Option B Human Biochemistry

IB CHEMISTRY HL

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B.7 Enzymes and proteins

Understandings:

- Inhibitors play an important role in regulating the activities of enzymes.
- Amino acids and proteins can act as buffers in solution.
- Protein assays commonly use UV-vis spectroscopy and a calibration curve based on known standards.

Applications and skills:

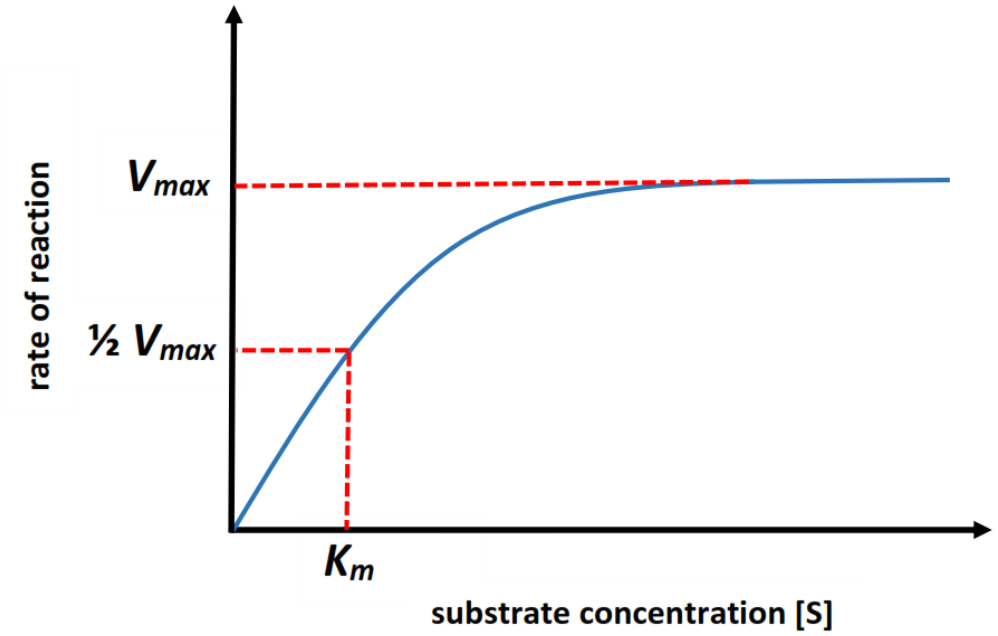
- Determination of the maximum rate of reaction (V_{max}) and the value of the Michaelis constant (K_m) for an enzyme by graphical means, and explanation of its significance.
- Comparison of competitive and non-competitive inhibition of enzymes with reference to protein structure, the active site and allosteric site.
- Explanation of the concept of product inhibition in metabolic pathways.
- Calculation of the pH of buffer solutions, such as those used in protein analysis and in reactions involving amino acids in solution.
- Determination of the concentration of a protein in solution from a calibration curve using the Beer–Lambert law.

Guidance:

- The effects of competitive and non-competitive inhibitors on K_m and V_{max} values should be covered.
- The Henderson–Hasselbalch equation is given in the data booklet in section 1.
- For UV-vis spectroscopy, knowledge of particular reagents and wavelengths is not required.

Enzyme kinetics

- Effect of substrate concentration on rate of reaction



- Maximum rate of reaction V_{max} - the point where all the active sites are bound to substrate (enzyme is saturated).
- Michaelis constant K_m - the substrate concentration which is equal to half its maximum value (½ V_{max}).

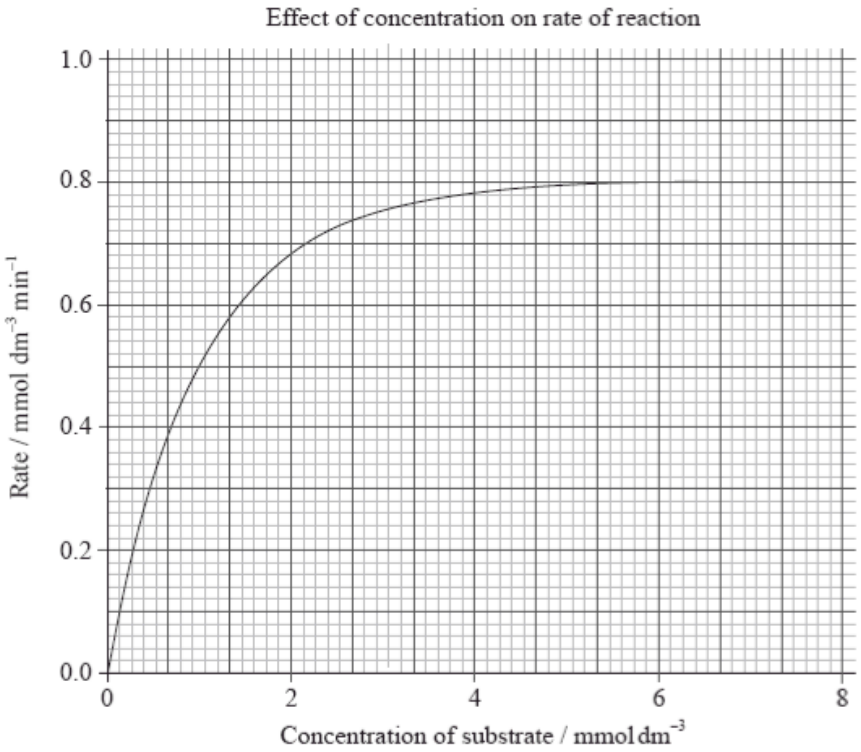
Value of V_{max}

- V_{max} reflects how fast the enzyme can catalyse the reaction.
- A low value of V_{max} means that the enzyme does not convert much substrate to product per unit time when the enzyme is saturated with substrate.
- A high value of V_{max} means the opposite. The V_{max} is a measure of how fast the enzyme can work when it is completely saturated with the substrate.

Value of K_m

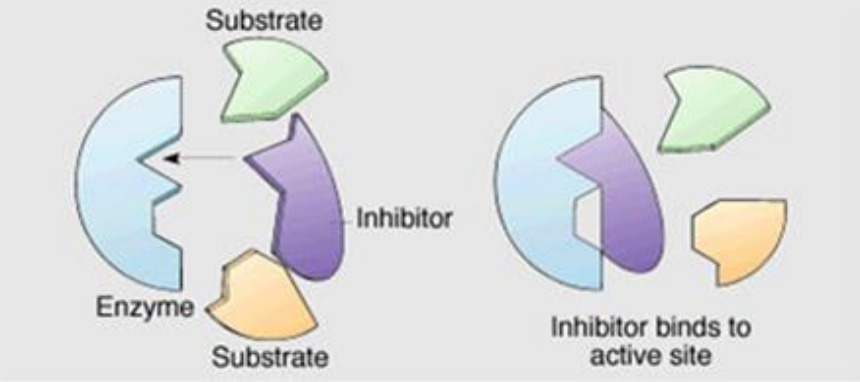
- Enzymes have varying tendencies to bind their substrates (affinity).
- A high value of K_m means a high concentration of substrate must be present to saturate the enzyme, therefore the enzyme has a low affinity for the substrate.
- A low value of K_m means only a small amount of substrate is needed to saturate the enzyme, indicating a high affinity for the substrate.

Exercise: Use the graph to determine V_{max} and the Michaelis constant K_m

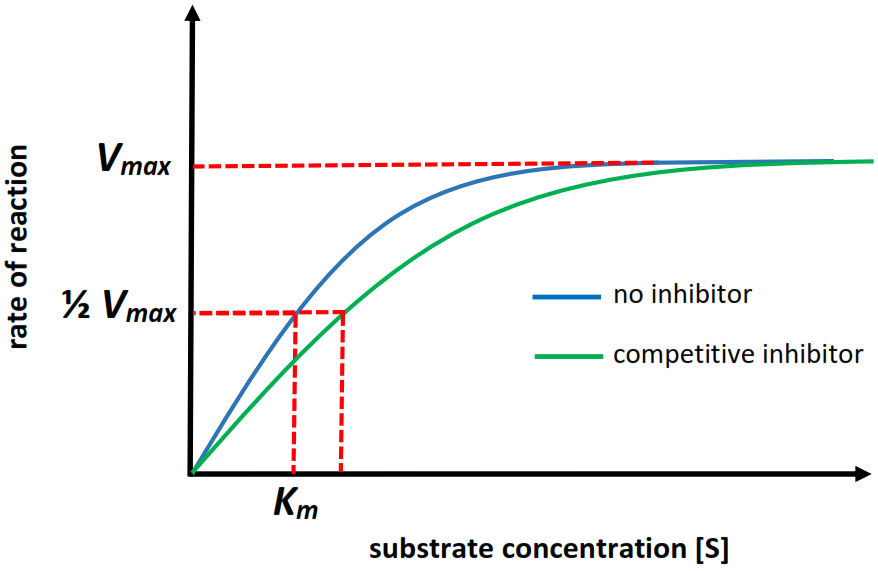


Competitive inhibitors

- Competitive inhibitors bind at the active site of the enzyme (they compete with the substrate for the active site).
- They usually have a chemical structure similar to the substrate.
- Once they bind to the active site, they do not form products, they just block the active site and make it unavailable to the substrate.



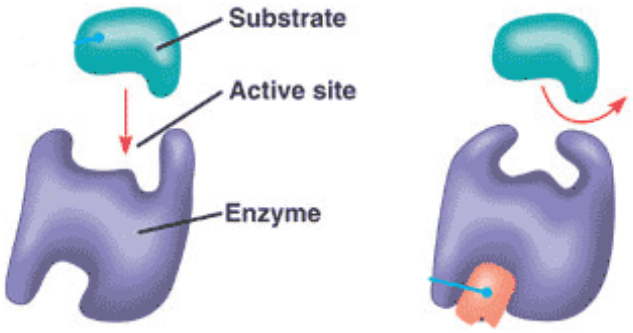
- Increasing the [substrate] reduces the extent of the inhibition as fewer of the inhibitor molecules are able to bind at the active site.

