BIOCHEMISTRY

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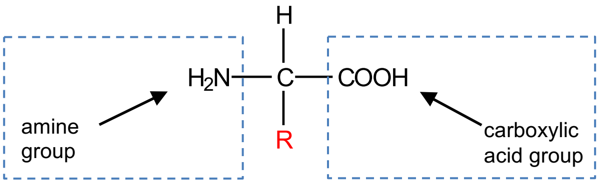
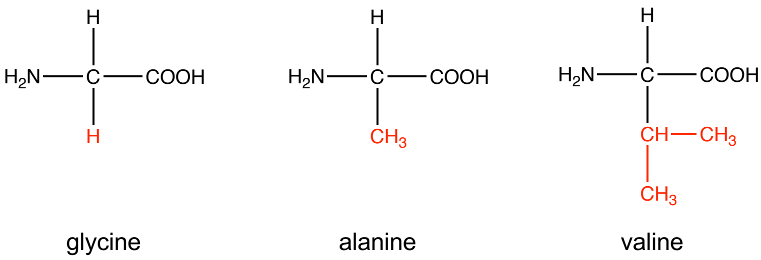
AMINO ACIDS

The structure of amino acids

- Amino acids all contain an amine group and a carboxylic acid group.
- α-amino acids have one amine and one acid group are separated by one C atom.



- There are 20 of these α-amino acids (usually just called amino acids) that occur naturally in proteins.
- The R group varies between these amino acids.



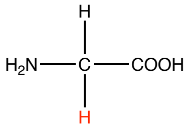
- The structures are shown on the next page – you do not need to learn these at A level.
- In reality, amino acids usually exist as zwitterions. Zwitterions are species that have one part that is positive and one part that is negative. An acid group from one amino acid protonates the amine group of another amino acid.

e.g. alanine

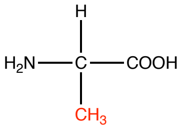
- Amino acids are solids at room temperature as they exist as zwitterions with ionic attractions between the positive part of one zwitterion and the negative part of another.

AMINO ACIDS with NON-POLAR R groups

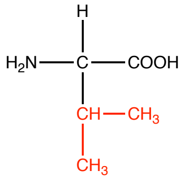
glycine
Gly



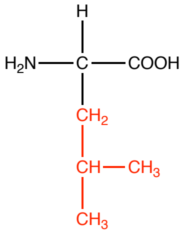
alanine
Ala



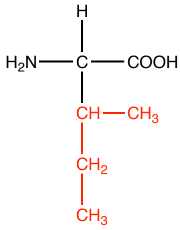
valine
Val



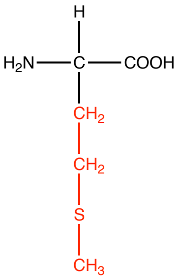
leucine
Leu



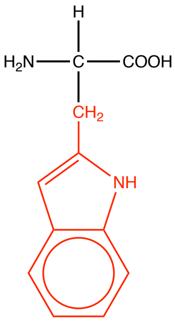
isoleucine
Ile



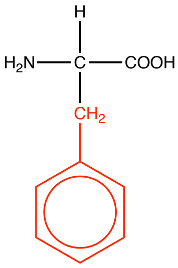
methionine
Meth



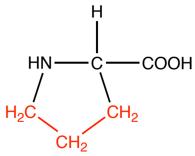
tryptophan
Trp



phenylalanine
Phe

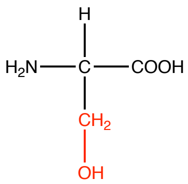


proline
Pro

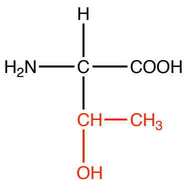


AMINO ACIDS with POLAR R groups

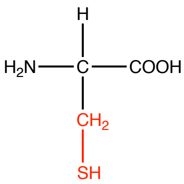
serine
Ser



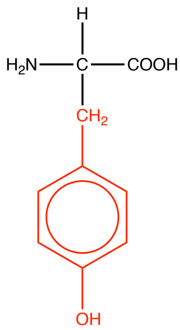
threonine
Thr



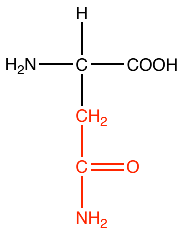
cysteine
Cys



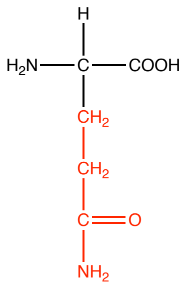
tyrosine
Tyr



asparagine
Asn

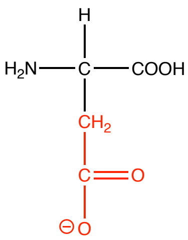


glutamine
Gln

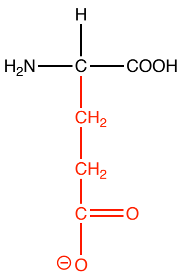


AMINO ACIDS with CHARGED R groups

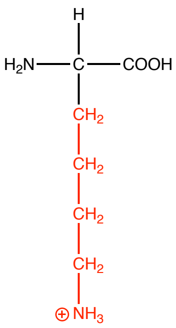
aspartic acid
Asp



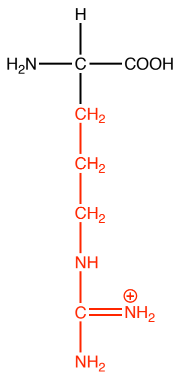
glutamic acid
Glu



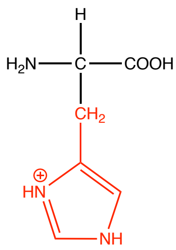
lysine
Lys



arginine
Arg

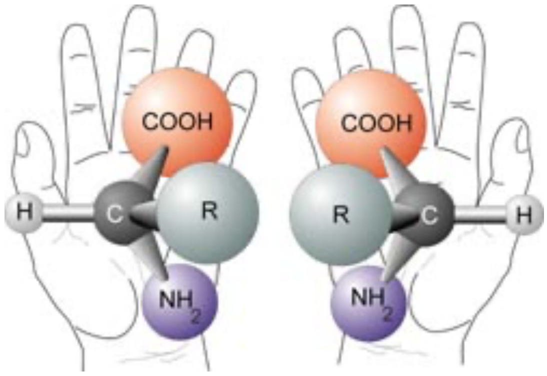


histidine
His



Optical isomerism of amino acids

- Amino acids contain a chiral (asymmetric) C atom, i.e. a C atom with four different groups (apart from glycine).
- In nature, only one of the two enantiomers is present.



