

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**



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! 😊

Chemistry

Biochemistry

Amino acids, Proteins & DNA

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>



The screenshot shows the Protein Data Bank (PDB) website interface. The main content area displays the entry for Hemoglobin A (Human, Deoxy, High Salt) with a 1.5 Å resolution X-ray diffraction structure. The structure is shown as a 3D model with different subunits colored. The page includes sections for 'Function and Biology', 'Ligands and Environments', and 'Citations'. The 'Function and Biology' section lists biochemical functions such as heme binding, bicarbonate transport, and extracellular region. The 'Ligands and Environments' section shows one bound ligand. The 'Citations' section lists 4 review citations, including a 2015 paper by Yuan et al. on hemoglobin allostery. The website header includes the PDB logo and navigation links for Services, Research, Training, and About us. The browser address bar shows the URL <https://www.ebi.ac.uk/pdbe/entry/pdb/1bzo>.

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.

Navigation icons: Home, Star, Settings

Navigation icons: Back, Forward, Refresh, Stop

Address bar: <http://chemistrylearningresources.weebly.com/c>

Browser tabs: BT | Using the power..., Staff Homepage - Ne..., Citrix Receiver, PDB 1bz0 structure su..., Chemistry Resour...

Menu: File, Edit, View, Favorites, Tools, Help

Navigation: HOME, PDBe PROJECT, CONTACT

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](#)

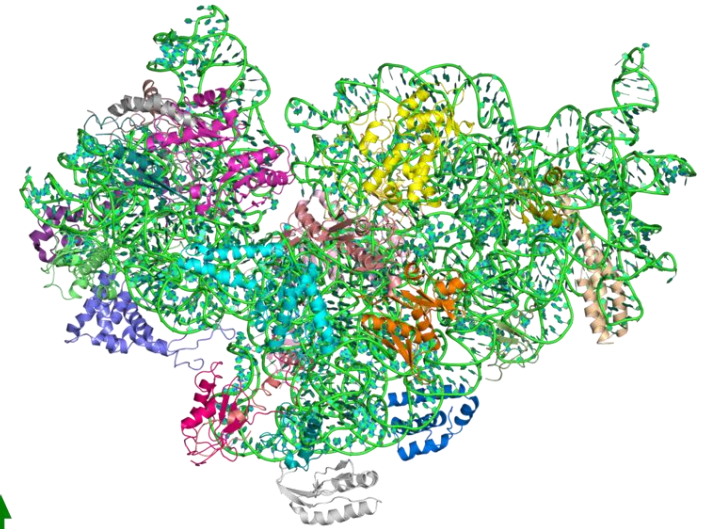
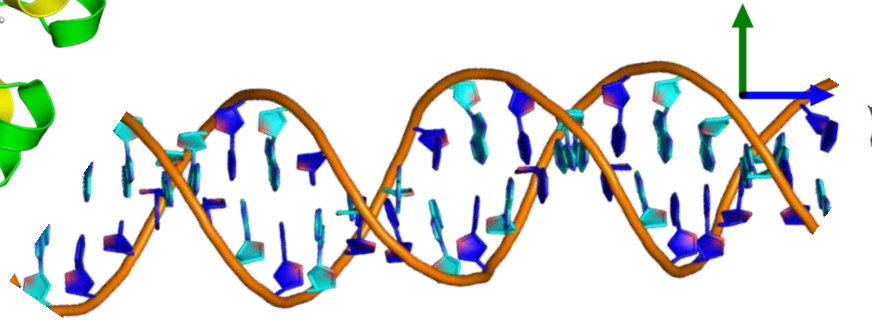
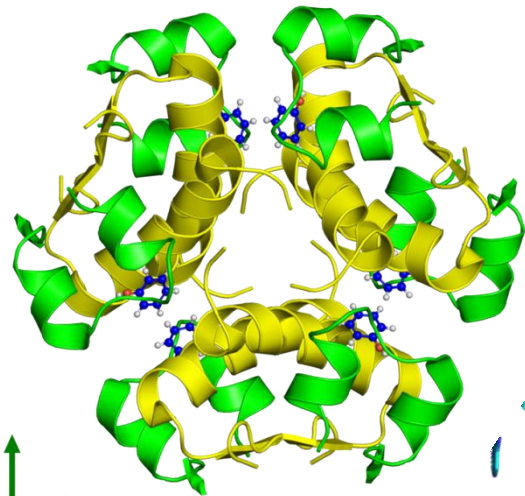
Taskbar: Windows logo, File Explorer, Internet Explorer, Google Chrome, VLC media player, 3D software, Citrix Receiver, Calculator, PowerPoint

System tray: 75%, 15:28, 26/11/2017

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

The screenshot displays the PDB 1bz0 structure viewer interface. The main view shows a 3D ribbon model of a protein structure, colored by chain (beige, purple, cyan, blue). A configuration panel on the right allows users to adjust settings for the model. The panel includes sections for Source, Validation Report, Domain Annotations, Polymer, and Interacting Residues. The Polymer section is currently expanded, showing settings for Type (Cartoon) and Coloring (Chain ID). A 'Density' tooltip is visible at the bottom of the viewer, indicating that streaming is enabled and that clicking on a residue or atom will display data.

Browser address bar: <https://www.ebi.ac.uk/pdbe/entry/pdb/1bz0>

EMBL-EBI logo and navigation links: Services, Research, Training, About us

Close button: Close

Viewer controls: Rotate, Zoom, Pan, Reset, Close

Configuration Panel:

- Source: Source Assembly, Asm. Name 1, Apply
- Validation Report: Apply
- Domain Annotations: Type Select, Apply
- Polymer: Type Cartoon, Coloring Chain ID
- Interacting Residues

Viewer Status: Density Streaming enabled, click on a residue or an atom to view the data.

Page Content: PDB HEMOGLOBIN Source on Primary p Accom alpha-Glu Kavanaugh Biochemist PMID: 844 Function Biochem Biological Cellular component: extracellular region Sequence domains: New look at hemoglobin allostery. Yuan et al. (2015)

System Tray: 100%, 15:13, 26/11/2017

Structure viewer – software - PyMOL

PyMOL Viewer

/1bz0//A/1 6 11 16 21 26 31 36 41 46 51 56 61 66 71 76 81 86 91 96 101 106 111 116 121 all

VLSPADKTNVKAAWGKVGAGHAGEYGAELERMFLSFPTTKTYFPHFDLSHGSAQVKGHGKVVADALTNVAHVDDMPNALSALSDLHAHKLKRVDPVNFKLLSHCLLVTLAAHLPAEFTPAVHA 1bz0 1/1

For Educational Use Only

Mouse Mode 3-Button Viewing
Buttons L M R Wheel
& Keys Rota Move MovZ Slab
Shft +Box -Box Clip MovS
Ctrl +/- PkAt Pk1 MovSZ
CtSh Sele Orig Clip MovZ
SnglClk +/- Cent Menu
Db1Clk Menu - PkAt
Selecting Residues
State 1/ 1

PyMOL>_

15:21
26/11/2017

Chemistry

Biochemistry

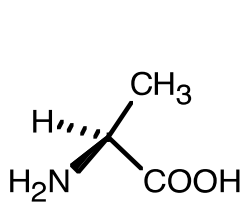
Session #1

Amino acids

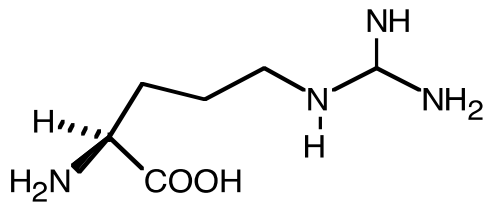
Amino acids

- **α -amino acids have the general formula $\text{RCH}(\text{NH}_2)\text{COOH}$**
- **There are 20 commonly-occurring amino acids**

