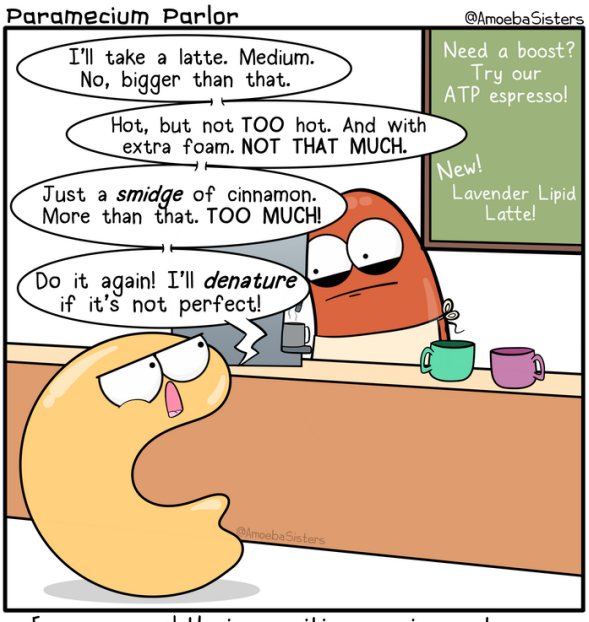
Name:	Class:	Date:

CORE IDEA 1: THE CELL AND BIOMOLECULES OF LIFE

PROTEINS



Enzymes and their sensitive requirements can make them very fussy coffee customers.

Your syllabus requires you to:

(g) describe the structure and properties of the following monomers:
- 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:
- iii. peptide bond

(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 disulphide 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)

Contents

1. Introduction

Proteins are highly diverse. The diversity in protein structures allow them to carry out many different functions (Figure 1).

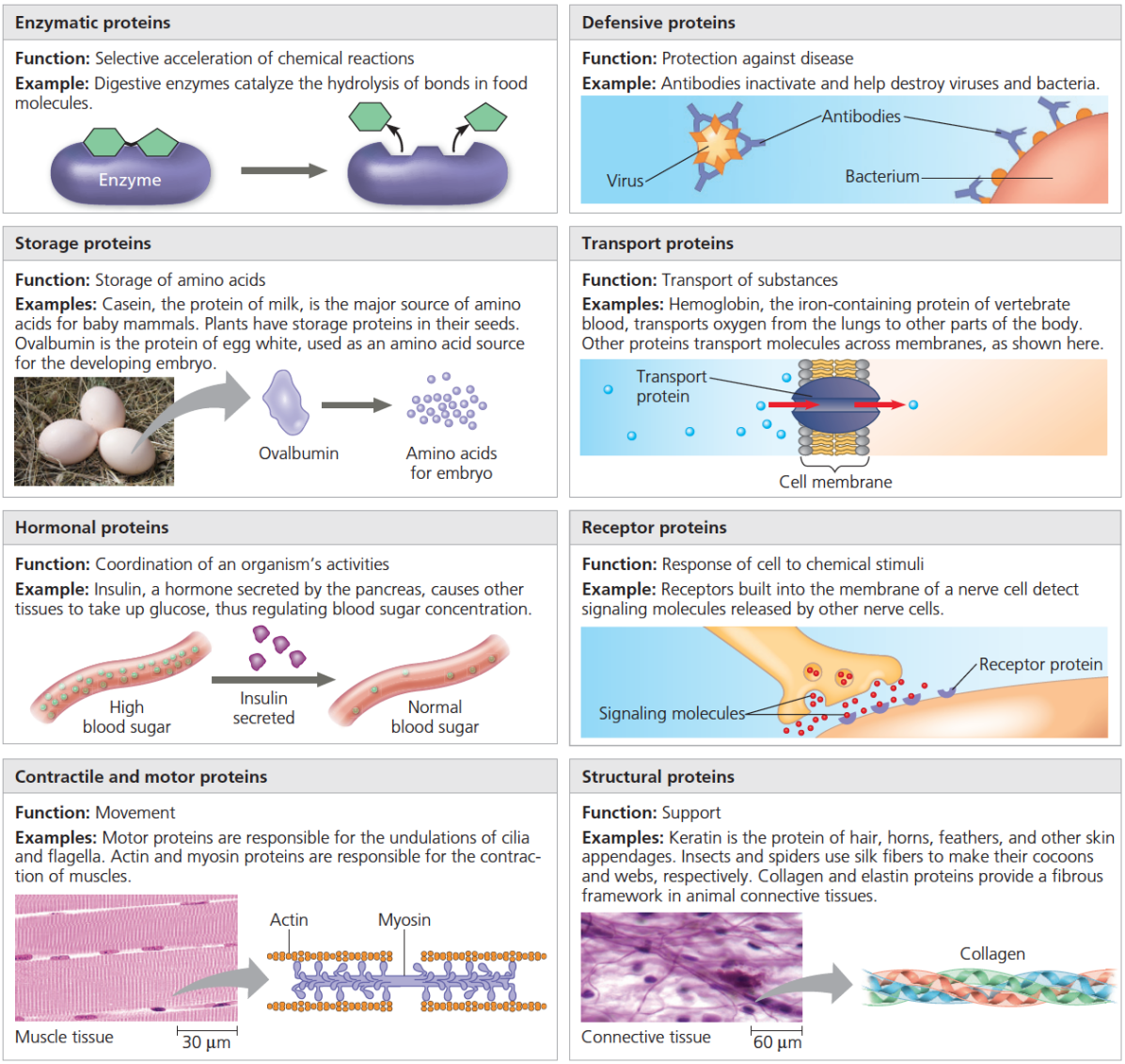


Figure 1: Overview of protein functions (*Campbell, et al., 2018*).

2. Amino acids

LO: (g) describe the structure and properties of the following monomers: amino acids (in proteins) (knowledge of chemical formulae of specific R-groups of different amino acids is not required)

Amino acids are the building blocks or monomers of proteins. There are 20 common amino acids that are used in the biosynthesis of proteins by cells. These amino acids can be divided into essential and non-essential amino acids.

- Essential amino acids must be obtained from the diet because organisms lack the long and complex reaction pathways required for their synthesis. This is to ensure proper nitrogen balance and adequate growth.
- Non-essential amino acids are synthesized from readily available metabolites.

a. Basic structure of an amino acid

Figure 2 shows the general structure of an amino acid which consists of a **central carbon** atom, known as the **α-carbon**, bonded to 4 different groups:

- a **hydrogen atom**
- an **amino group** ($-NH_2$)
- a **carboxyl group** (-COOH)
- a variable **R group** / side chain which is unique to each amino acid.

The R group may be a hydrogen atom or hydrocarbon chain or cyclic structure containing varying functional groups, The different R groups of amino acids determines their physical and chemical properties.

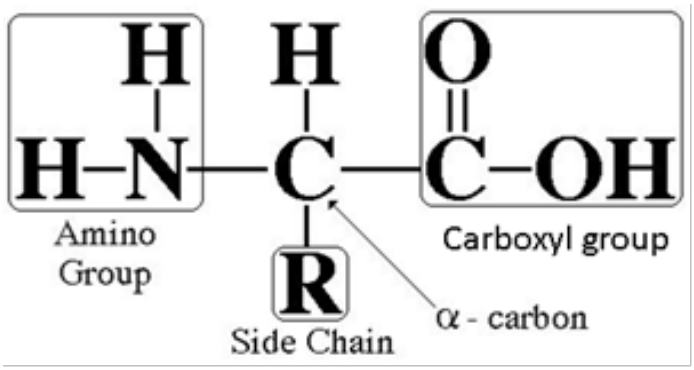


Figure 2: General structure of an amino acid

b. Properties of Amino acids

- Amino acids are **amphoteric** because they contain a basic group (amino group which can accept H^+) and an acidic group (carboxyl group which can donate H^+) (Figure 3).

- Amino acids are soluble in water and ionise to form **zwitterions**, ions with both positive and negative charges (Figure 3).
  - The amino group receives an H^+ and becomes positively-charged.
  - The carboxyl group dissociates, releasing H^+ and becomes negatively-charged.

- Due to their amphoteric property, amino acids can resist slight pH changes, thus serving as **pH buffers** (Figure 3). A buffer minimises changes in pH when a small amount of acid or alkali is added to it. Such property is essential in biological system where any sudden change in pH could adversely affect the performance of proteins like enzymes.

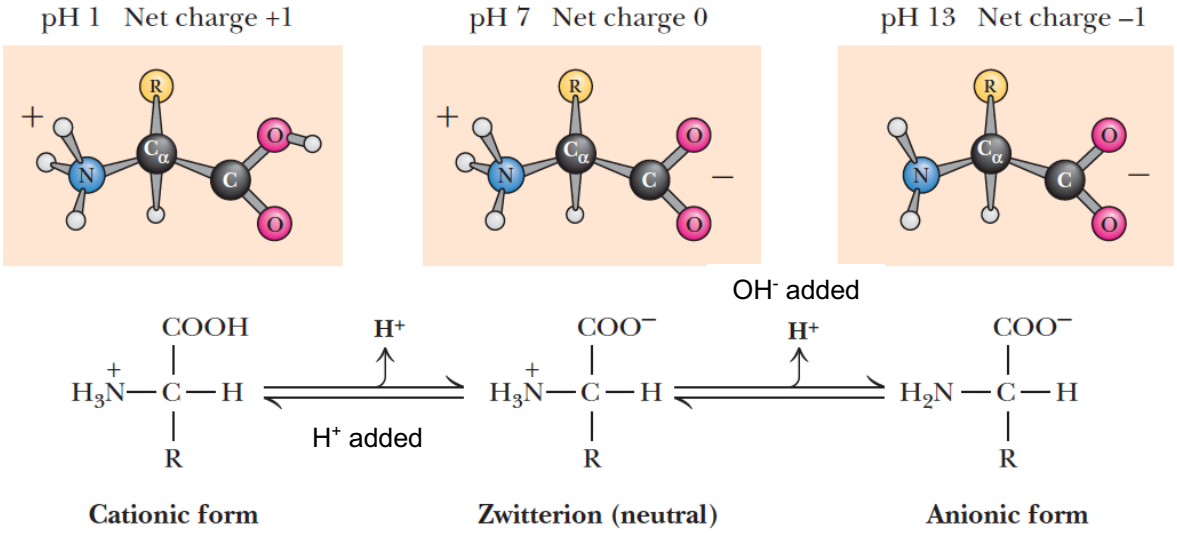


Figure 3: Amino acids can act as acid and as base (Garrett & Grisham, 2010)

Amino acids are classified according to the properties of their R group (Figure 4 and Figure 5).

