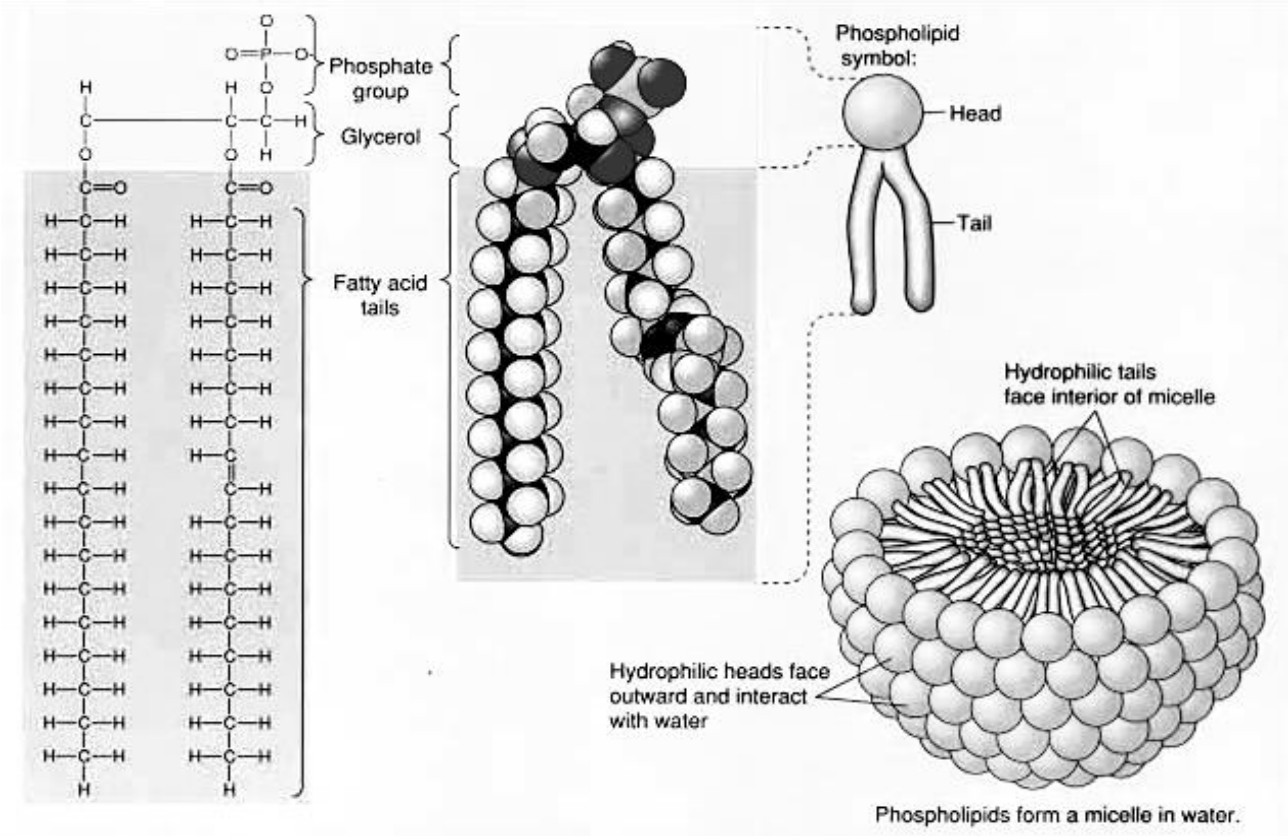
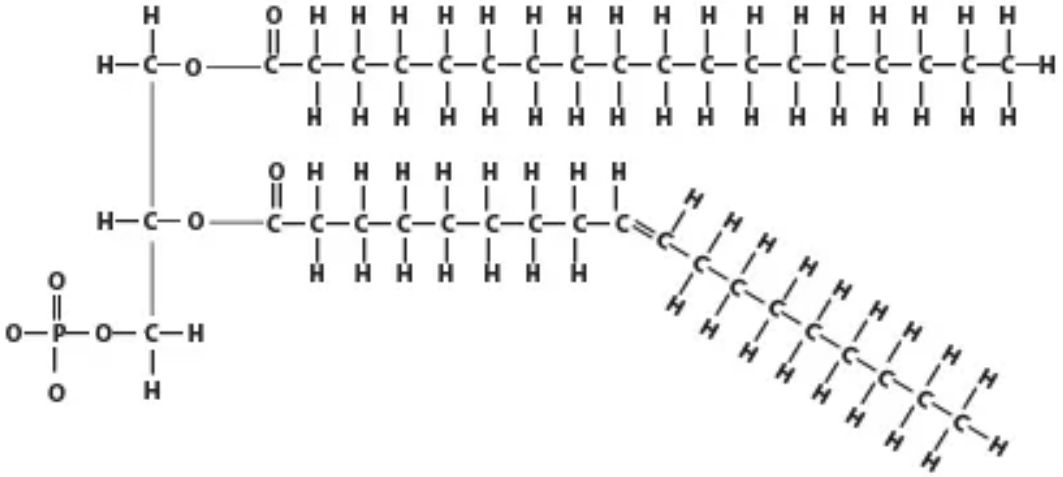


Fig. 3.3.2 Molecular structure of phospholipid and micelle formation in water

Checkpoint 3

On the diagram of the phospholipid below,

1. *Circle and label the glycerol backbone, 1 fatty acid tail and phosphate group.*
2. *Label 1 ester bond.*



4 PROTEINS

- Proteins are polymers of amino acids (monomers).

- They are a group of organic compounds consisting mainly of the elements carbon (C), hydrogen (H), oxygen (O), nitrogen (N) and sometimes sulphur (S).

- Proteins serve multiple functions in the cell:
  - Enzymatic (e.g. protein kinase)
  - Immunity (e.g. antibodies)
  - Storage (e.g. ovalbumin)
  - Hormonal (e.g. insulin)
  - **Transport (e.g. haemoglobin)**
  - **Structural (e.g. collagen)**
  - **Signalling (e.g. G-protein linked receptor)**
  - Contractile (e.g. actin)

Learning Outcome (g)(iii):

Describe the structure and properties of the following monomers:

iii. amino acids (in proteins) (chemical formulae of specific R-groups of different amino acids are not required)

4.1 STRUCTURE OF AMINO ACIDS

- There are 20 commonly occurring amino acids. They have the same basic structure but **differ in their R-groups**.

- Each amino acid is made up of a central α-carbon atom bonded to a hydrogen (H), an amine group (NH_2), a carboxyl group (COOH) and a variable R group (side chain).

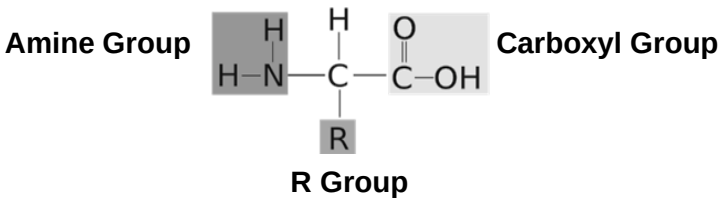
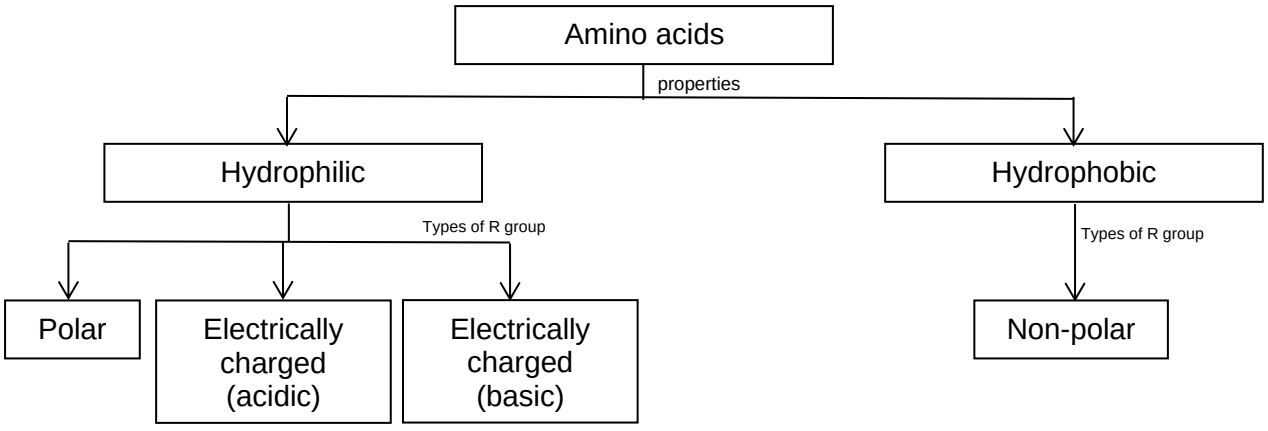


Fig. 4.1.1 Structure of an amino acid

- Amino acids are usually abbreviated based on the first 3 letters of their names, e.g. alanine is ala, glycine is gly. The 20 commonly occurring amino acids can be classified based on the properties of their R groups.