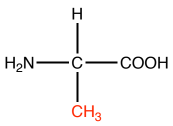
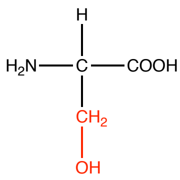
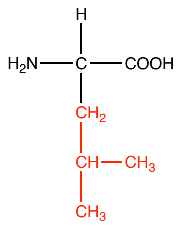
Reactions of amino acids

Amine group (NH_2)		
with acids	to protonate the amine group	acid-base reaction
with halogenoalkanes	to replace H atoms with alkyl groups	nucleophilic substitution
with acyl chlorides and acid anhydrides	to form amides	acylation (nucleophilic addition-elimination)

Acid group (COOH)		
with bases	to deprotonate the acid group	acid-base reaction
with alcohols (with conc acid catalyst)	to form ester group in place of acid group	esterification

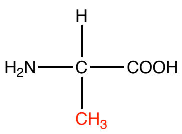
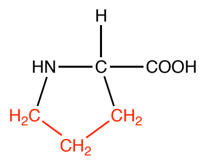
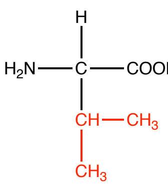
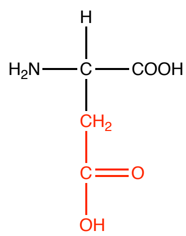
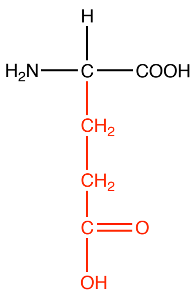
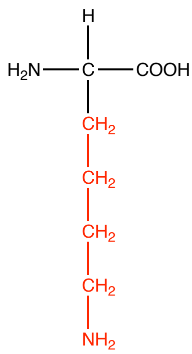
TASK 1 – Amino acid problems

1) Give the IUPAC names for these amino acids:

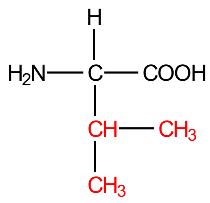
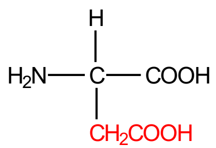
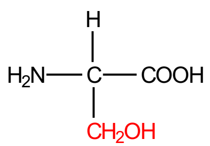
alanine	serine	leucine
		

2) Sketch a 3D diagram to show the two enantiomers of serine.

3) Draw the species formed from each amino acid at the pH shown.

a) alanine at pH 1 	d) proline at pH 2 
b) valine at pH 13 	e) glutamic acid at pH 1 
c) aspartic acid at pH 12 	f) lysine at pH 1 

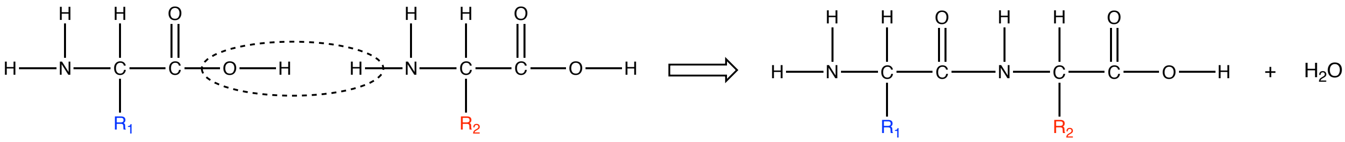
TASK 2 – Reactions of amino acids

Amino acid	Reaction with NaOH	Reaction with hydrochloric acid	Reaction with methanol in the presence of a small amount of conc H_2SO_4	Reaction with ethanoyl chloride
 *valine*				
 *aspartic acid*				
 *serine*				

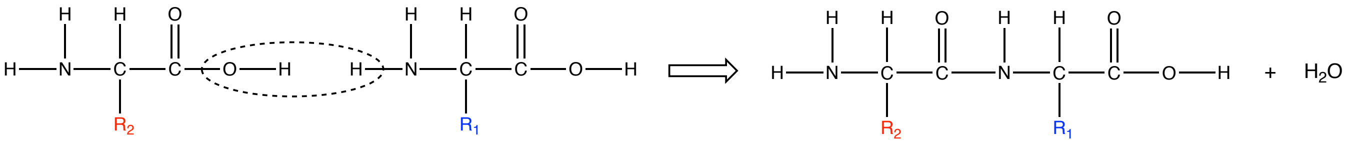
Joining amino acids together

- Amino acids can react with each other and join together in a **condensation reaction**. This makes a **dipeptide** and water.

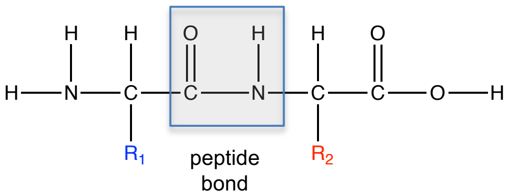
- Two amino acids can join together either way round making two different dipeptides.



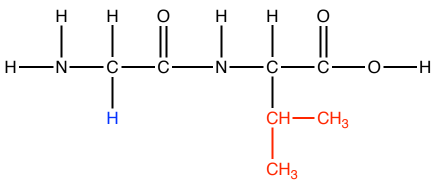
OR



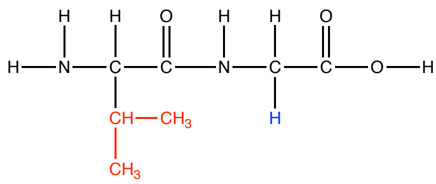
- The bond between the two amino acids is called a **peptide bond** or **peptide link**. It is the C–N bond between the CO group of one amino acid and the NH group of another amino acid.