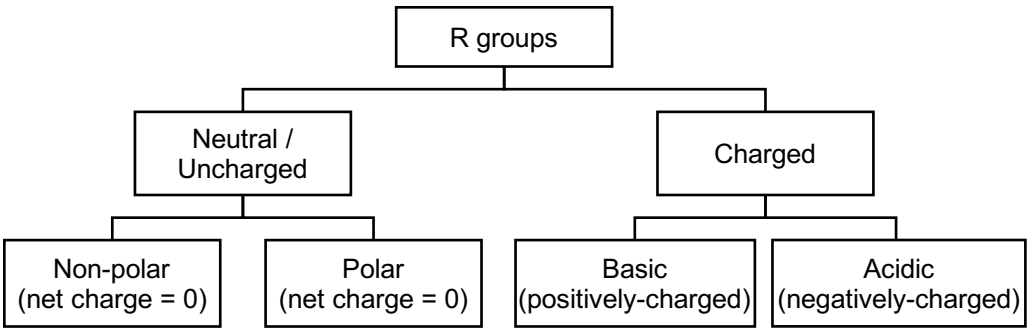


Figure 4: Classification of R groups of amino acids

Within your syllabus, you will need to be familiar with the following amino acids:

- The simplest amino acid is glycine (Gly or G) as it only has a hydrogen atom as the R-group.
- Lysine (Lys or K) has a basic R group (positively-charged), which is important for the packing of negatively-charged DNA (cross reference to topic: Eukaryotic Genomes).
- Cysteine (Cys or C) is the only amino acid with a sulfhydryl (–SH) group and hence the only amino acid that can form disulfide bond.
- Methionine (Met or M) is an important amino acid for protein synthesis is it is coded by the start codon AUG.
- Glutamate (Glu or G) has a carboxyl group in its side chain which makes it hydrophilic. In sickle cell anaemia, mutation in haemoglobin causes glutamate to be substituted with valine (Val or V), an amino acid with a non-polar R-group, and so it is hydrophobic (cross reference to topic: Mutations).

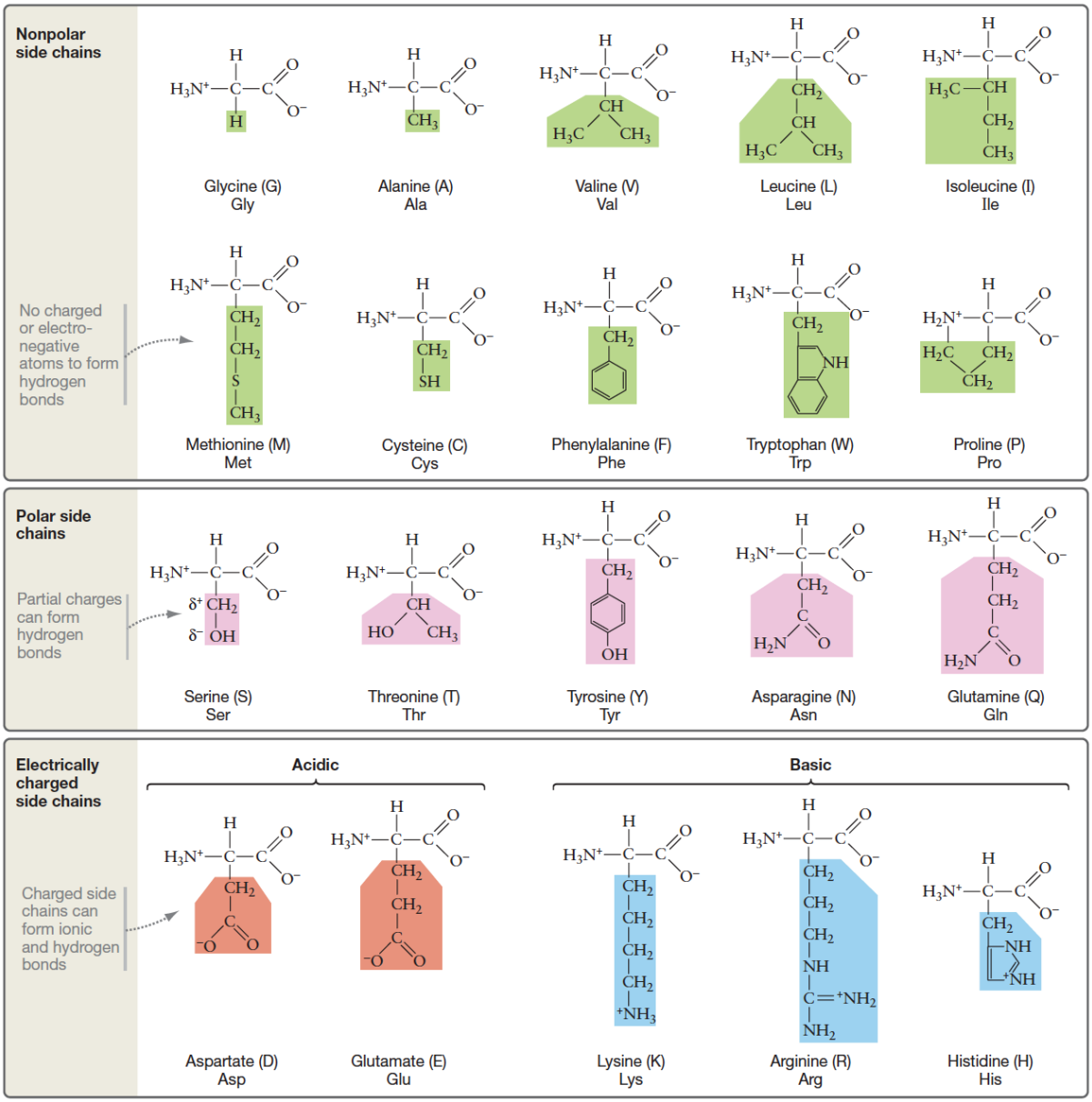


Figure 5: Structures of 20 major amino acids at pH 7 (Freeman, et al., 2014)

3. Polypeptides

LO: (h) Describe the formation and breakage of peptide bonds.

- A **peptide bond** is formed by a **condensation** reaction between the amino group of one amino acid and the carboxyl group of another amino acid, with the elimination of a molecule of water (Figure 6).
- The reverse reaction is a **hydrolysis** reaction which breaks the peptide bond (Figure 6).

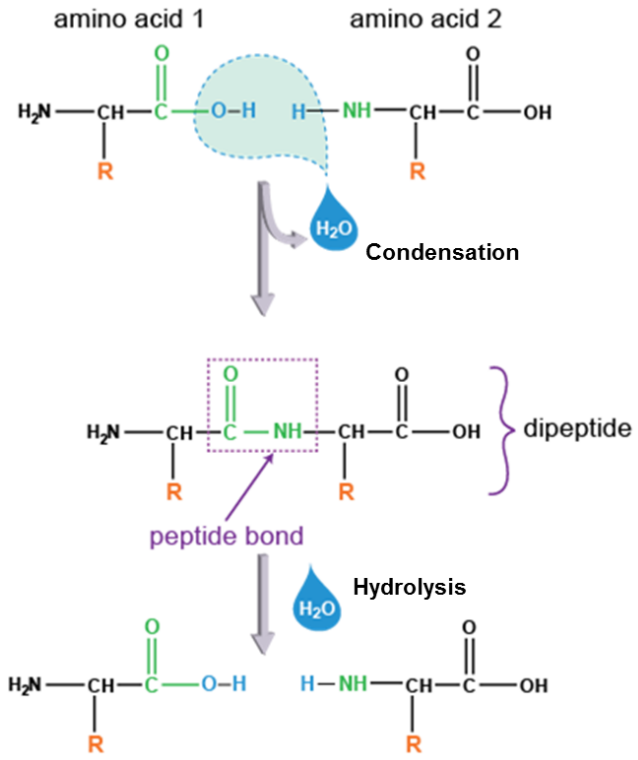


Figure 6: Formation and breakage of peptide bond.

- Successive condensation reactions lead to the addition of more amino acids to the chain, forming a polypeptide.
- The resulting polypeptide has a **free –NH₂** group at one end (known as the **N-terminus** or **amino terminal end**) and a **free –COOH** group at the other end (known as the **C-terminus** or **carboxyl terminal end**).
- By convention, the N-terminus is taken to be the start of a polypeptide chain. Therefore, the amino acid sequence of a polypeptide chain is always written with the N-terminus residue first.