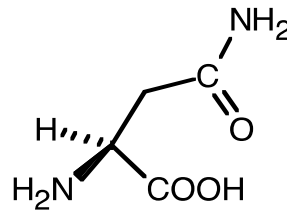
Amino acids



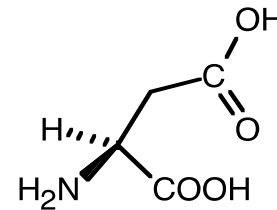
L-Alanine



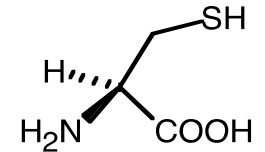
L-Arginine



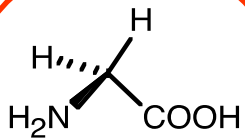
L-Asparagine



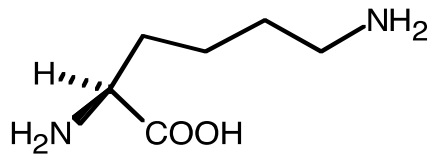
L-Asparagic acid



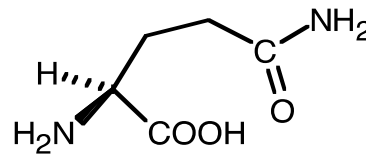
L-Cysteine



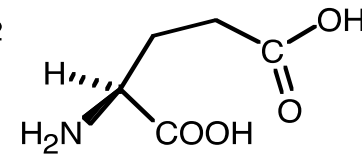
Glycine



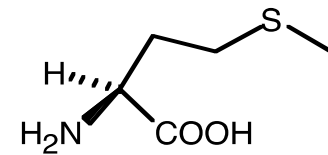
L-Lysine



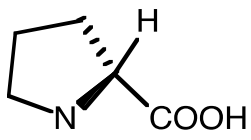
L-Glutamine



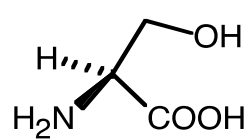
L-Glutamic acid



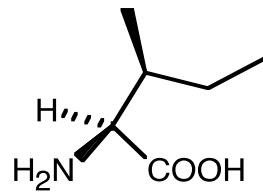
L-Methionine



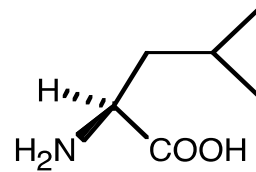
L-Proline



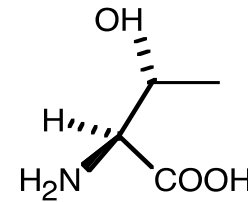
L-Serine



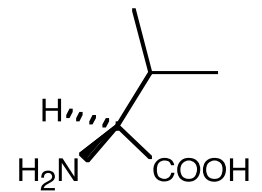
L-Isoleucine



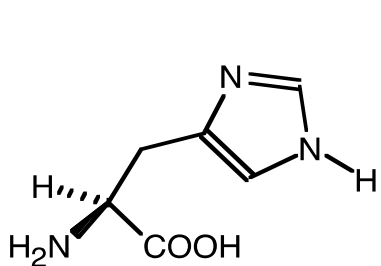
L-Leucine



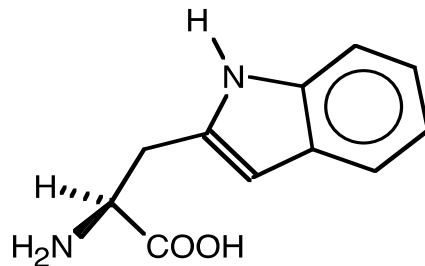
L-Threonine



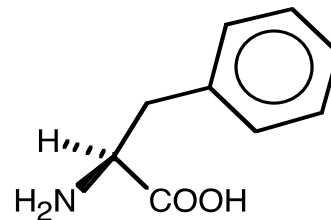
L-Valine



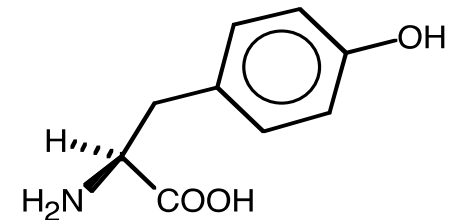
L-Histidine



L-Tryptophan



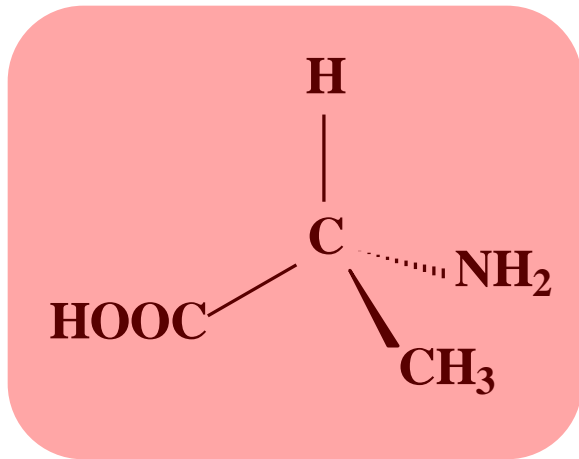
L-Phenylalanine



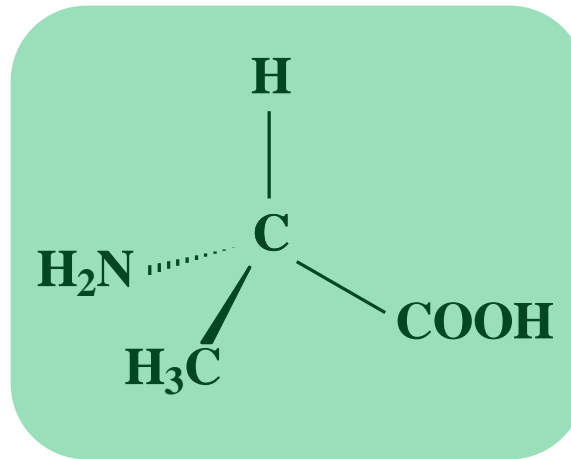
L-Tyrosine

Amino acids

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



D-alanine

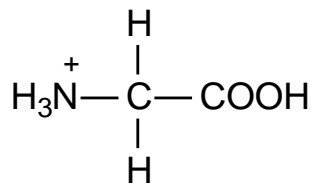


L-alanine

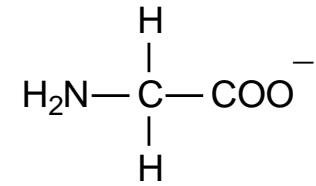
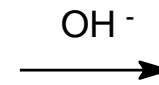
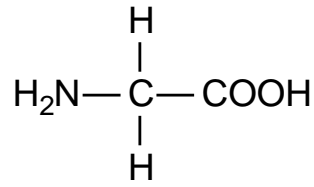
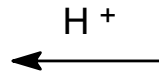
- should exist as pairs of optical isomers* - only 1 occurs in nature!

Amino acids – effect of pH on structure?

- Structure in aqueous solutions:



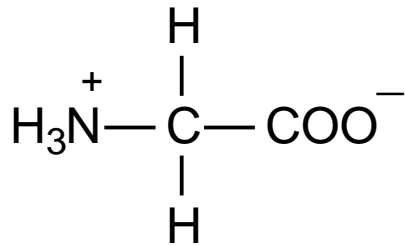
pH < 7



pH > 7

Amino acids – in neutral solution

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



$$\text{pH} = 7$$

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

Chemistry

Biochemistry

Session #2

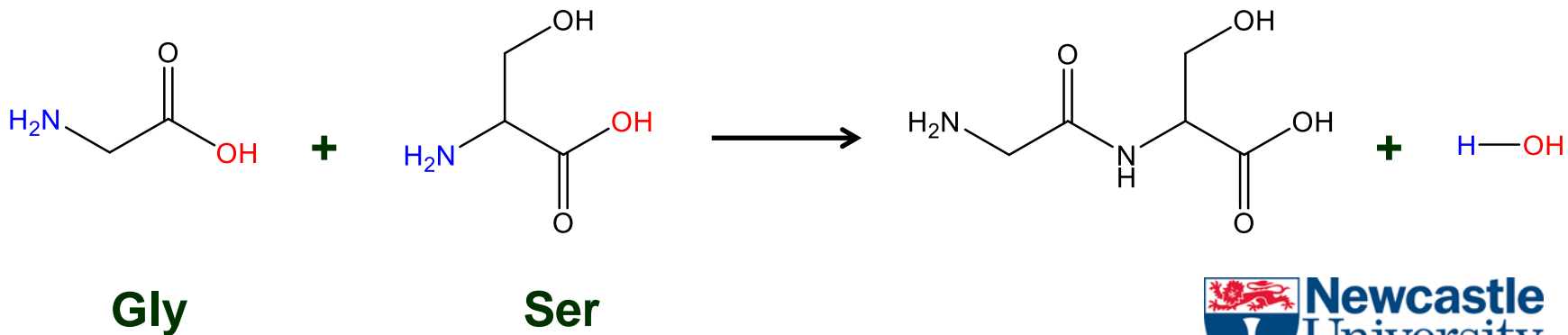
Peptides, Proteins & Polymers

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**)

