Chemistry

A2 Chemistry Revision Lecture

- DNA, Proteins & Amino-Acids

Tuesday 26th March 2019, 7.00 p.m. – 8.00 p.m.

Welcome! ☺

Dr Peter Hoare, Outreach Officer, SAgE Faculty
Dr Matthew Conroy, EMBL-EBI / PDBe

PDBe
Protein Data Bank in Europe

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A2 Examinations

Time allocation

- 1 mark = 1 scoring point

LEARN the content!

- 35% of marks overall are for factual recall ! ☹

The crucial piece of advice *re*. examinations technique:

- R Read
- T The
- F **FULL**
- Q Question! ☺

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Biochemistry

Amino acids, Proteins & DNA

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Learning Resources – Proteins/Biomolecules

Uses **FREE** online viewer of 3D protein structures via the PDBe website: **www.pdbe.org**

Peer-produced: stage 4 MChem & summer UG project student & yr12 Nuffield Research Placement students. Trialled in schools.

Activities for post-16 study on a range of topics for **chemistry** & **biology** including; basic protein structure, intermolecular forces, esp. H-bonding, ligand-protein interactions & links to drug design. Also 3D modelling with TangleProtein™ & MSOE Amino-Acids kits.

Access via website: **http://tiny.cc/proteinLR**

PDBe Protein Data Bank in Europe

Nuffield Foundation

Newcastle University

Protein & DNA Learning Resources Using the Protein Data Bank in Europe (PDBe)

About

These project resources are peer-produced. The objective of the project was to develop resources for either student self-study or to support learning and teaching.

This project has been running since 2014 in collaboration with colleagues at the Protein Data Bank in Europe (PDBe), initially Dr Gary Battle and latterly Dr Matt Conroy. The PDBe is part of the European Bioinformatics Institute and is based at the Wellcome Genome Campus at Hinxton, near Cambridge.

The objective of the project was initially to develop resources to support the teaching and learning of protein structure, function and application for post-16 biology and chemistry. These resources are for either student self-study or teacher support. They could also be used for on-campus outreach sessions.

All resources use the PDBe's online worldwide protein database and viewer, LiteMol, which is free to access online.

TA1 - Biochemistry Basics Explains the basic biochemical principles of amino acids, proteins, enzymes, and DNA

download here: ta1_biochemistry_basics.pdf

TA2 - Amino Acids Explains fundamental amino acid biochemistry including structure, zwitterions, and triplet codes

download here: ta2_amino_acids.pdf

TA3 - Peptide Bonds Describes the formation of peptide bonds, including the mechanisms involved. The chemistry of amide bonds, and the principles of hydrolysis and condensation reactions are explained, as well as equilibria.

download here: ta3_peptide_bonds.pdf

TA9 - Primary Structure Explains the nature of the primary structure of a protein

download here: ta9_primary_structure.pdf

TA4 - Secondary Structures Explains the different forms of protein secondary structure, including their chemical and biological causes.

download here: ta4_secondary_structures.pdf

TA5 - Tertiary and Quaternary Structures Explains the reasons why proteins fold into specific 3D shapes, including the different interactions which cause this. The relationship between the genetic code and overall protein structure is also briefly discussed.

download here: ta5_tertiary_and_quaternary_structures.pdf

TA6 - Enzymes and Inhibitors Explains how proteins act as enzymes, including the complementary of active sites, and the effect of inhibitors

download here: ta6_enzymes_and_inhibitors.pdf

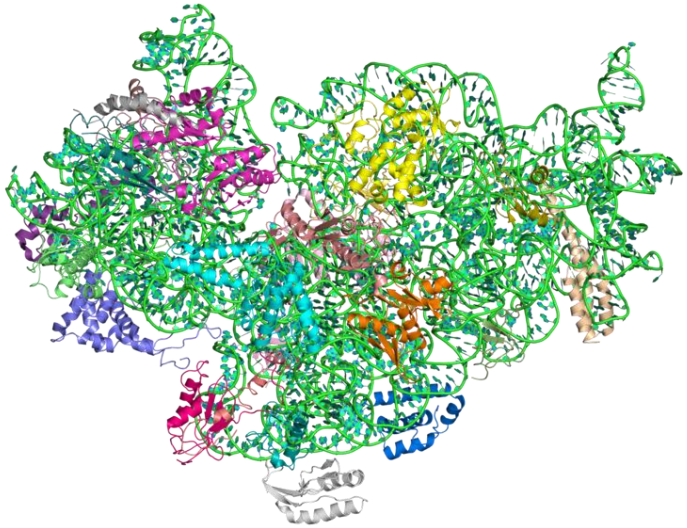
TA7 - DNA Structure and Base Pairing Explains the structure of nucleotides and DNA, including complementary base pairing

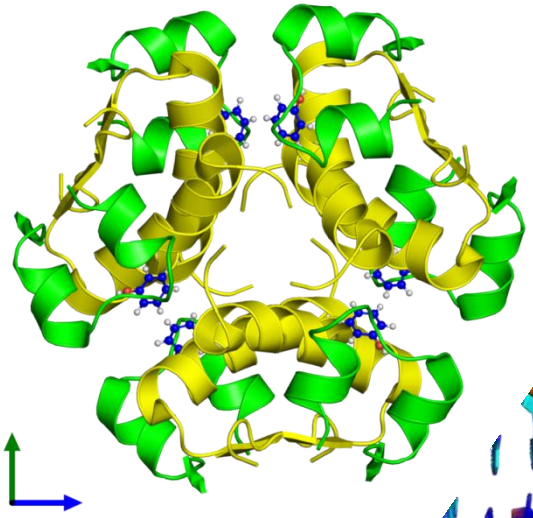
download here: ta7_dna_structure_and_base_pairing.pdf

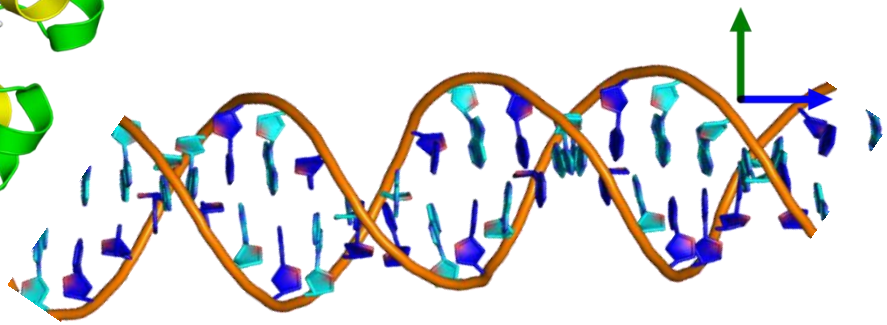
What is the **Protein Data Bank (PDB)?**

An archive of ***experimentally determined*** 3-dimensional structures of biological macromolecules

Protein, nucleic acids, sugars



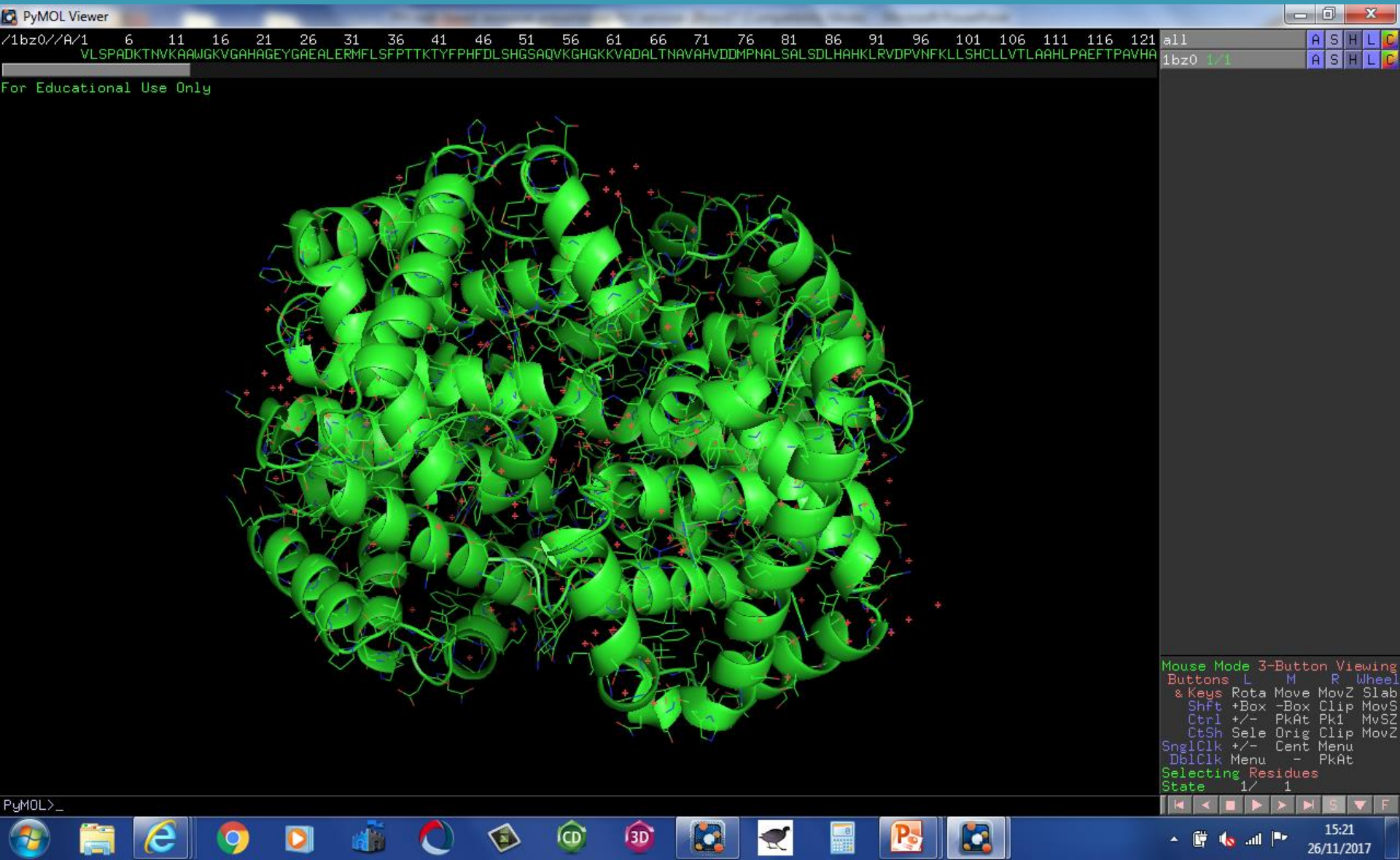




Available to anyone online for free

Structure viewer – website - LiteMol

Structure viewer – software - PyMOL



Biochemistry

Session #1

Amino acids

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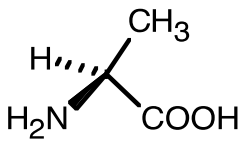
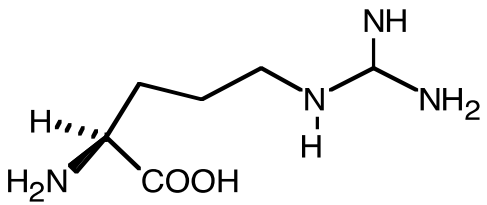
Amino acids