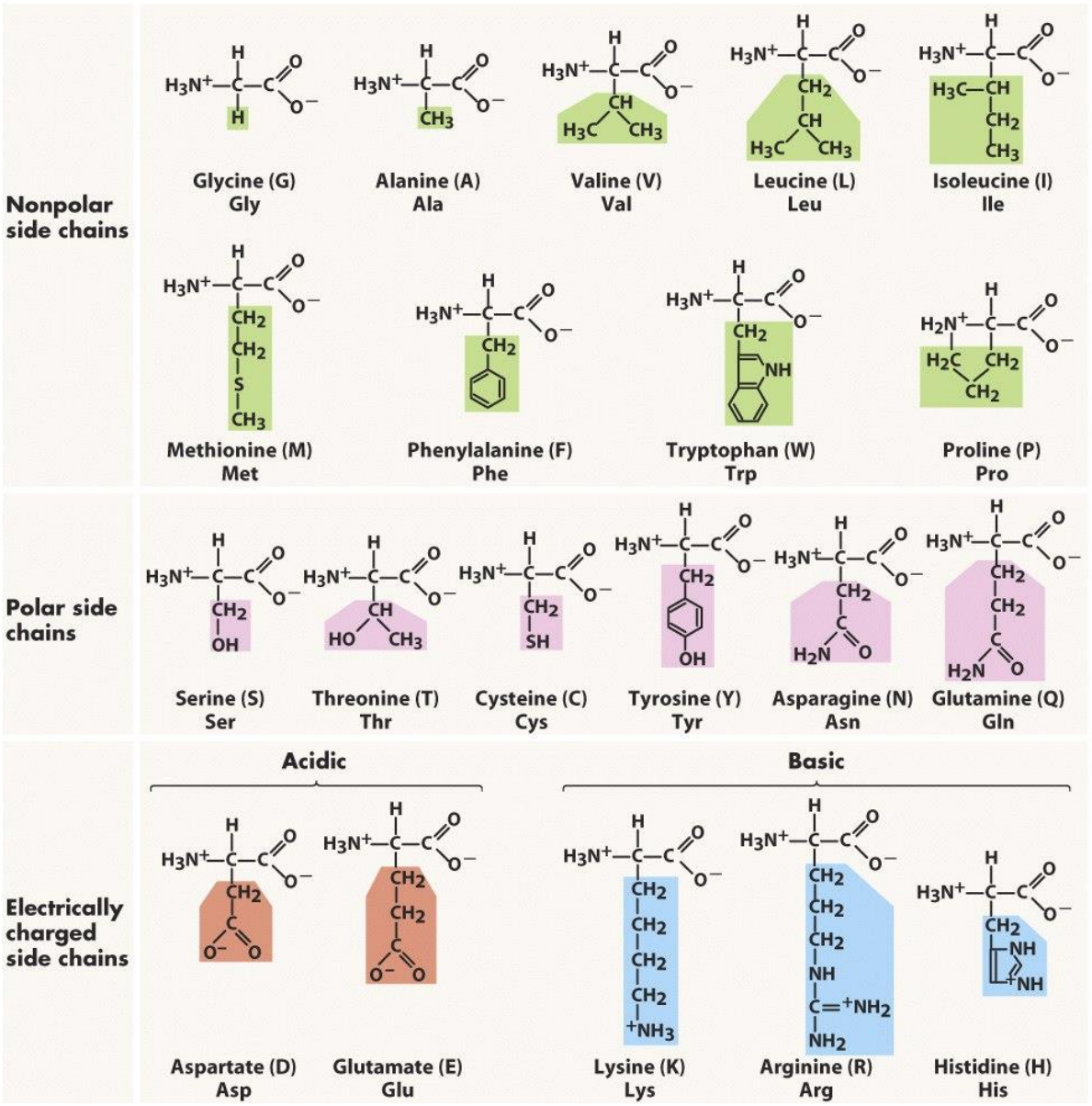


Fig. 4.1.2 Classification of amino acids

4.2 PROPERTIES OF AMINO ACIDS

- **Amino acids** exist as dipolar zwitterions in neutral solutions (i.e. they have both positive and negative charges).

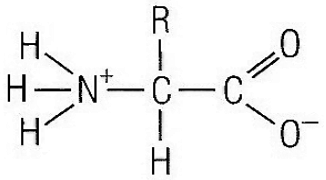


Fig. 4.2.1 Amino acid existing as a zwitterion at pH 7

Amino acids are **amphoteric** in nature (i.e. have both basic and acidic properties). The amine group ($-NH_2$) can accept a proton (H^+) to become NH_3^+, thus acting as a base. The carboxyl group (-COOH) can donate a proton (H^+) to become COO^-, thus acting as an acid.

- Hence, **amino acids (zwitterions) can act as pH buffers** (solutions that resist pH changes). This means that the amino acids in the solution can act as an acid or base depending on the pH of the solution.

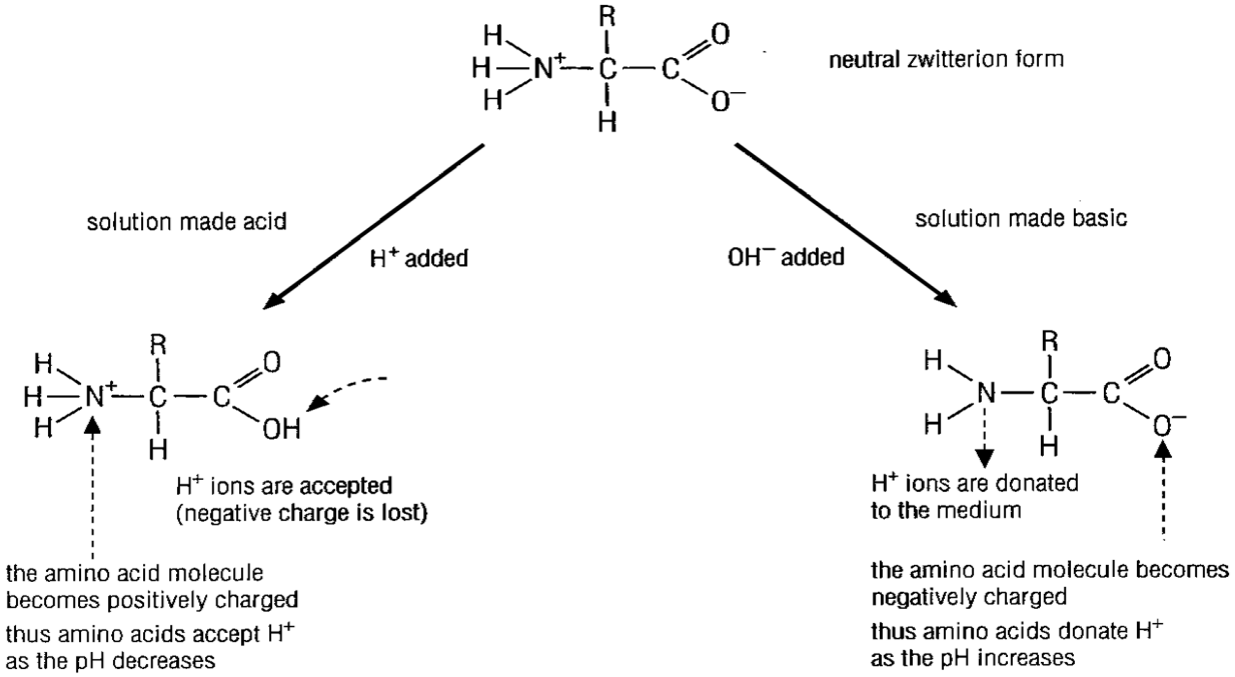


Fig. 4.2.2 Amino acid act as pH buffer

Decrease in pH (i.e. more acidic) **Amino acid acting as a base**	**Increase in pH** (i.e. more alkaline) **Amino acid acting as an acid**
• There is an increase in the concentration of hydrogen ions (H^+). • COO^- group removes the excess H^+ to form COOH, thus restoring the original pH of the solution.	• There is an increase in the concentration of hydroxyl ions (OH^-). • NH_3^+ group releases H^+ to neutralize excess OH^- to H_2O, thus restoring the original pH of the solution.

Learning Outcome (h)(iii):

Describe the formation and breakage of the following bonds:

iii. peptide bond

4.3 FORMATION OF PEPTIDE BOND

- **Peptide bond** is formed between two amino acids via **condensation** reaction between the carboxyl group (-COOH) of one amino acid and the amine group ($-NH_2$) of another amino acid, with the elimination of one water molecule.