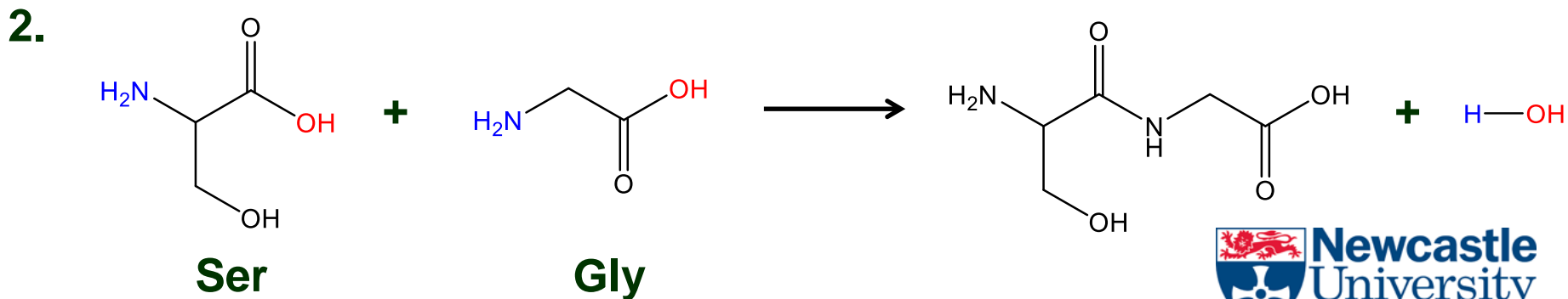
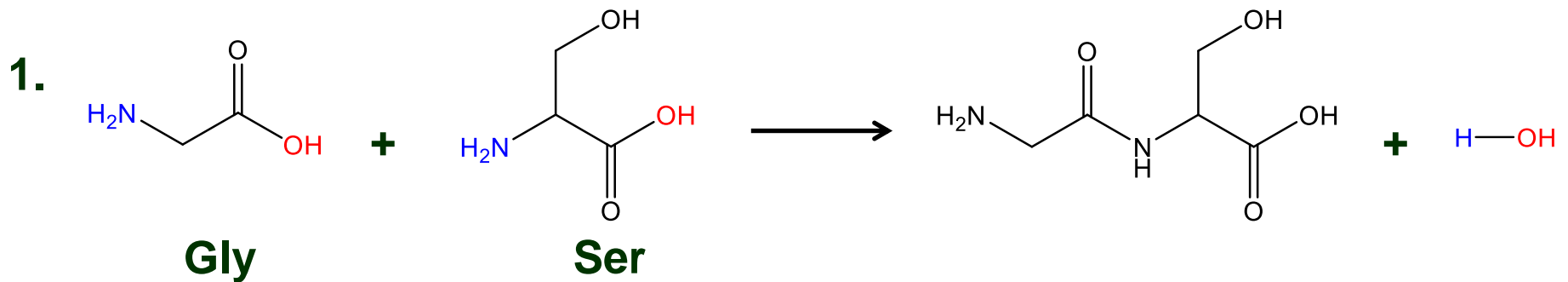
e.g. the reaction between glycine (Gly) and serine (Ser):



Peptides

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

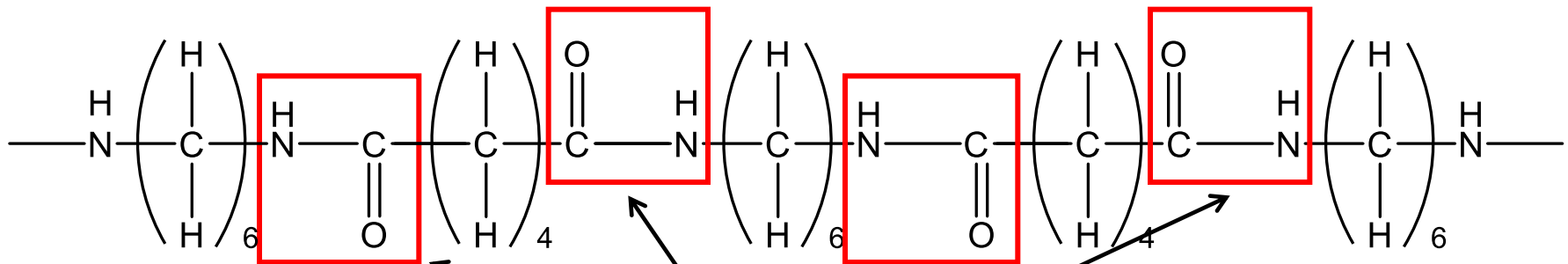
e.g. for the reaction between glycine (Gly) and serine (Ser):



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:

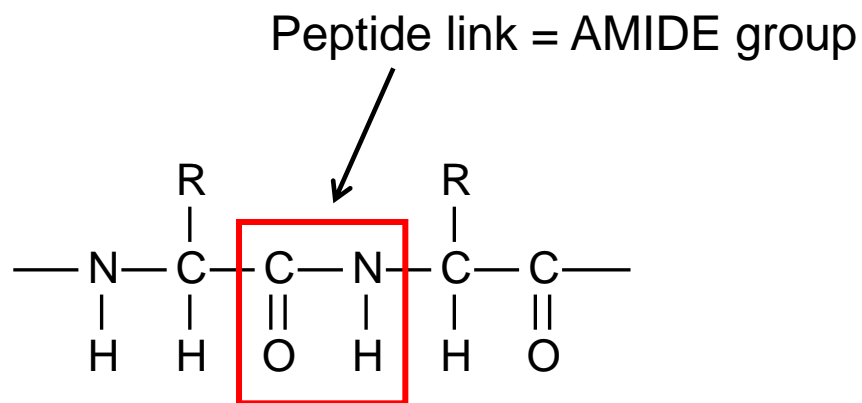


AMIDE links – NOT peptide links

Peptide link

Hydrolysis of peptides

- peptide (AMIDE) link can be broken (hydrolysed) using dilute acid
- reforms component amino acids – thus can be used to identify amino acids in a peptide via TLC – see theory sheet TC3



Chemistry

Biochemistry

Session #3

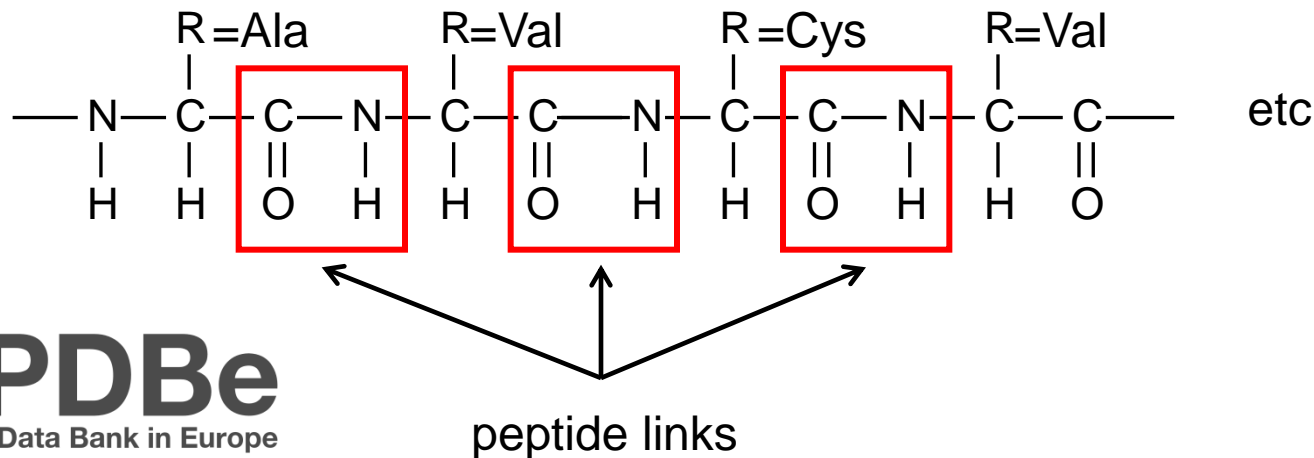
Proteins

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

Types of structure - Primary

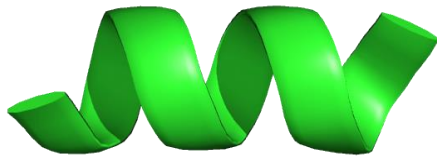
- **Primary**
- The order of the amino acids in the polymer, e.g.
- Ala-Val-Cys-Val-Tyr-Arg-Thr-Cys-Asp-Lys-Asp-...
- A V C V Y R T C D K D



Types of structure - Secondary

- **Secondary**

- Alpha helix



- beta 'pleated' sheet



- AVCVYRTCCKDKRRGYRSGKCNNACKCYPY

- How the sequence is shaped locally -

- the angle of the bonds in the protein backbone
 - principally stabilised by hydrogen bonds (IMFs)

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.