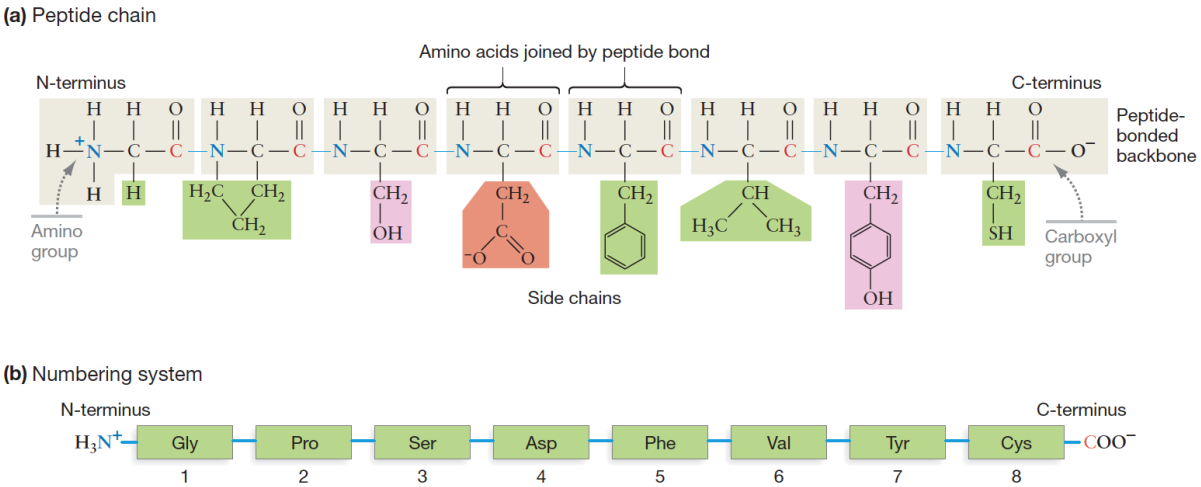
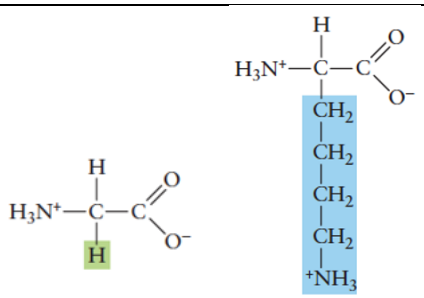


Figure 7: Formation of peptide chain (Freeman, et al., 2014)

Concept Check!

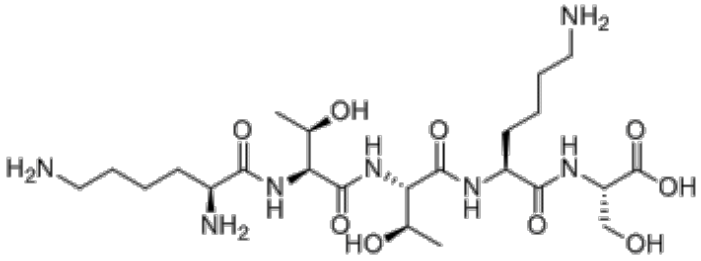


Glycine (G)
Gly

Lysine (K)
Lys

1. Given the structures of the above amino acids, draw the formation of a dipeptide, glycine-lysine.

2. How many amino acids are there in this peptide? Draw out the structure of all the amino acids, in the form of zwitterions, produced upon hydrolysis of all peptide bonds.



4. Four Levels of Protein Structure

LO: (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)

There are four levels of structural organisation in proteins: **primary**, **secondary**, **tertiary** and **quaternary**. Note that not all proteins possess all four levels.

a. Primary structure

- The primary structure of a protein refers to the **specific number and sequence of amino acids** joined by **peptide bonds** in a polypeptide chain.
- The total possible number of different combinations of polypeptide chains can be denoted as n^r, where n = number of different amino acids and r = number of residues in polypeptide chain.
- The sequence of amino acids determines the type and location of chemical interactions, and hence the pattern of folding which confers the specific three-dimensional conformation of a particular protein.
- The sequence of amino acids is determined by the sequence of DNA in the cell (cross reference topic: Nucleic Acids and Central Dogma).

b. Secondary structure

- The secondary structure of proteins consists of **repeated coiling or folding of a polypeptide chain in a specific pattern**.
- These coils and folds are maintained by **hydrogen bonds** between **oxygen of –C=O in a peptide bond and hydrogen of –N-H in a peptide bond**.
- The side chains or R-groups are not involved in the secondary structure.
- There are two common types of secondary structure: **α-helix** and **β-pleated sheet**.
- Regions of polypeptide chains without a regular secondary structure are described to have a random coil or loop conformation.

i. α-helix

- Each α-helix is made up of a single polypeptide chain coiled into a **right-handed spiral** structure.
- There are **3.6 amino acid residues per turn** (Figure 8).
- The structure is maintained by **hydrogen bonds** between groups at every 4th peptide bond. The hydrogen bond is formed between the **O of –C=O of one amino acid and hydrogen of –N-H four amino acids away** in a single polypeptide chain (Figure 9).
- Each successive turn of the α-helix is held to adjacent turns by three to four hydrogen bonds, conferring significant stability on the overall structure.
- The primary structure affects the stability of the α-helix as interactions between side chains can stabilise or destabilise helical structure.

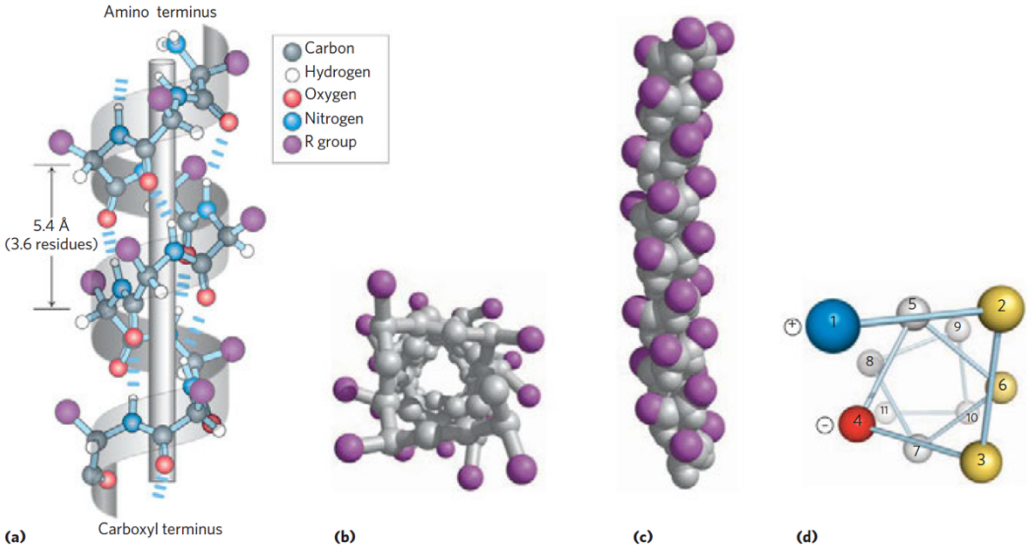


Figure 8: Different aspects of the alpha-helix (David & Michael, 2013)
(a) Ball-and-stick model showing the intrachain hydrogen bonds. The repeat unit is a single turn of the helix, 3.6 residues. (b) The α-helix viewed from one end, looking down the longitudinal axis. (c) This space-filling model shows that the atoms in the centre of the α-helix are in very close contact. (d)This is a helical wheel projection representation of the α-helix. The residues usually coloured to identify properties, such as yellow (hydrophobic), red (negative), and blue (positive).

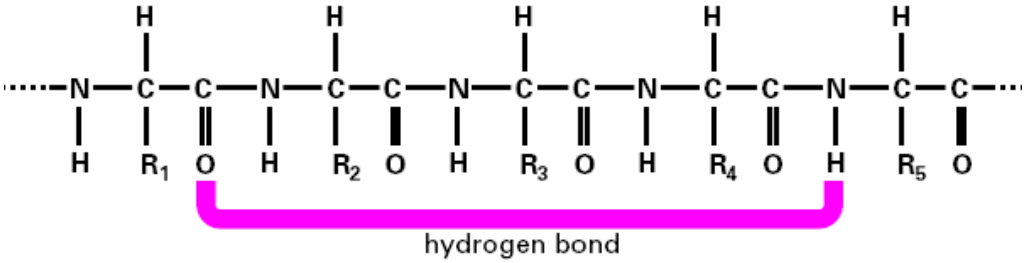


Figure 9: Hydrogen bonding in α-helix between –C=O of residue 1 and –N-H of residue 5

ii. β-pleated sheet

- Each β-pleated sheet consists of **two or more β-pleated strands** (pleated = zigzag structure) **aligned side by side** and held together by **hydrogen bonds** (Figure 10).
- The hydrogen bond is formed between the **–C=O of an amino acid on one region/segment and the –N-H group of an amino acid on an adjacent region/segment** of a single polypeptide chain.
- The β-pleated strands may run **parallel** (same) or **anti-parallel** (opposite) directions, forming a β-pleated sheet (Figure 10).