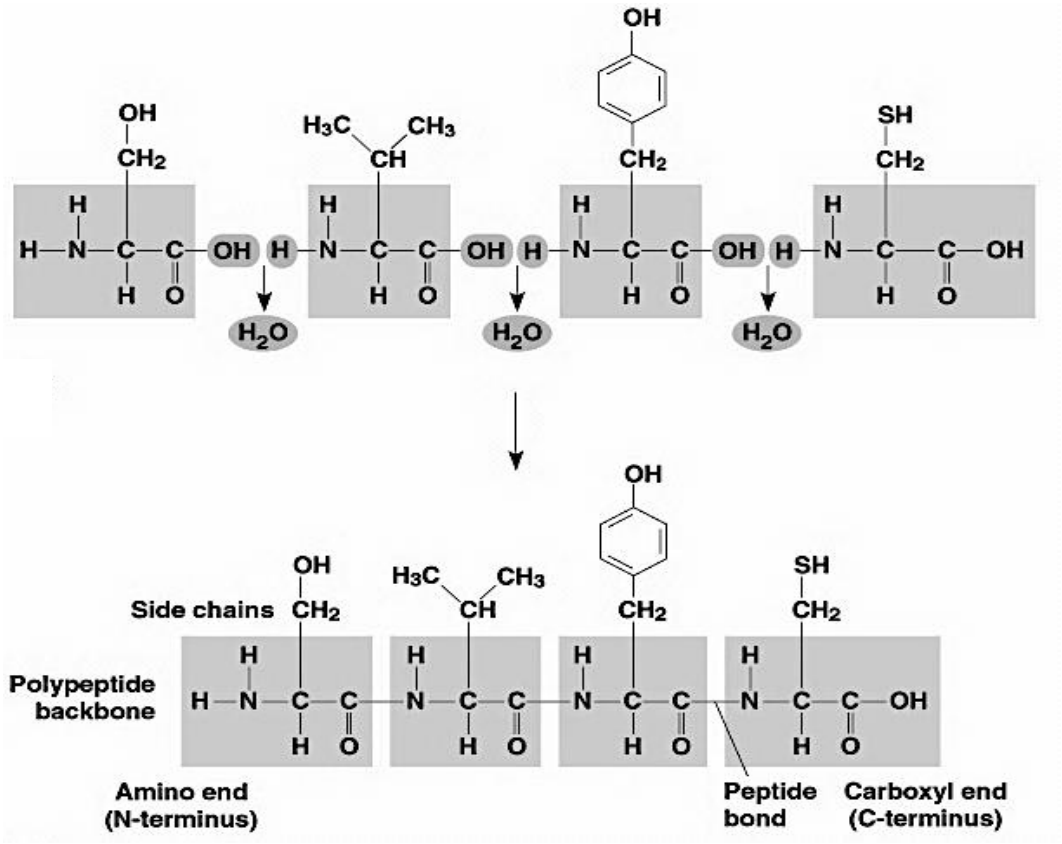


Fig. 4.3 Condensation reactions to form peptide bonds

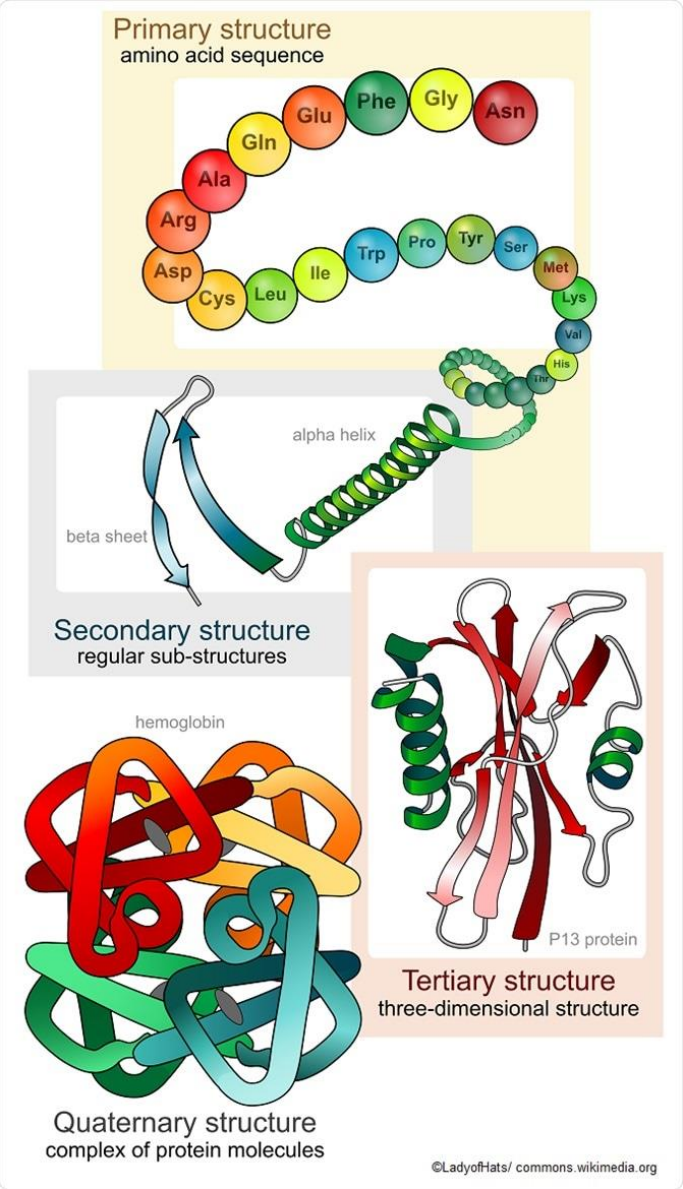
- Many amino acids are linked by peptide bonds to form a polypeptide (unfolded protein).

- A polypeptide contains an N-terminus ending with an amine group ($-NH_2$) and a C-terminus ending with a carboxyl group (-COOH). It is hence amphoteric and possesses pH-buffering properties.

- The linear polypeptide must fold into its specific 3D configuration to form a functional protein.

Learning Outcome (m):

Explain primary structure, secondary structure, tertiary structure and quaternary structure of proteins, and describe the types of bonds that hold the molecule in shape (hydrogen, ionic, disulfide bonds and hydrophobic interactions).



4.4 ORGANIZATION OF PROTEIN STRUCTURE

Protein structure is organized into 4 levels – primary, secondary, tertiary and quaternary.

4.4.1 PRIMARY STRUCTURE

The primary structure is the unique, linear sequence of amino acids linked by peptide bonds. This linear sequence of amino acids is determined by the sequence of nucleotides in DNA i.e. gene *(more details will be covered in Protein Synthesis)*.

4.4.2 SECONDARY STRUCTURE

The secondary structure results from folding of primary structure. Its shape is maintained by hydrogen bonds formed between the O of the C=O and H of the NH of different peptide bonds.

Secondary protein structure exists in 2 forms: **α-helix** and **β-pleated sheet**. Some proteins may only contain only α-helix or β-pleated sheet while some contain both.

Fig. 4.4.2.1 Primary structure (top) and secondary structure with α-helix and β-pleated sheets (bottom)

(a) α-helix (e.g. keratin in hair, nails, beaks of birds)

- The α-helix results from folding of the primary structure (polypeptide) into helical structure.
- The helix contains **3.6 amino acids per turn**.
- The spiral structure is stabilised by **hydrogen bonds between O of C=O and H of N-H groups of the peptide bonds** between the n^{th} and $(n+4)^{th}$ amino acid.
- The hydrogen bonds are **parallel to the long axis of the helix**.

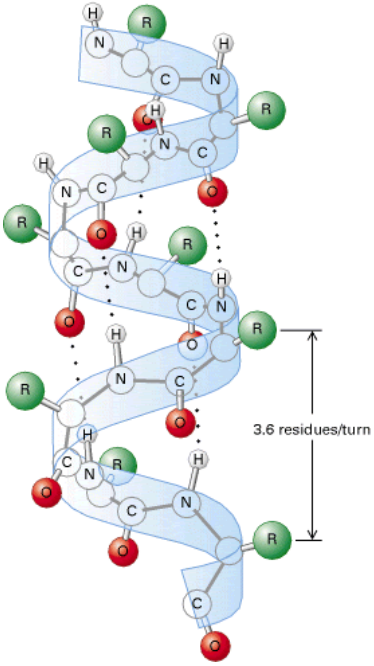


Fig. 4.4.2.2 Structure of α-helix

(b) β-pleated sheet (e.g. silk)

- β-pleated sheets consist of **extended chains of polypeptide strands lying side by side** to form a pleated sheet.
- The peptide backbone makes a zigzag pattern with the α-carbon lying at the folds of the pleats.
- The structure is stabilised by **hydrogen bonds between O of C=O and H of N-H of the peptide bonds**. The hydrogen bonds are **perpendicular to the long axis of the pleated sheet**.
- The sheet can be arranged in parallel or anti-parallel forms. Adjacent polypeptide chains of parallel sheets run in the same direction while those in anti-parallel sheets run in opposite directions.

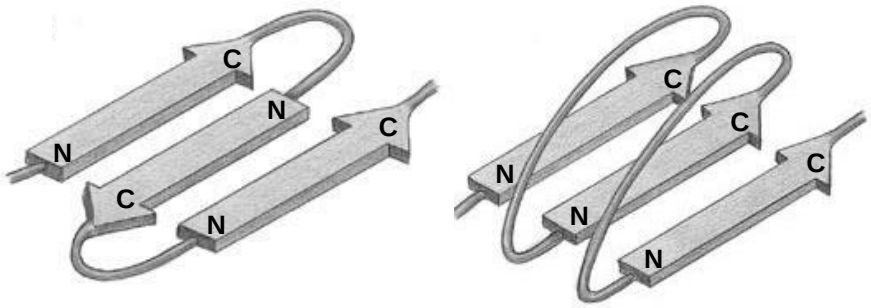


Fig. 4.4.2.3 Anti-parallel (left) and parallel form (right) of β-pleated sheets

4.4.3 TERTIARY STRUCTURE

- The **tertiary protein structure** results from the **further folding of the secondary structures** (both α-helix and β-pleated sheets) to form a **globular** molecule.