- Peptides can be named by listing the sequence of the amino acids. The convention is to start from the amine group end. For example the two different dipeptides made from glycine and valine (Gly-Val and Val-Gly) are shown:



Gly–Val



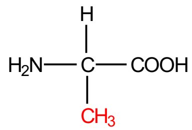
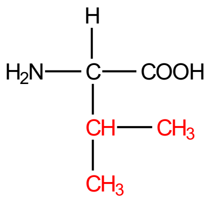
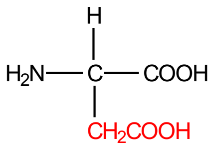
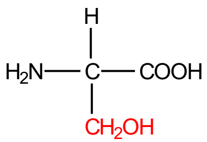
Val–Gly

- Tripeptides contain three amino acids joined together.

- Polypeptides contain many amino acids joined together.

- Proteins typically contain 50-2000 amino acids joined together.

TASK 3 – Formation of dipeptides

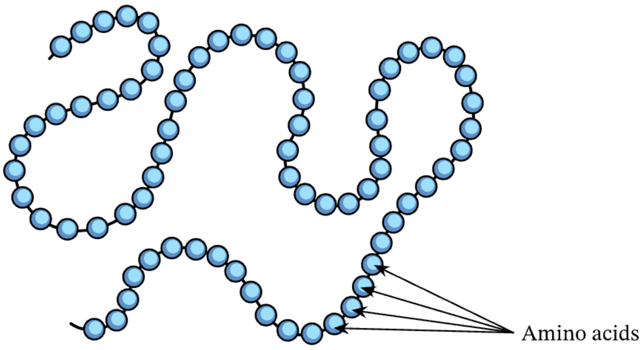
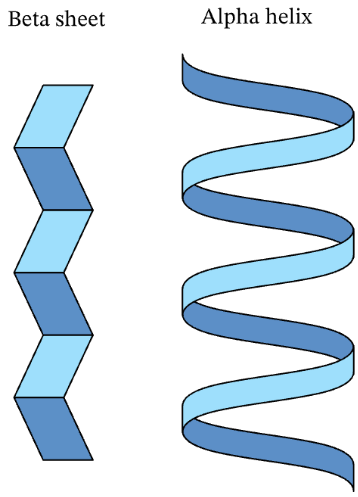
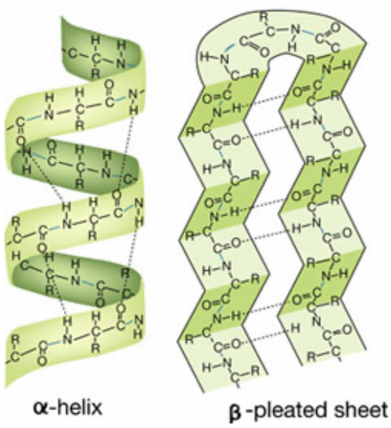
Amino acid	Reaction with alanine (Ala) 	
	Product 1 (structure and name)	Product 2 (structure and name)
 *valine (Val)*		
 *aspartic acid (Asp)*		
 *serine (Ser)*		

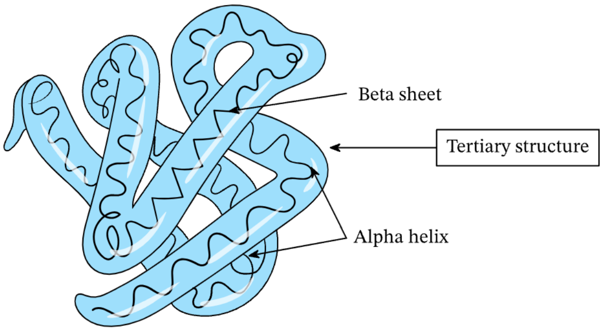
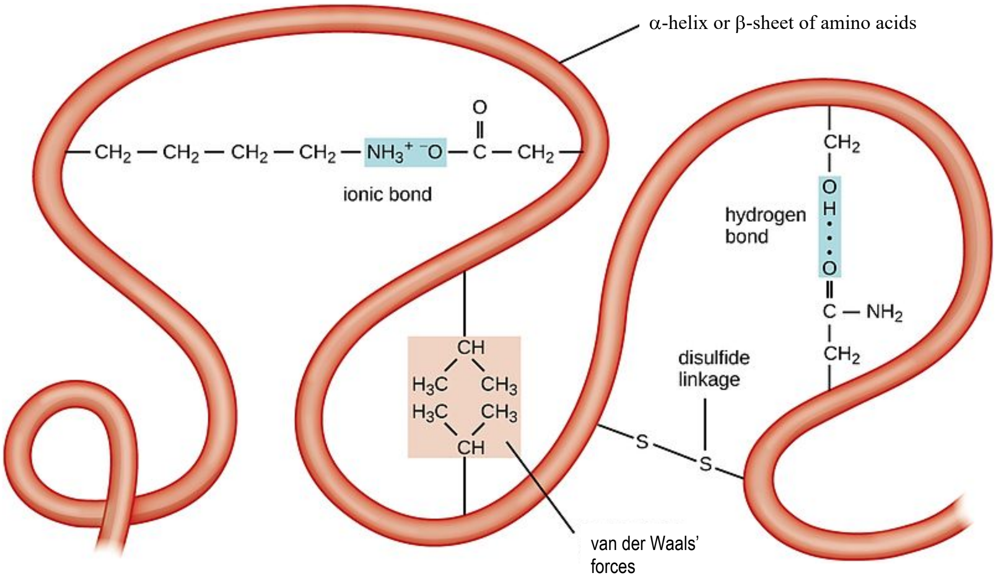
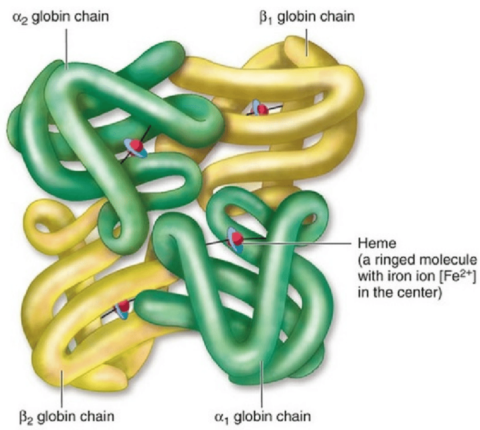
TASK 4 – Tripeptides

Draw and name the six tripeptides formed from alanine (Ala), valine (Val) and cysteine (Cys).