Intermolecular forces

Hydrogen “bonding”

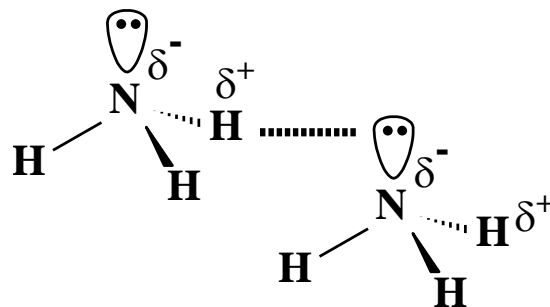
- A specific and extreme type of dipole-dipole force
- Molecule must have **two** specific structural requirements:
 1. an **H atom** bonded to either **N, O or F**
 2. an electronegative atom with at least **one lone pair** (this is often, but not always, the same **N, O or F** atom to which the H is 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! ☹️

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^{δ^+} atom to a **lone pair**

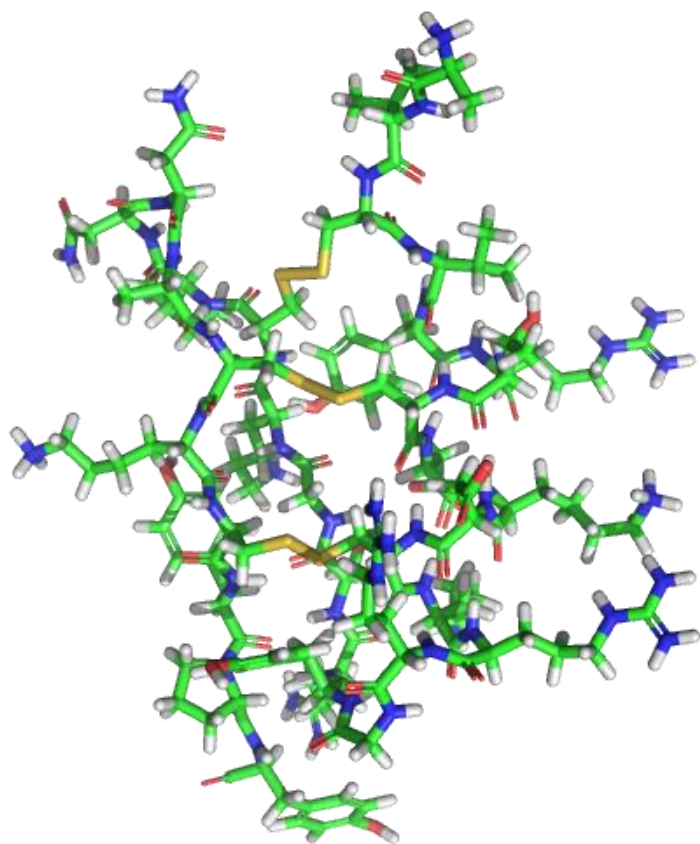
Types of structure - Tertiary

- **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)



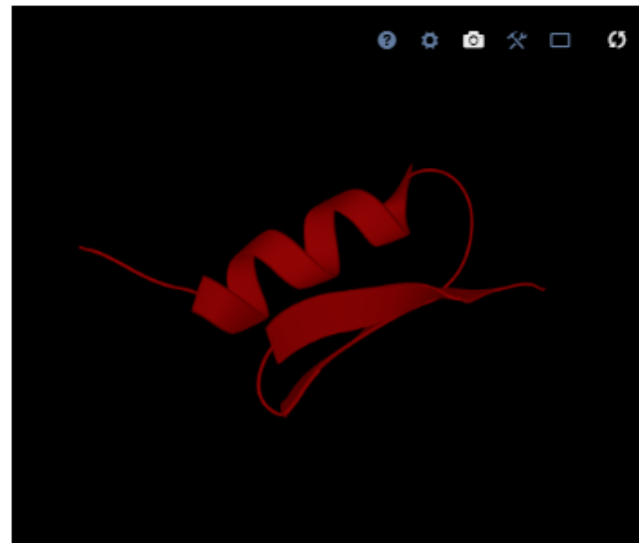
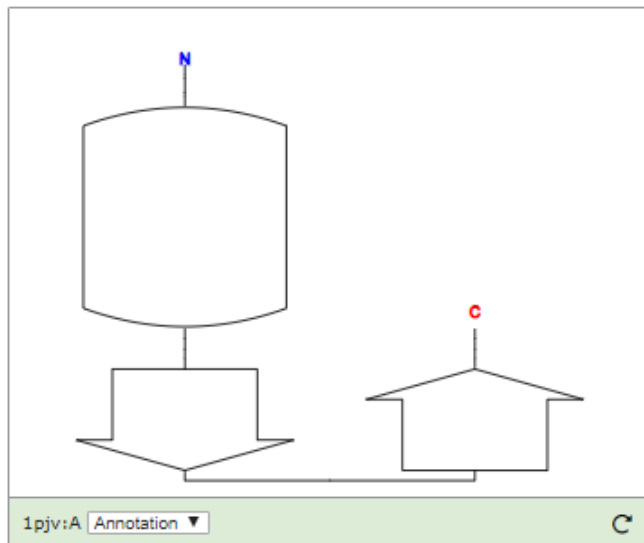
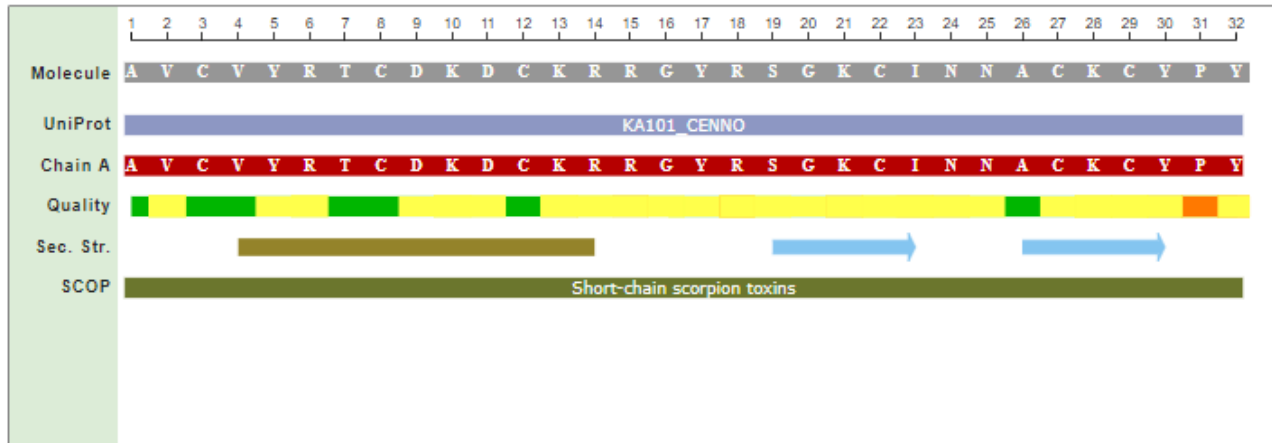
A real protein - Scorpion toxin