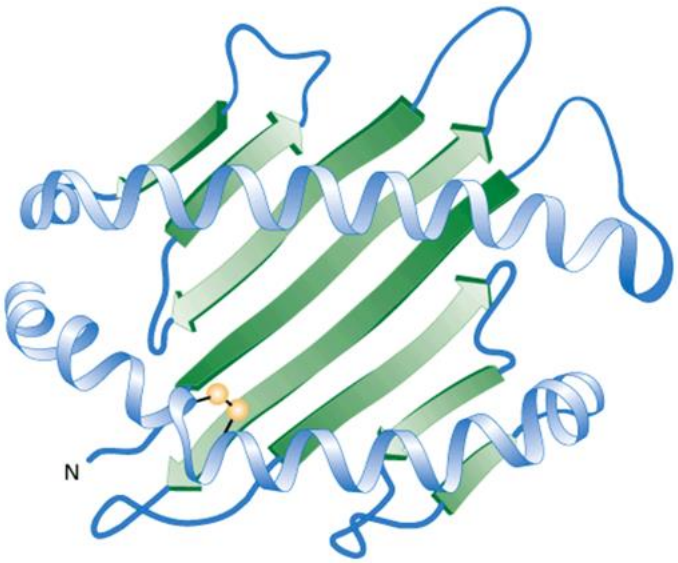


Fig. 4.4.3.1 Folding of secondary structures to form tertiary structure

- The globular shape is mainly stabilized by interactions between R groups of amino acids:

1. **Hydrogen bonds** between amino acids with polar R groups
2. **Ionic bonds** formed between amino acids with oppositely charged R groups
3. **Hydrophobic interactions** between amino acids with non-polar R groups
4. **Disulfide bridges (S-S)** formed by oxidation between sulfhydryl groups (-SH) in cysteine residues.

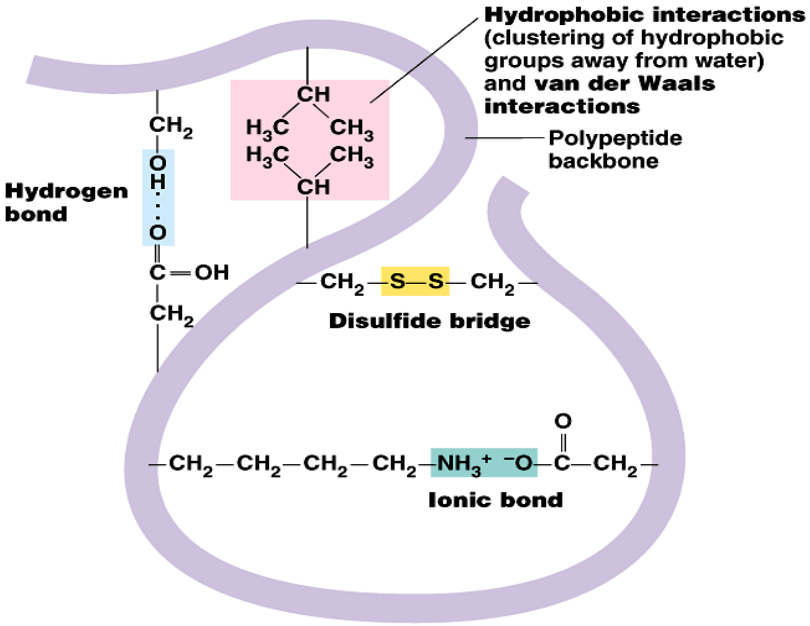


Fig. 4.4.3.2 R group interactions in tertiary structure

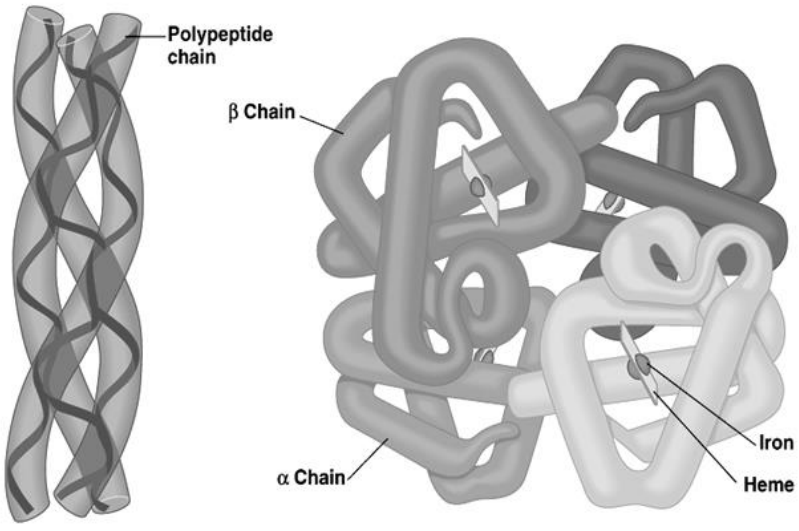
4.4.4 QUATERNARY STRUCTURE

- Proteins with a quaternary structure consist of a **complex aggregation of 2 or more polypeptide chains (subunits)** to form a biologically active molecule. E.g. collagen and haemoglobin

- Each polypeptide chain (one subunit) typically folds into independent globular conformations that interacts with each other via R group interactions:

    - hydrogen bonds between polar R groups
    - hydrophobic interactions between non-polar R-groups
    - ionic bonds between oppositely charged R groups
    - disulfide bridges between R groups in non-adjacent cysteine residues

- The specific 3-dimensional (3D) configuration of a protein is dependent on the way the polypeptide chain folds which in turn is dependent on the position and type of the bonds formed between the R groups. Therefore, the **shape of a protein is determined by its primary structure**.



(a) collagen (b) haemoglobin

Fig. 4.4.4.1 Quaternary proteins - collagen (left) and haemoglobin (right)

Checkpoint 4

Match each statement below with the corresponding level of protein structure. Each statement can be used more than once.

Only found in proteins consisting of more than one polypeptide	The overall 3-D shape of a polypeptide or protein	Held together by R group interactions	Unique sequence of amino acids as determined by the gene
alpha helix	Ala-Gly-Tyr-Met-Phe-Gly	Hydrogen bonds formed between the CO and NH groups of the peptide bonds	beta pleated sheet

Primary structure	**Secondary Structure**	**Tertiary Structure**	**Quaternary Structure**

4.5 PROTEIN DENATURATION

- The 3D configuration of the protein determines its biological function.

- Denaturation is the loss of specific 3D configuration of the protein, causing a loss of function. This usually involves unfolding of the tertiary and secondary structures of the protein via **disruption of bonds stabilising the protein structure**. Denaturation occurs due to changes in the protein environment (e.g. change in temperature, pH, salt concentration).

    - When proteins are heated, **excess heat disrupt hydrogen bonds and hydrophobic interactions** due to the increased amount of kinetic energy.

    - When proteins are subjected to pH changes, **hydrogen bonds and ionic bonds are disrupted**. This is due to the neutralisation of the carboxyl and amine groups hence, hydrogen bonds and ionic bonds cannot be formed.

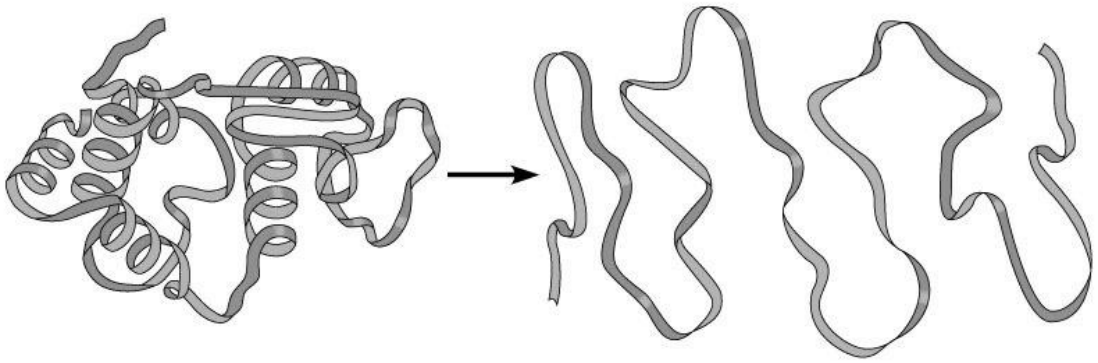


Fig. 4.5 Denaturation of tertiary protein leading to unfolding of protein

Learning Outcome (o):

Describe the molecular structure of the following proteins and explain how the structure of each protein relates to the function it plays:

i. haemoglobin (transport)
ii. collagen (structural)
iii. G-protein linked receptor (signalling) (Details of the number of amino acid and types of secondary structures present are not required.)

4.6 TERTIARY PROTEIN – RELATING STRUCTURE TO FUNCTION

4.6.1 G-PROTEIN LINKED RECEPTOR (GPLR) / G-PROTEIN COUPLED RECEPTOR (GPCR)

- **G-protein linked receptors (GPLR)** is a family of proteins, with **tertiary structure**, **embedded in the cell surface membrane**. ***This protein will be revisited in Topic 3.1: Cell Signalling.***

- These membrane proteins bind to signal molecules (ligand) outside the cell and activate signal transduction pathways inside the cell to eventually result in a cellular response.

- GPLR are so named because they use G-proteins to relay the signal to the cell's interior.