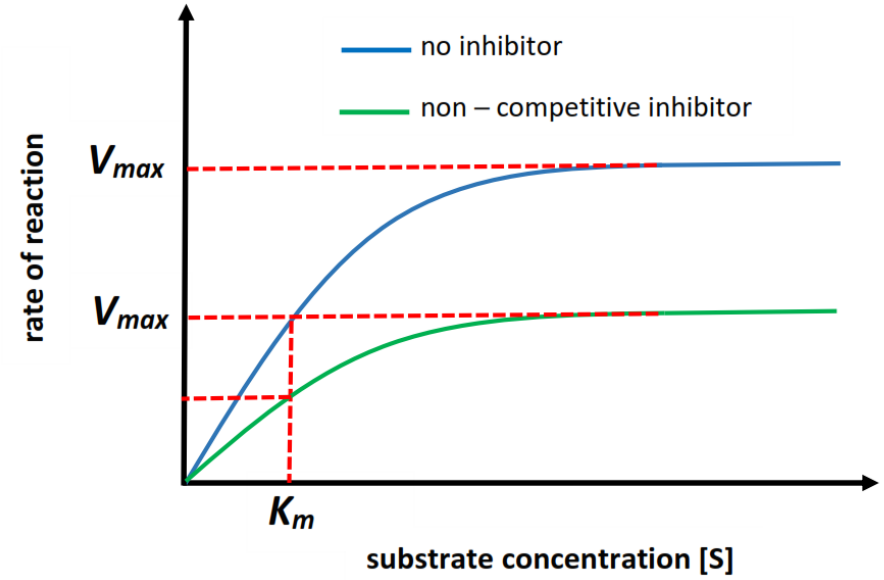


- V_{max} is not changed as there is still a substrate concentration where full enzyme activity can be achieved.
- K_m is increased as it takes a higher substrate concentration to reach V_{max}

Non-competitive inhibitors

- Non - competitive inhibitors bind away from the active site (called the allosteric site).
- This results in a change in the proteins' conformation which alters the shape of the active site, inhibiting its ability to bind to the substrate.





- Increasing the concentration of substrate does not reduce this type of inhibition as the active site is unavailable.
- The value of V_{max} is decreased but the value of K_m is unchanged.

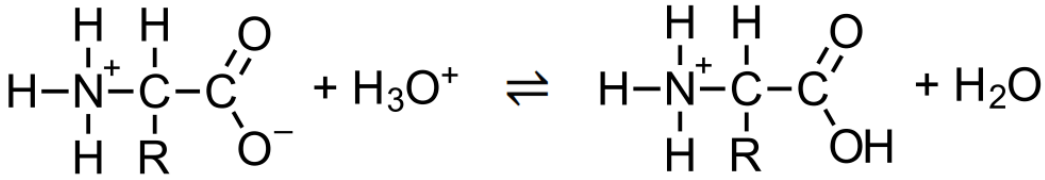
Summary:

Competitive inhibitor	Non-competitive inhibitor
Binds at active site	Binds away from active site (allosteric site)
Is similar in structure to the substrate	May have different structure to substrate
V_{max} is unchanged	V_{max} is lowered
K_m increased	No change in K_m
Increasing concentration of substrate has an effect	Increasing concentration of substrate has no effect

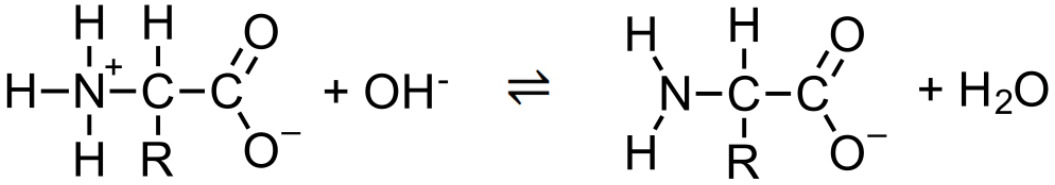
Calculating pH of buffer solutions

- Amino acids can act as acid-base buffers by reacting with the hydronium ion (H_3O^+) or the hydroxide ion (OH^-), minimizing the change in pH when small amounts of acid or base are added.

- Response to added acid (H_3O^+):



- Response to added base (OH^-)



- The Henderson-Hasselbalch equation can be found in section 1 of the data booklet.

$$\mathrm{pH} = \mathrm{p}K_a + \log_{10}\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

[HA] = initial concentration of the weak acid
[A^-] = the initial concentration of the salt

Assumptions when using the Henderson-Hasselbalch equation:

- The concentration of the weak acid at equilibrium is approximately equal to the initial concentration of the weak acid.

$$[\mathrm{HA}]_{\mathrm{initial}} \approx [\mathrm{HA}]_{\mathrm{equilibrium}}$$

- The salt fully dissociates, so the concentration of the A^- is approximately equal to the initial concentration of the salt.

$$[\mathrm{MA}]_{\mathrm{initial}} \approx [\mathrm{A}^-]_{\mathrm{equilibrium}}$$

Exercise: Calculate the pH of a solution prepared by mixing 50.0 cm^3 of 0.200 mol dm^{-3} $CH_3COOH_{(aq)}$ and 50.0 cm^3 of 0.100 mol dm^{-3} $NaOH_{(aq)}$. The pK_a of ethanoic acid is 4.75 at 298 K.

Beer-Lambert law

- The Beer – Lambert law expresses the linear relationship between the absorbance and concentration of a compound at a fixed wavelength.

$$\log_{10} \frac{I_o}{I} = \varepsilon l c$$

I_o – intensity of the light before it passes through the sample

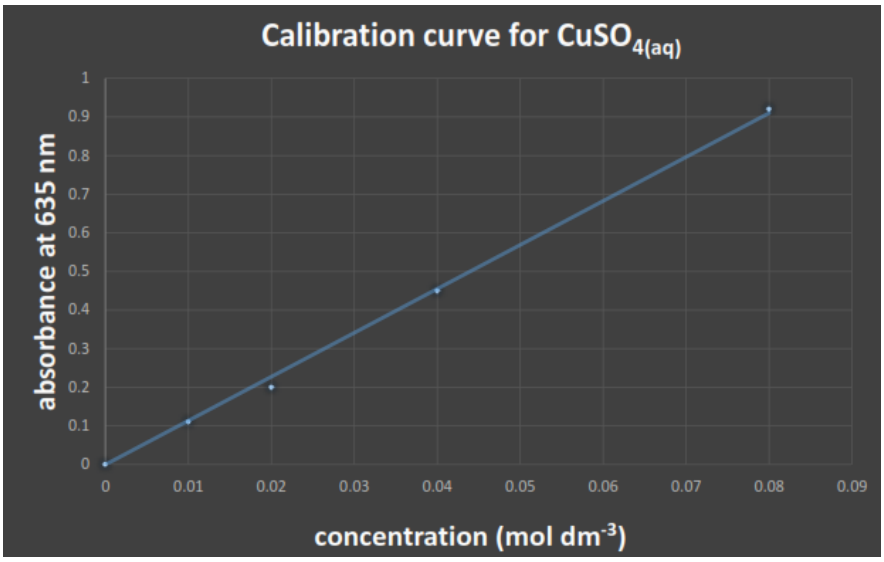
I – intensity of the light after it passes through the sample

ε – molar absorption coefficient

l – path length of absorbing solution (usually 1.00 cm)

c – concentration of the solution

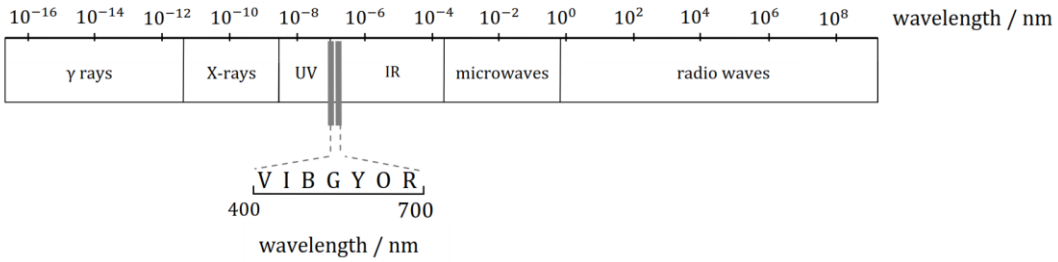
- A calibration curve can be obtained by using a range of solutions with known concentrations and measuring the absorbance using a spectrophotometer.



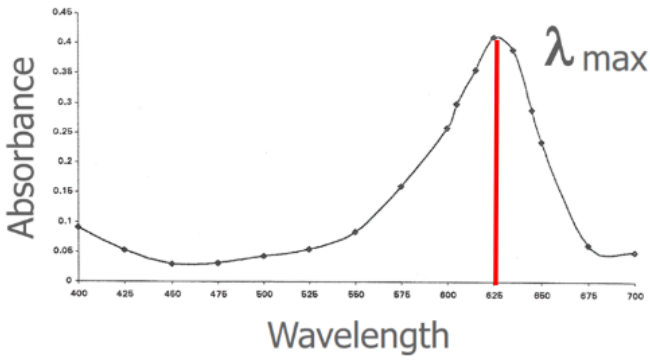
- The absorbance of a compound at a fixed wavelength is directly proportional to its concentration.
- The calibration curve can be used to determine the concentration of an unknown $CuSO_4$ solution by measuring its absorbance with the spectrophotometer.
- From the graph, we can determine the concentration of a copper sulfate pentahydrate solution with an absorbance of 0.170 at 635 nm (0.016 mol dm^{-3}).

Analysis of protein concentration

- UV-visible spectroscopy is a technique used in protein assays to measure the concentration of a protein in a sample.
- UV-vis spectroscopy depends on the interaction of molecules with the UV and visible light portions of the electromagnetic spectrum (180 - 750nm).