A real protein - Scorpion toxin

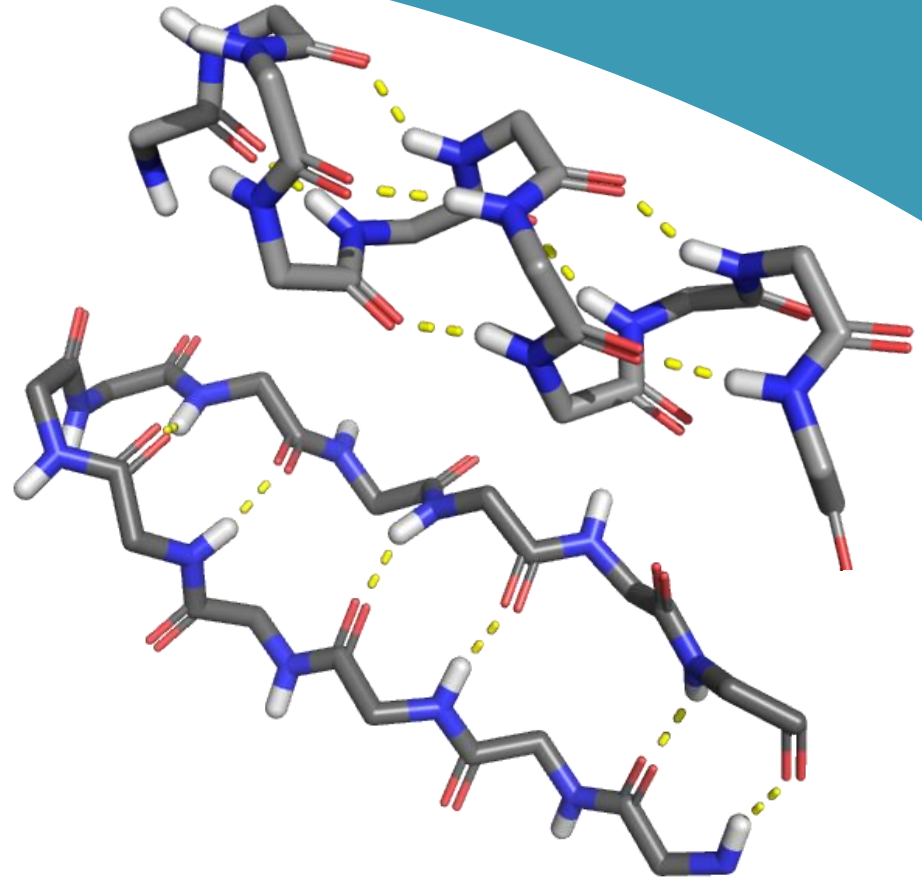
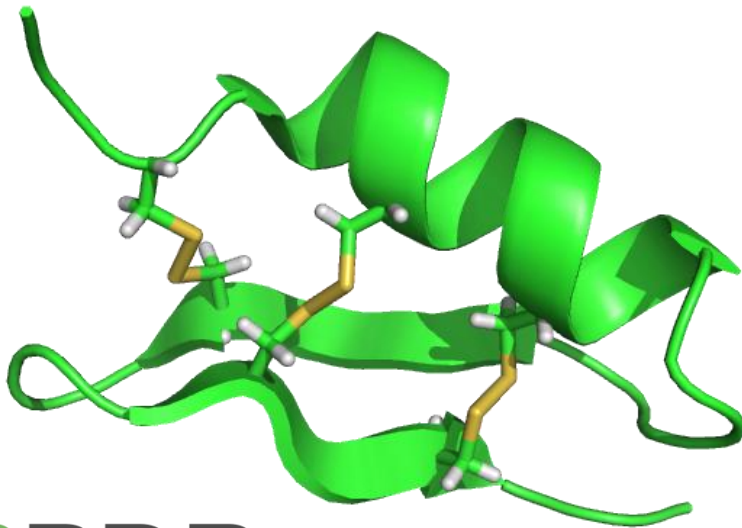
See MP4 file **RL1 - 1pju** for an animation
with audio description

All structures interlinked on PDBe webpages!



What holds a protein together - summary

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



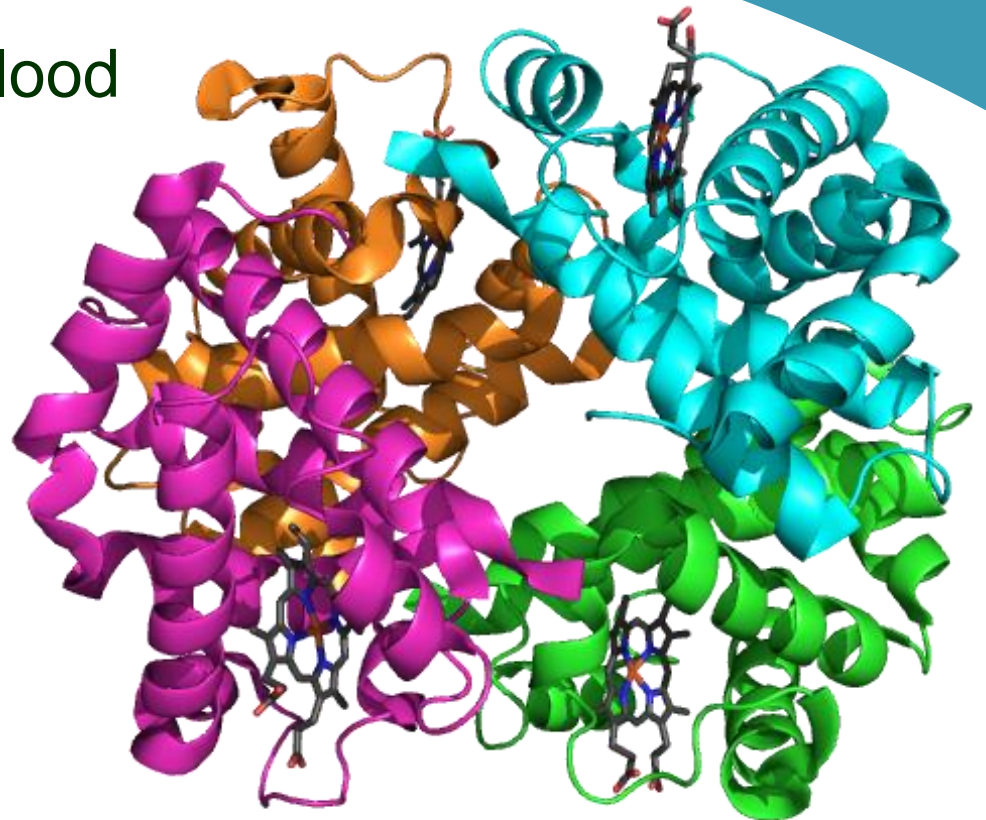
Specific examples of proteins #1

Haemoglobin

- carries oxygen in the blood
- only alpha helices

It also has

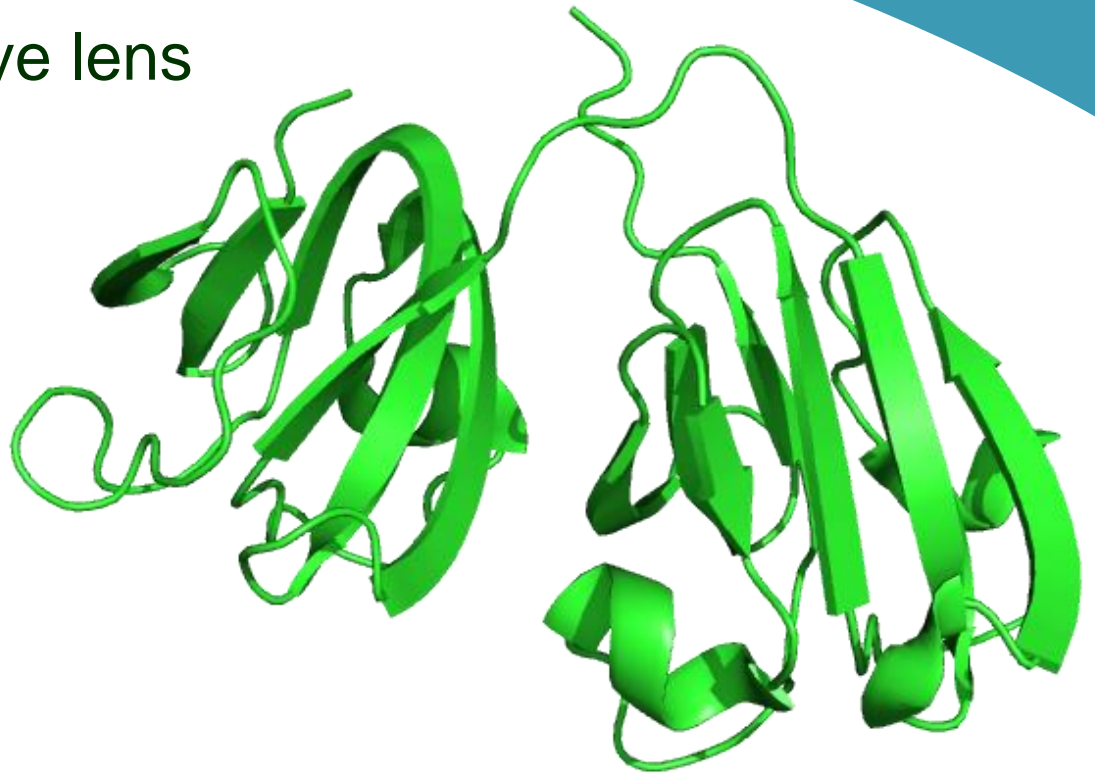
Quaternary structure
(not all proteins do!)