PROTEINS

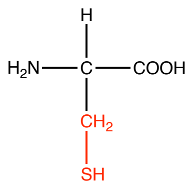
- Proteins typically contain 50 to 2000 amino acids joined together in a specific sequence.
- We can look at different aspects of the structure of proteins – these are known as the primary, secondary, tertiary and quaternary structure (we don't usually study the quaternary structure at A level).

Structure level	What it is all about
Primary structure	The sequence in which amino acids are joined together. e.g. Val-Gly-Phe-Gln-Thr-Gly-Met-etc…………….. 
Secondary structure	The chain of amino acids forms into an α-helix or β-sheet.  The secondary structure is held together by hydrogen-bonds These H-bonds are between the δ+H of an NH group to the lone pair on the O**:** of a CO group). 

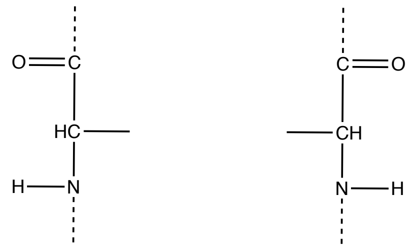
Tertiary structure	How the α-helix (or β-sheet) folds around into a specific shape  This tertiary shape is held together by interactions between the R groups on amino acids. These interactions could be • disulfide bonds • ionic attractions • hydrogen-bonds • van der Waals' forces 
Quaternary structure	Some proteins just contain a single polypeptide chain, but some are a combination of several polypeptide chain units. For example, haemoglobin is a combination of four globin subunits. The quaternary structure is also held together by interactions between the R groups on amino acids. 

TASK 5 – Tertiary structure of protein interactions

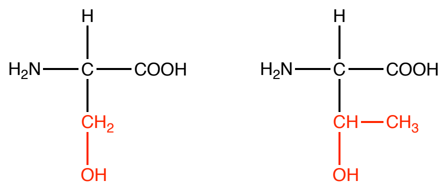
1 The structure of cysteine is shown.



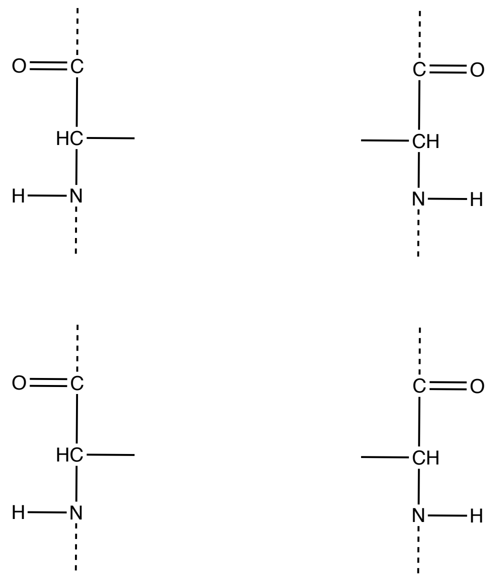
Complete the diagram to show the disulfide bond that can form between two cysteine units in separate parts of the protein structure.



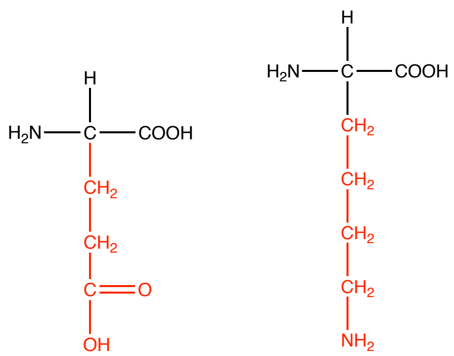
2 The structure of serine and threonine are shown.



Complete the diagrams to show the two ways in which a hydrogen bond that can form between serine and threonine in separate parts of the protein structure.



3 The structure of aspartic acid and lysine are shown.



Complete the diagram to show the ionic attraction that can form between aspartic acid and lysine in separate parts of the protein structure.

Heating proteins

- The secondary structure and aspects of the tertiary (and quaternary) structure of proteins is held together by hydrogen bonds. These hydrogen bonds are overcome when proteins are heated above about 40ºC and so these proteins lose their shape.

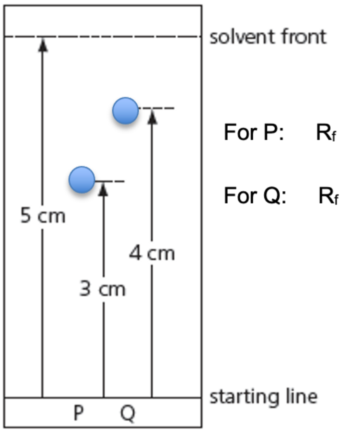
Hydrolysis of proteins

- Proteins can be broken down into their constituent amino acids by hydrolysis.
- The peptide bonds are broken in the hydrolysis reaction.
- This can be done by reacting the protein with 6 mol dm^{-3} hydrochloric acid at 110ºC.

Chromatography of amino acids

- One way to distinguish amino acids is by thin-layer chromatography (TLC).
- The amino acids can be seen on the TLC plate under UV light or by staining with ninhydrin.
- Different amino acids have different R_f values in different solvents.

$$R_f = \frac{distance\ travelled\ by\ sample}{distance\ travelled\ by\ solvent}$$