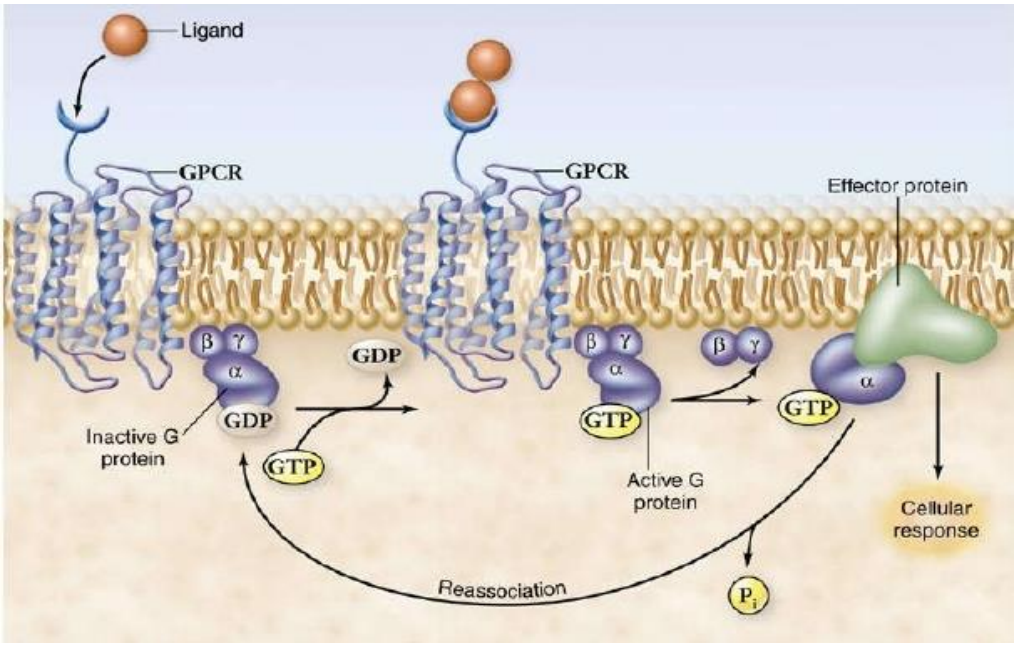


Fig. 4.6.1.1: GPLR allows cell to respond to external stimuli by relaying signals from outside of cell to interior of cell

- GPLR consists of a **single polypeptide chain** with **7 transmembrane α-helices**.
- The structure of the receptor can be separated into 3 regions:
    - **Extracellular region**
    - **Transmembrane region** (consisting of portions of the 7 α-helices that span across the cell surface membrane)
    - **Intracellular region**

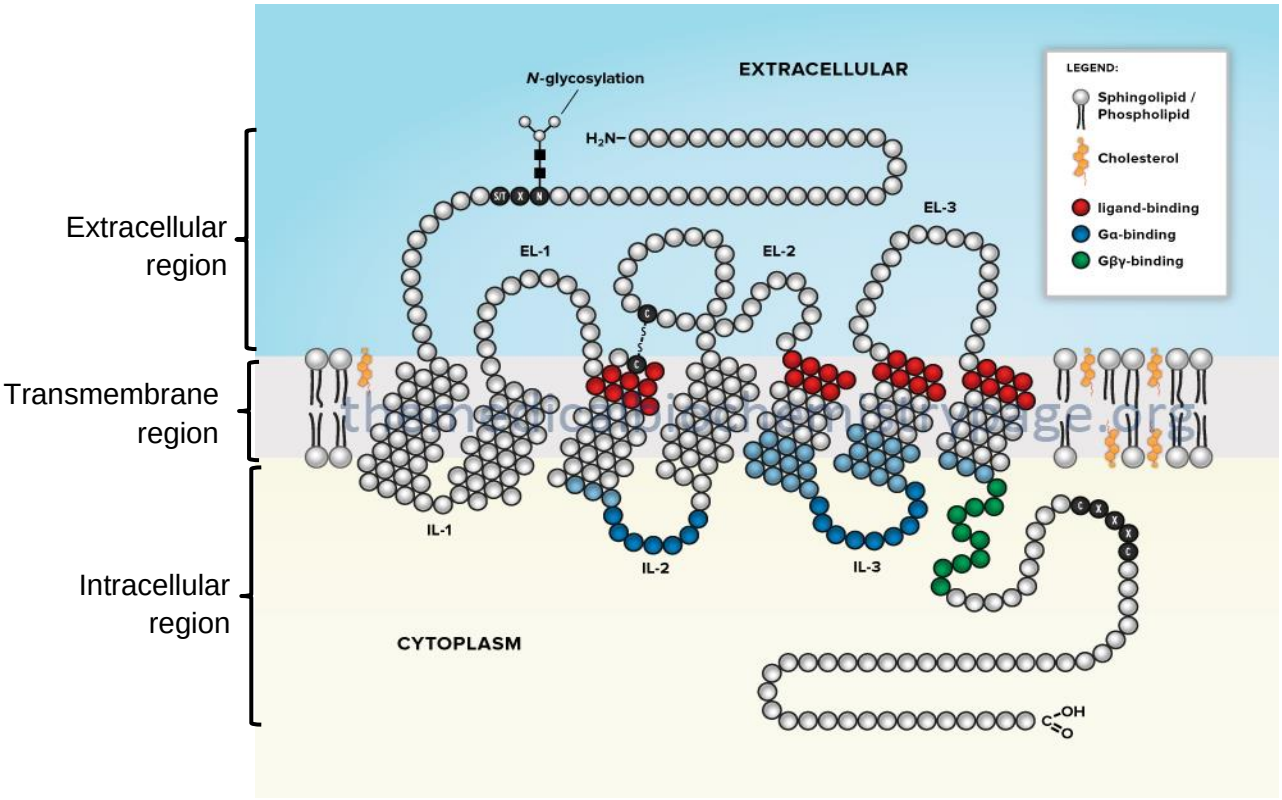


Fig. 4.6.1.2: Structure of GPLR showing extracellular, transmembrane and intracellular regions and sites where ligand and G-protein binds.

EL and IL represents extracellular and intracellular loop respectively

- Each of the 3 abovementioned regions help G-protein linkedreceptor to serve its function.

1. **Extracellular region: <u>Binds ligand</u>**
    - Extracellular segments of the receptor protein contains ligand binding pocket where the ligand can bind to activate the receptor.
    - Shape of ligand binding pocket is complementary to shape of ligand, hence only ligand specific to the receptor can bind and activate it
    - Extracellular region is stabilized by disulfide bridges formed between sulfhydryl-group of cysteines present in extracellular segments.

2. **Transmembrane region**: **<u>Anchors receptor in the cell surface membrane</u>**

    - The polypeptide is folded in such a way that the transmembrane region mainly consists of **amino acids with hydrophobic R groups**.

    - These amino acids form **hydrophobic interactions** with the fatty acid tails of phospholipids in the cell surface membrane to embed the receptor in the membrane.

    - This allows the receptor to serve as a bridge between the extracellular and intracellular environment (i.e. able to bind to ligand outside of cell and activate proteins inside the cell in response to signal).

    - Once the ligand binds and the receptor is activated, the transmembrane helices also undergo conformation change exposing the G-protein binding site to which the G-protein can bind.

3. **Intracellular region**: **<u>Binds G-protein and activate signalling cascade to bring about cellular response</u>**

    - Intracellular region contains the G-protein binding site. When the transmembrane helices undergo a conformation change, G-protein binding site is exposed and can bind to G-protein to active it.

    - Active G-protein can now activate other proteins in the signalling pathway to eventually bring about a cellular response. ***This will be revisited in Topic 3.1: Cell Signalling.***

G-protein linked receptors - Structural features adapted to function as a mediator in signalling pathways

Structural features	Function Adaptations
Extracellular region of receptor contains ligand binding pocket.	Allows receptor to bind to specific signal molecules (ligands) on the exterior of the cell so as to trigger a response from the cell.
Shape of binding pocket is complementary to shape of ligand.	Ensure specificity of receptor i.e. only ligand specific to receptor can bind and activate it.
Sulfhydryl-group of cysteines present in the extracellular segments forms disulfide bridge.	Stabilize conformation of extracellular region.
Folding of polypeptide chain such that the transmembrane region of the receptor contains amino acids with hydrophobic R-groups.	Allows hydrophobic interactions to be formed between the hydrophobic R-group of these amino acids and the fatty acid tails of phospholipids so as to anchor receptor in the cell surface membrane.
Transmembrane helices undergo conformational change upon ligand binding to expose G-protein binding site in intracellular region.	Allows G-protein to bind to intracellular region of receptor. This induces G-protein to release GDP and bind GTP, hence activating it. Active G-protein can go on to activate other proteins which would eventually result in cellular response.

4.7 QUARTERNARY PROTEINS – RELATING STRUCTURE TO FUNCTION

4.7.1 HAEMOGLOBIN (Hb)

- Haemoglobin (Hb) is a **globular protein** with quaternary structure found in large amounts inside red blood cells.

- It functions to transport oxygen from the lungs to the cells in tissues via blood vessels.

- In adults, the major form of haemoglobin present is Haemoglobin A (HbA).

- Each molecule of Hb is a **tetramer** (i.e. made up of 4 subunits) consisting of 2 α-globin and 2 β-globin chains of polypeptides. Each globin subunit is globular.