Specific examples of proteins #2

Crystallin

- bends light in your eye lens
- mostly beta sheets



Chemistry

Biochemistry

Session #4

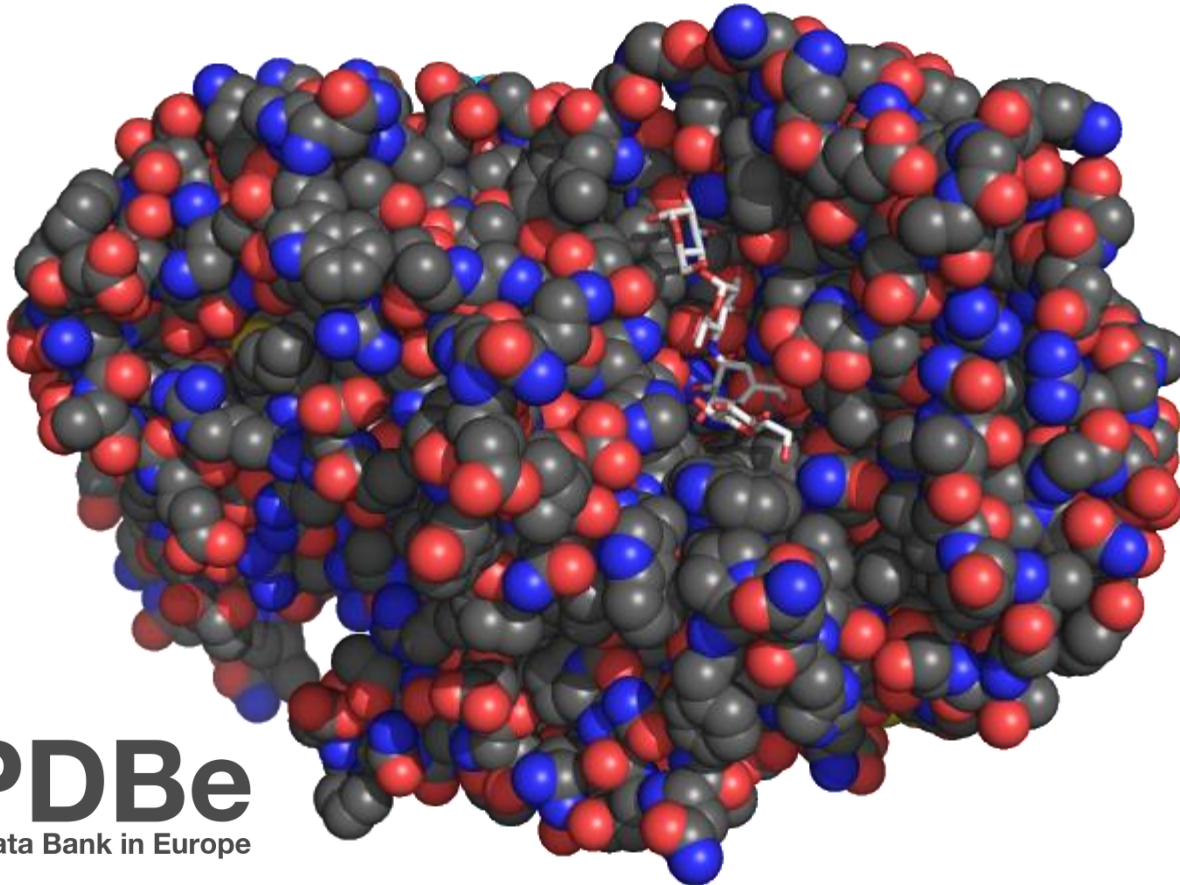
Enzymes

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! ☹️

Salivary Amylase

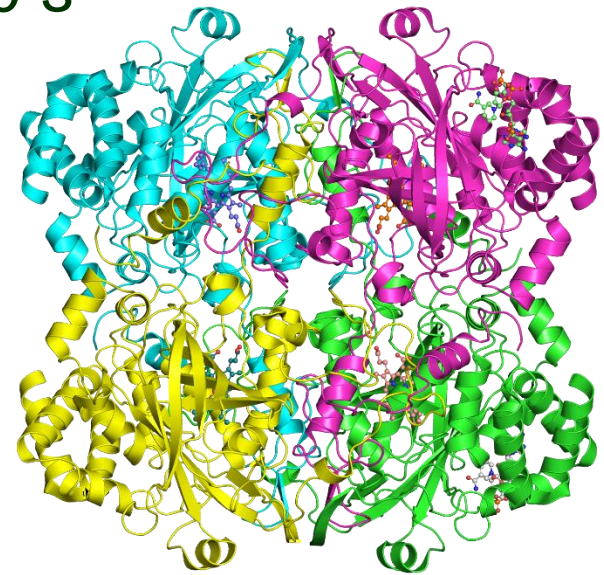
- 'chops up' starch to sugars in your mouth
- has both alpha helices & beta sheets!



[PDBe.org/3dhp](https://pdbe.org/3dhp)

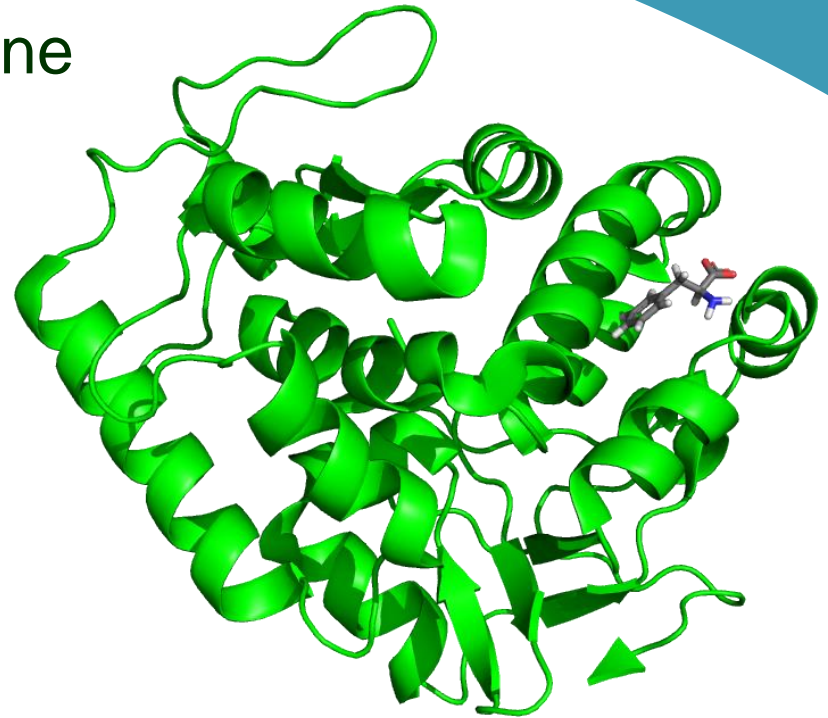
How fast do enzymes work?

- Slowest: RuBisCO - 3 or 4 per second
 - fixes CO₂ in plants
- Acetylcholine esterase - around 15,000 s⁻¹
 - inhibited by Novichok
- Fastest: catalase - up to 1 million s⁻¹
 - 2 H₂O₂ → 2 H₂O + O₂
- How fast do chemical catalysts work?