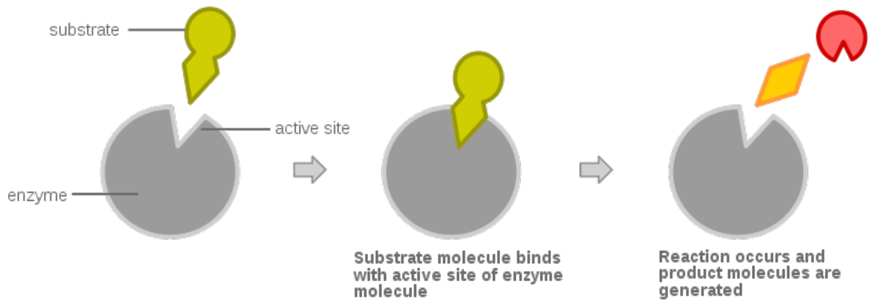
For P: $R_f = \frac{3}{5} = 0.60$

For Q: $R_f = \frac{4}{5} = 0.80$

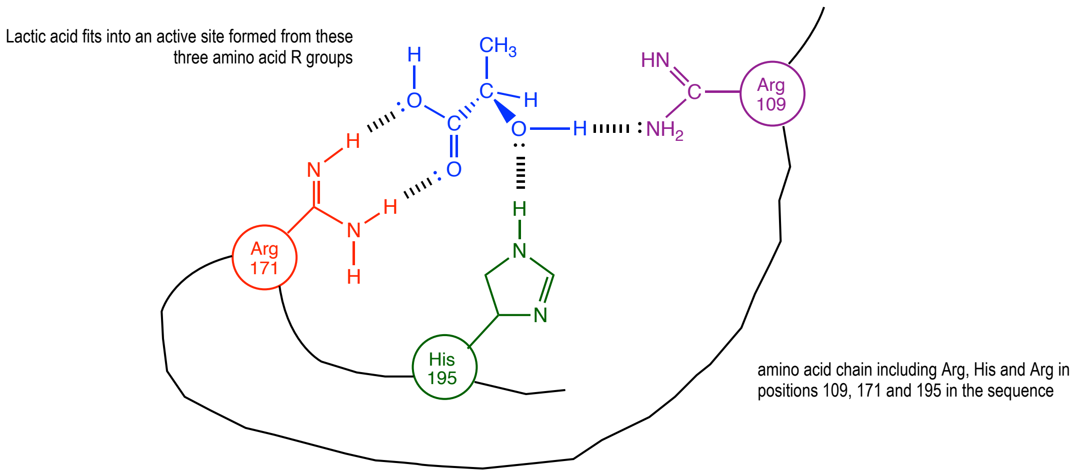
- Some amino acids have similar R_f values in some solvents, but using different solvents may better distinguish those amino acids.

ENZYMES

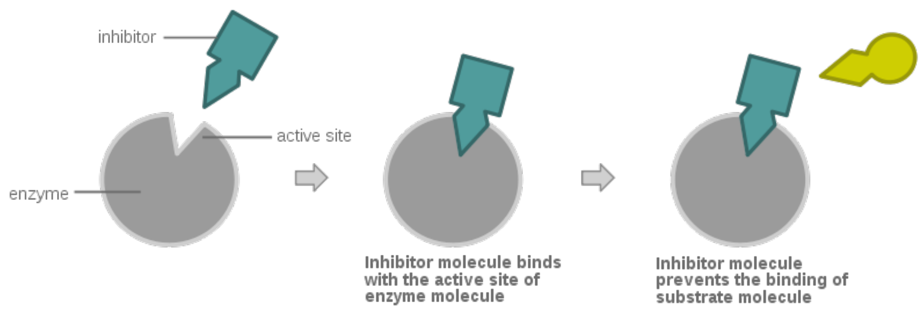
- Enzymes are proteins that act as catalysts in biochemical reactions.
- Enzymes are highly effective and typically increase the rate of a reaction by factors of millions or more.
- Enzymes are also highly specific with each enzyme catalysing a specific reaction.
- They work by attracting a reactant (substrate) to an active site where the reaction occurs with a lower activation energy.



- The specific shape and the atoms in an active site is often formed by the R groups on amino acids.
- For example (you do not need to learn this), the enzyme LDH catalyses the oxidation of lactic acid to pyruvic acid. Only one enantiomer of lactic acid fits this active site.

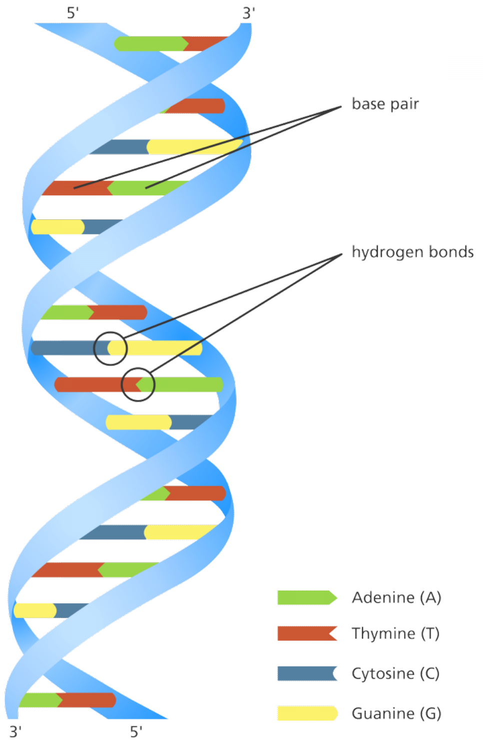


- Enzymes can be deactivated by other molecules that bind strongly to the active site and block it.
- Molecules that block active sites are called **inhibitors**.



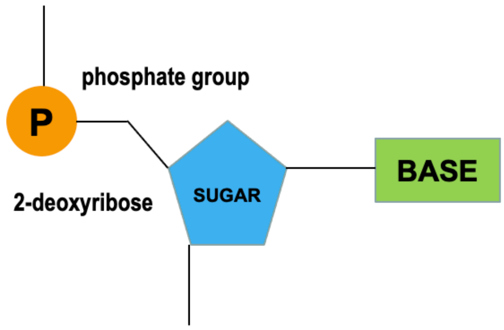
- An as example, ibuprofen is a pain killer that works by blocking the active site that makes pain-causing prostaglandins.
- Computer modelling is used to design molecules to fit active sites.

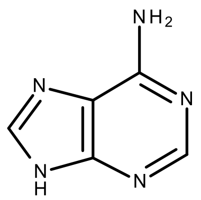
DNA



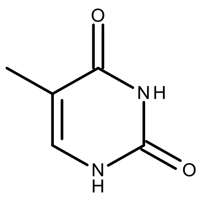
- DNA (deoxyribonucelic acid) is found in the nucleus of most cells. All the information cells require to develop, survive and reproduce are in DNA. The instructions in DNA are used to build proteins from amino acids.
- While over 99% of humans' DNA is the same, each human has their own unique DNA (except identical twins).
- DNA is made up of two strands held together in a double helix by hydrogen bonds.
- Each strand of DNA is made up from four different nucleotides. Each DNA strand contains thousands of these nucleotides in a specific sequence.