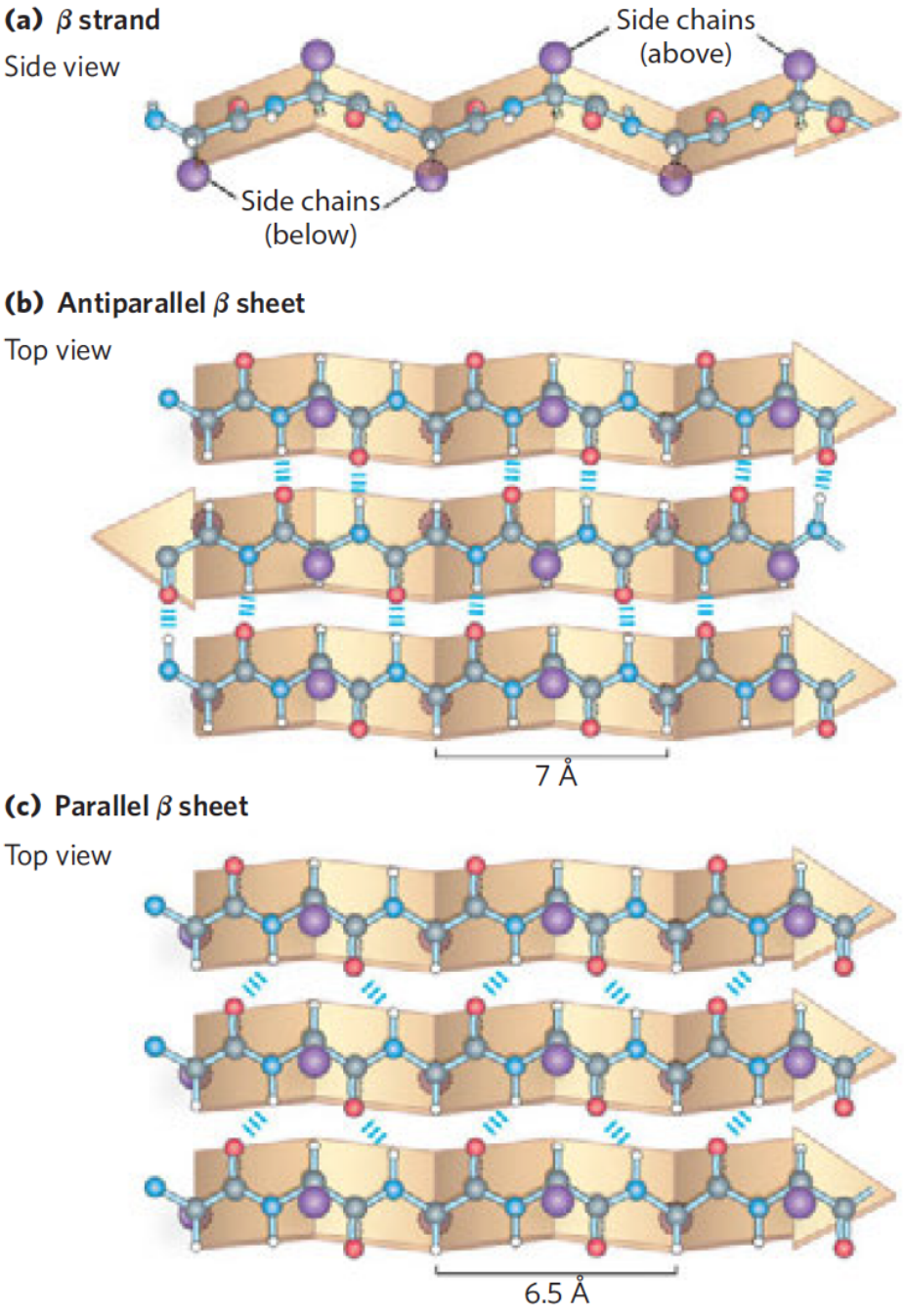


Figure 10: Conformation β-pleated sheets (David & Michael, 2013)

c. Tertiary structure

- The tertiary structure of proteins refers to the **unique three-dimensional conformation** formed by further coiling and folding of a single polypeptide.
- As a result of the coiling and folding, amino acids that are far apart in the primary structure and in different types of secondary structure may interact within the completely folded protein.
- It is stabilised by four types of interactions: **hydrogen bonds, ionic bonds, hydrophobic interactions, and disulfide bonds between R groups of amino acids** (Figure 11).

i. Hydrogen bonds

- Hydrogen bonds are formed between **an electronegative atom and a hydrogen atom bonded to an electronegative atom**.
- Oxygen and nitrogen are highly electronegative whereas hydrogen and carbon are less electronegative.
- Hydrogen bonds are formed between polar R groups of amino acids.
- Individually, a hydrogen bond is weak, but collectively hydrogen bonds are strong and is able to hold the protein structure together.

ii. Ionic bonds

- Ionic bonds are electrostatic attractions formed between **oppositely charged R groups**.
- E.g. COO^- of acidic amino acids and NH_3^+ of basic amino acids.
- While ionic bonds are relatively stronger than hydrogen bonds, they can be easily disrupted by changes in pH.

iii. Hydrophobic interactions

- Hydrophobic interaction is caused by the **exclusion of non-polar substances by water**.
- Hydrophobic interactions are formed between non-polar R groups which interact and cluster at the core of the protein to avoid contact with water.
- This causes the polypeptide to fold in a way so as to shield as many of the hydrophobic R groups from the aqueous environment as possible.

iv. Disulfide bonds/linkages

- Disulfide bonds are covalent bonds between **sulfhydryl (-SH) groups of two cysteine** residues which are brought close together by the folding of polypeptide.
- Disulfide bonds are strong (strongest amongst these four interactions), and they contribute to higher stability of a protein.

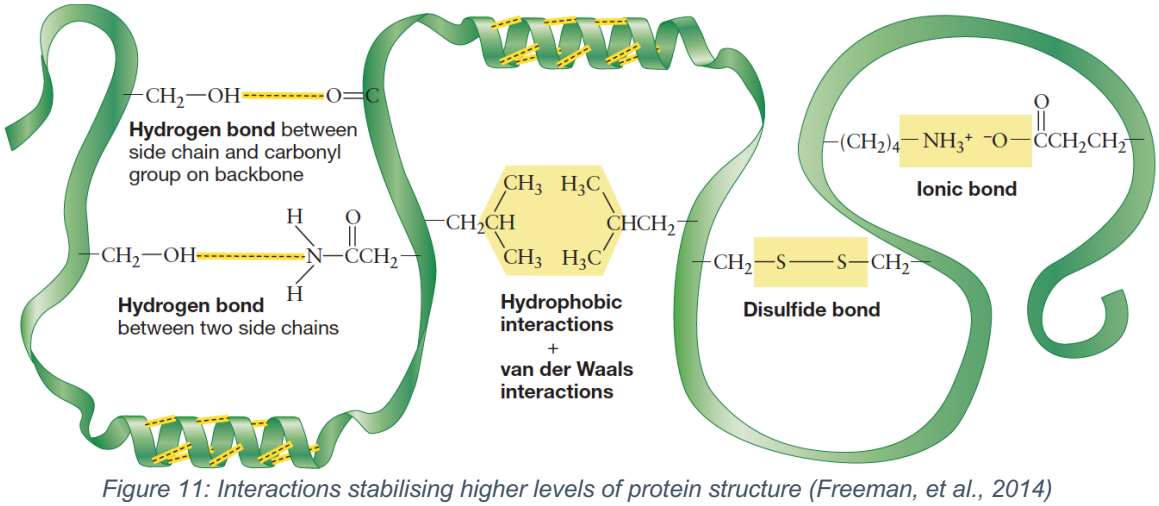


Figure 11: Interactions stabilising higher levels of protein structure (Freeman, et al., 2014)

d. Quaternary structure

- Quaternary structure refers to the association of **two or more polypeptide chains** to form one functional protein.
- Each polypeptide forms a subunit, and the subunits are held together by **hydrogen bonds, ionic bonds, hydrophobic interactions, and disulfide bonds between R groups of amino acids** to form a multimeric protein.
- Note: Not all proteins have a quaternary structure. Some proteins, such as myoglobin, only have one polypeptide and hence are organised up to tertiary level only.

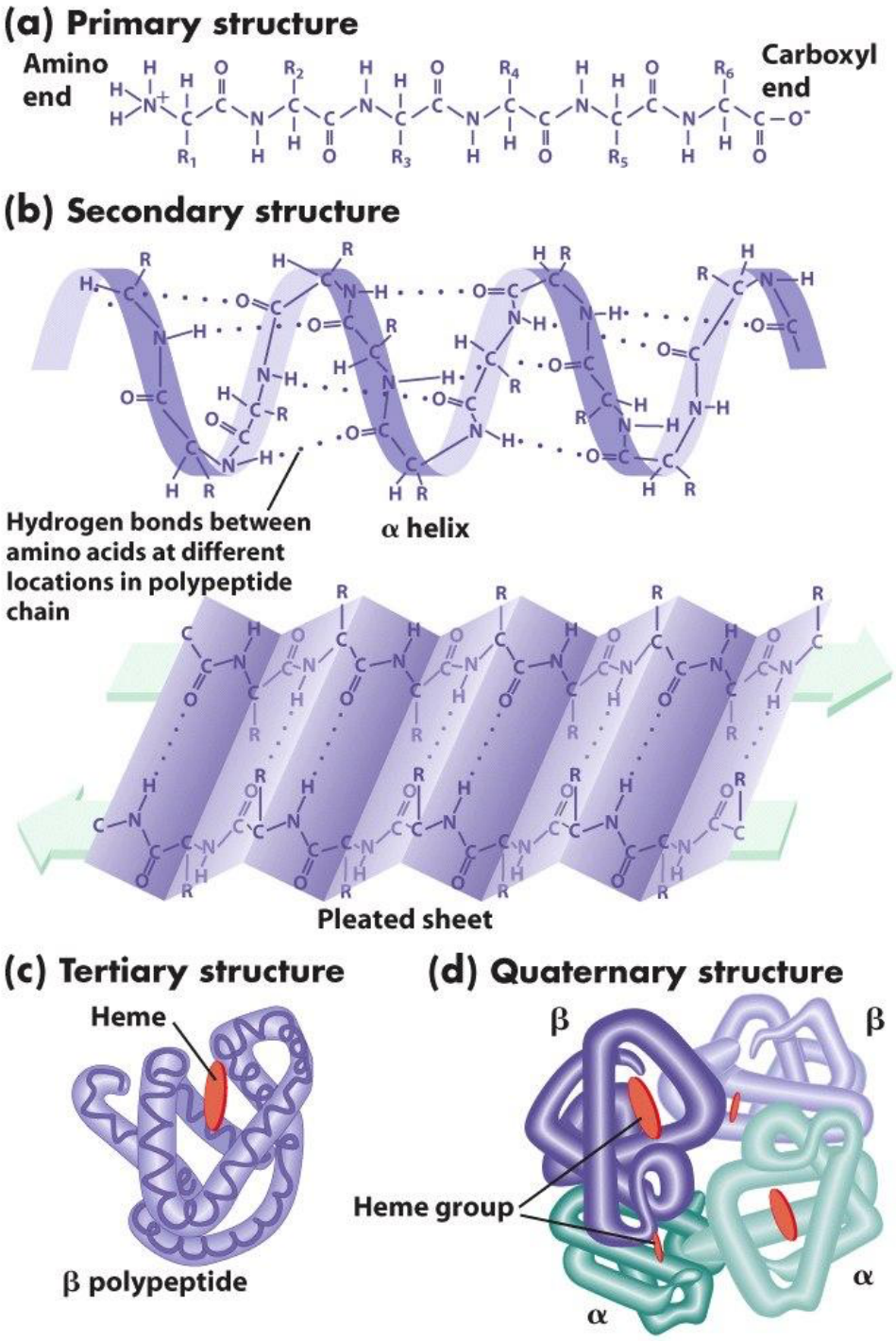


Figure 12: Four levels of protein structure (Gupta, et al., 2017)

For your information

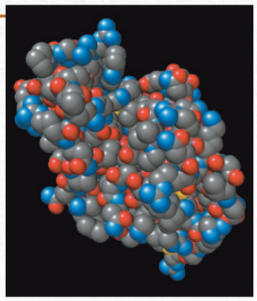
Proteins can be represented in different ways, depending on the goal of the illustration.