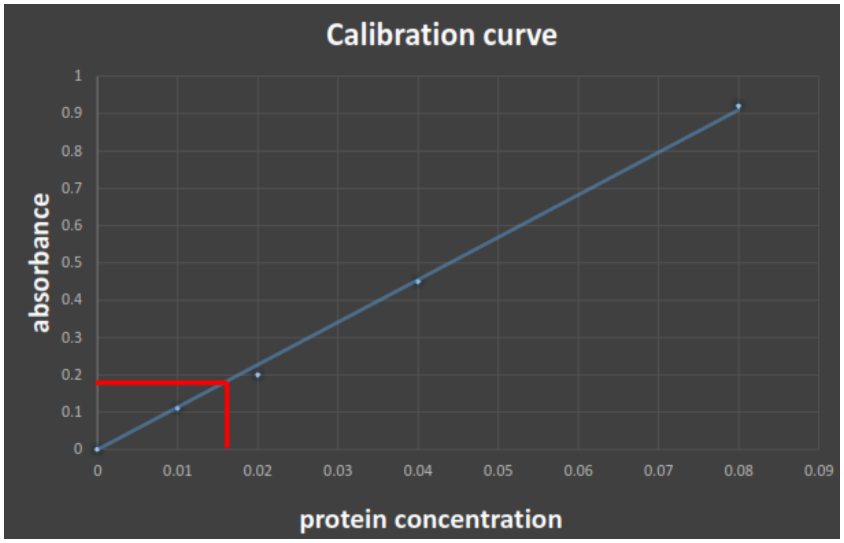
- Absorption spectra are produced using a spectrophotometer.
- The protein is made into a coloured compound using a dye so that the intensity of the colour depends upon the concentration of protein in the sample.
- The wavelength of maximum absorbance is selected.
- The λ_{max} is the wavelength at which absorption is the greatest.



- The amount of light absorbed at this wavelength is given by the equation for the Beer – Lambert law.

$$\log_{10} \frac{I_o}{I} = \varepsilon l c$$

- A calibration curve can be obtained by using a range of solutions with known concentrations and measuring the absorbance using a spectrophotometer.



- The calibration curve can then be used to determine the concentration of an unknown protein solution.

B.8 Nucleic acids

Understandings:

- Nucleotides are the condensation products of a pentose sugar, phosphoric acid and a nitrogenous base—adenine (A), guanine (G), cytosine (C), thymine (T) or uracil (U).
- Polynucleotides form by condensation reactions.
- DNA is a double helix of two polynucleotide strands held together by hydrogen bonds.
- RNA is usually a single polynucleotide chain that contains uracil in place of thymine, and a sugar ribose in place of deoxyribose.
- The sequence of bases in DNA determines the primary structure of proteins synthesized by the cell using a triplet code, known as the genetic code, which is universal.
- Genetically modified organisms have genetic material that has been altered by genetic engineering techniques, involving transferring DNA between species.

Applications and skills:

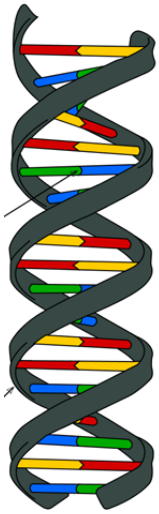
- Explanation of the stability of DNA in terms of the interactions between its hydrophilic and hydrophobic components.
- Explanation of the origin of the negative charge on DNA and its association with basic proteins (histones) in chromosomes.
- Deduction of the nucleotide sequence in a complementary strand of DNA or a molecule of RNA from a given polynucleotide sequence.
- Explanation of how the complementary pairing between bases enables DNA to replicate itself exactly.
- Discussion of the benefits and concerns of using genetically modified foods.

Guidance:

- Structures of the nitrogenous bases and ribose and deoxyribose sugars are given in the data booklet in section 34.
- Knowledge of the different forms of RNA is not required.
- Details of the process of DNA replication are not required.
- Limit expression of DNA to the concept of a four-unit base code determining a twenty-unit amino acid sequence. Details of transcription and translation are not required.

Nucleic acids (polynucleotides)

- DNA stores the information that controls the genetic characteristics of an organism and RNA enables the information stored in DNA to be expressed.
- DNA and RNA are both examples of polynucleotides which are polymers composed of nucleotides (monomers).



DNA
Deoxyribonucleic acid

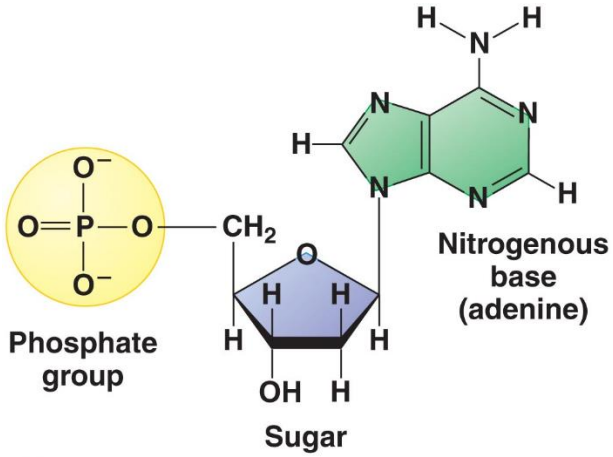
DNA has a double helix structure (double stranded polynucleotide).
The sugar phosphate backbone is on the outside and the nitrogenous bases are on the inside.
The two strands are held together by hydrogen bonds between the nitrogenous bases.

RNA
Ribonucleic acid

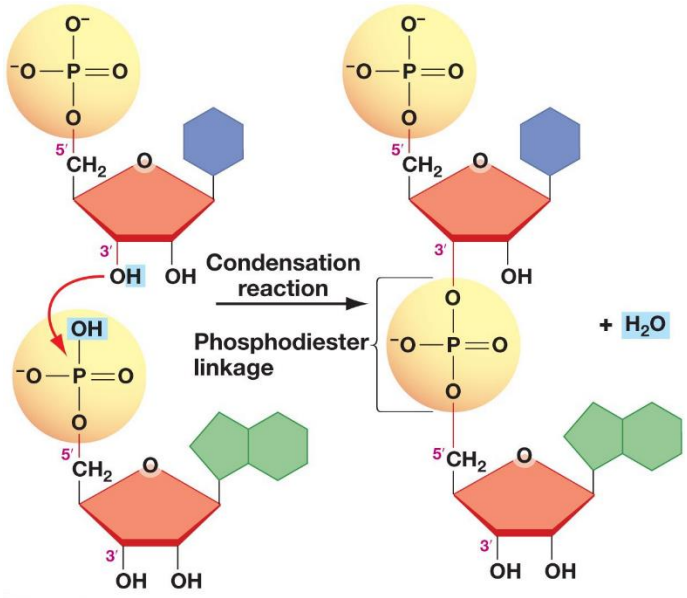
RNA is a single stranded polynucleotide

Nucleotides

- A nucleotide contains a phosphate group, a pentose (5 carbon) sugar and an organic nitrogenous base.
- The nitrogenous base, pentose sugar and phosphate group bond in condensation reactions, releasing a molecule of water.

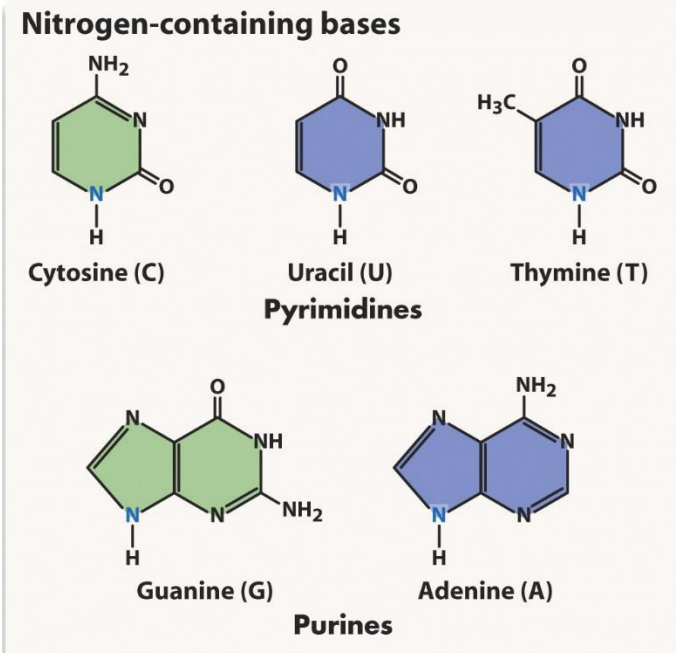


- The nitrogenous base joins at the C_1 of the sugar and the phosphate to C_5, the 5 prime position (5').
- Nucleotides bond in condensation reactions involving the phosphate group at the 5' position of one nucleotide and the OH group at the 3' position of the next nucleotide.
- These bonds are called phosphodiester links.



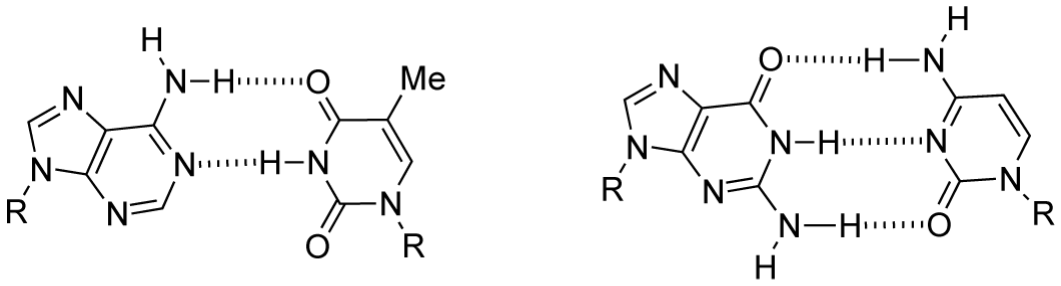
Nitrogenous bases

- There are two types of nitrogenous bases, purines and pyrimidines.
- Pyrimidines are smaller and contain only 1 ring.
- Purines are larger and contain 2 fused rings.



Base pairing

- Only certain base pairings involving one purine and one pyrimidine are possible.
- In DNA, adenine forms 2 hydrogen bonds with thymine and guanine forms 3 hydrogen bonds with cytosine.