- **α-amino acids have the general formula $RCH(NH_2)COOH$**
- **There are 20 commonly-occurring amino acids**

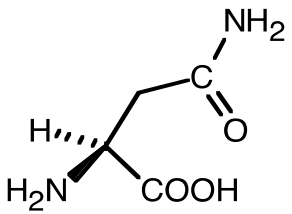
Amino acids



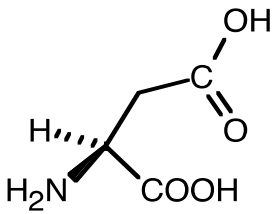
L-Alanine



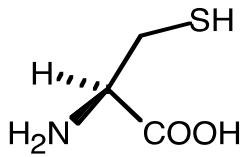
L-Arginine



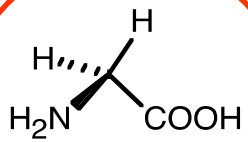
L-Asparagine



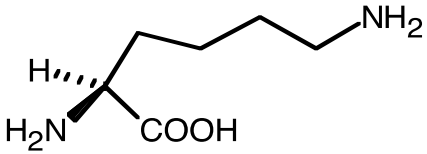
L-Asparagic acid



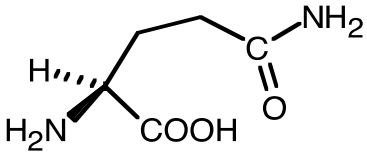
L-Cysteine



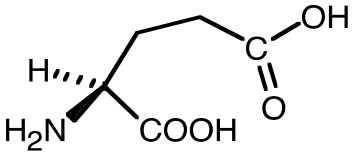
Glycine



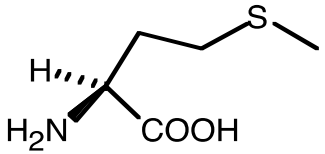
L-Lysine



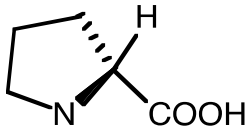
L-Glutamine



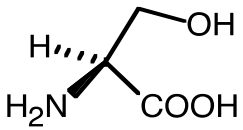
L-Glutamic acid



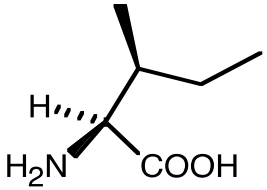
L-Methionine



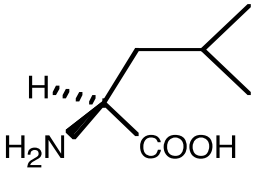
L-Proline



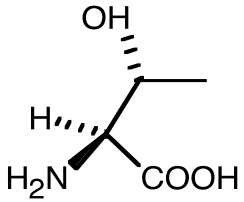
L-Serine



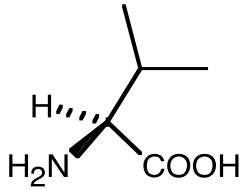
L-Isoleucine



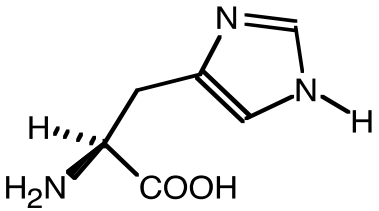
L-Leucine



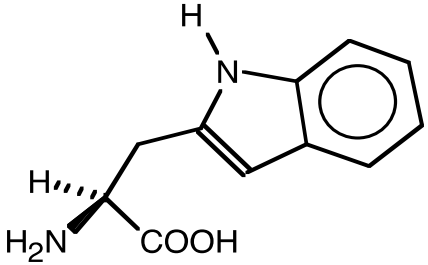
L-Threonine



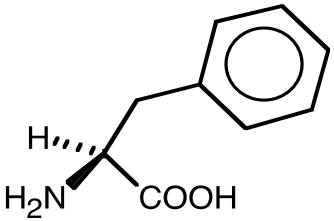
L-Valine



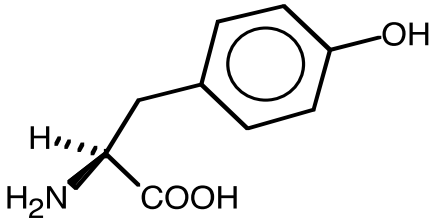
L-Histidine



L-Tryptophan



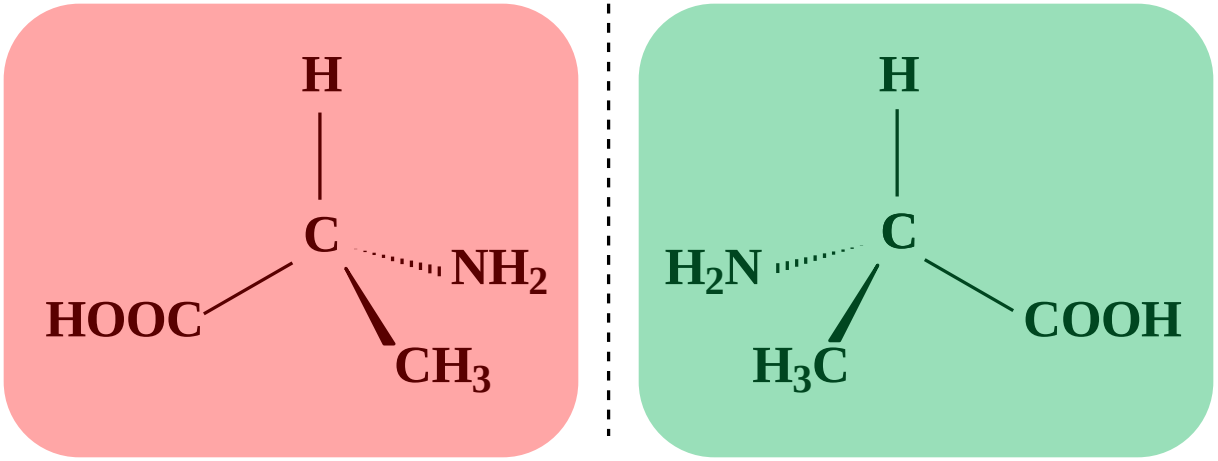
L-Phenylalanine



L-Tyrosine

Amino acids

- **ALL are optically active bar *glycine* (R = H)**

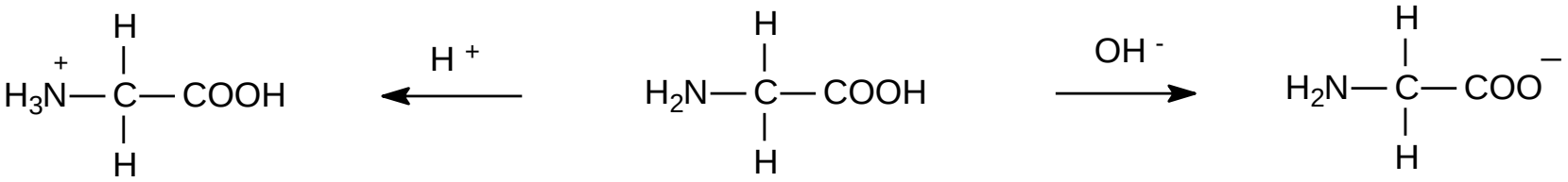


D-alanine **L-alanine**

- ***should* exist as pairs of optical isomers - only 1 occurs in nature!**

Amino acids – effect of pH on structure?