Structural Models

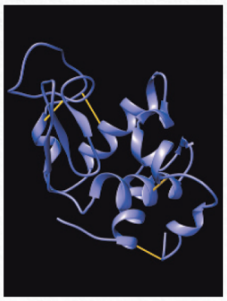
Using data from structural studies of proteins, computers can generate various types of models. Each model emphasizes a different aspect of the protein's structure, but no model can show what a protein actually looks like. These three models depict lysozyme, a protein in tears and saliva that helps prevent infection by binding to target molecules on bacteria.

1 *In which model is it easiest to follow the polypeptide backbone?*

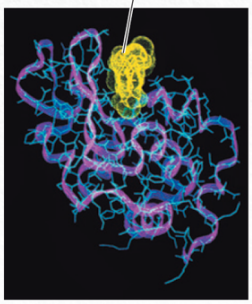
MB **Instructors:** The tutorial "Molecular Model: Lysozyme," in which students rotate 3-D models of lysozyme, can be assigned in MasteringBiology.



Space-filling model: Shows all the atoms of the protein (except hydrogen), emphasizing the overall globular shape. The atoms are color-coded: gray = carbon, red = oxygen, blue = nitrogen, and yellow = sulfur.



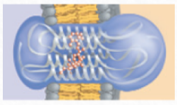
Ribbon model: Shows only the backbone of the polypeptide, emphasizing how it folds and coils to form a 3-D shape, in this case stabilized by disulfide bridges (yellow lines).



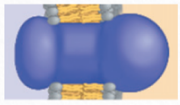
Wireframe model (blue): Shows the backbone of the polypeptide chain with side chains (R groups) extending from it (see Figure 5.15). A ribbon model (purple) is superimposed on the wireframe model.

Simplified Diagrams

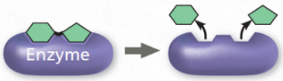
It isn't always necessary to use a detailed computer model; simplified diagrams are useful when the focus of the figure is on the function of the protein, not the structure.



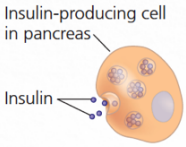
In this diagram of the protein rhodopsin, a simple transparent shape is drawn around the contours of a ribbon model, showing the overall shape of the molecule as well as some internal details.



When structural details are not needed, a solid shape can be used to represent a protein.



A simple shape is used here to represent a generic enzyme because the diagram focuses on enzyme action in general.



Sometimes a protein is represented simply as a dot, as shown here for insulin.

2 *Draw a simple version of lysozyme that shows its overall shape, based on the molecular models in the top section of the figure.*

3 *Why is it unnecessary to show the actual shape of insulin here?*

Concept Check!

Level of protein structure	Definition	Bond(s) used to stabilise structure	No. of polypeptide chains
Primary			
Secondary			
Tertiary			
Quaternary			

5. Types of Proteins

LO: (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).

Proteins can be broadly grouped into three major classes according to their shape and solubility: globular, fibrous, or membrane.

- **Globular proteins** have **hydrophobic R-groups in the interior of the protein while the hydrophilic R-groups are on the exterior**, making them **soluble**, such as haemoglobin.
- **Fibrous proteins** have **regular repeating structure** which gives **high tensile strength**. So, they often perform structural role, such as collagen, the major component of connective tissue.
- **Membrane proteins** often serve as receptors such as G-protein linked receptor, or protein channels.

a. Haemoglobin

- Haemoglobin is the red pigment in red blood cells responsible for transporting oxygen in blood.
- Haemoglobin is a **quaternary globular protein** with **4 subunits** (*Figure 13*):
  - 2 α globin chains of 141 amino acids each
  - 2 β globin chains of 146 amino acids each
- Each subunit consist of a globin chain associated with a prosthetic group called **haem group**.

Structure	Function
Each globin chain coils into **α-helices** (no β-pleated sheets) and folded into a 3D tertiary structure. Four subunits associate and packed tightly in a **tetrahedral conformation**.	.
Each subunit is associated with a **haem group**, which resides in a **hydrophobic pocket**. The haem group is a **prosthetic group**, consisting of a **porphyrin ring with an iron (II) ion (Fe^{2+})** in the centre (Figure 14).	$Hb + 4O_2 \underset{unloading}{\overset{loading}{\rightleftharpoons}} HbO_8$ haemoglobin — oxygen — oxyhaemoglobin The haem group allows **reversible binding to oxygen**, so haemoglobin can **take up oxygen in the lungs and release it to the rest of the body**.
Each haemoglobin molecule has **four haem** groups and can carry four oxygen molecules.	
The quaternary structure of haemoglobin is maintained by **weak intermolecular forces** such as **hydrogen bonds, ionic bonds, and hydrophobic interaction**s. No disulfide bonds.	This gives **flexibility** to the molecule to change conformation upon binding to oxygen, enabling **cooperative binding** of oxygen to haemoglobin (Figure 15), in which the **binding of one oxygen molecule results in a conformation change in the adjacent subunits, increasing their affinity to oxygen**.
Haemoglobin has a globular structure, with the **hydrophobic R-groups are in the interior** of the structure while **hydrophilic R-groups are on the exterior** surface in contact with the aqueous medium.	

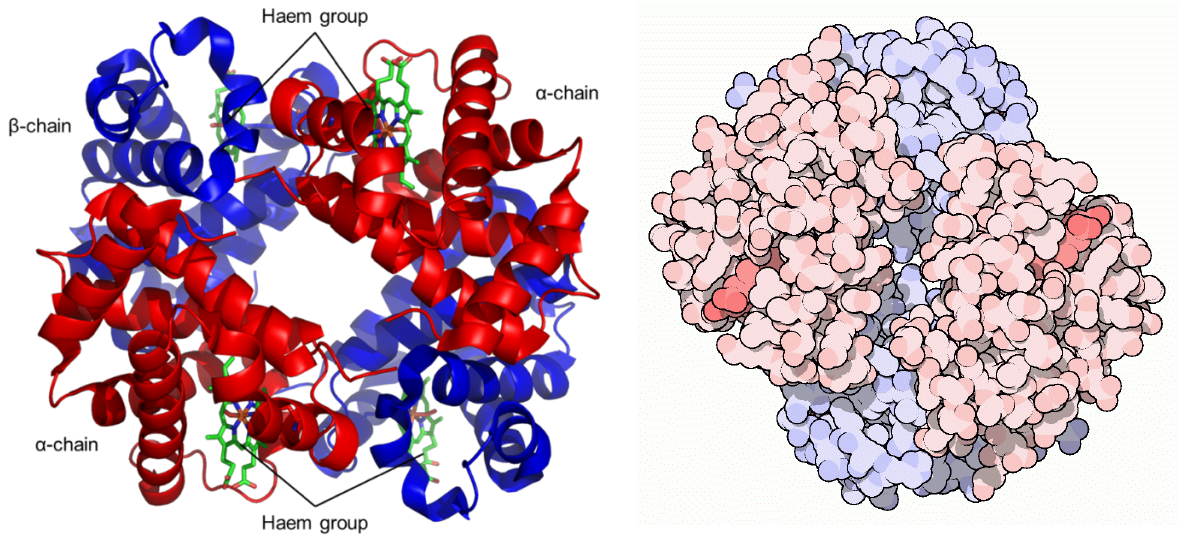


Figure 13: Structure of Haemoglobin

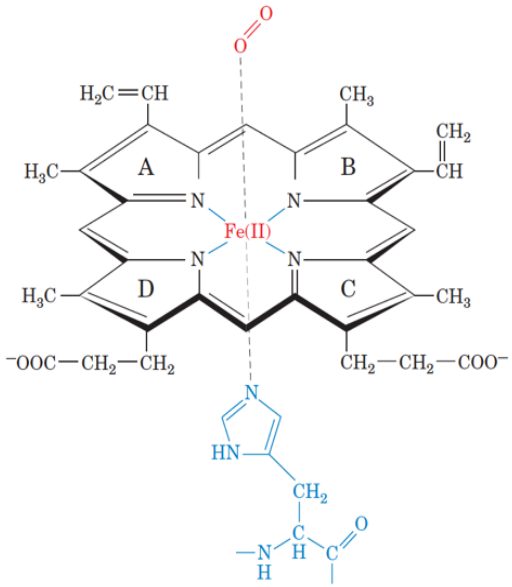


Figure 14: Haem group with bound oxygen (Voet & Voet, 2011)

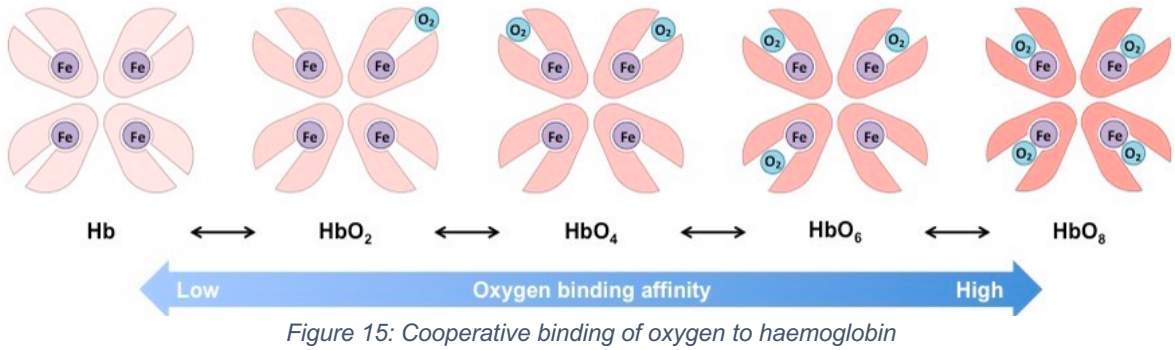


Figure 15: Cooperative binding of oxygen to haemoglobin

b. Collagen

- Collagen is a structural protein found in connective tissue such as tendons, cartilages, and skin.
- Collagen is a fibrous protein, consisting of a basic triple helix structure, called **tropocollagen**.
- Each collagen polypeptide chain contains about 1000 amino acids, usually with a **repeating triplet sequence** of **Gly-X-Y**, where **X is often proline**, and **Y is often hydroxyproline**.
- Each chain is coiled into a left-handed helix (not α-helix), which wound around one another to form a triple helix structure, called tropocollagen (Figure 16).
- The 3 helical chains are held together by **hydrogen bonds between –NH and –C=O of peptide bonds in adjacent polypeptide chains** (Figure 17).
- Tropocollagen molecules lie **parallel** to each other in a **staggered arrangement** to form **fibrils**, with **strong covalent cross-links** occur between **adjacent tropocollagen molecules**.
- The cross-links occur between **two lysine or hydroxylysine residues at the C-terminus of one collagen chain with two similar residues at the N-terminus of an adjacent chain**.
- Many **fibrils unite to form fibres**.