- Nucleotides are made from one
  - phosphate group
  - deoxyribose group (a sugar)
  - one of these four bases:
    - adenine (A)
    - cytosine (C)
    - guanine (G)
    - thymine (T)

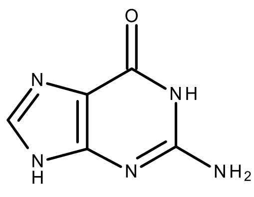




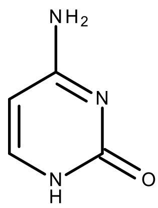
adenine (A)



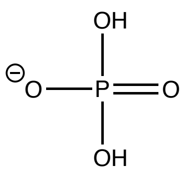
thymine (T)



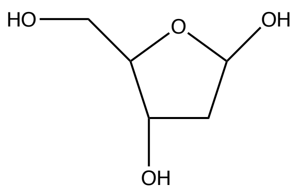
guanine (G)



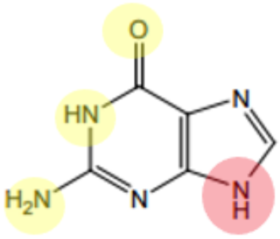
cytosine (C)



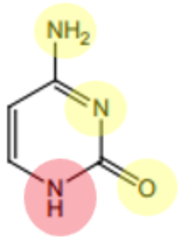
phosphate group



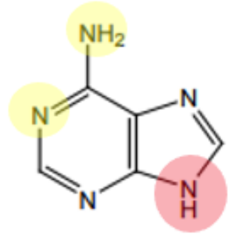
2-deoxyribose



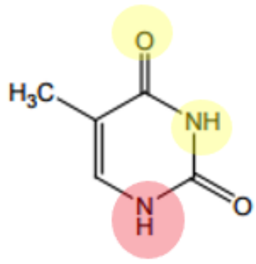
guanine



cytosine



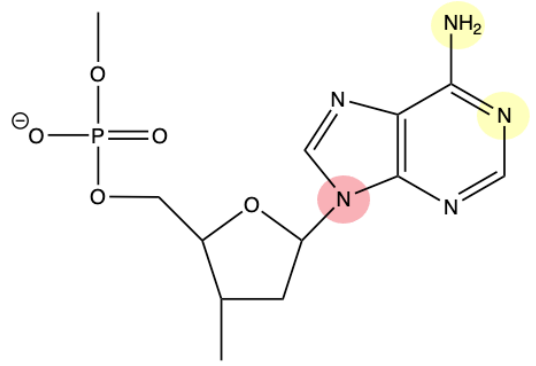
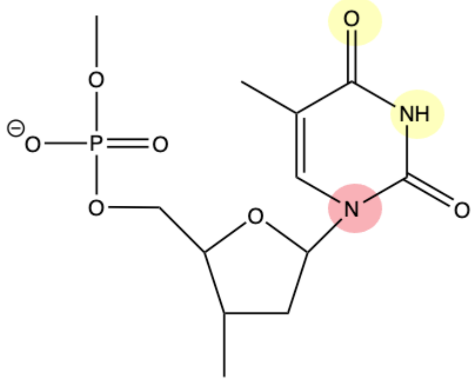
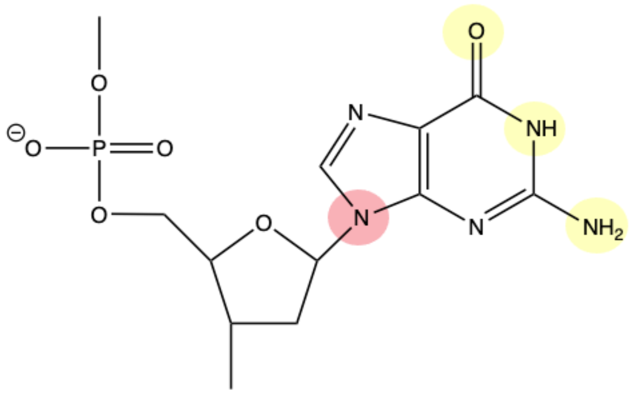
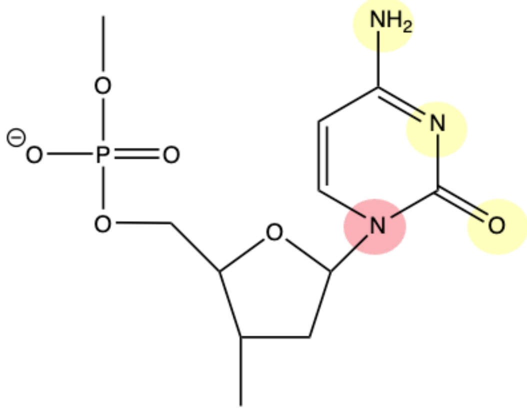
adenine