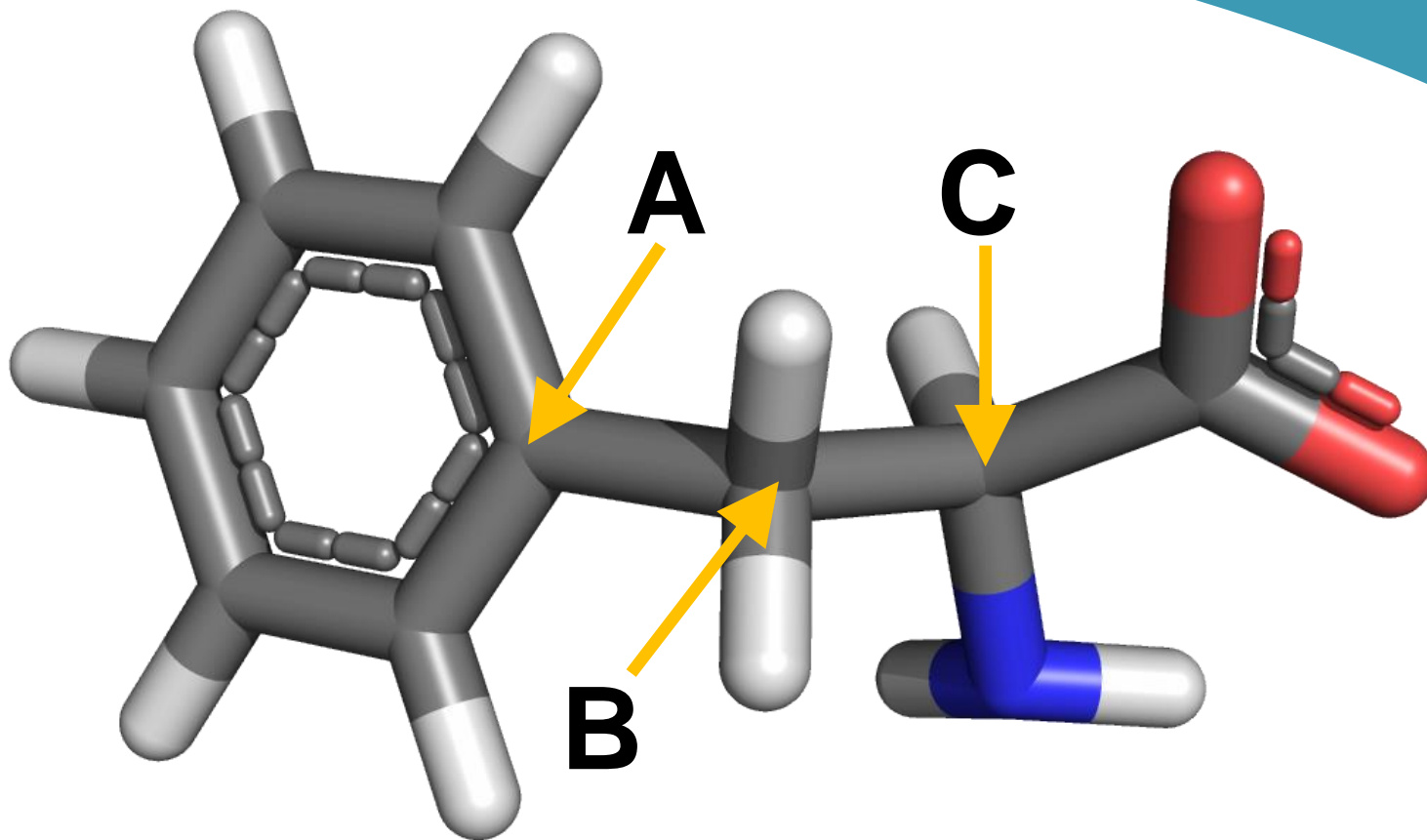


Stereospecificity of enzymes

- Phenylalanine hydroxylase
 - only recognises L-phenylalanine
- If enzyme doesn't work ->
 - Phenylketonuria



Where is the chiral centre?



Stereospecificity of enzymes

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

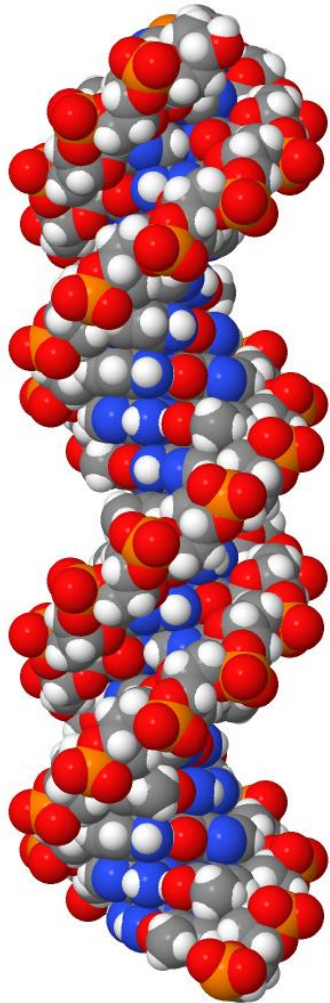
Chemistry

Biochemistry

Session #5

DNA

DNA - Summary

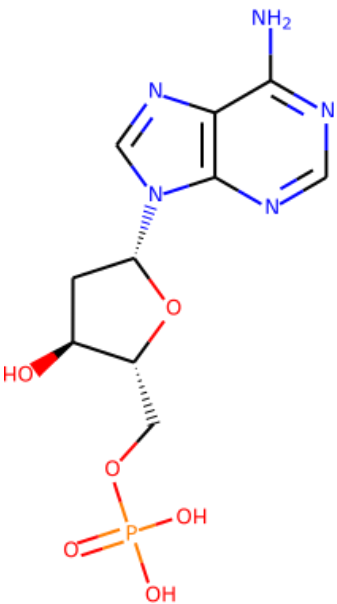


- Definition – NOT a protein! 😊
- Structure of repeat unit –
 - sugar, base, phosphate
- Double helix
 - H-bonding between base pairs

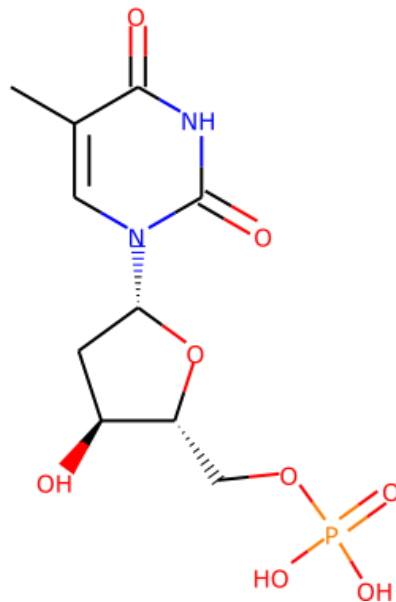
[PDBe.org/1saa](https://pdbe.org/1saa)