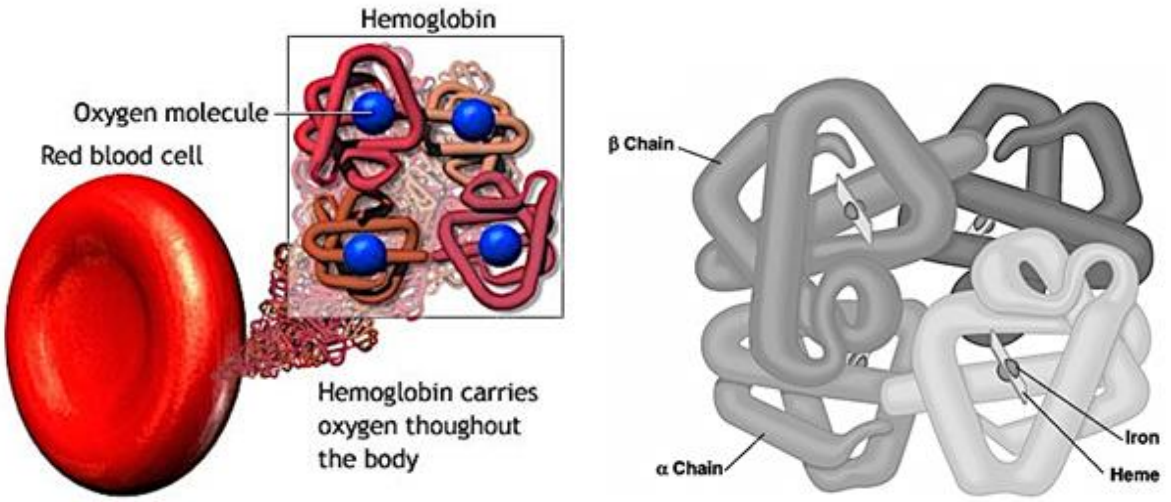


Fig. 4.7.1.1 Structure of haemoglobin

- The **quaternary structure** of Hb is stabilized by R groups interactions:

    - **interchain hydrophobic interactions** (between one α-chain and one β-chain to form stable αβ dimers) **and intermolecular hydrogen and ionic bonds** (between two αβ dimers), forming the tetramer.

    - Each globin subunit contains a prosthetic group called **haem** (a non-protein complex) that holds an iron ion (Fe^{2+}) that can bind to oxygen reversibly. Therefore, **each Hb molecule can bind 4 oxygen molecules (O_2).**

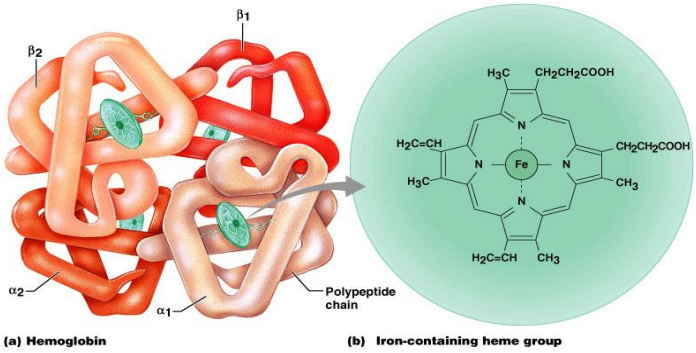


Fig. 4.7.1.2 Structure haem group in each subunit holding a Fe^{2+}

- Haemoglobin exhibits **cooperative binding of oxygen** where the O_2 affinity of the subunits increases with each successive binding of O_2 molecule.

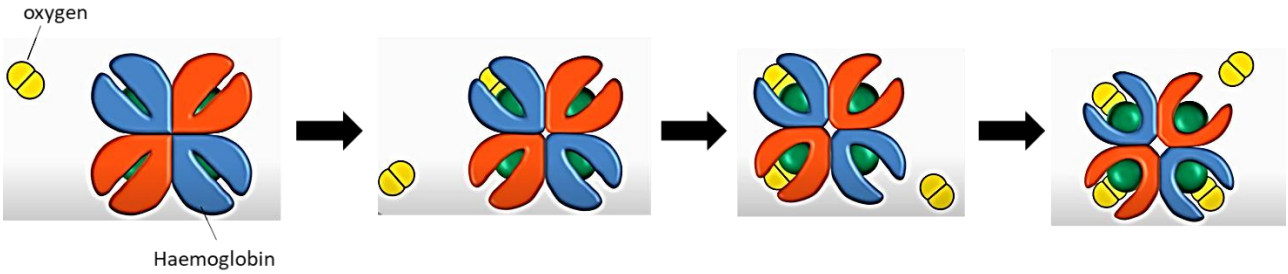


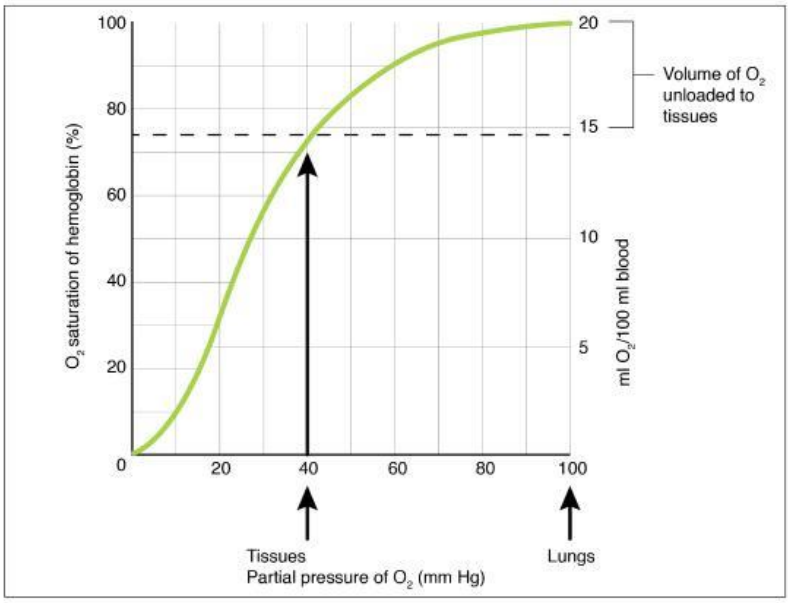
Fig. 4.7.1.3 Cooperative binding of oxygen to haemoglobin

- Haemoglobin is **soluble** in the cytoplasm of red blood cells. This is because the folding of polypeptide chains in Hb keeps hydrophobic amino acids in the interior of the protein away from the aqueous medium.

- Close packing of Hb makes it also make it compact, hence allowing more Hb molecules to dissolve in a given volume of solvent.

DID YOU KNOW?

Cooperative binding allows Hb to be highly saturated at high oxygen partial pressure (e.g. in lungs) and releases more oxygen at low oxygen partial pressure (e.g. in tissues). As a consequence, the oxygen-binding curves of Hb is sigmoidal, or S-shaped.



(a) Partial pressure of oxygen and hemoglobin saturation

Table 4 Structure to function adaptations of haemoglobin

Structural features	Function Adaptations
Hb contains haem group with Fe^{2+}.	Allow Hb to bind O_2 reversibly
Hb has 4 subunits (tetramer), each containing 1 haem group.	Four O_2 molecules can be bound to each Hb.
Presence of weak intermolecular hydrogen and ionic bonds (between dimers)	Allows for cooperative binding of O_2, as breaking of bonds results in increase in O_2 affinity in subsequent subunits after O_2 has bound to one subunit.
Folding of polypeptide chains into globular shape keeps hydrophobic amino acids in the interior of the protein, with hydrophilic amino acids facing the exterior.	Allows Hb to dissolve in the cytoplasm of red blood cell, enabling red blood cells to transport oxygen.
Close packing of Hb	Makes Hb more compact thus more molecules of Hb can be dissolved per volume of blood, i.e. more O_2 can be carried per unit volume.

4.7.2 COLLAGEN

- Collagen is an abundant structural protein in all animals. It is a principal component of connective tissue in tendons, cartilage, bones, teeth, skin and blood vessels etc. It is rigid and inextensible and is able to withstand severe stresses of high impact activities like running and jumping.

- In humans, collagen comprises one-third of the total protein, accounts for three-quarters of the dry weight of skin, and is the most prevalent component of the extracellular matrix (ECM).