A·T base pair G·C base pair

Stability of DNA

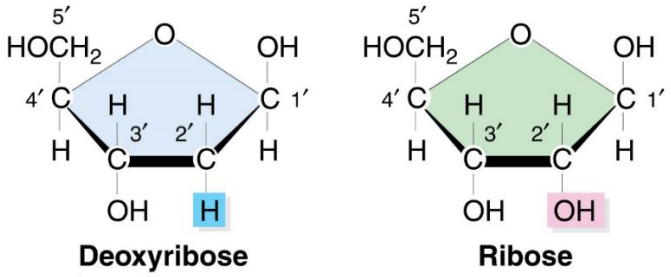
- The double helix structure places the non-polar bases in the centre surrounded by the charged phosphate groups.
- Base stacking (London dispersion forces) and hydrogen bonding both contribute to the stability of the double helix structure.
- The cellular environment is aqueous and therefore polar, so surrounding the non-polar bases with charged phosphates maximizes the solubility of DNA.

DNA packaging

- DNA is tightly packed in the nucleus of every cell.
- DNA wraps around special proteins called histones, which form loops of DNA called nucleosomes.
- Histones contain a large proportion of the positively charged basic amino acids lysine (Lys) and arginine (Arg).
- DNA is negatively charged due to the phosphate groups that link the deoxyribose sugars in the backbone of the molecule.
- The result of these opposite charges is a strong attraction and high binding affinity between histones and DNA.

Differences between DNA and RNA

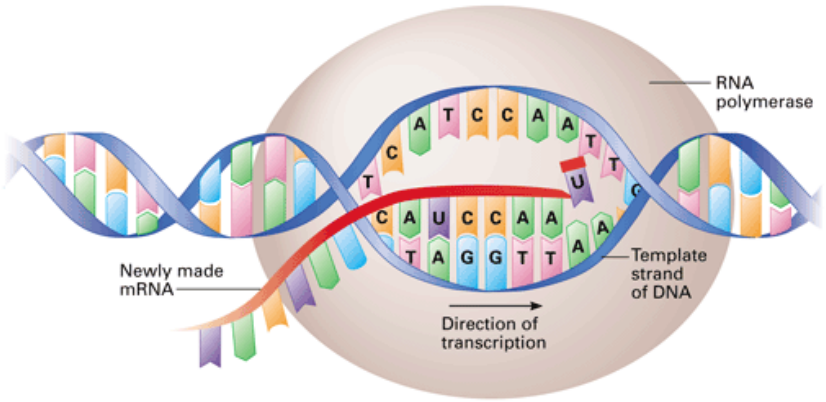
- DNA has deoxyribose as its pentose sugar.
- RNA has ribose as its pentose sugar.
- Deoxyribose lacks an oxygen atom on carbon 2.



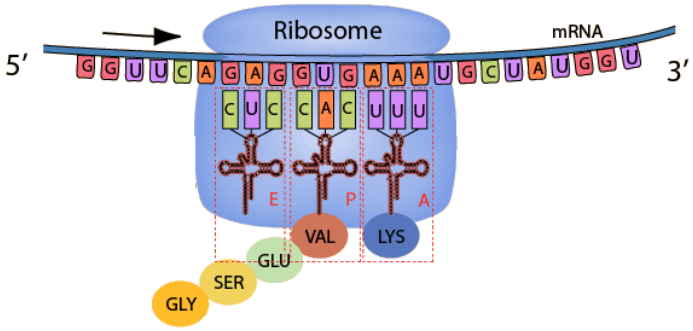
- RNA has uracil instead of thymine as its base.
- RNA is a single-strand nucleic acid; DNA is a double-strand nucleic acid.

Protein synthesis

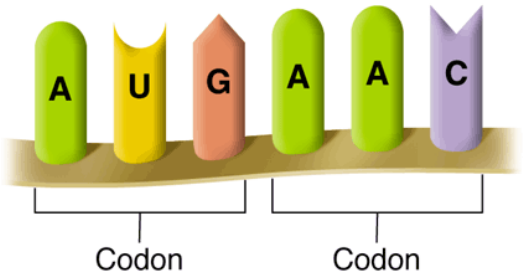
- The information required to make proteins is passed from DNA to mRNA in a process called transcription.



- In transcription, a segment of DNA is copied into mRNA by the enzyme RNA polymerase.
- The newly formed mRNA leaves the nucleus for the ribosome, where translation takes place.



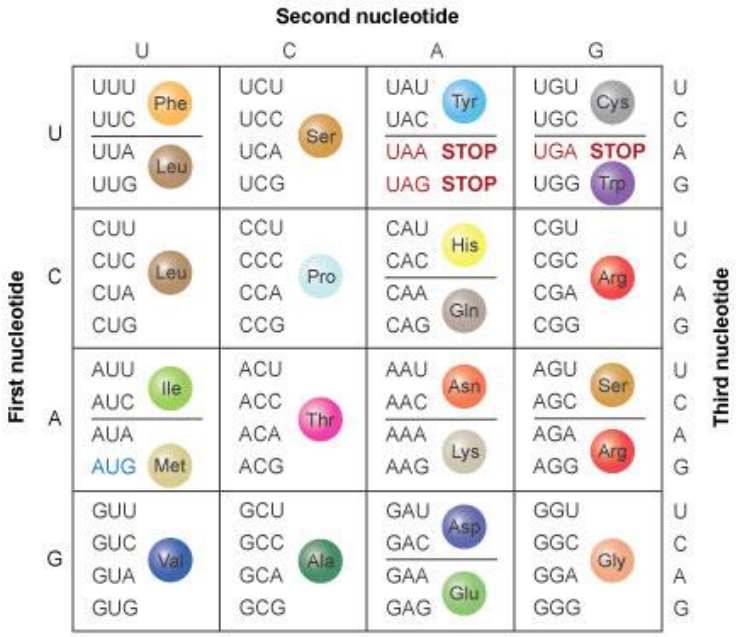
- In translation, messenger RNA (mRNA) is decoded by a ribosome to produce a polypeptide chain.
- In translation, a triplet code is used with each sequence of three nucleotides (bases) representing one amino acid.
- The triplet code allows for up to 64 permutations, known as codons.



- Each codon consists of three nucleotides, corresponding to a single amino acid.
- The 64 permutations represent the 20 naturally occurring amino acids.

The table below shows the DNA codon, the RNA codon and amino acid for which it codes.

DNA codon	AAA	TAA	AGA	GTG	CTT
RNA codon	UUU	AUU	UCU	CAC	GAA
Amino acid	Phe	Ile	Ser	His	Glu



GM foods

- Genetically modified foods (GM foods), are foods produced from genetically modified organisms that have had changes introduced into their DNA through genetic engineering.
- Genetic engineering allows DNA to be transferred from one species to another.
- An example is corn that has been genetically modified to express a protein taken from bacteria that acts as a natural insecticide.

Benefits of GM foods:

- Increased crop yields, which could help by feeding more people in developing countries.
- Improved food quality - a tomato was genetically engineered to stay fresher for longer, extending its shelf life in the supermarket.
- Increased resistance to disease or pests thereby reducing the use of pesticides.
- Increased resistance to adverse weather such as droughts.
- GM foods can be engineered to have a high content of a specific nutrient that is lacking in the diet of a local population group.

Concerns over GM foods:

- The ability of a GM food to trigger an allergy in humans. Genes used in GM technology might be taken from a food that causes allergies in certain people.
- Lack of information regarding the long-term effects of GM foods.
- Other organisms in the ecosystem could be harmed, which would lead to a lower level of biodiversity.
- Given that some GM foods are modified using bacteria and viruses, there is concern regarding the emergence of new diseases.

B.9 Biological pigments

Understandings:

- Biological pigments are coloured compounds produced by metabolism.
- The colour of pigments is due to highly conjugated systems with delocalized electrons, which have intense absorption bands in the visible region.
- Porphyrin compounds, such as hemoglobin, myoglobin, chlorophyll and many cytochromes are chelates of metals with large nitrogen-containing macrocyclic ligands.
- Hemoglobin and myoglobin contain heme groups with the porphyrin group bound to an iron(II) ion.
- Cytochromes contain heme groups in which the iron ion interconverts between iron(II) and iron(III) during redox reactions.
- Anthocyanins are aromatic, water-soluble pigments widely distributed in plants. Their specific colour depends on metal ions and pH.
- Carotenoids are lipid-soluble pigments, and are involved in harvesting light in photosynthesis. They are susceptible to oxidation, catalysed by light.

Applications and skills:

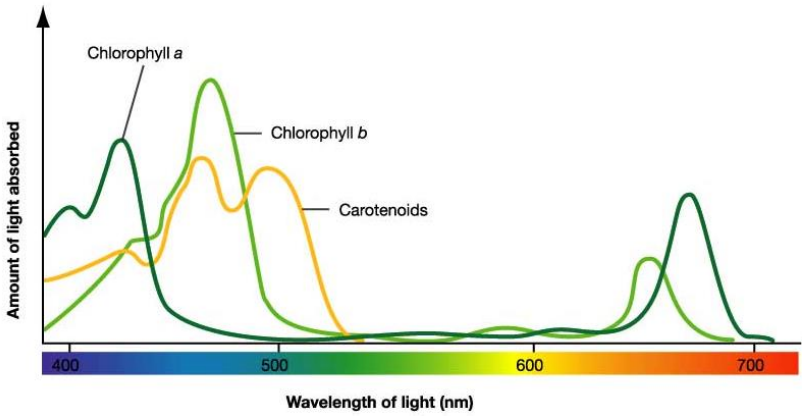
- Explanation of the sigmoidal shape of hemoglobin's oxygen dissociation curve in terms of the cooperative binding of hemoglobin to oxygen.
- Discussion of the factors that influence oxygen saturation of hemoglobin, including temperature, pH and carbon dioxide.
- Description of the greater affinity of oxygen for foetal hemoglobin.
- Explanation of the action of carbon monoxide as a competitive inhibitor of oxygen binding.
- Outline of the factors that affect the stabilities of anthocyanins, carotenoids and chlorophyll in relation to their structures.
- Explanation of the ability of anthocyanins to act as indicators based on their sensitivity to pH.
- Description of the function of photosynthetic pigments in trapping light energy during photosynthesis.
- Investigation of pigments through paper and thin layer chromatography.