thymine

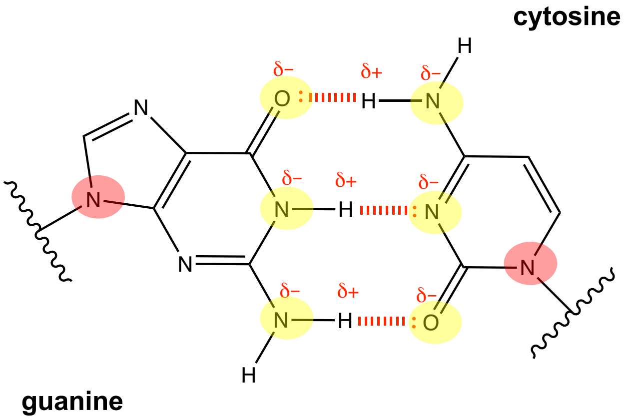
bonding site to deoxyribose

H bonding site to base partner

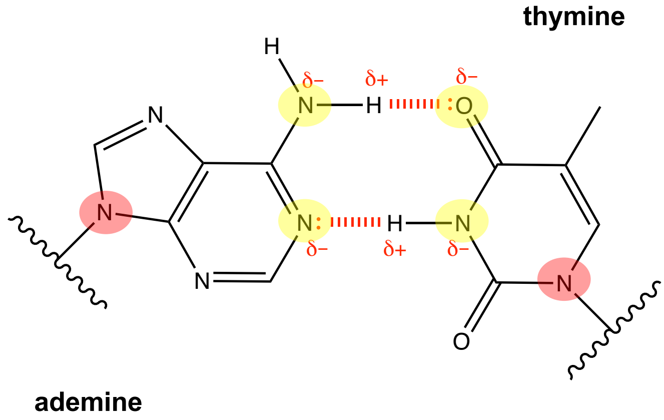
 adenine	 thymine
 guanine	 cytosine

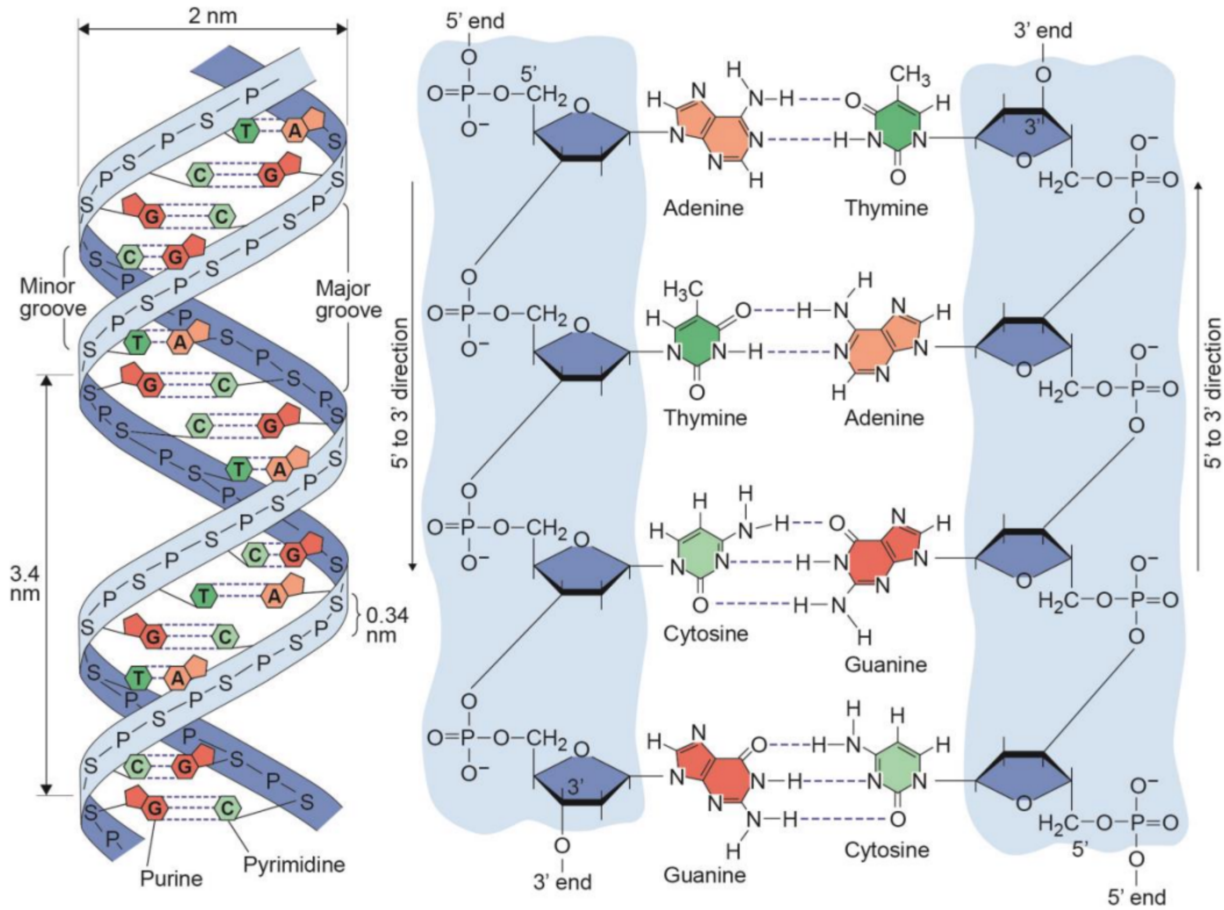
- Hydrogen bonding between groups on the bases hold the two strands together.

C and **G** are held together by 3 hydrogen bonds.

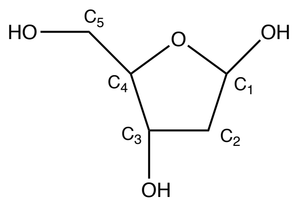


A and **T** are held together by 2 hydrogen bonds.



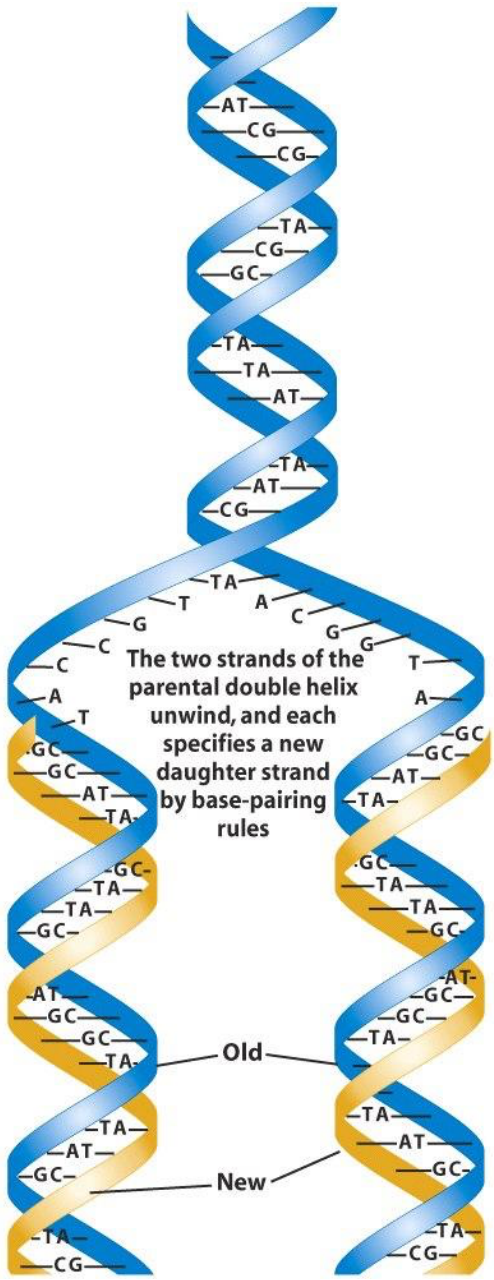


- Note that we refer to the direction of the DNA strand as being 3' to 5' direction or 5' to 3' direction. The 3 and 5 refer to whether C3 or C5 is closest to the end of the chain. One strand runs in the 3' to 5' direction and one in the 5' to 3' direction.