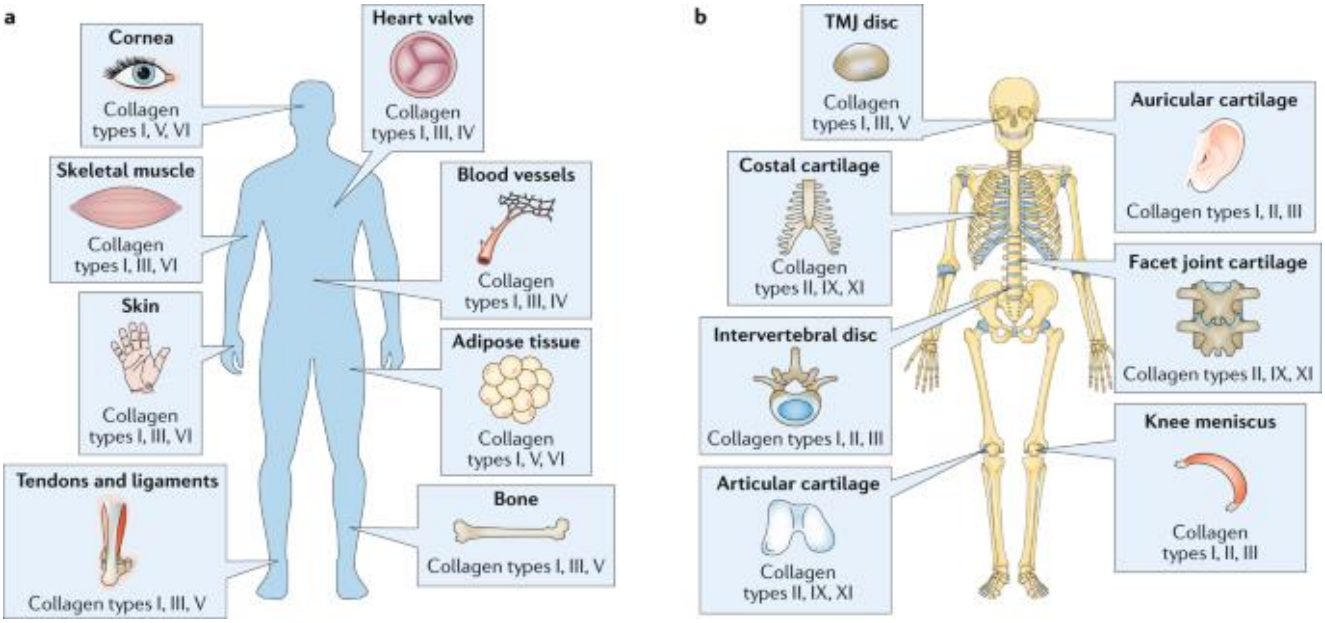
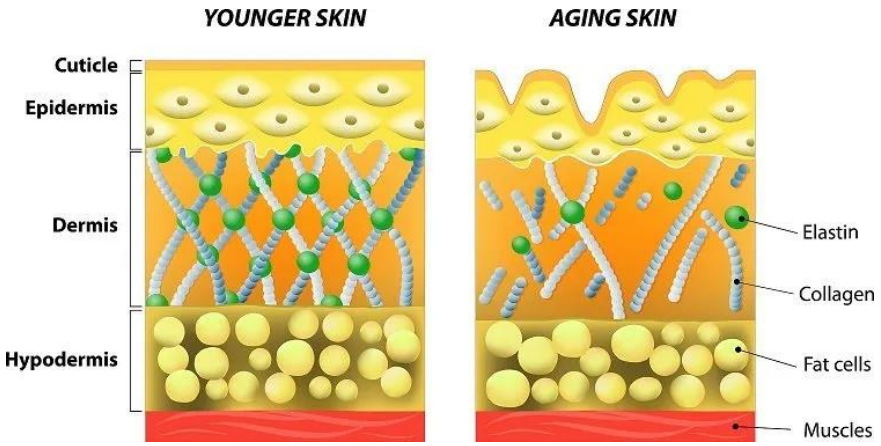


Fig. 4.7.2.1 Location of collagen in the human body

Why your skin loves vitamin C?

Vitamin C bolsters the production of collagen in the skin and the formation of elastin. Good collagen production increases the strength and firmness of your skin. Low levels of Vitamin C can result in poor collagen production which in turn destabilises the foundation of the skin resulting in lines and wrinkles.



Vitamin C also protects the skin from ultra violet light damage, reducing premature ageing in the skin and inhibits the production of melanin a major contributor of skin pigmentation.

Source: https://customcompounding.com.au/skin-loves-vitamin-c/

- Collagen is a **fibrous quaternary protein structure** consisting of polypeptide chains organized in a parallel fashion to produce long fibres.

- The basic structural unit of collagen is **tropocollagen**, a triple helix consisting of 3 intertwined polypeptide chains. Each polypeptide chain is twisted with 3.3 amino acids per turn.

- Each polypeptide chain consists of a frequently **repeating Gly-x-y motif** where x is often proline (Pro) and y is often proline or hydroxyproline (Hyp).

- **Glycine (Gly) is found as every 3rd residue** in the polypeptide chain, facing the crowded centre of the triple helix. As gly is the smallest amino acid (R group = H), this allows the triple helix to twist tightly.

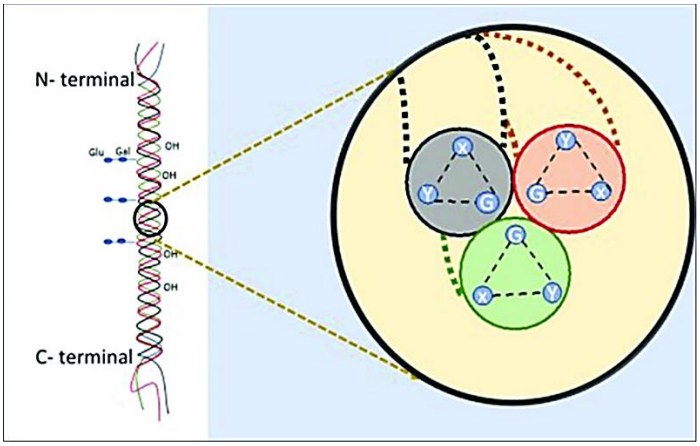


Fig. 4.7.2.2 Glycine in the centre of the triple helix

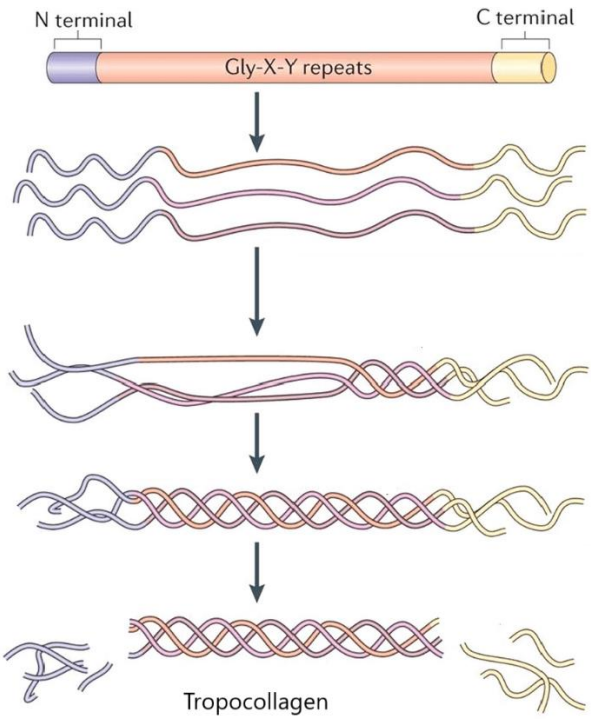


Fig. 4.7.2.3 Formation of a tropocollagen

- The **triple helix is stabilised by**:
  - **Hydrogen bonds** between adjacent polypeptide chains formed at the **length and tip** of the tropocollagen molecule.

  - **Covalent cross-links** formed at the **N-terminals between polypeptide chains**

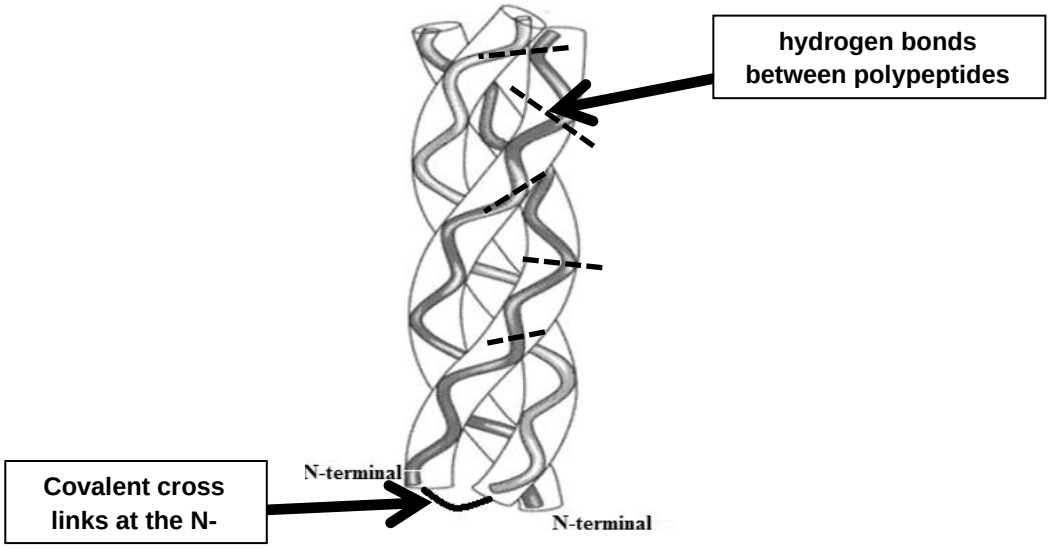


Fig. 4.7.2.4 Bonds stabilising the triple helix

- The tropocollagen molecules will self-assemble in staggered arrays (banded pattern) to form a collagen fibril.

- Staggered arrangement results in gap region between tropocollagen molecules along a row. These gaps allow the covalent attachment of sugars that may help in fibril assembly and allow deposition of minerals during bone formation.

- The **collagen fibril is stabilised by** bonds *between* tropocollagen molecules:

  - **Covalent cross-links** between amino acids at the **N-terminal of one tropocollagen and the C-terminal region of an adjacent tropocollagen** in the fibril.

- Collagen fibrils are further bundled to form collagen fibres.

- In the electron micrograph, collagen fibers exhibit banded patterns of alternating light and dark bands. The dark bands correspond to the gap regions between pairs of aligned tropocollagen.