Guidance:

- The structures of chlorophyll, heme B and specific examples of anthocyanins and carotenoids are given in the data booklet in section 35; details of other pigment names and structures are not required.
- Explanation of cooperative binding in hemoglobin should be limited to conformational changes occurring in one polypeptide when it becomes oxygenated.
- Knowledge of specific colour changes with changing conditions is not required.
- International-mindedness:
- Artificial colours are commonly added during the commercial preparation and processing of food. The list of approved food colours varies greatly by country, which raises questions for international trade.

Biological pigments

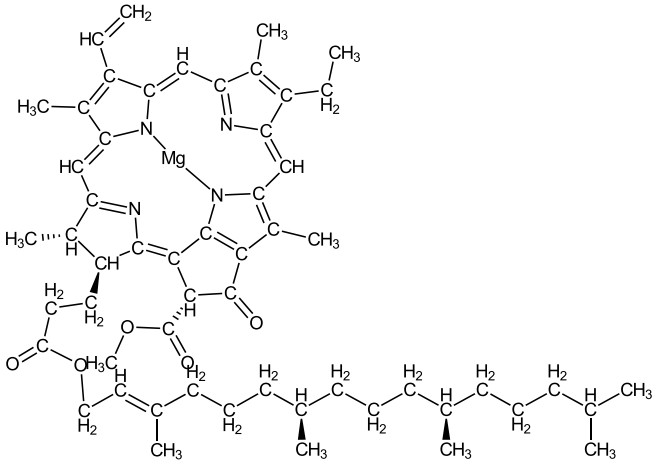
- Biological pigments are coloured compounds produced by living organisms (by metabolism).
- Pigment molecules absorb light in the visible region of the spectrum (400 – 700 nm).



- Chlorophyll appears green because it absorbs wavelengths of visible light at 430 and 660 nm and reflects the remaining wavelengths.

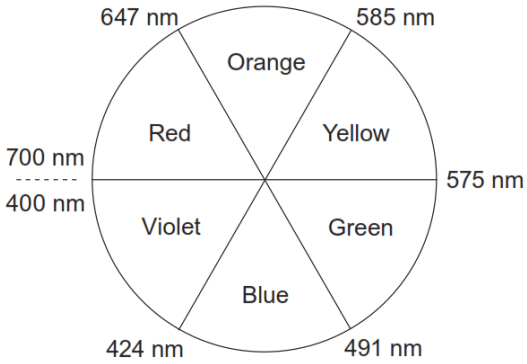
Conjugated systems

- Highly conjugated systems (alternating single and double bonds) absorb wavelengths of light in the visible region of the spectrum (400 – 700 nm).



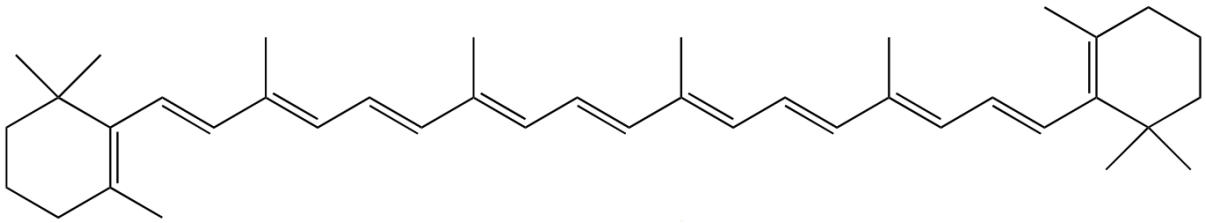
- A conjugated system has a region of overlapping p orbitals with delocalized π electrons.
- The delocalized π electrons absorb wavelengths of light in the visible region and are excited to higher energy levels.
- A colour wheel can be used to determine the colour of a pigment.
- The colour that is reflected (the colour that we see) is the complementary colour of the colour that is absorbed.

- A pigment that absorbs wavelengths of green light will appear red (the complementary colour).

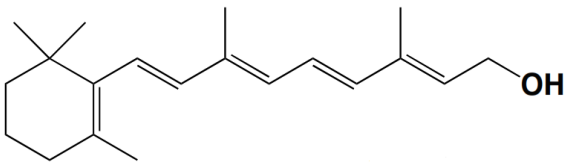


Examples of biological pigments

- β-carotene (absorbs blue light, reflects orange)



- Retinol (absorbs violet light, reflects yellow)



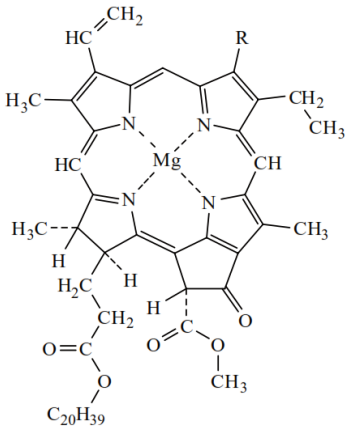
Exercise:
Use the colour wheel to determine the wavelength of light absorbed and reflected by β-carotene and retinol.

Porphyrin compounds

- Porphyrin compounds are planar ring structures with extensive conjugated systems.
- Porphyrin compounds are chelates of metals with large nitrogen containing macrocyclic ligands.
- The porphyrin structure is made up of four rings that act as ligands.
- The non-bonding pairs of electrons on the nitrogen atoms form coordinate covalent bonds with the central metal ion.

Chlorophyll

- Chlorophyll is a biological pigment found in plant cells.
- The metal ion in chlorophyll is the magnesium ion (Mg^{2+}).
- In chlorophyll-a, the R group is a methyl (CH_3) group, and in chlorophyll-b, an aldehyde (CHO) group.

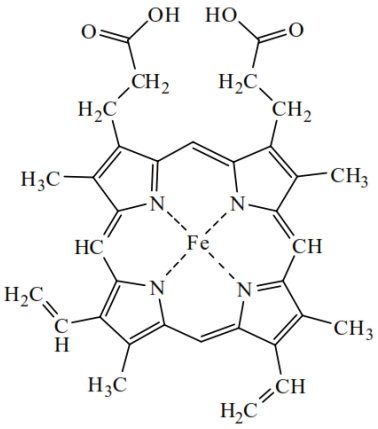


Stability of chlorophyll

- The thermal stability of chlorophyll depends on the pH.
- When heated, the cell membrane of the plant deteriorates, releasing acids which decrease the pH.
- This magnesium ion in the porphyrin ring is displaced by two hydrogen ions, resulting in the formation of a brown colour.
- Sodium hydrogen carbonate is added to cooked vegetables to keep their green colour (chlorophyll is more stable in an alkaline solution).

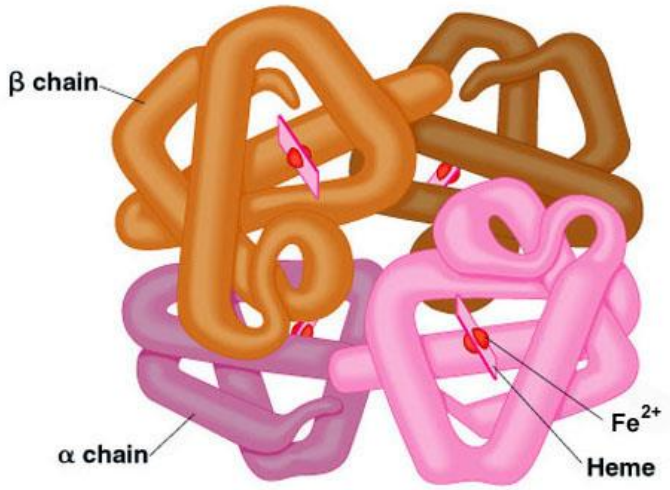
Heme

- Heme is the prosthetic group of hemoglobin, myoglobin, and the cytochromes.
- The iron(II) ion in heme can form two additional coordinate bonds with a protein residue (histidine) and molecular oxygen (O_2).



Hemoglobin

- Hemoglobin carries molecular oxygen (O_2) within the blood.
- It contains four heme groups, each bound within a polypeptide chain (quaternary protein).
- The porphyrin group is bonded to an iron(II) ion.



Myoglobin

- Myoglobin is a protein composed of a single polypeptide chain and one heme group.
- It is found in muscle cells, where it stores molecular oxygen (O_2).
- The porphyrin group is bonded to an iron(II) ion.
- Myoglobin only binds one O_2 molecule compared to four in hemoglobin.

Summary:

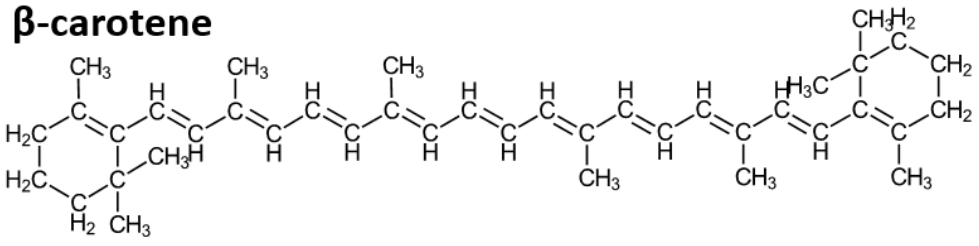
- Porphyrin compounds are composed of 4 nitrogen containing macrocyclic ligands which are bonded to a central metal ion by coordinate covalent bonds.
- Because of their highly conjugated systems, they absorb light in the visible region of the spectrum.
- Chlorophyll is the light absorbing pigment in plants.
- Hemoglobin and myoglobin are protein molecules and are able to bind molecular oxygen (O_2); hemoglobin transports O_2 in blood cells and myoglobin stores O_2 in muscle cells.

Colour stability of haem

- The purplish-red colour of meat is caused by myoglobin.
- In myoglobin iron is in the Fe^{2+} state (+2 oxidation state). When it is oxidized, the state of the iron changes from Fe^{2+} to Fe^{3+} (from +2 to +3 oxidation state).
- In the Fe^{3+} state (+3 oxidation state), it is called metmyoglobin (MMb) and has an undesirable brown colour.
- The stability of colour and the rate of brown MMb formation can be minimized if the meat is stored in oxygen free conditions by using packaging films with low gas permeabilities.
- Air is removed from the package and a storage gas (100% CO_2) is used.

Carotenoids

- The carotenoids are an important group of pigments in plants, where they function as accessory light-harvesting pigments in photosynthesis.
- Carotenoids have extensive conjugated systems (alternating single and double bonds with delocalized π electrons).