Structure	Function
Every 3rd amino acid residue is a glycine. Glycine being the **smallest amino acid** is able to **fit into the centre of the tropocollagen**.	
Presence of **large number of proline and hydroxyproline** which have **bulky and inflexible R group**, contributing to the **rigidity** of the polypeptide chains.	This rigidity helps to **maintain the precise alignment** of the polypeptide chains within the triple helix structure. Hydroxyproline, derived from proline through post-translational hydroxylation, further **enhances stability** of the triple helix by forming **additional hydrogen bonds**.
Hydrogen bonding between collagen chains of tropocollagen, **covalent cross-linking** between tropocollagen molecules, and **bundling** of collagen fibrils into fibres.	
The tropocollagen are arranged in a **staggered** pattern.	

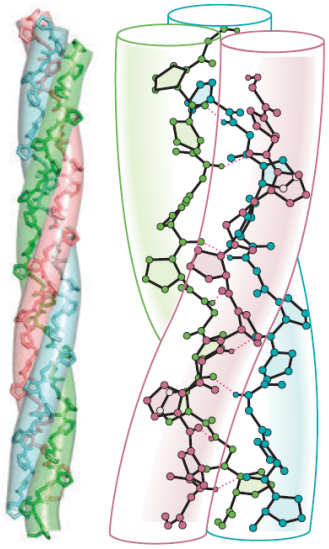


Figure 16: Tropocollagen (Garrett & Grisham, 2010)

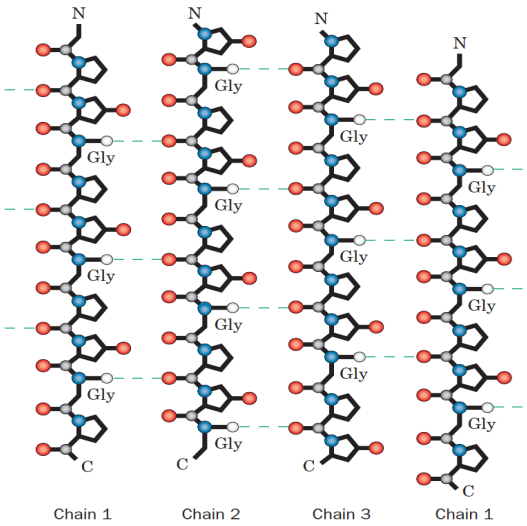


Figure 17: A schematic diagram showing the interchain hydrogen bonding in collagen (Voet & Voet, 2011)

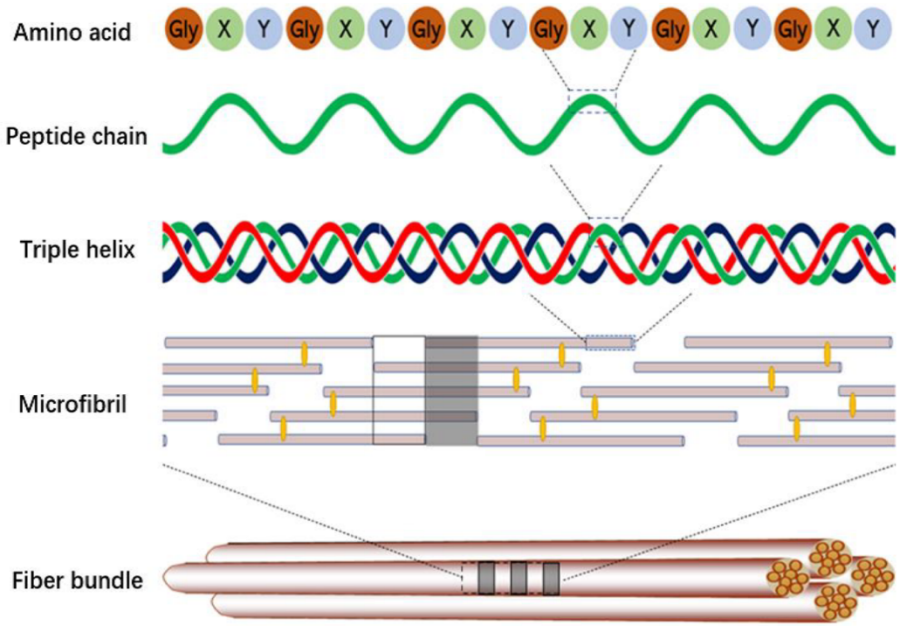


Figure 18: Structural Characteristics of Collagen (He Xiaofeng, et al., 2021)

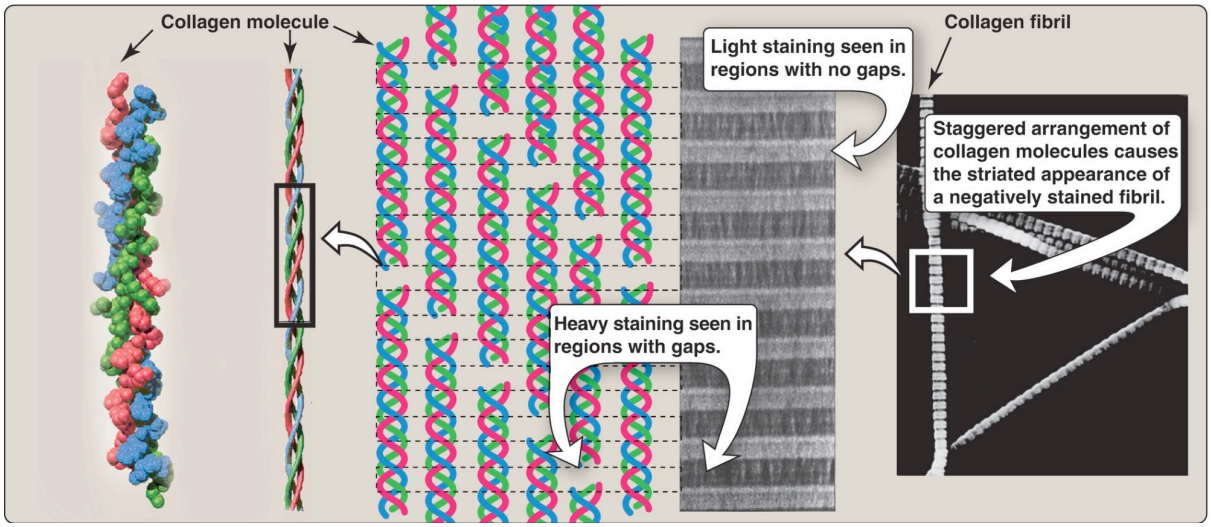
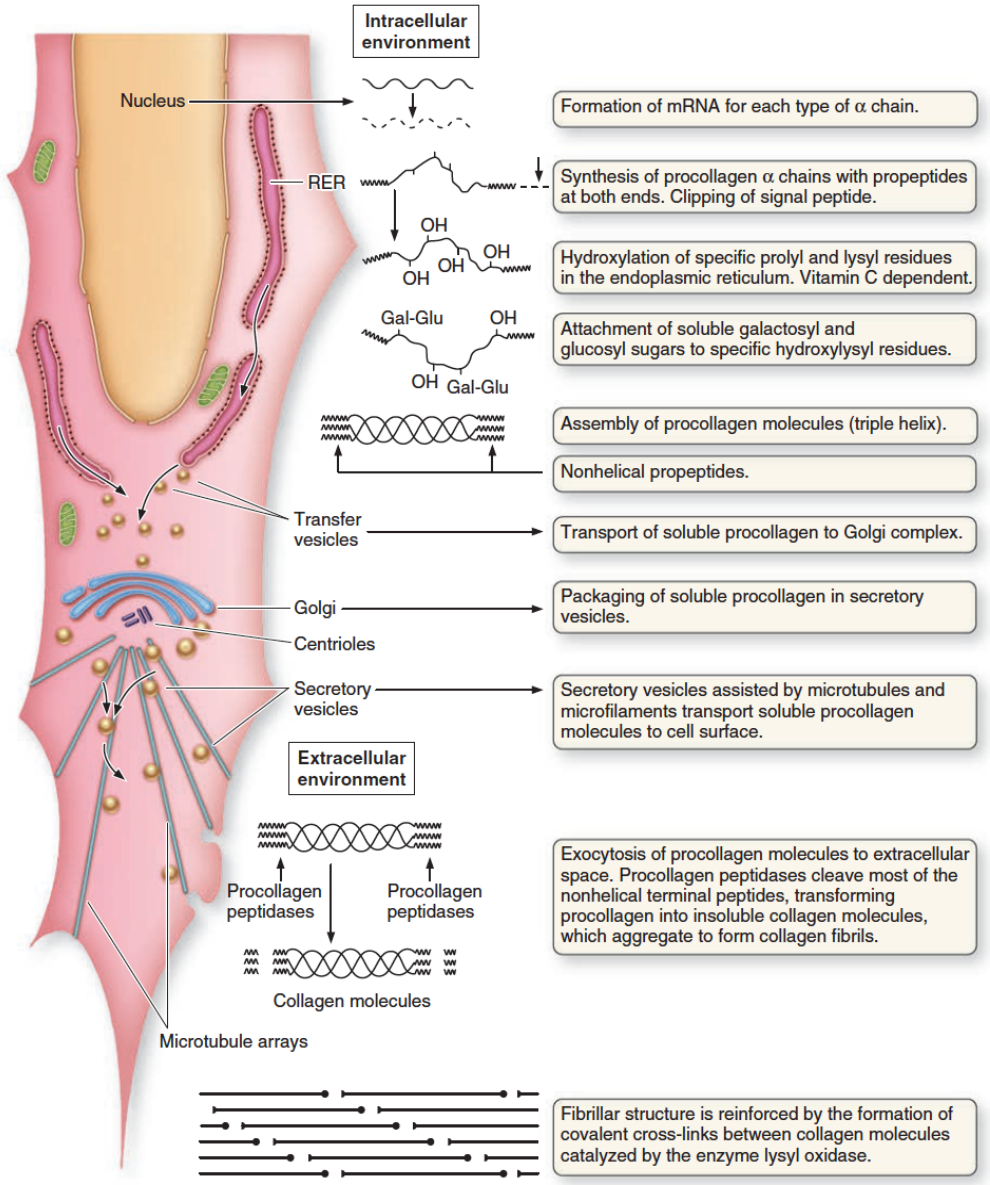