- **Structure in aqueous solutions:**

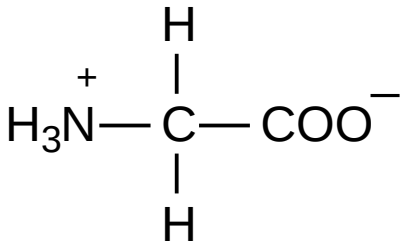


pH < 7

pH > 7

Amino acids – in neutral solution

- **Exist in neutral solution as *zwitterions***



pH = 7

- ***Note that this is an intermolecular proton (H^+) transfer between the acid group of one amino acid and the amino group of another molecule***

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Chemistry

Biochemistry

Session #2

Peptides, Proteins & Polymers

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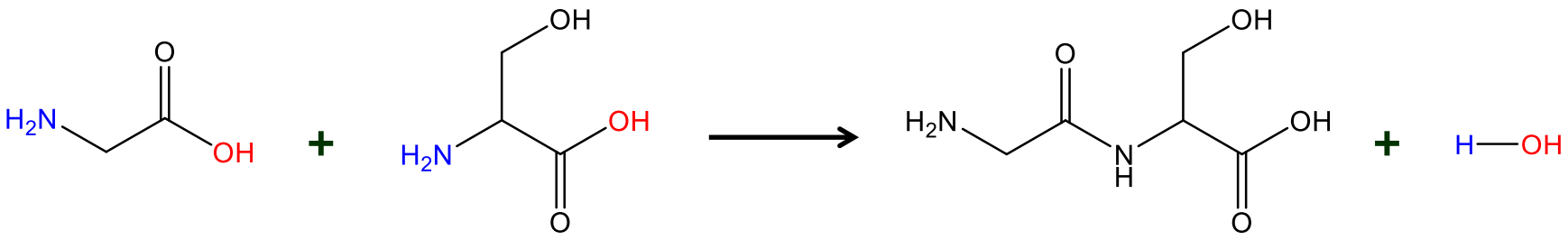
Peptides

- **Formation of peptides**

  - peptide = 2 or more amino acids bonded together with AMIDE (*peptide*) links

  - condensation reaction between amino group and acid group with elimination of a water molecule (H-OH)

***e.g.* the reaction between glycine (Gly) and serine (Ser):**



Gly **Ser**

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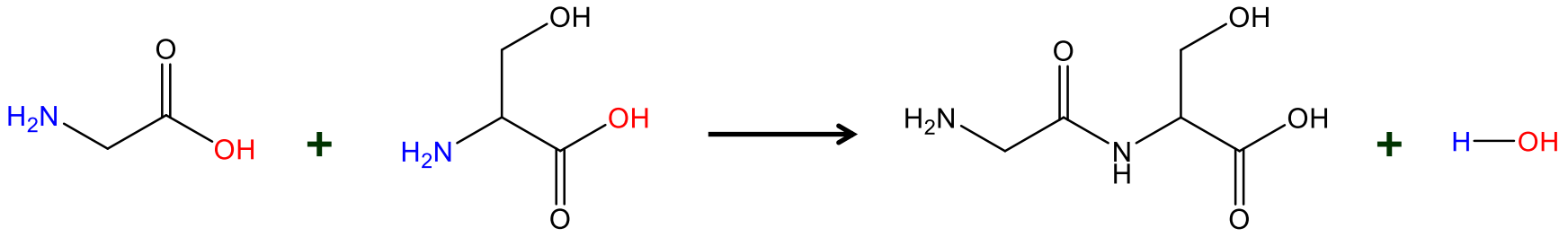
Peptides

- **each amino acid has both functional groups so it can form a *peptide* link to the second one in two ways:**

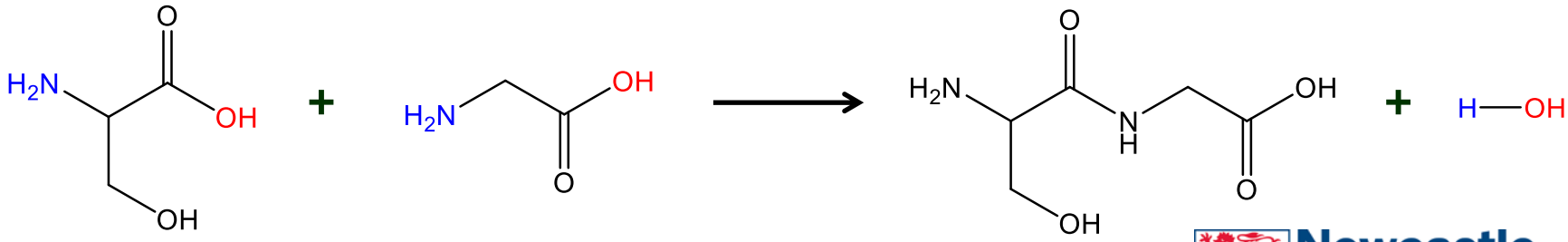
***e.g.* for the reaction between glycine (Gly) and serine (Ser):**

1.



Gly **Ser**

2.



Ser **Gly**

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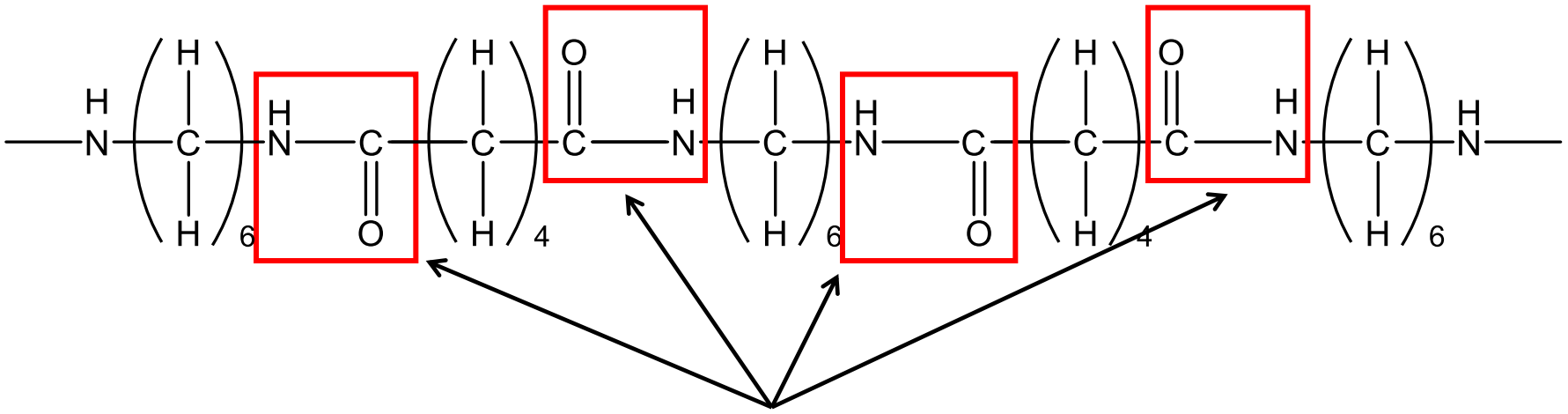
Condensation Polymers

- ***cf.* formation of condensation polymers**

  - 2 monomers bonded together with AMIDE links

  NOT peptide links as the monomers are NOT α-amino acids! ☹

***e.g*. the Nylon-6,6 polymer:**



AMIDE links – NOT peptide links

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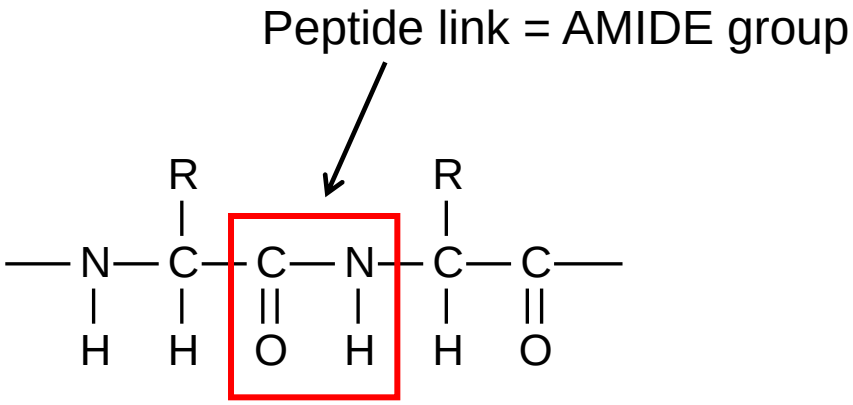
Peptide link

- **Hydrolysis of peptides**

  - peptide (AMIDE) link can be broken (hydrolysed) using dilute acid

  - reforms component amino acids – thus can be used to id amino acids in a peptide via TLC – see theory sheet TC3



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Chemistry

Biochemistry

Session #3

Proteins

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Proteins Section - Summary

- Definition – a linear polymer of amino acids
- Of any length – longest in humans is 34,000!

- Fold up into a precise shape in 3D

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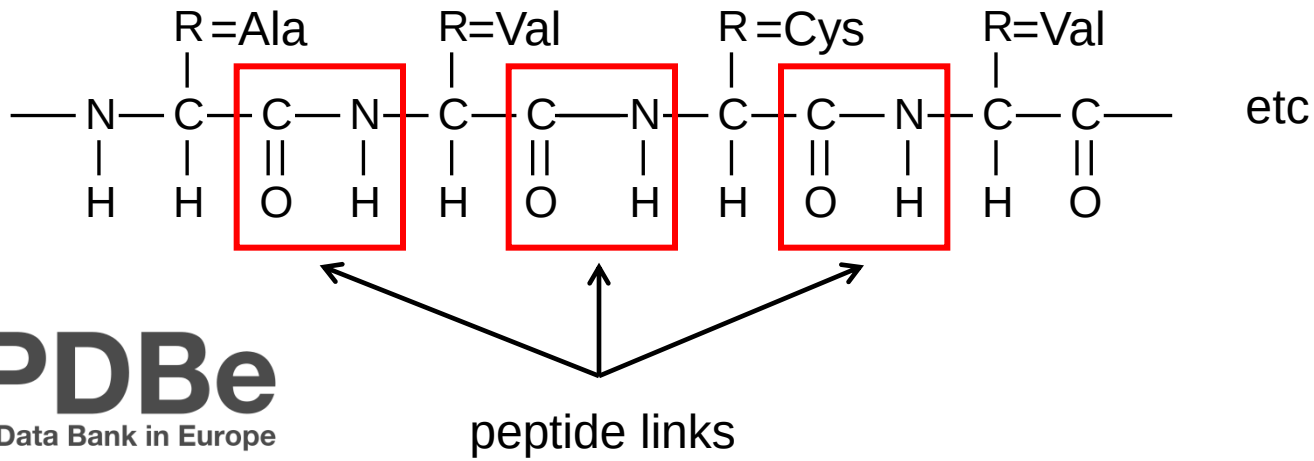
Types of structure - Primary

- **Primary**
- The order of the amino acids in the polymer, *e.g.*

- Ala-Val-Cys-Val-Tyr-Arg-Thr-Cys-Asp-Lys-Asp-…
- A V C V Y R T C D K D



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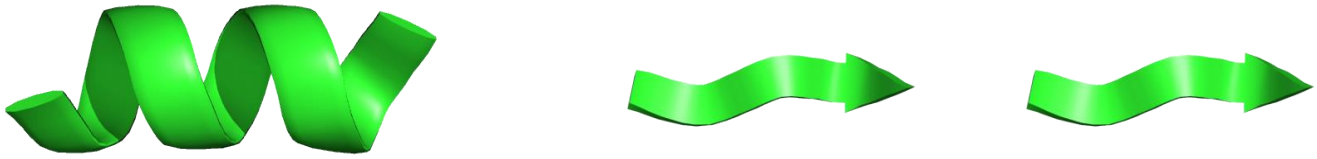
Types of structure - Secondary

- **Secondary**
  - Alpha helix
  - beta ‘pleated’ sheet



- AVCVYRTCDKDCKRRGYRSGKCINNACKCYPY
- How the sequence is shaped locally -
  - the angle of the bonds in the protein backbone
  - principally stabilised by hydrogen bonds (IMFs)

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Intermolecular forces

Summary

These only occur between simple molecules. There are three types:

1. **Van der Waals / London / Dispersion**
2. **Dipole-Dipole**
3. **Hydrogen “bonding” - most significant IMF between biomolecules**

You need to know the important features of each type and be able to recognise which type(s) are present between any given molecule.