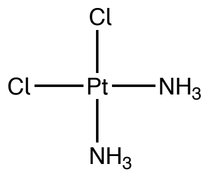
DNA Replication

- The two DNA strands are only held together by hydrogen bonds.
- When a cell replicates by **mitosis,** the two DNA strands separate.
- Two new complementary strands are built up by connecting the appropriate nucleotides to match the sequence on the other strand. This leads to two DNA double helices made from one DNA double helix, each being identical to the original.
- Occasionally, there is a problem with the DNA replication and the sequence is incomplete or changed in some way. These damaged cells may replicate themselves leading to cancer.



Cis-platin

- Cancer by treated by chemotherapy (use of anti-cancer medicines) and/or radiotherapy (the use of radiation) and/or surgery.
- Cis-platin is a highly effective chemotherapy drug, especially for treatment of testicular cancer.



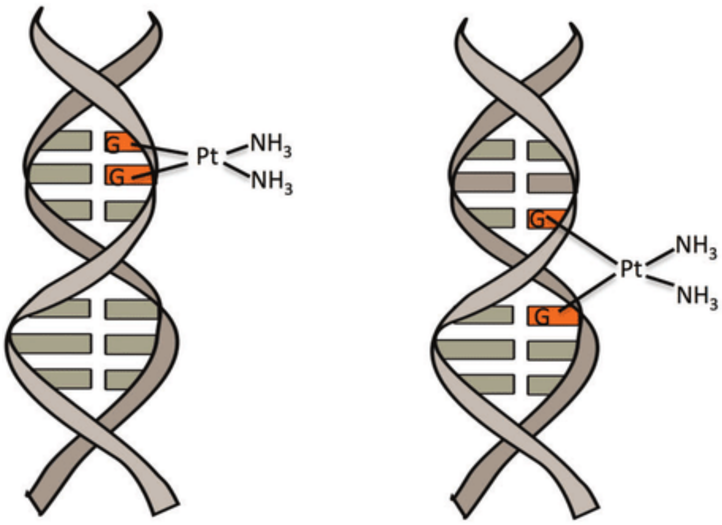
- The mechanism by which cis-platin works is

1. $Pt(NH_3)_2Cl_2$ reacts with water in cell with H_2O replacing one Cl^- ligand:

   $$Pt(NH_3)_2Cl_2 + H_2O \rightarrow Pt(NH_3)_2(H_2O)Cl^+ + Cl^-$$

2. a guanine bonds to the Pt via an N atom replacing the H_2O
3. a second guanine bonds to the Pt via an N atom replacing the Cl^-
4. if the two guanines are on different DNA strands then the two strands cannot separate preventing replication of the DNA, or

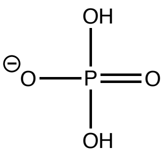
   if the two guanines are on the same DNA strand, then the strand becomes kinked and cannot replicate



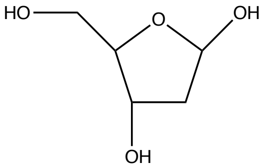
same strand　　　different strands

- Most chemotherapy medicines have the same effect on healthy cells as they do on cancer cells, and this leads to unpleasant side effects for the patient.

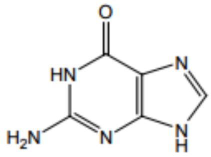
TASK 6 – DNA Problems



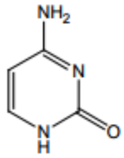
phosphate



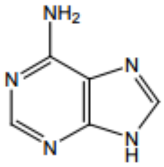
2-deoxyribose



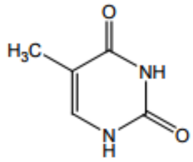
guanine (G)



cytosine (C)



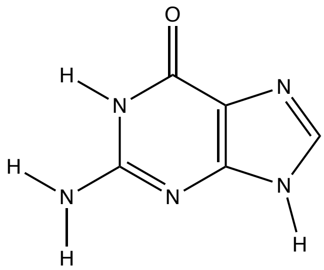
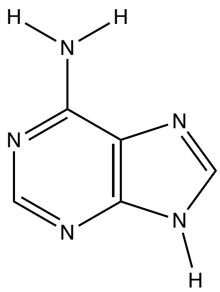
adenine (A)



thymine (T)

1	Sketch part of the DNA backbone showing two phosphate units joined to two 2-deoxyribose units.
2	At the top of the page, circle the N atoms on the four bases through which they bond to the 2-deoxribose units.

3	Sketch the nucleotide containing one phosphate, one 2-deoxyribose and one guanine unit.
4	Sketch the nucleotide containing one phosphate, one 2-deoxyribose and one cytosine unit.
5	Sketch the nucleotide containing one phosphate, one 2-deoxyribose and one adenine unit.
6	Sketch the nucleotide containing one phosphate, one 2-deoxyribose and one thymine unit.

7	DNA consists of two strands each made of nucleotides. What holds the two DNA strands together?
8	Explain why the interaction between cytosine and guanine units is stronger than that between an adenine and a thymine unit.
9	Sketch how a cytosine unit hydrogen bonds to this guanine unit. 
10	Sketch how a thymine unit hydrogen bonds to this adenine unit. 

11	Draw one 2-deoxyribose unit and show how the C atoms are numbered.
12	Scientists talk about '3 prime' and '5 prime' ends in DNA. What do these terms refer to?
13	Draw *cis*-platin.
14	Explain how *cis*-platin stops DNA replication and so can act as an anti-cancer drug.
15	Draw *trans*-platin and explain why this would not stop DNA replication.