Figure 19: Banded pattern of collagen fibrils, reflecting the regular staggered arrangement (Ferrier, 2017)

For your information



Hydroxylation and glycosylation of procollagen α chains and their assembly into triple helices occur in the RER, and further assembly into fibrils occurs in the ECM after secretion of procollagen. Because there are many slightly different genes for procollagen α chains and collagen production depends on several posttranslational events involving several other enzymes, many diseases involving defective collagen synthesis have been described.

Figure 20 – Synthesis of collagen (Mescher, 2018)

c. G-protein linked receptor (GPLR) or G-protein coupled receptor (GPCR)

- G-protein linked receptor (GPLR) is a **transmembrane protein**, embedded in the cell surface membrane, involved in cell signalling.
- GPLR is a tertiary protein (no quaternary structure) with a single polypeptide that has large variety in terms of length and sequence of amino acids.
- GPLRs constitute one of the largest and most diverse known protein families (>800 genes in humans).
- They serve as cell surface receptors to mediate most cellular responses to hormones and neurotransmitters, as well as being responsible for vision, olfaction, and taste.
- In general, GPLR binds to a **specific signal molecule or ligand** on the **extracellular domain**, and **induces a conformational change** on the **cytoplasmic domain**, transmitting an external signal into the cell (cross reference to topic: Cell Signalling).

Structure	**Function**
GPLR consists of **7 transmembrane α-helices,** spanning the phospholipid bilayer seven times, with **hydrophobic R groups projected out of the helices**.	
There are a **large variety** of GPLRs in terms of length and sequence of amino acids, contributing to a large variety of extracellular and intracellular domains.	
The **hydrophilic extracellular domain** of the GPLR is folded into a **ligand binding site** with a **specific conformation that is complementary to its ligand**.	This allows **binding of ligand** to the GPLR. The binding **triggers a conformational change** in the GPLR.
The **hydrophilic intracellular domain** of the GPLR is folded into a **specific conformation complementary to G-protein**.	This allows **weak association** with G-protein, enabling the **transmission of an external signal into the cell**, as the **conformational change in the GPLR activates the G-protein** for **downstream signalling**.

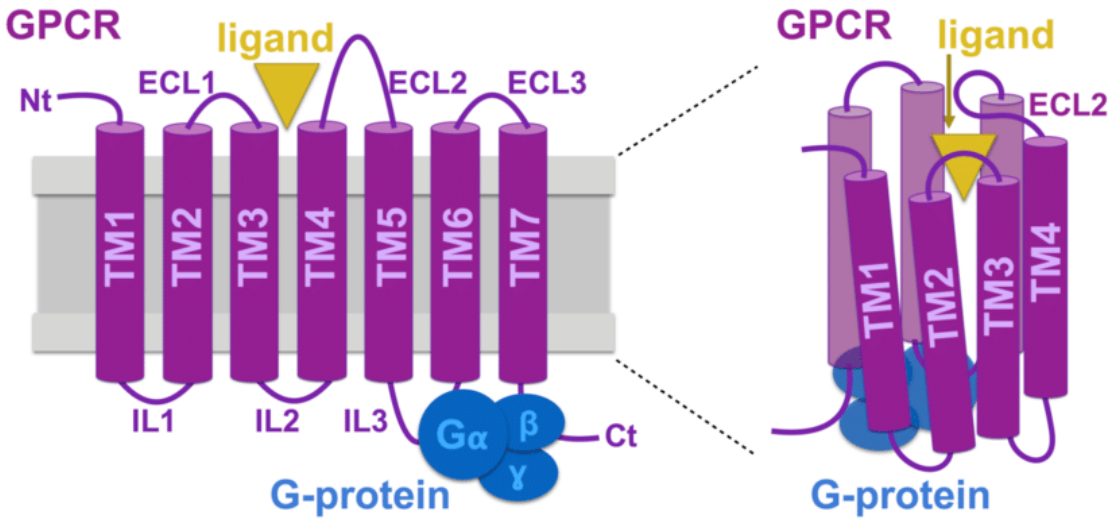


Figure 21 – Schematic diagram of structure of a G-protein linked receptor (Schneider, et al., 2018)
(TM = transmembrane helix, ECL = extracellular loop, IL = intracellular loop, Nt = N-terminus, Ct = C-terminus)

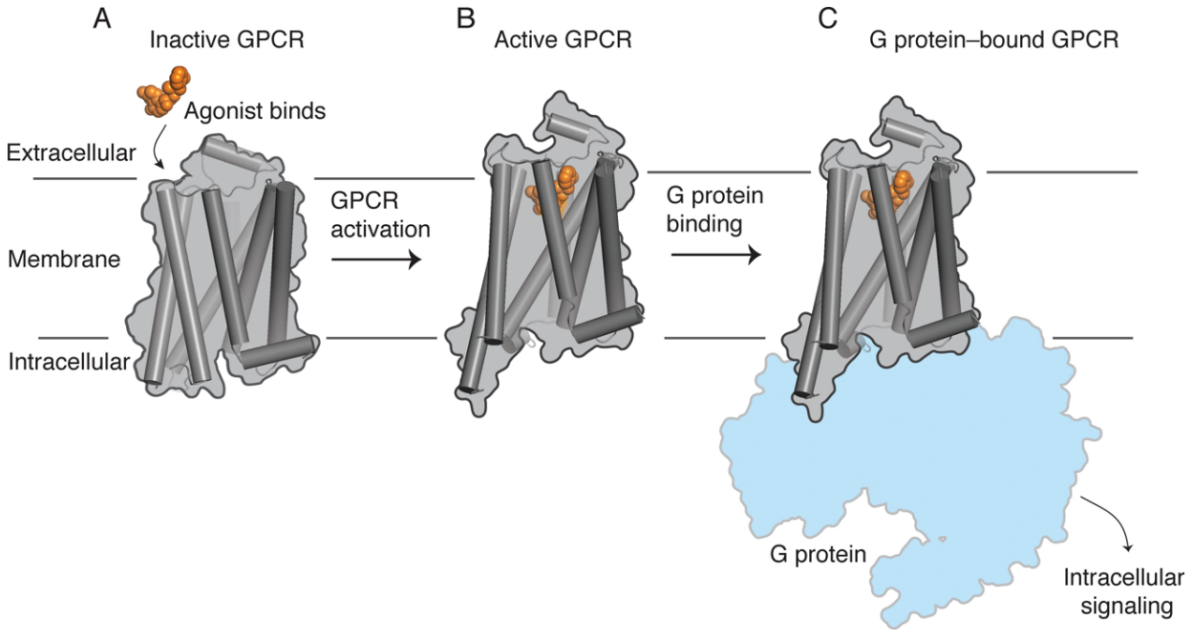


Figure 22 - GPCR signalling: (A) a ligand (orange) binds an inactive GPCR; (B) ligand-bound GPCR undergoes a conformational change to its active state; and (C) an active GPCR binds a G protein, which results in downstream intracellular signalling pathways (Latorraca, 2017).

6. Denaturation

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

a. Normal protein folding is crucial to function

- The combination of primary, secondary, tertiary, and quaternary levels of structure is responsible for the diversity of sizes and shapes observed in proteins.
- Protein folding is directed by the sequence of amino acids present in the primary structure.
- Protein folding is spontaneous. In terms of energy, the folded molecule is more stable than the unfolded molecule.
- The secondary, tertiary, and quaternary levels of protein structure maintained by weaker interactions can be disrupted by heat or chemical treatment.
- Denaturation is the loss of three-dimensional structure sufficient to cause loss of function.
- The denatured state does not necessarily equate with complete unfolding of the protein and randomisation of conformation.
- Denaturation may be reversible or irreversible.
- Renaturation is the regaining of native three-dimensional structure and biological activity.