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Intermolecular forces

Hydrogen "bonding"

- A specific and extreme type of dipole-dipole force
- Molecule must have **two** specific structural requirements:
  1. an **H atom** bonded to either **N, O or F**
  2. an electronegative atom with at least **one lone pair** (this is often, but not always, the same **N, O or F** atom to which the H is bonded)
- Very strong attractive force between electron-deficient $H^{\delta+}$ atom and the lone pair
- Strongest type of IMF – but still an IMF, **NOT** a covalent bond! ☹

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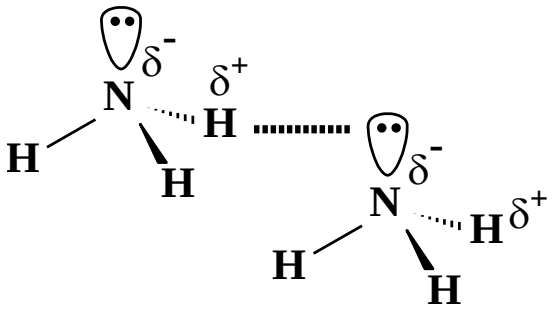
Intermolecular forces

Hydrogen “bonding” – diagrams

If you are asked to draw a diagram to illustrate H-bonding in a specific molecule, it **MUST** have **3** features (worth **3 marks**)

e.g. for ammonia:



1. δ+ and δ- shown correctly on at least one H-X bond
2. The correct number of lone pairs shown on each X atom
3. The H-bond is clearly shown from a $H^{\delta+}$ atom to a **lone pair**

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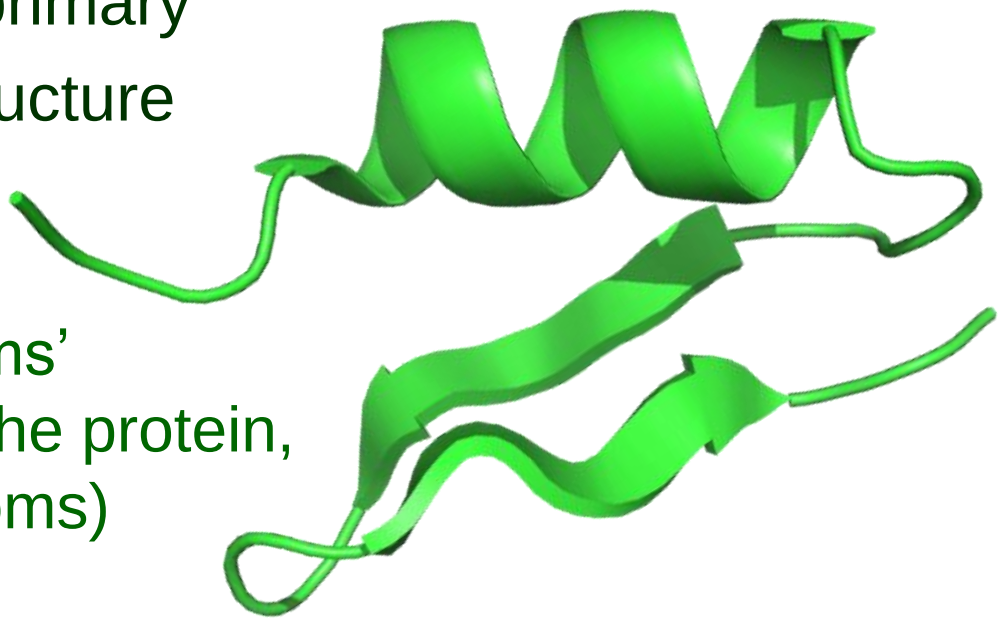
Types of structure - Tertiary

- **Tertiary**
- How all the parts are folded up in 3D space

- Amino acids distant in primary

can be close in tertiary structure



Cartoons or ‘ribbon diagrams’
show the overall shape of the protein,
(but without showing all atoms)

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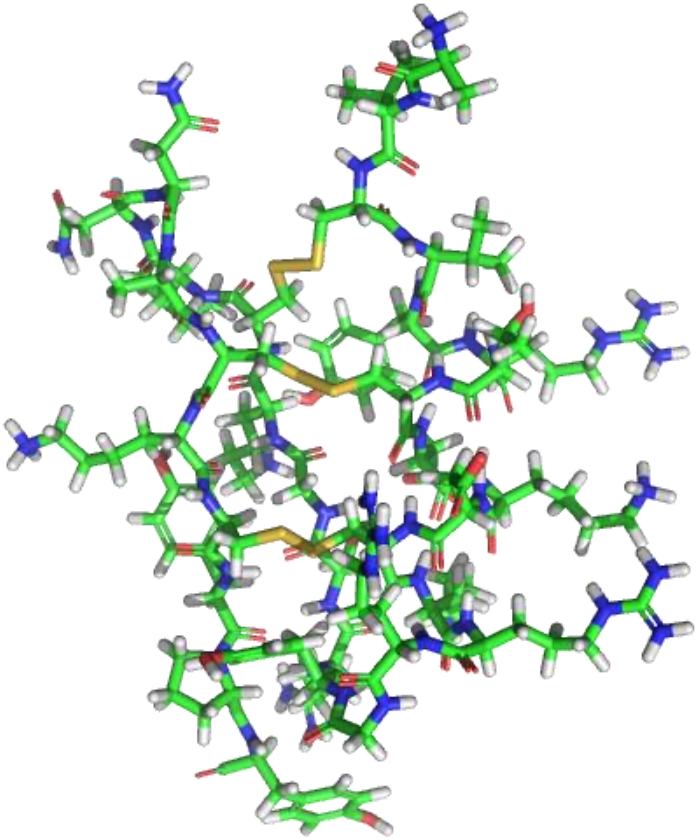
A real protein - Scorpion toxin



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PDBe.org/1pjv

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A real protein - Scorpion toxin

See MP4 file **RL1 - 1pjv** for an animation with audio description

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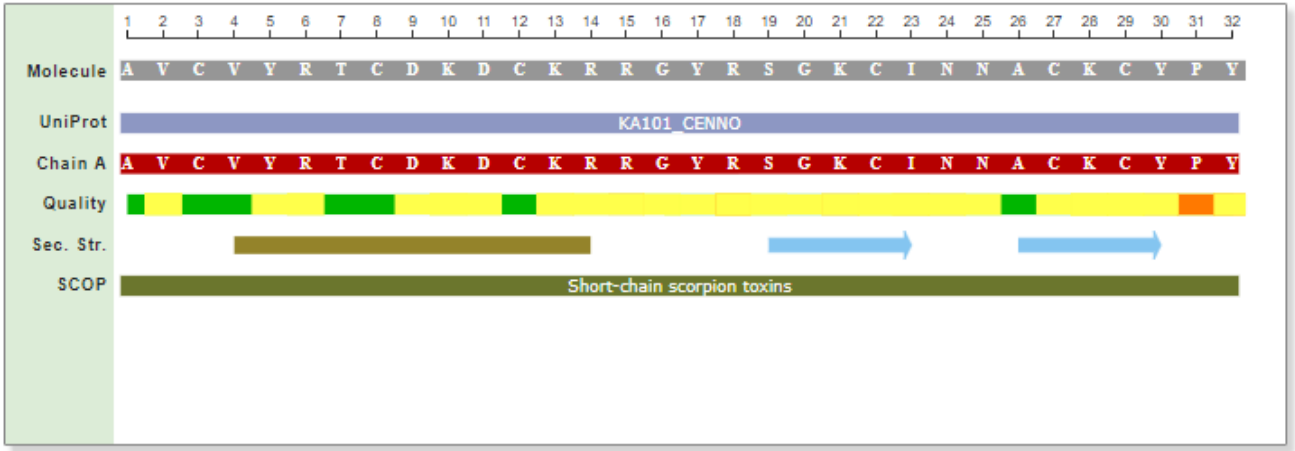
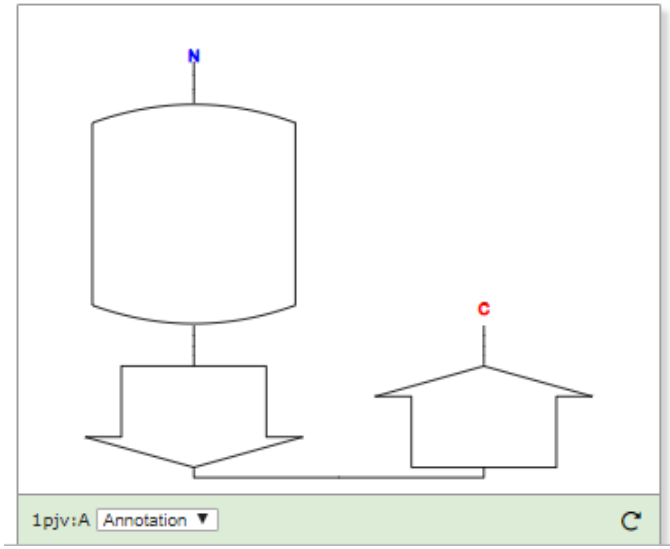
All structures interlinked on PDBe webpages!