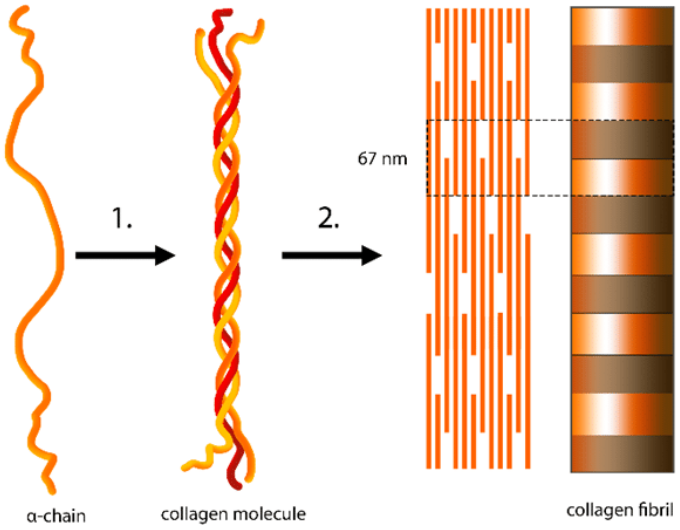


Fig. 4.7.2.5 Banded patterns in collagen fibre due to staggered arrays of tropocollagen

Table 5 Structure to function adaptions of collagen

Structural features	Function adaptions
Tropocollagen is a **triple helix** made of **3 intertwined polypeptide chains** with a repeating **Gly-x-y motif** and **3.3 amino acids per turn**.	Gly positioned in the centre allowed **tight twisting in tropocollagen** increasing tensile strength.
Hydrogen bonds between adjacent polypeptide chains formed at the length and tip of the tropocollagen molecule. **Covalent cross-links** formed at the N-terminals between polypeptide chains	These interchain bonds **stabilizes** the triple helix structure and increase tensile strength.
Staggered arrays of tropocollagen molecules result in gap regions.	Allows **covalent attachment of sugars** to aid in fibril assembly to increase tensile strength
Covalent cross-links between amino acids at the N-terminal of one tropocollagen and the C-terminal region of another tropocollagen molecule in the fibril.	**Stabilizes** collagen fibril structure and increase tensile strength.
Bundling of many collagen fibrils to form collagen fibre.	Increases tensile strength.

Checkpoint 5

Complete the table below.

	GPCR	Haemoglobin	Collagen
Number of polypeptides			
Molecular Appearance			
Amino acid composition			
Types of bonds within each polypeptide			
Types of bonds between polypeptides			
Solubility			
Presence of prosthetic group			
Function			
Level of protein organisation			

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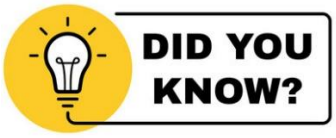
Answers



What are the following disaccharides made up of?

1. Maltose (commonly known as malt) — Glucose + Glucose
2. Sucrose (commonly known as table sugar) — Glucose + Fructose
3. Lactose (commonly known as milk sugar) — Glucose + Galactose

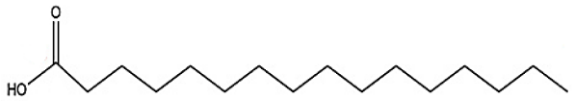
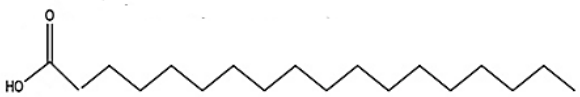
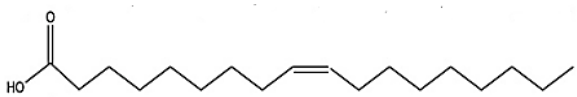
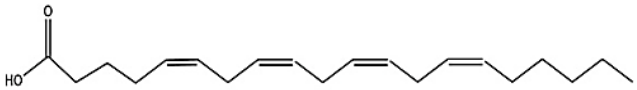
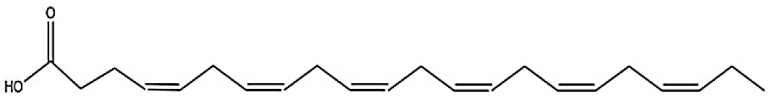
Checkpoint 1

Complete the following table.

Polysaccharide	Starch	Glycogen	Cellulose
Sugar monomer	*α-glucose*	*α-glucose*	*β-glucose*
Bond(s) present between monomers	*α-1,4 glycosidic bond* *α-1,6 glycosidic bond*	*α-1,4 glycosidic bond* *α-1,6 glycosidic bond*	*β-1,4 glycosidic bond*
Appearance of molecule	Amylose: *helical* Amylopectin: *branched*	Similar to amylopectin but more highly branched	*Linear*
Orientation of adjacent monomers	adjacent monomers in same orientation	*adjacent monomers in same orientation*	*adjacent monomers inverted 180° to each other*
Location	storage organs in plants	animal cells in liver & skeletal muscles	*cell wall in plant cells*
Function	storage	storage	structural

Checkpoint 2

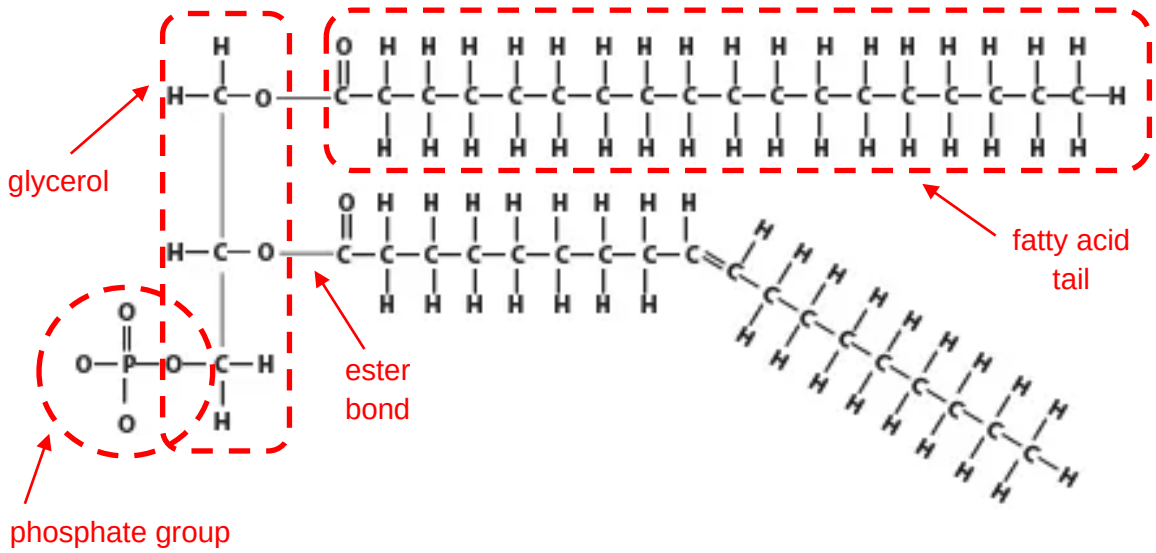
Complete the following table.

Fatty Acid	No. of carbon	Degree of saturation	Number of C=C
 **Palmitic acid (PA)**	16	saturated	0
 **Stearic acid (SA)**	18	saturated	0
 **Oleic acid (OA)**	18	unsaturated	1
 **Arachidonic acid (AA)**	20	unsaturated	4
 **Docosahexaenoic (DHA)**	22	unsaturated	6

Checkpoint 3

On the diagram of the phospholipid below,

1. *Circle and label the glycerol backbone, 1 fatty acid tail and phosphate group.*
2. *Label 1 ester bond.*



Checkpoint 4

Match each statement below with the corresponding level of protein structure. Each statement can be used more than once.

Only found in proteins consisting of more than one polypeptide	The overall 3-D shape of a polypeptide or protein	Held together by R group interactions	Unique sequence of amino acids as determined by the gene
alpha helix	Ala-Gly-Tyr-Met-Phe-Gly	Hydrogen bonds formed between the CO and NH groups of the peptide bonds	beta pleated sheet

Primary structure	**Secondary Structure**	**Tertiary Structure**	**Quaternary Structure**
Unique sequence of amino acids as determined by the gene	alpha helix	Held together by R group interactions	Only found in proteins consisting of more than one polypeptide
Ala-Gly-Tyr-Met-Phe-Gly	beta pleated sheet	The overall 3-D shape of a polypeptide or protein	Held together by R group interactions
	Hydrogen bonds formed between the CO and NH groups of the peptide bonds		

Checkpoint 5

Complete the table below.

	GPCR	Haemoglobin	Collagen
Number of polypeptides	*1*	*4*	*3*
Molecular Appearance	*globular*	*globular*	*fibrous*
Amino acid composition	*variable*	*variable*	*Majority are repeating motifs of Gly-X-Y*
Types of bonds within each polypeptide	*Hydrogen bond, hydrophobic interactions, ionic bond, disulfide bond*	*Hydrogen bond, hydrophobic interactions, ionic bond*	
Types of bonds between polypeptides		*Hydrogen bond, hydrophobic interactions, ionic bond*	*Hydrogen bond, covalent bond*
Solubility	*Insoluble*	*Soluble*	*Insoluble*
Presence of prosthetic group	*No*	*yes*	*No*
Function	*Cell Signalling*	*Transport protein*	*Structural protein*
Level of protein organisation	*Tertiary*	*Quaternary structure*	