- Carotenoid pigments exhibit strong light absorption in the blue portion of the visible spectrum.
- Carotenoids are responsible for the yellow, orange, and red colours of many plants (carrots, tomatoes, pumpkins).

Accessory pigments

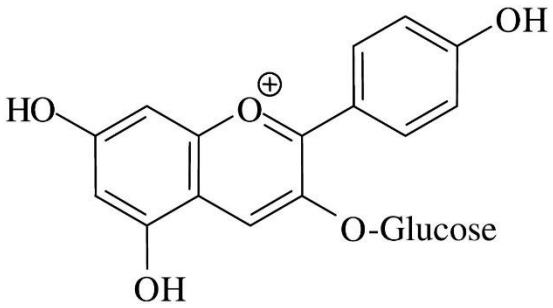
- While the chlorophylls are efficient in absorbing the red and blue portions of the light spectrum, they do not efficiently absorb other parts of the sunlight spectrum.
- The range of light absorption in leaves is extended by accessory pigments such as the carotenoids.
- Carotenoids cannot transfer sunlight energy directly to the photosynthetic pathway, but instead pass their absorbed energy to chlorophyll.

Oxidation of carotenoids

- The presence of multiple carbon to carbon double bonds makes carotenoids susceptible to oxidation in the presence of oxygen catalysed by light (photo-oxidation).
- Oxidation results in the loss of colour, loss of vitamin A activity and off-odors.
- The oxidation of carotenoids can be reduced by preventing exposure to air (oxygen) and light.

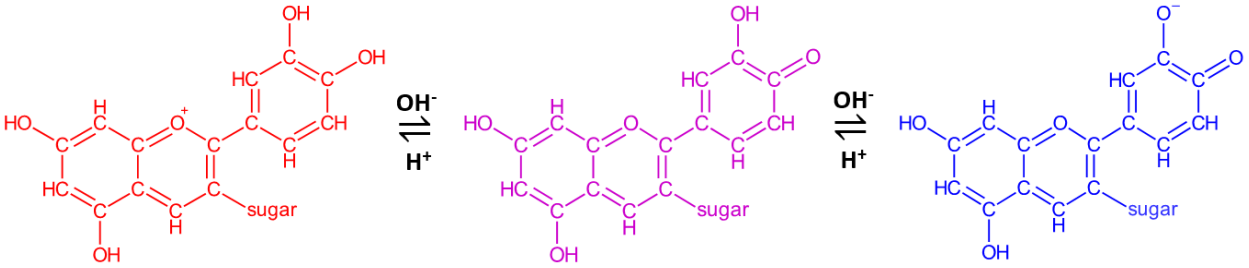
Anthocyanins

- Anthocyanins are water soluble pigments that appear red, blue, or purple depending on the pH.
- They belong to a class of molecules called flavonoids.
- As with all biological pigments, they have highly conjugated systems (alternating single and double bonds) with delocalised π electrons that absorb light in the visible region of the spectrum.



- The polar hydroxyl groups allow the molecule to form hydrogen bonds with water molecules.

- Anthocyanins can act as pH indicators.



red at low pH **violet at pH 7-8** **blue at high pH**

- Cyanidin has less conjugation at low pH; green light is absorbed and red light transmitted.
- Cyanidin has more conjugation at high pH; orange light is absorbed and blue light transmitted.

Stability of anthocyanins

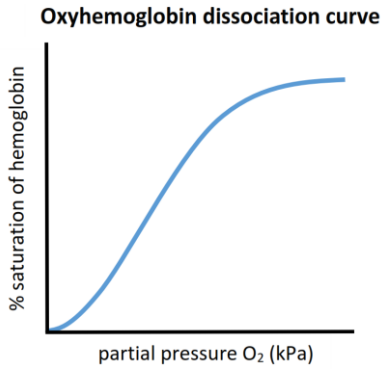
- Anthocyanins are stable and the most highly coloured at low pH and low temperature.
- Anthocyanins form deeply coloured coordination complexes with Fe^{3+} and Al^{3+} ions, a source of which can be metal cans - this can cause a discoloration in canned fruit.
- Anthocyanins also become less stable when exposed to heat, causing a loss of colour and browning.

Cytochromes

- Cytochromes are a group of protein molecules that contain the heme prosthetic group.
- They are responsible for electron transport during the redox reactions that take place during aerobic respiration and photosynthesis.
- Cytochromes become successively reduced and re-oxidized as they accept and pass electrons.
- The iron ion in the heme group interconverts between iron(II) and iron(III) during these redox reactions.

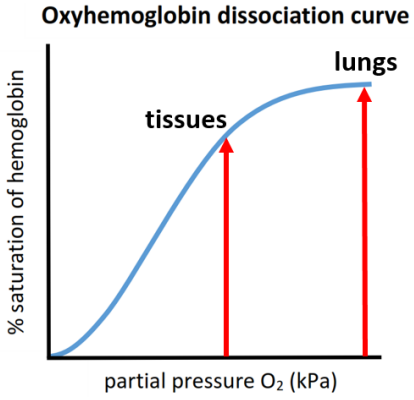
Oxygen saturation of hemoglobin

- Hemoglobin carries oxygen in the blood and myoglobin stores oxygen in the muscles.
- They do this by binding reversibly with oxygen, which forms a weak bond with the iron(II) ion in heme.
- The binding of oxygen does not change the oxidation state of the iron ion (+2), therefore hemoglobin and myoglobin are oxygenated rather than oxidized.
- The oxygenated products are known as oxyhemoglobin and oxymyoglobin.



- The binding of oxygen to hemoglobin is a cooperative process.
- The ability to bind oxygen is increased by the initial binding of the first oxygen molecule.
- The first oxygen molecule binds with low affinity, but increases the binding affinity of further oxygen molecules.
- This results in a sigmoidial or S-shaped saturation curve.

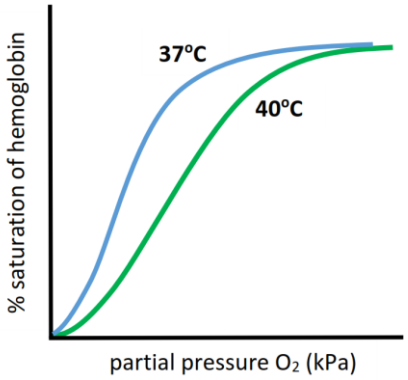
Effect of partial pressure on % saturation of hemoglobin



- The ability of hemoglobin to bind or release oxygen depends on the partial pressure of the oxygen (pO_2).
- When the pO_2 is high (in the lungs), each molecule of hemoglobin can carry its maximum of four oxygen molecules.

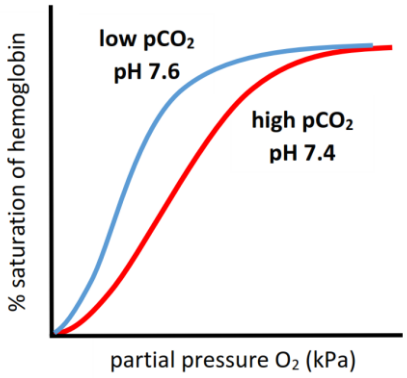
- As the blood circulates around the body, the blood experiences lower levels of partial pressure.
- At low pO_2 the hemoglobin releases some of the oxygen it is carrying.

Effect of temperature on the oxygen saturation of hemoglobin



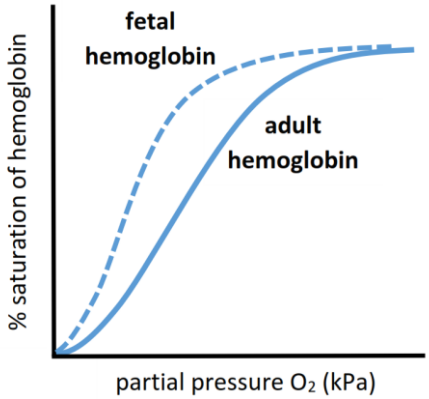
- An increase in temperature reduces the affinity of hemoglobin for oxygen (the dissociation curve has shifted to the right).
- Therefore, hemoglobin more readily releases oxygen at higher temperatures in the cells during high metabolic activity such as exercise.

Effect of pH and [CO_2] on the oxygen saturation of hemoglobin



- A decrease in pH reduces the affinity of hemoglobin for oxygen (the dissociation curve has shifted to the right).
- Increasing the [CO_2] has the same effect as CO_2 dissolves to form carbonic acid (H_2CO_3).
- During cellular respiration, CO_2 is produced which decreases the pH, causing hemoglobin to release oxygen.

Greater affinity of fetal hemoglobin for oxygen



- Hemoglobin exists as a different form in fetal blood.
- It has a greater affinity for oxygen than normal hemoglobin so more oxygen binds at lower partial pressures (the dissociation curve has shifted to the left).
- This allows the fetal blood in the placenta to take up oxygen from the mother's blood.

Effect of CO on the binding of oxygen to hemoglobin

- Carbon monoxide (CO) is an odorless, colourless gas that is highly toxic.
- CO is produced during incomplete combustion of hydrocarbons (car exhausts, tobacco smoke).

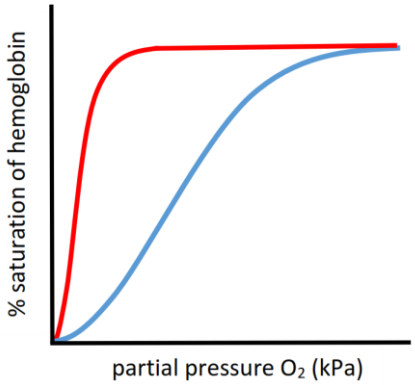
$$C_4H_{10(g)} + 4½O_{2(g)} \rightarrow 4CO_{(g)} + 5H_2O_{(l)}$$

- CO has a much higher affinity for hemoglobin than oxygen (it is a stronger ligand).
- It acts as a competitive inhibitor and therefore prevents oxygen from binding to hemoglobin.
- Carbon monoxide forms an irreversible complex with the iron(II) ion in hemoglobin (carboxyhemoglobin).

$$Hb + CO \rightarrow Hb–(CO)$$

- Competitive inhibitors bind to the active site of an enzyme as they are similar in structure to the substrate.
- CO acts like a competitive inhibitor; it effectively binds irreversibly to the heme.