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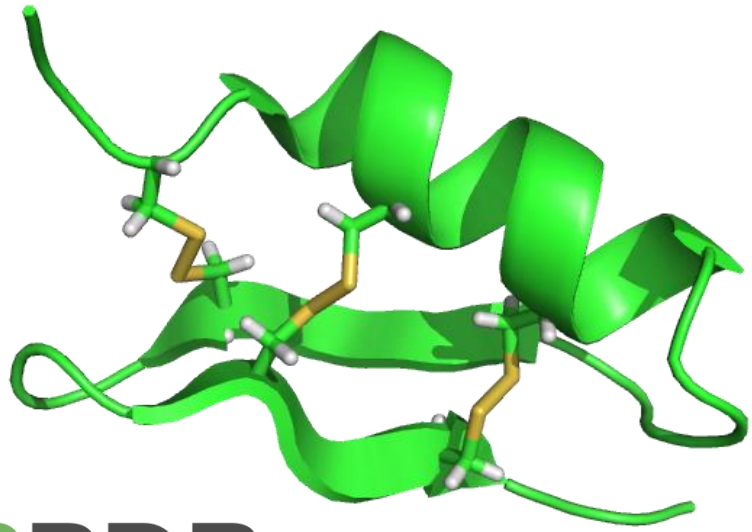
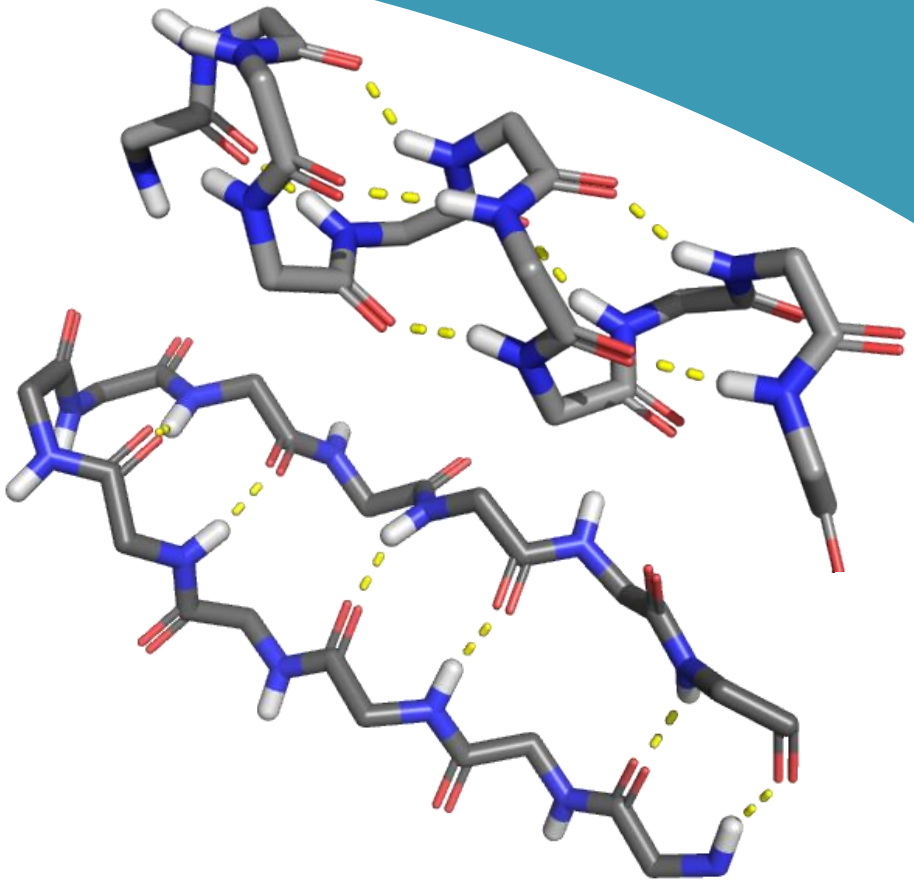
What holds a protein together - summary

- Many hydrogen bonds
- Fewer (if any) covalent S-S bonds





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Specific examples of proteins #1

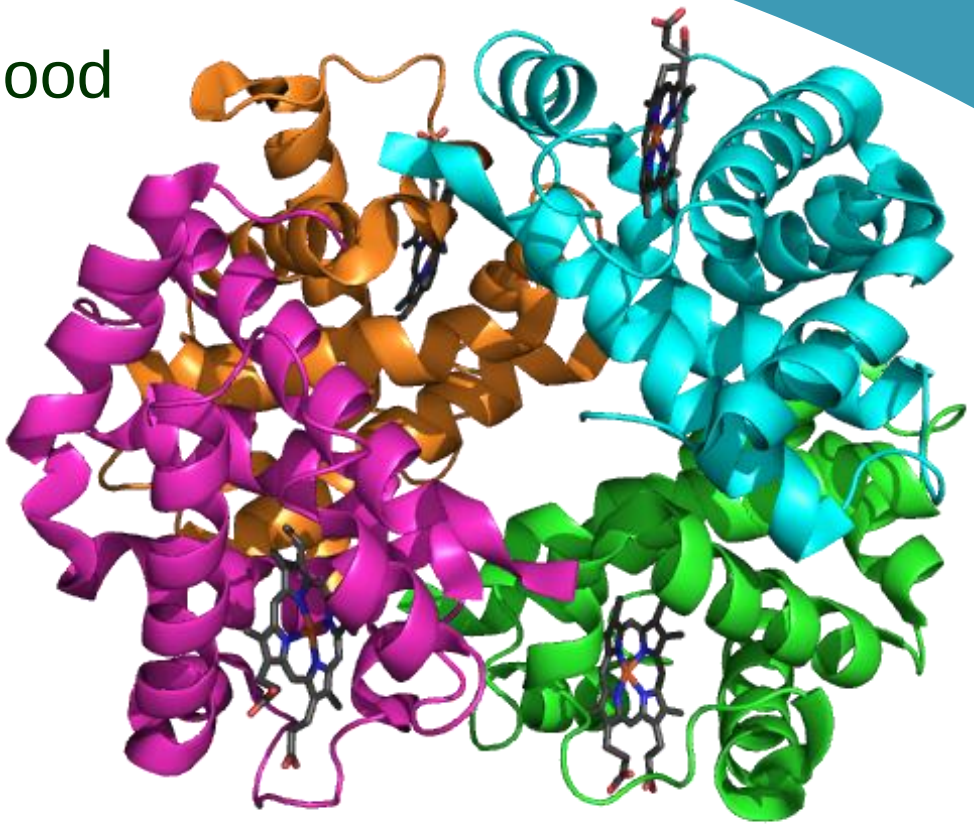
Haemoglobin

- carries oxygen in the blood
- only alpha helices

It also has

Quaternary structure

(not all proteins do!)



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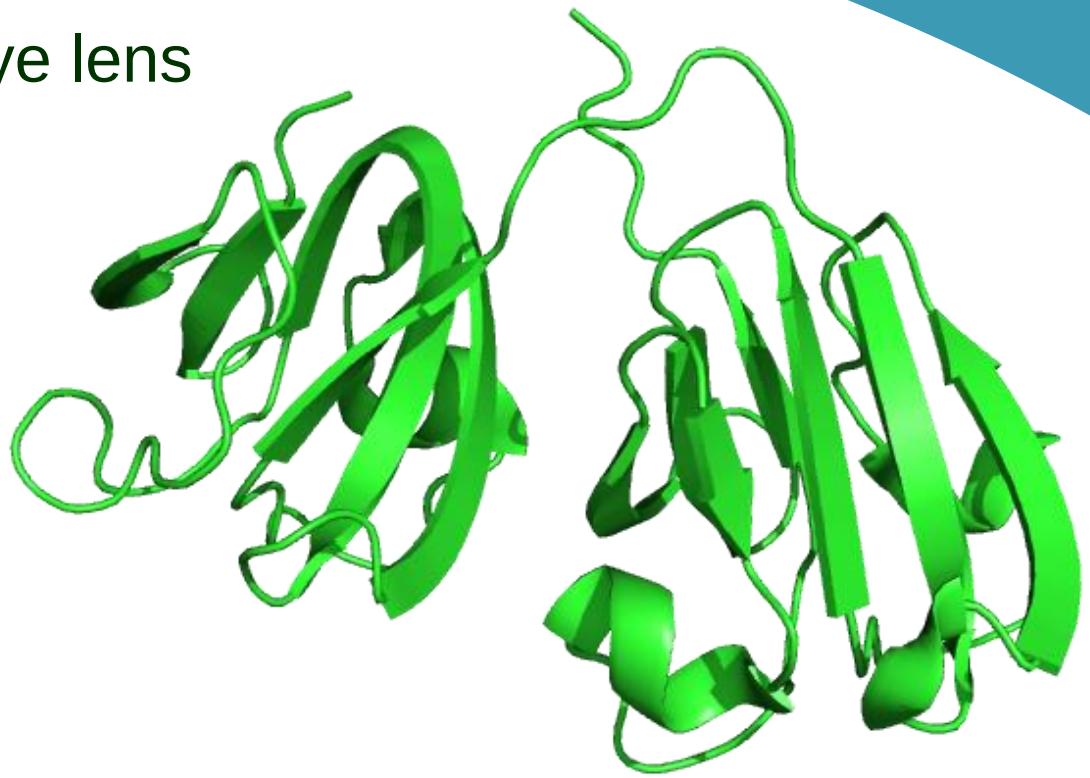
Specific examples of proteins #2

Crystallin

- bends light in your eye lens
- mostly beta sheets



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Chemistry

Biochemistry

Session #4

Enzymes

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Enzymes Section - Summary

- Definition – biological catalysts
- A-level chemistry definition of a catalyst:
- increases the rate of reaction by providing

  - an alternative reaction pathway with

  - a lower E_a
- *NB* the Activation Energy (E_a) is the **MINIMUM** energy needed for reaction to occur
- Mode of action - lower E_a by binding to substrate
- Remarkable efficiency and rate of reaction of enzymes vs chemical catalysts! ☹