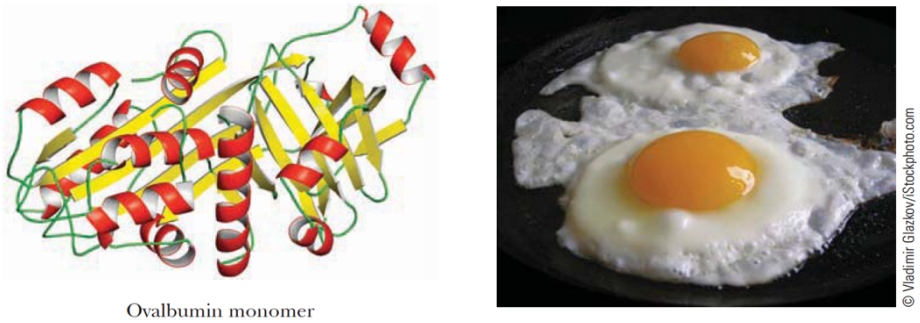


Figure 14 - Cooked egg whites are denatured protein ovalbumin (Garrett & Grisham, 2010)
About 10% of the mass of an egg white is protein, and 54% of that is ovalbumin. Cooking causes the nearly transparent raw egg white proteins to unfold precipitate out of solution. The unfolded proteins aggregate into the solid white mass that we are familiar with.

b. Effect of temperature on protein structure

- Increasing temperature increases the average **kinetic energy** of atoms, causing them to **vibrate faster**.
- This **disrupts the hydrogen bonds, ionic bonds and hydrophobic interactions** in secondary, tertiary and quaternary structures, causing protein structure to **unfold**.
- **Non-polar side chains**, previously folded in the core of the protein, **becomes exposed to aqueous environment**.
- This causes them **aggregate randomly** with other polypeptides, resulting in irreversible change to the protein structure.

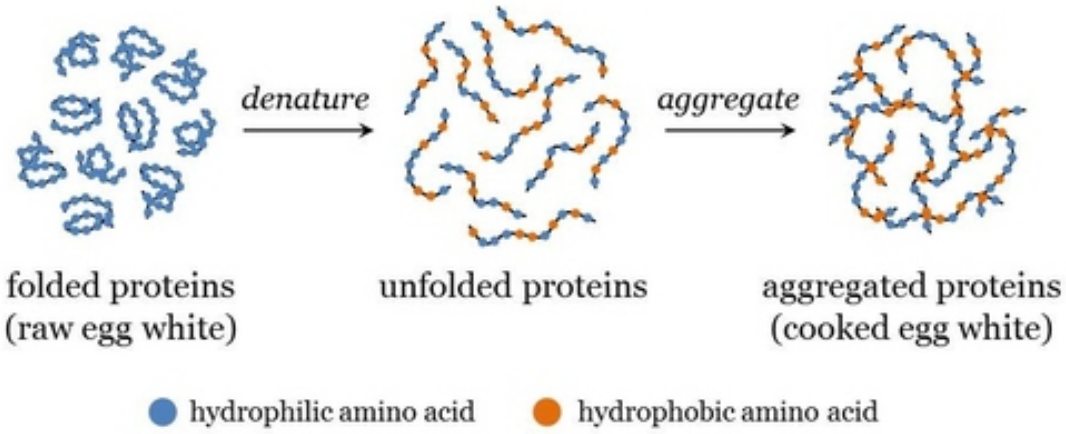


Figure 23 – Heat denaturation of egg white

c. Effect of pH on protein structure

- Changes in pH may **disrupt ionic interactions and hydrogen bonding** between side chains.
- Decreasing pH through the addition of acids, increases H^+ concentration in the solution. The additional H^+ combines with R groups e.g. $–COO^-$ to form –COOH, and $–NH_2$ to form $–NH_3^+$.
- Increasing pH through the addition of alkalis, increases OH^- concentration in the solution. The additional OH^- removes the H^+ from R groups e.g. $–NH_3^+$ to form $–NH_2$, and –COOH to form $–COO^-$.
- If either $–COO^-$ or $–NH_3^+$ become uncharged, ionic bonds will be disrupted.
- If either –COOH or $–NH_2$ become charged, hydrogen bonds will be disrupted.

Conditions	Disruption of ionic bonds	Disruption of hydrogen bonds
Decreasing pH	Ionic bonds between $–COO^-$ and $–NH_3^+$ are disrupted due to $–COO^-$ accepting H^+ from the solution and form –COOH.	Hydrogen bonds between $–NH_2$ and another polar group are disrupted due to $–NH_2$ accepting H^+ from the solution and form $–NH_3^+$.
Increasing pH	Ionic bonds between $–NH_3^+$ and $–COO^-$ are disrupted due to $–NH_3^+$ losing a H^+ to the solution and form $–NH_2$.	Hydrogen bonds between –COOH and another polar group are disrupted due to –COOH losing a H^+ from the solution and form $–COO^-$.

- Presence of very high concentration of H^+ may even cause peptide bonds to be broken (acid hydrolysis).

For your information

d. Effect of other chemicals on protein structure

- Detergents are amphipathic and can disrupt hydrophobic interactions by associating with non-polar R groups in a protein and increase its solubility.
- Reducing agents, such as β-mercaptoethanol, can disrupt disulfide bonds between cysteine residues by reducing the disulfide bonds (–S-S–) to –S-H (sulfhydryl) groups.
- Heavy metals are positively charged and form strong bonds with negatively charged carboxyl R groups of proteins, disrupting ionic bonds.

For your information

Death by Misfolding: Prion Diseases (David & Michael, 2013)

A misfolded brain protein seems to be the causative agent of several rare degenerative brain diseases in mammals. Perhaps the best known of these is bovine spongiform encephalopathy (BSE; also known as mad cow disease). Related diseases include kuru and Creutzfeldt-Jakob disease in humans, scrapie in sheep, and chronic wasting disease in deer and elk. These diseases are also referred to as spongiform encephalopathies, because the diseased brain frequently becomes riddled with holes (Fig. 1). Progressive deterioration of the brain leads to a spectrum of neurological symptoms, including weight loss, erratic behavior, problems with posture, balance, and coordination, and loss of cognitive function. The diseases are fatal.

In the 1960s, investigators found that preparations of the disease-causing agents seemed to lack nucleic acids. At this time, Tikvah Alper suggested that the agent was a protein. Initially, the idea seemed heretical. All disease-causing agents known up to that time—viruses, bacteria, fungi, and so on—contained nucleic acids, and their virulence was related to genetic reproduction and propagation. However, four decades of investigations, pursued most notably by Stanley Prusiner, have provided evidence that spongiform encephalopathies are different.

The infectious agent has been traced to a single protein (M_r 28,000), which Prusiner dubbed **prion** protein (PrP). The name was derived from *pro*teinaceous *in*fectious, but Prusiner thought that "prion" sounded better than "proin." Prion protein is a normal constituent of brain tissue in all mammals. Its role is not known in detail, but it may have a molecular signaling function. Strains of mice lacking the gene for PrP (and thus the protein itself) suffer no obvious ill effects. Illness occurs only when the normal cellular PrP, or PrP^{C}, occurs in an altered conformation called PrP^{Sc} (Sc denotes scrapie). The structure

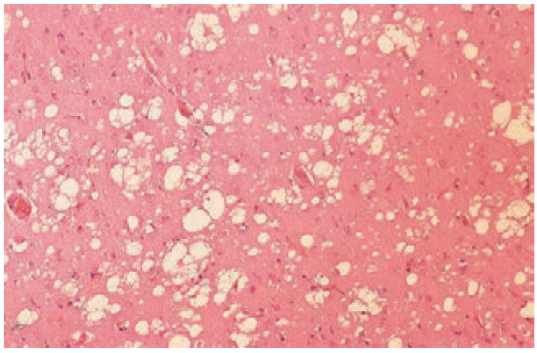


FIGURE 1 Stained section of cerebral cortex from autopsy of a patient with Creutzfeldt-Jakob disease shows spongiform (vacuolar) degeneration, the most characteristic neurohistological feature. The yellowish vacuoles are intracellular and occur mostly in pre- and postsynaptic processes of neurons. The vacuoles in this section vary in diameter from 20 to 100 μm.

7. Biuret Test for Proteins

To test for the presence of proteins in a sample, you'll need to do the Biuret test:

Procedure:

1. Add 2 cm^3 of sodium hydroxide (NaOH) to 2 cm^3 of test sample in a test tube. Mix well.
2. Then add a few drops of copper (II) sulfate ($CuSO_4$) and mix well.

Observation:

1. If proteins are present, the solution turns purple.
2. If proteins are absent, the solution remains blue.

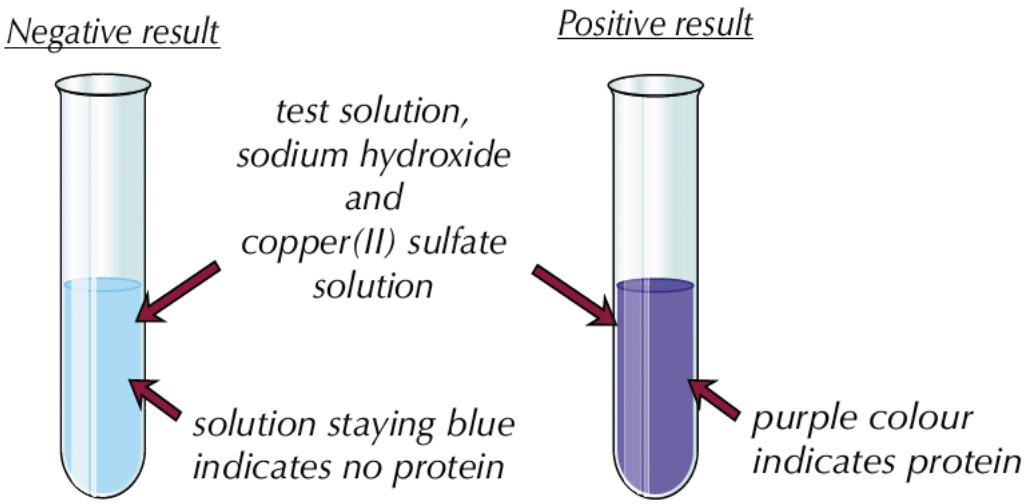


Figure 24: Positive result of emulsion test

Glossary

Complete the table by filling up the definitions of the key words and phrases.

Key words/phrases	Definition
Amino acid	
Amphoteric	
Zwitterion	
Peptide bond	
Primary structure	
Secondary structure	
Tertiary structure	
Quaternary structure	
α-helix	
β-pleated sheet	
Hydrogen bond	
Ionic bond	
Hydrophobic interaction	
Disulfide bond	
Denaturation	
Globular protein	
Fibrous protein	
Membrane protein	
Haemoglobin	
Prosthetic group	
Haem group	
Collagen	
Tropocollagen	
G-protein linked receptor	