Oxygen-hemoglobin saturation curve



- Carbon monoxide shifts the oxygen-hemoglobin saturation curve to the left and changes it to a more hyperbolic shape.
- Therefore, less oxygen is available for body tissues.
- Hemoglobin has four oxygen binding sites. The binding of CO at one of these sites increases the oxygen affinity of the remaining three sites. This causes hemoglobin to retain oxygen that would otherwise be delivered to body tissues.

B.10 Stereochemistry in biomolecules

Understandings:

- With one exception, amino acids are chiral, and only the L-configuration is found in proteins.
- Naturally occurring unsaturated fat is mostly in the *cis* form, but food processing can convert it into the *trans* form.
- D and L stereoisomers of sugars refer to the configuration of the chiral carbon atom furthest from the aldehyde or ketone group, and D forms occur most frequently in nature.
- Ring forms of sugars have isomers, known as α and β, depending on whether the position of the hydroxyl group at carbon 1 (glucose) or carbon 2 (fructose) lies below the plane of the ring (α) or above the plane of the ring (β).
- Vision chemistry involves the light activated interconversion of *cis*- and *trans*-isomers of retinal.

Applications and skills:

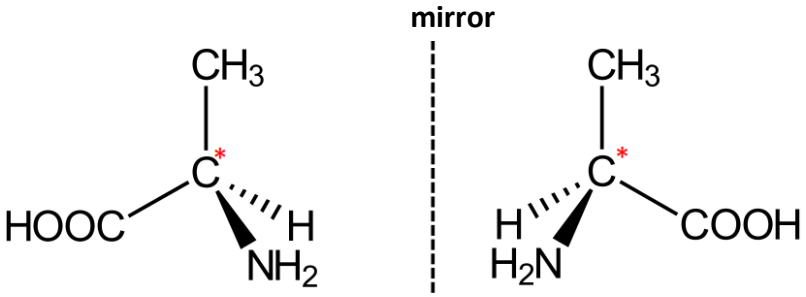
- Description of the hydrogenation and partial hydrogenation of unsaturated fats, including the production of *trans*-fats, and a discussion of the advantages and disadvantages of these processes.
- Explanation of the structure and properties of cellulose, and comparison with starch.
- Discussion of the importance of cellulose as a structural material and in the diet.
- Outline of the role of vitamin A in vision, including the roles of opsin, rhodopsin and cis and trans retinal.

Guidance:

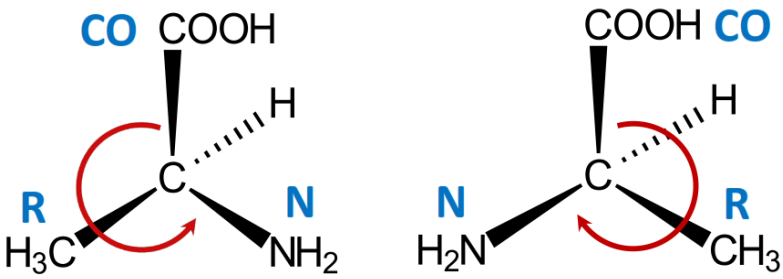
- Names of the enzymes involved in the visual cycle are not required.
- Relative melting points of saturated and *cis*-/*trans*-unsaturated fats should be covered.

Stereochemistry of amino acids

- A chiral carbon atom is a carbon atom bonded to four different atoms or groups.
- Amino acids are optically active (with the exception of glycine) and exist as enantiomers.



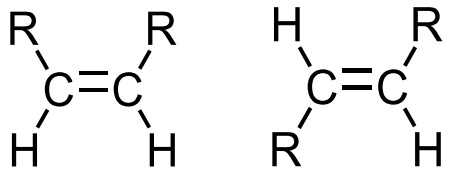
- The CORN rule can be applied to name the two stereoisomers.



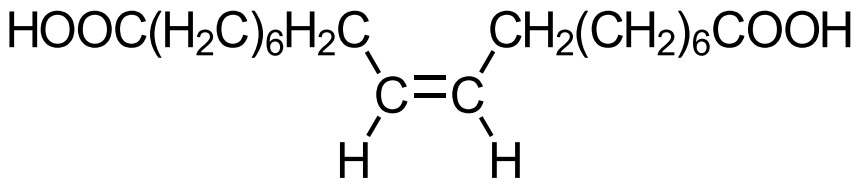
- If the CORN ($COOH - R - NH_3$) is clockwise, it is the D-isomer.
- If the CORN ($COOH - R - NH_3$) is counter-clockwise, it is the L-isomer.
- All naturally occurring amino acids are the L-configuration.
- The proteins in our bodies are only composed of the L-enantiomers of amino acids - 19 of the 20 naturally occurring amino acids exist as L-enantiomers.
- The D and L convention refers to the optical activity of the enantiomers of glyceraldehyde.
- D-glyceraldehyde is dextrorotatory (right) and L-glyceraldehyde is levorotatory (left).
- This refers to the direction of the rotation of plane-polarized light.

Stereochemistry of lipids

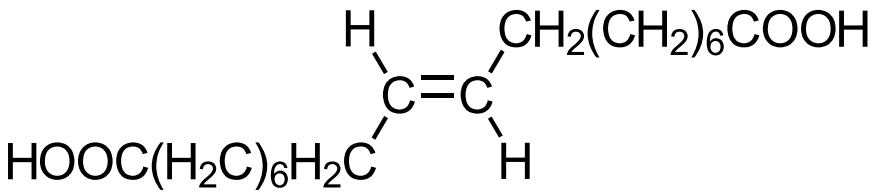
- Unsaturated fats and oils contain carbon to carbon double bonds.
- They exist in two forms which are known as *cis*-*trans* isomers.



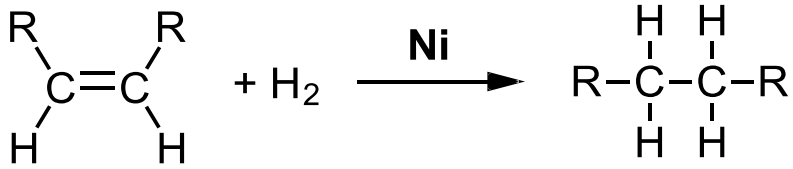
- oleic acid – *cis* isomer (melting point 13^{o}C)



- elaidic acid – *trans* isomer (melting point 45^{o}C)



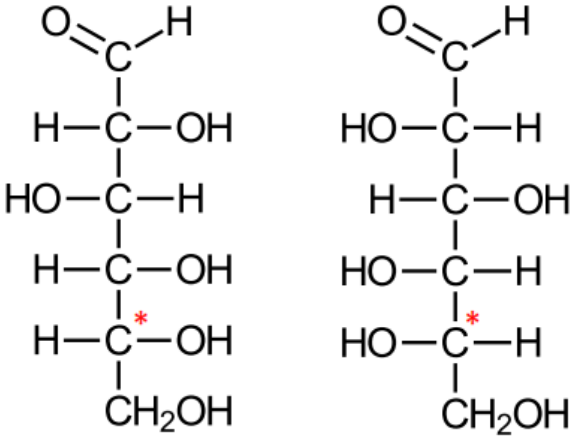
- *Trans*-fatty acids have higher melting points than *cis*-fatty acids because the molecules in the *trans*-fatty acids are able to pack more closely together.
- This results in stronger intermolecular forces between molecules and therefore a higher melting point.
- Naturally occurring unsaturated fat is mostly in the cis form, but the processing of food can convert it to the trans form.



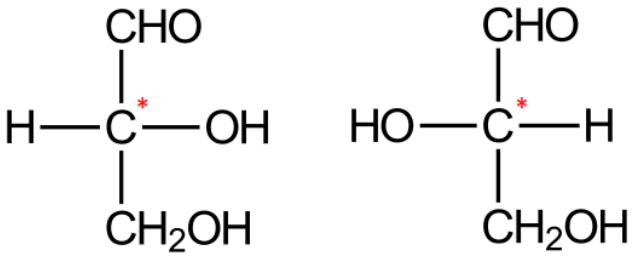
- In partial hydrogenation, only some of the carbon to carbon double bonds are broken and those that remain get modified from the *cis* position to the *trans* position (*trans* fats).
- *Trans* fats increase the level of LDL cholesterol which can cause heart disease; they also lower levels of HDL cholesterol.

Stereochemistry in carbohydrates

- All simple sugars are chiral molecules as they contain at least one chiral carbon atom.

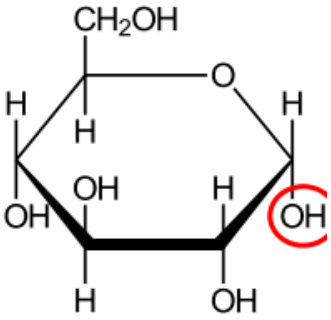


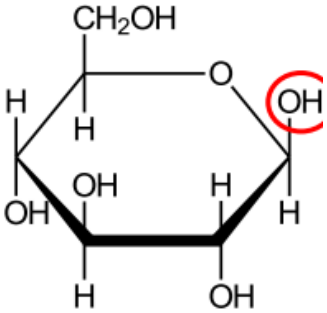
- Naturally occurring sugars are D isomers.
- The D and L isomers are determined on the basis of the chiral carbon atom and how its orientation compares to glyceraldehyde.
- The D isomer has the OH group to the right of the chiral carbon atom.



- In aqueous solutions, glucose forms a ring structure.
- Due to the restricted rotation around the carbon atoms, two isomers are formed, alpha (α) glucose and beta (β) glucose.

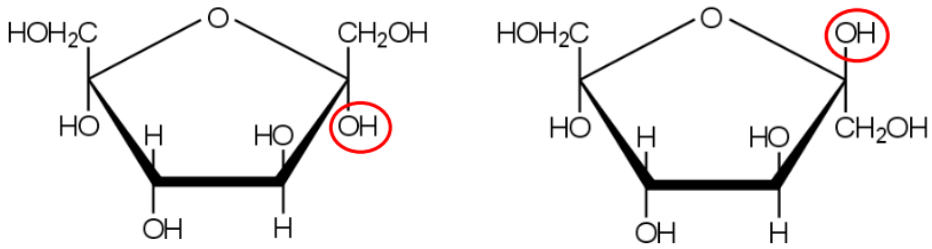
α-glucose
The OH group on carbon 1 is below the plane of the ring.