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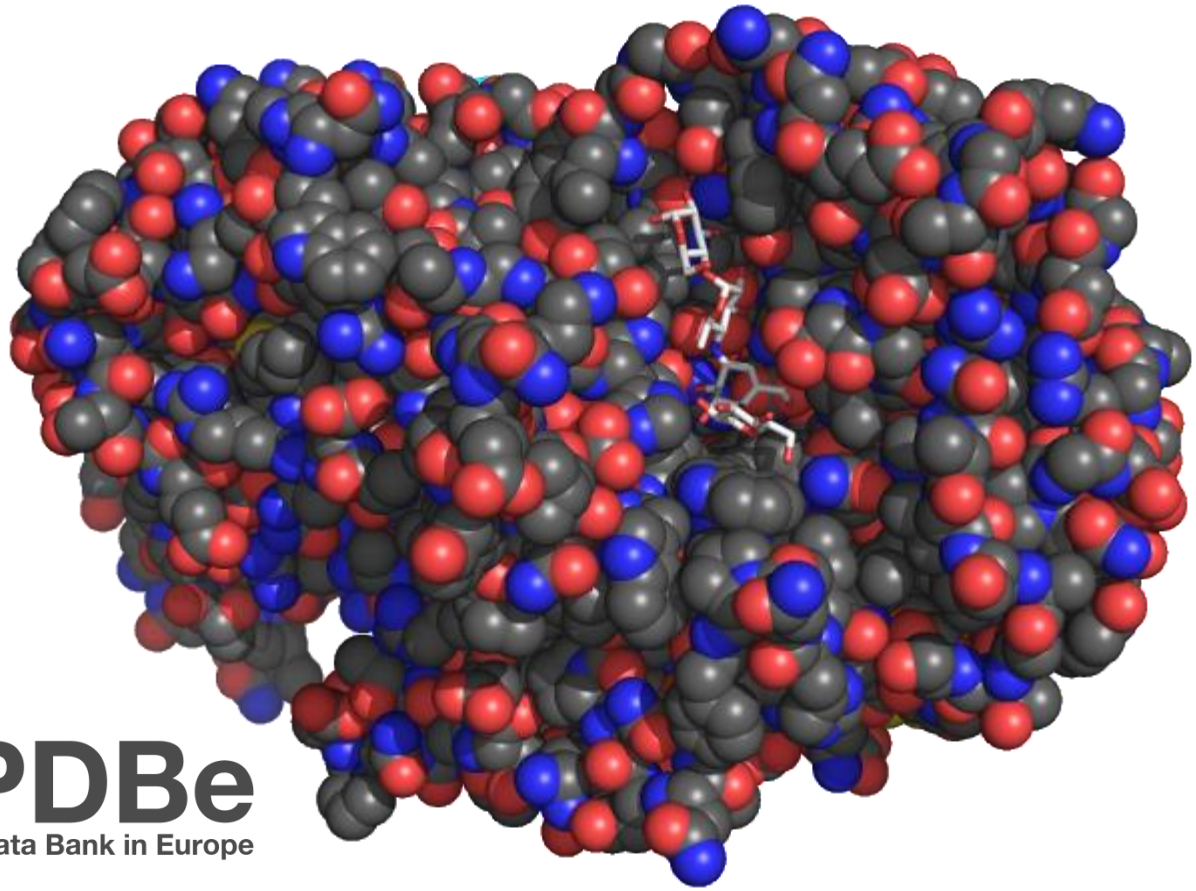
Salivary Amylase

- ‘chops up' starch to sugars in your mouth
- has both alpha helices & beta sheets!



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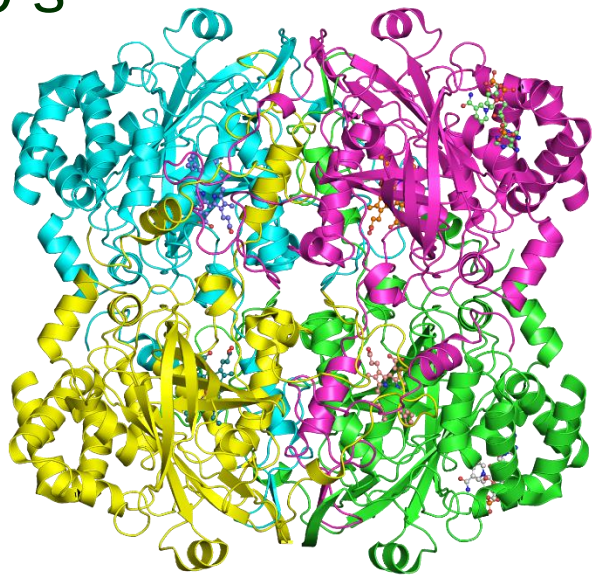
How fast do enzymes work?

- Slowest: RuBisCO - 3 or 4 per second
  - fixes CO_2 in plants
- Acetylcholine esterase - around 15,000 s^{-1}
  - inhibited by Novichok
- Fastest: catalase - up to 1 million s^{-1}
  - $2\ H_2O_2 \rightarrow 2\ H_2O + O_2$
- How fast do chemical catalysts work?



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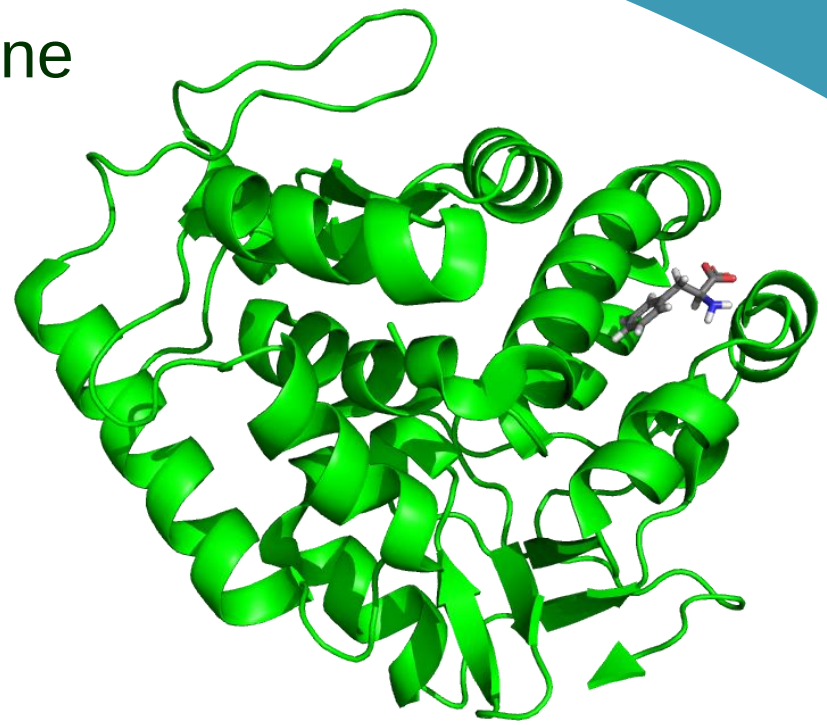
Stereospecificity of enzymes

- Phenylalanine hydroxylase

- only recognises L-phenylalanine

- If enzyme doesn't work ->
  - Phenylketonuria



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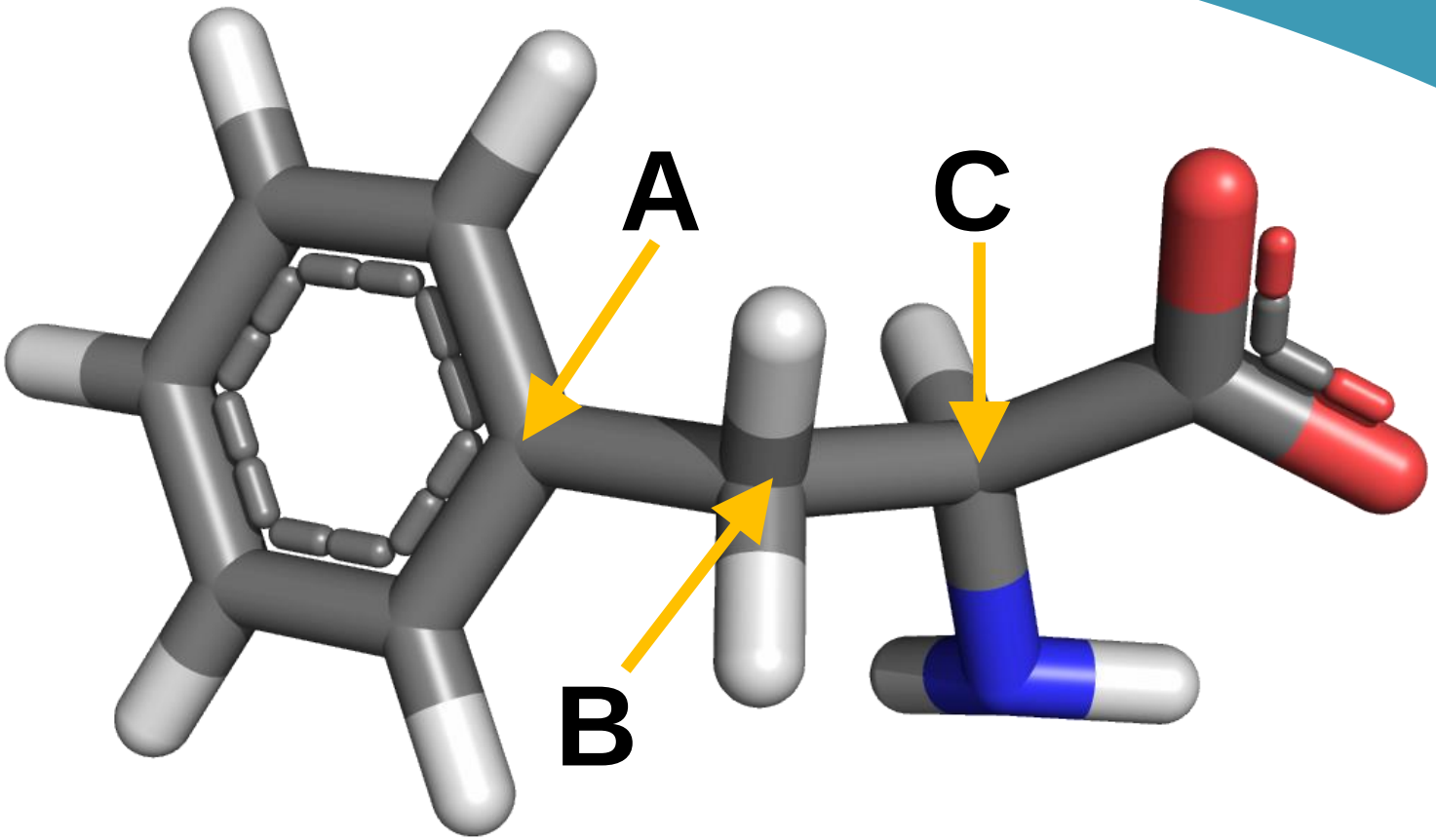
Where is the chiral centre?



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Stereospecificity of enzymes

See MP4 file **RL2 - 4jpy** for an animation with audio description

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Chemistry

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Session #5

DNA

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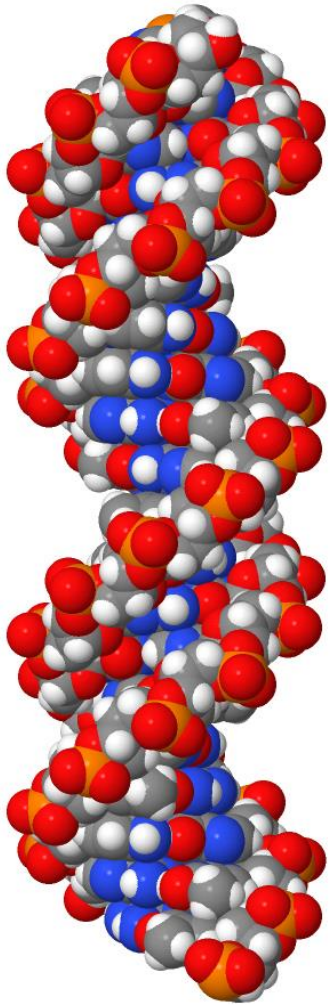
DNA - Summary



- Definition – NOT a protein! ☺
- Structure of repeat unit –
  - sugar, base, phosphate
- Double helix
  - H-bonding between base pairs

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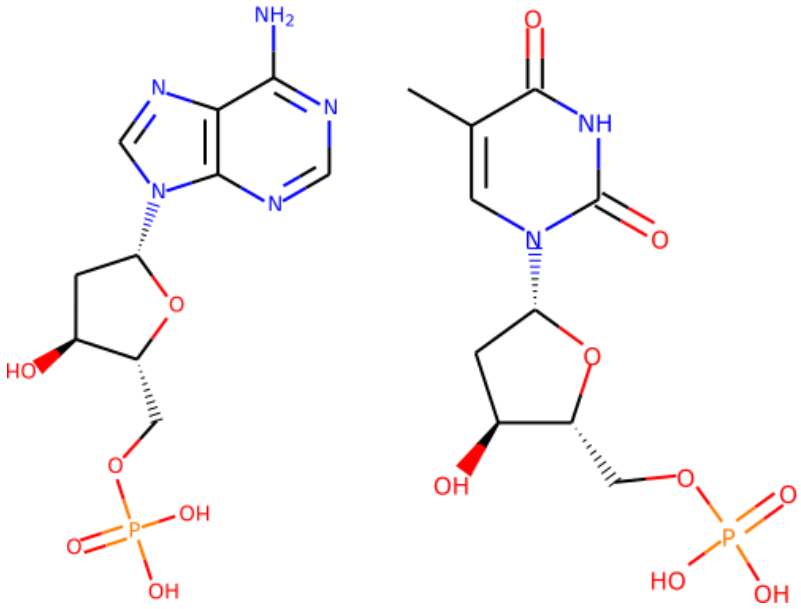
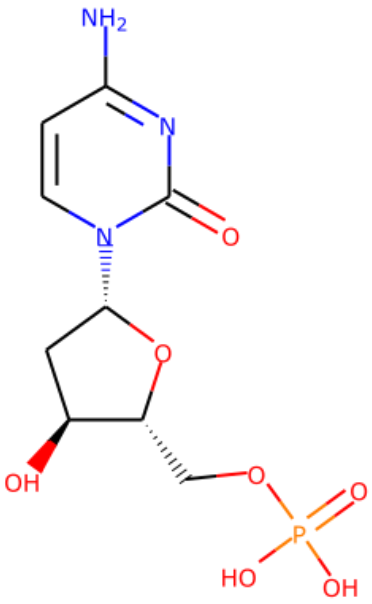
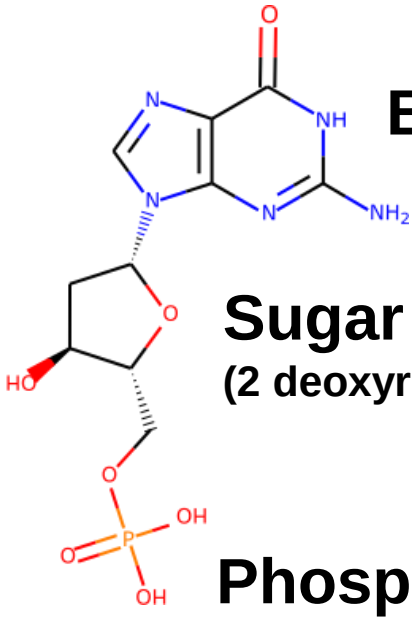
The building blocks of DNA

Adenine **Thymine** **Cytosine** **Guanine**







Base

Sugar
(2 deoxyribose)

Phosphate

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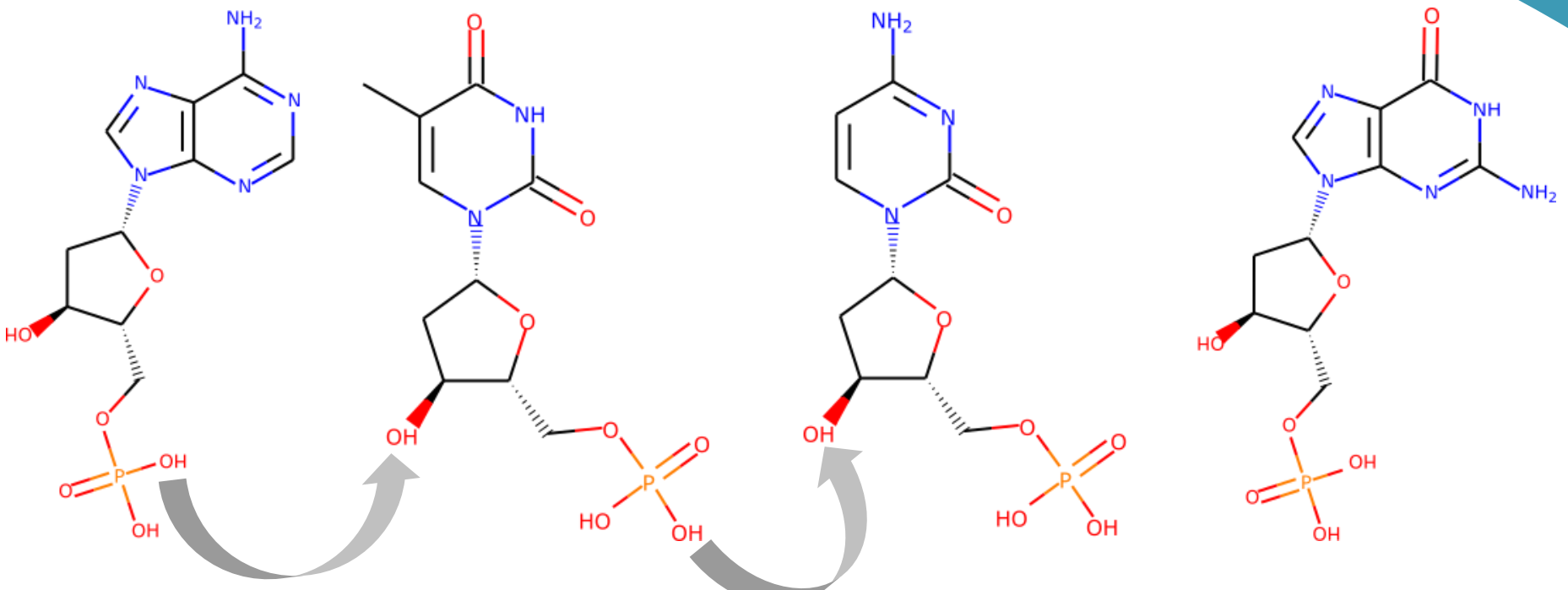
Bases polymerise via phosphodiester bonds



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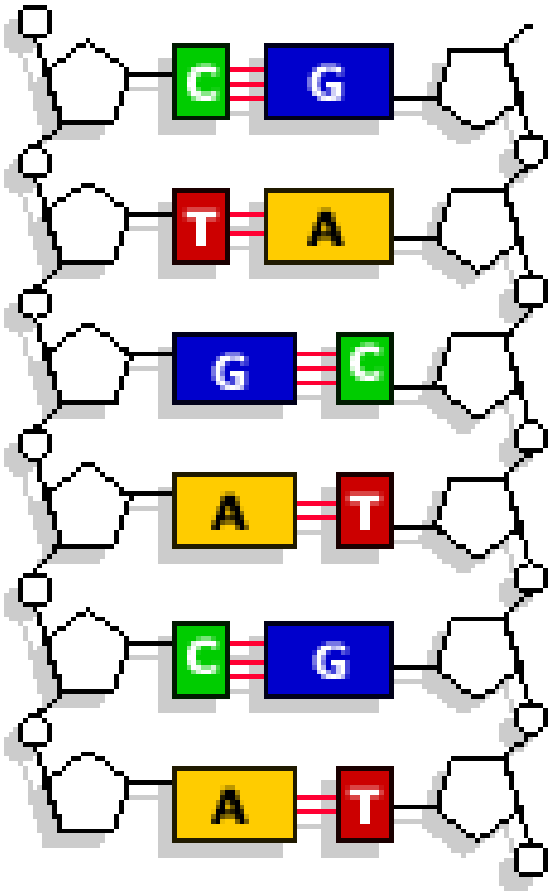
Complementary strands