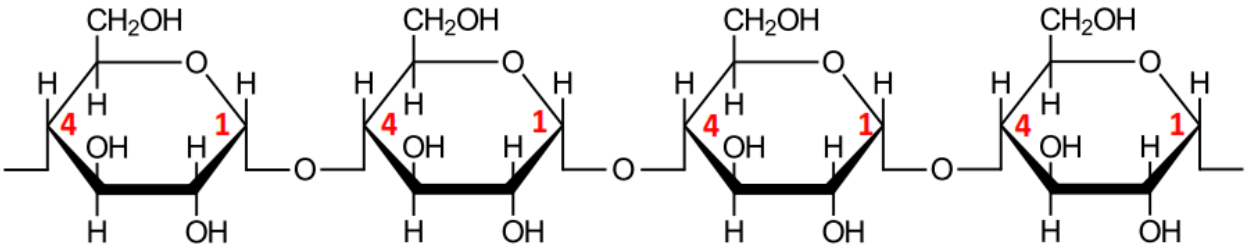
β-glucose
The OH group on carbon 1 is above the plane of the ring.

Exercise: Classify the isomers of fructose as α or β

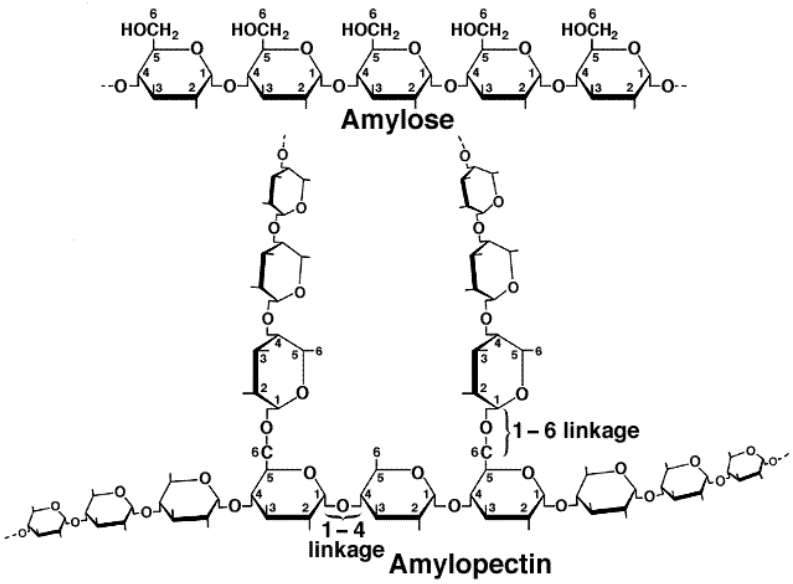


Starch, glycogen and cellulose

- Starch is used as carbohydrate storage in plants.
- It is a polymer composed of α-glucose with α-1,4 glycosidic links between glucose molecules.

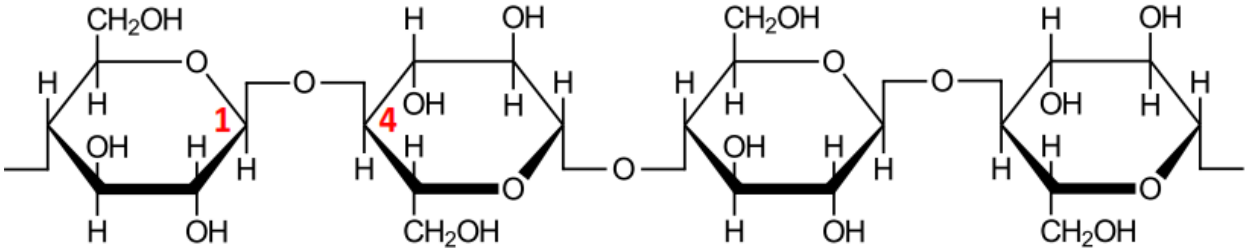


- Starch is a mixture of two polysaccharides; amylose and amylopectin.
- Amylose has α-1,4 glycosidic links and amylopectin has α-1,4 and α-1,6 glycosidic links.

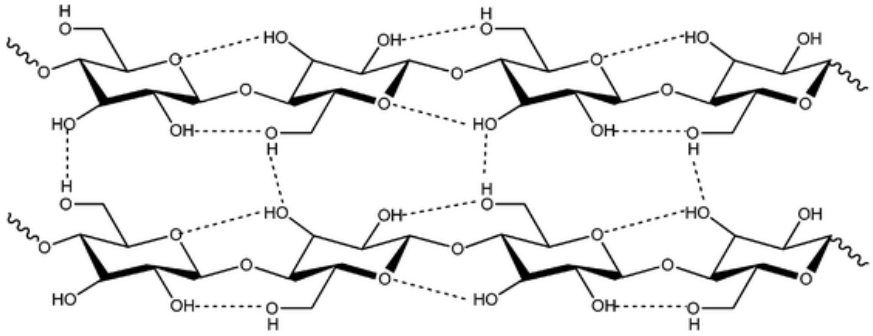


Cellulose

- Cellulose is used as the structural material in plants and as dietary fiber as part of a balanced diet.
- It is a polymer of β-glucose with β-1,4 glycosidic links.
- The alternating β-glucose molecules are upside down with respect to each other.



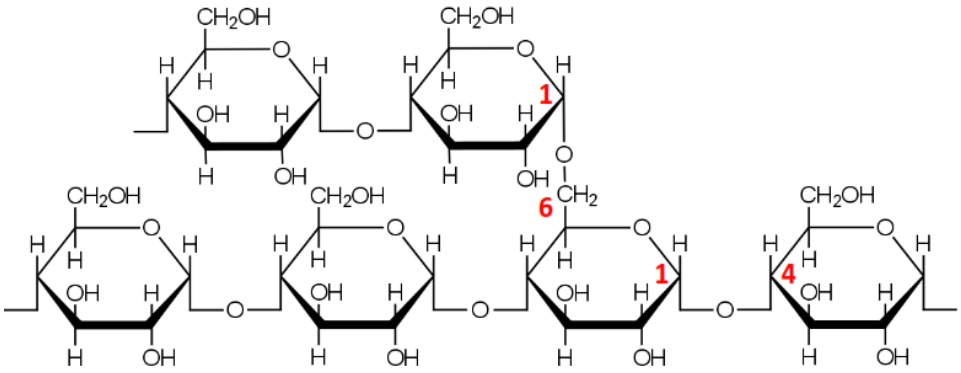
- The hydroxyl groups in the cellulose molecules form hydrogen bonds with the hydroxyl groups of other cellulose molecules lying parallel to each other.



- Cellulose forms cables, known as microfibrils, of parallel chains that give it a rigid structure.
- Wood, which is composed of cellulose, has a rigid structure and is a useful building material.

Glycogen

- Glycogen is used as carbohydrate storage in animals.
- It is a polymer of α-glucose with α-1,4 glycosidic and α-1,6 glycosidic links.



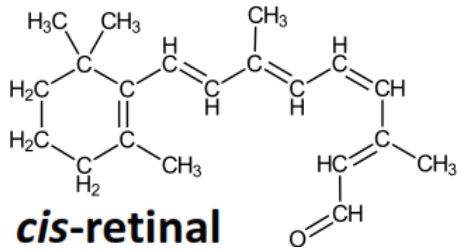
Dietary fibre

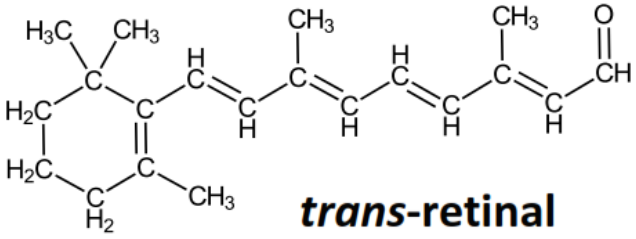
- During digestion, polysaccharides such as starch are broken down by enzymes into glucose before passing into the blood stream.
- The human body lacks the enzyme *cellulase* to break down the polysaccharide cellulose.
- Therefore, cellulose passes through the alimentary canal intact.
- Cellulose is known as dietary fibre.
- It stimulates the walls of the digestive tract producing mucus that allows for the smooth passage of undigested food.
- Dietary fibre helps reduce conditions such as haemorrhoids and irritable bowel syndrome.

Stereochemistry in vitamins

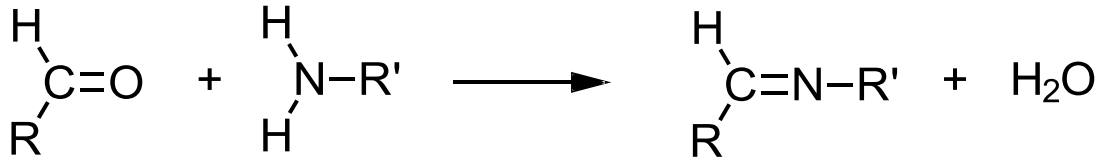
- Vitamin A (retinal) is involved in the visual cycle.

cis / trans isomers of retinal





- The visual cycle involves the biological conversion of light into electrical signals in the retina of the eye.
- The retina of the eye contains two types of light sensitive cells; rods and cones.
- The major photoreceptor in the rods is rhodopsin, a large conjugated protein molecule.
- Opsins are a group of light-sensitive proteins found in photoreceptor cells of the retina.
- The aldehyde group of *cis*-retinal can reversibly bind to a lysine residue of the protein opsin, producing rhodopsin.



cis-retinal opsin rhodopsin

- Rhodopsin is also known as visual purple – it absorbs wavelengths of green light (500 nm).
- When rhodopsin is exposed to light, *cis*-retinal is converted to *trans*-retinal (isomerization).
- The *trans* form of retinal does not fit as well into the protein, and the protein undergoes a change in its conformation.
- As the conformation of the protein changes, it initiates a series of biochemical reactions which trigger a nerve impulse that is sent to the brain along the optic nerve.