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DNA structure

See MP4 file **RL3 - DNA** for an animation with audio description

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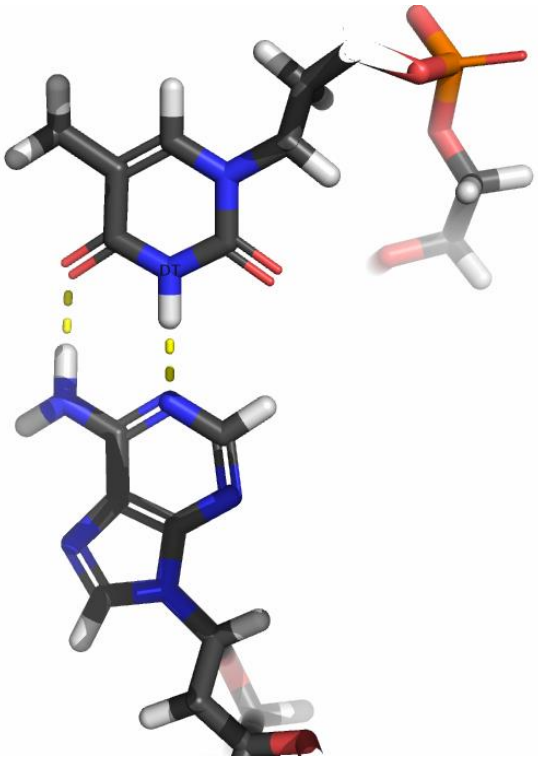
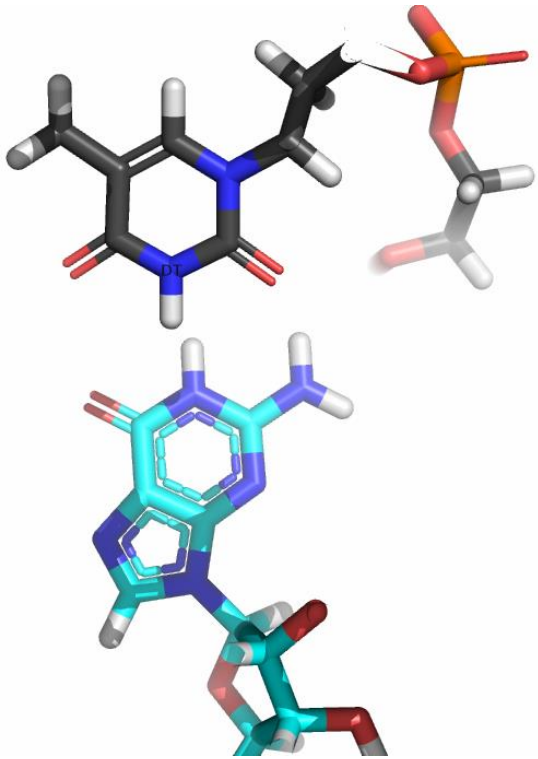
Why other base pairs don't work…..

AT pair
- works



GT pair
- doesn't work



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Session #6

Drug Action

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Drug Action - Summary

- Many drugs stop enzymes working
- Bind in the ‘active site’
  - where the substrate would normally bind

- *e.g.* Ibuprofen

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Video of ibuprofen inhibiting cyclooxygenase

See Video **VA5** on YouTube

Link: https://www.youtube.com/watch?v=fMBTPGLuFbc

A drug which binds to DNA - cisplatin

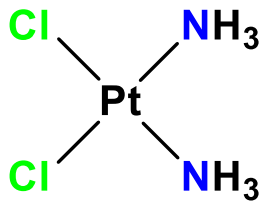
Covalently bonds 2 G bases together (via substitution of the two Cl ligands)

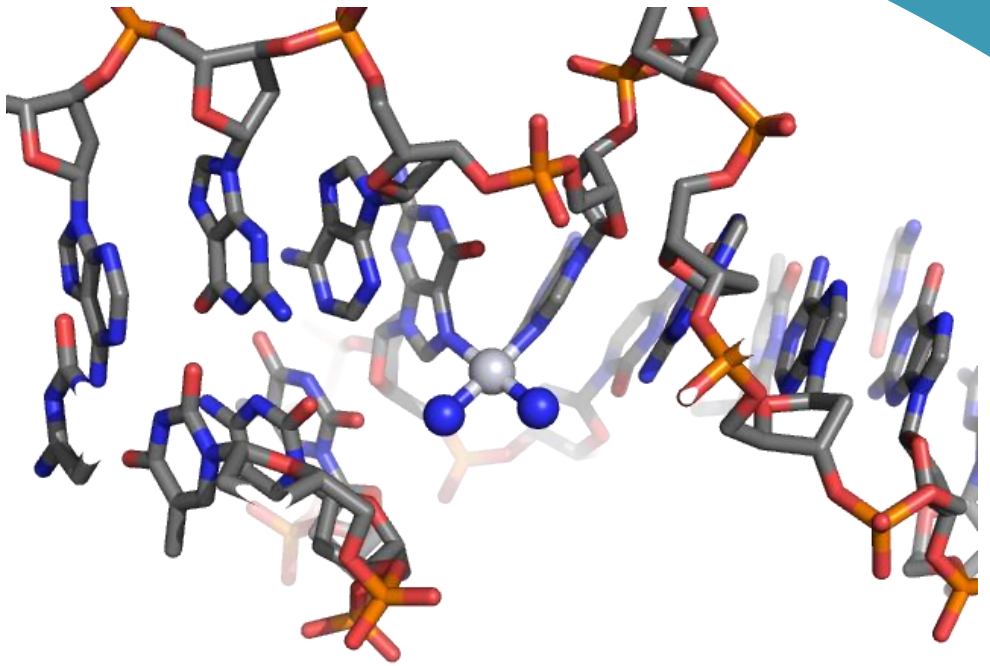
Makes it impossible for DNA to replicate

Anti-cancer drug

Side-effects?

See theory sheet TC5 & video VC2





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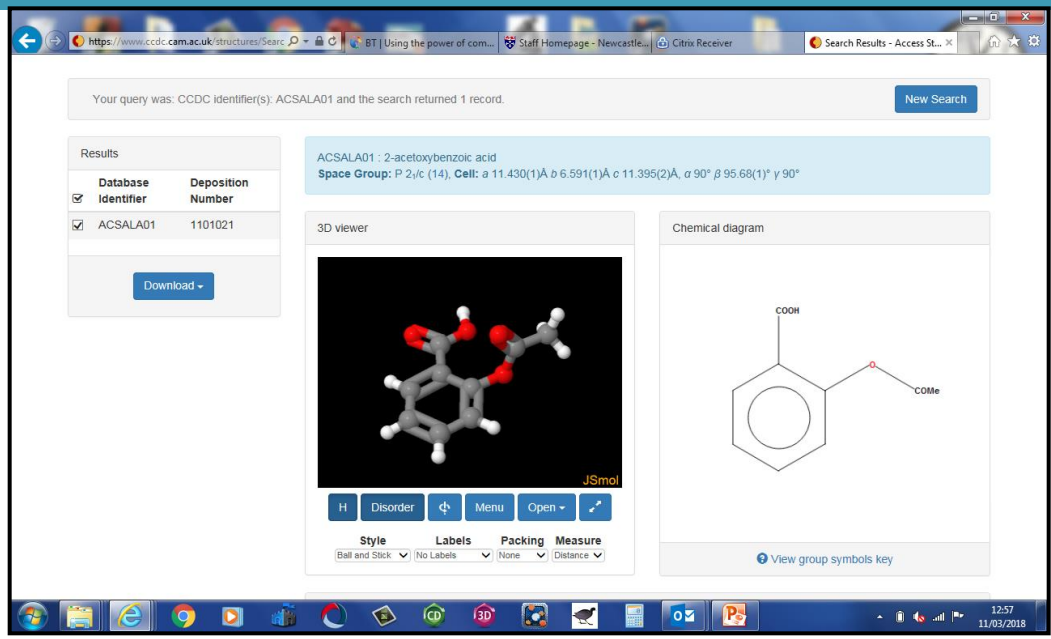
Learning Resources - Crystallography

Uses **FREE** online viewer of real X-ray xtallography 3D structures:
CSD Access Structures:

Peer-produced: Nuffield Bursary yr12 summer students & 4th year MChem project students.
Trialled worldwide!



Theory and work sheets on range of topics for AS/A2 chemistry, including; organic functional groups, E/Z and optical isomerism, structure of benzene, VSEPR, TM complex shapes, reaction mechanisms, intermolecular forces, *etc.*
Access via website: **http://tiny.cc/ccdcLR**

www.ccdc.cam.ac.uk

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Thanks - PDBe Learning Resources Project

EMBL-EBI/PDBe:

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- Lucy Jakubecz; MChem stage 4 project student 2013-14 (now teaching in Coventry)
- Dr Ian Hardcastle, Reader in Medicinal Chemistry
- Adam Stubbs; Summer UG Research Placement student 2017 (currently doing PGCE)

Nuffield Foundation Research Placement students 2015 & 17:

- Alexa Ramos; Heworth Grange School, Gateshead
- Toni Robinson; Excelsior Academy, Newcastle
- Alex Greer; Bedlington High School, Northumberland
- Anna McKie; Queen Elizabeth High School, Hexham, Northumberland
- Olivia Turnbull; Newcastle Sixth-Form Centre
- Wing Yan Ye; Longbenton Academy, Newcastle

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Chemistry

Thank you! ☺

- WMCTC Committee
- School of Chemistry, Birmingham University
- SAgE Faculty, Newcastle University
- Protein Data Bank in Europe (EMBL-EBI)

- Lastly and most importantly – yourselves!

- **GOOD LUCK with your summer exams! ☺**

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