The building blocks of DNA

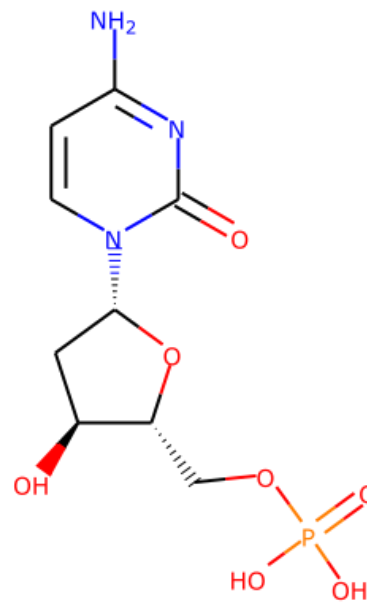
Adenine



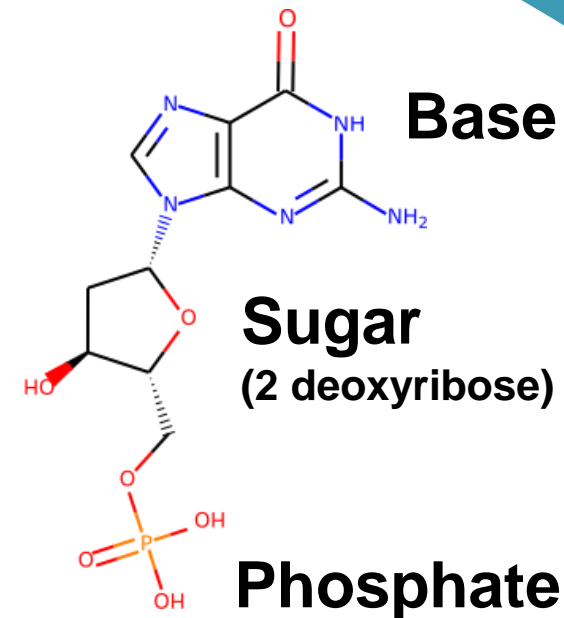
Thymine



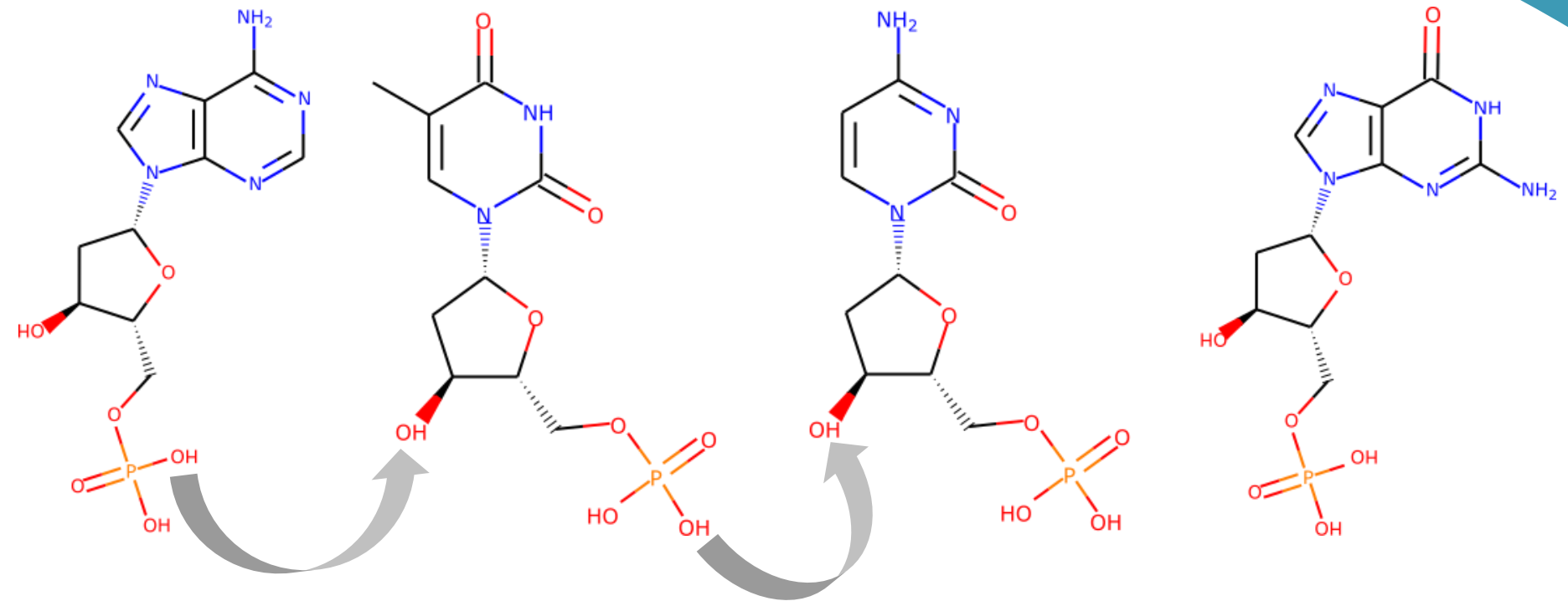
Cytosine



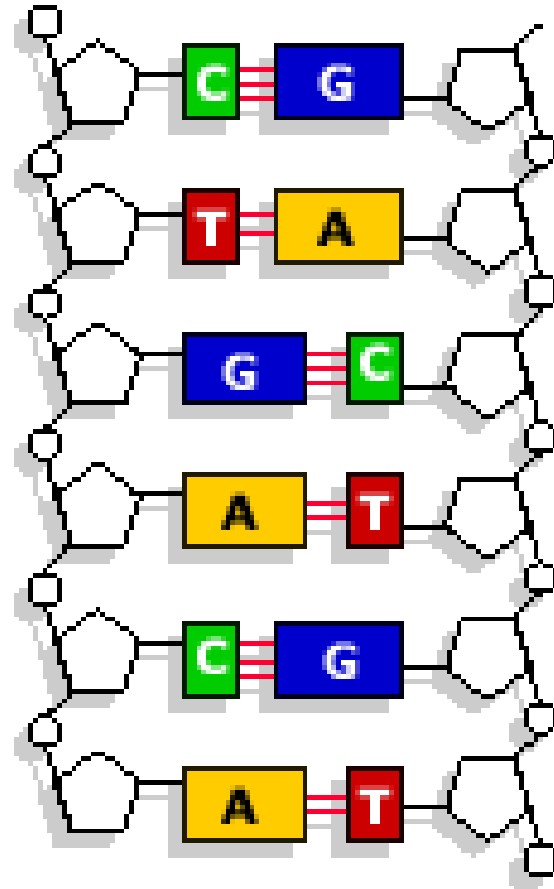
Guanine



Bases polymerise via phosphodiester bonds



Complementary strands

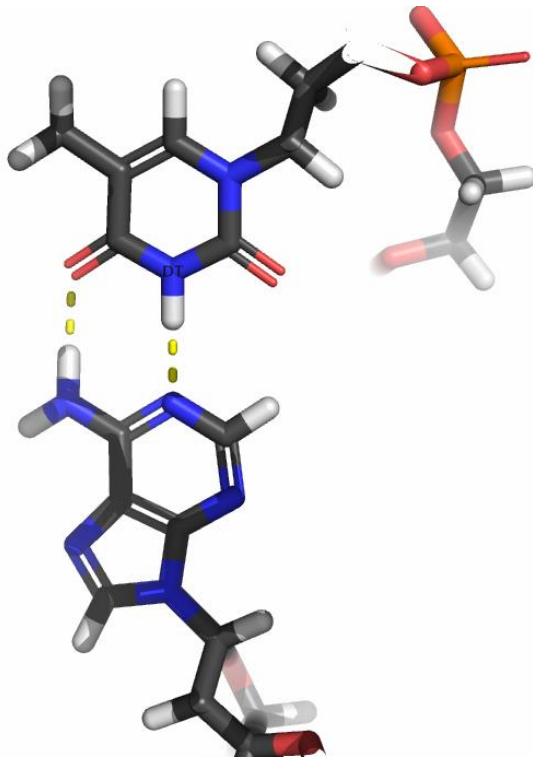


DNA structure

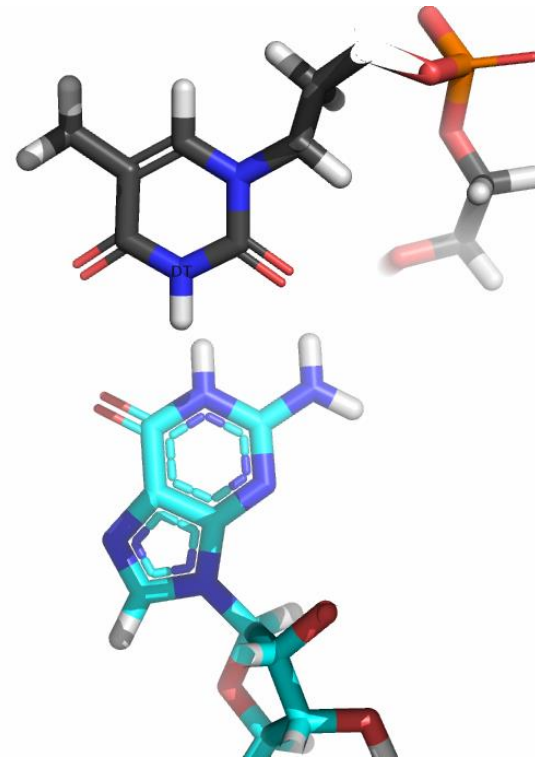
See MP4 file **RL3 - DNA** for an animation with audio description

Why other base pairs don't work.....

AT pair
- works



GT pair
- doesn't work



Chemistry

Biochemistry

Session #6

Drug Action

Drug Action - Summary

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

- e.g. Ibuprofen



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

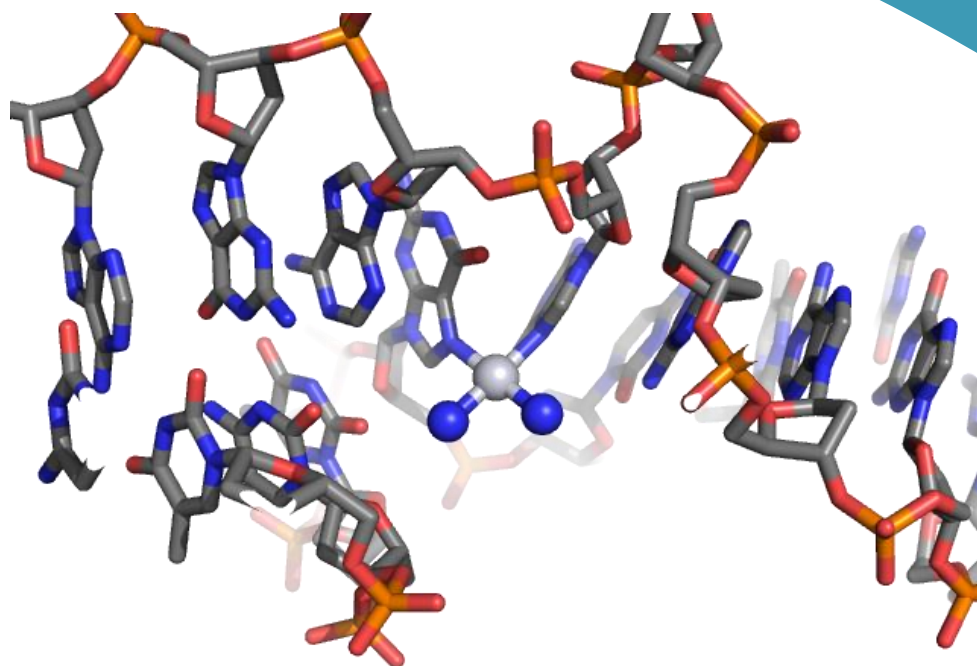
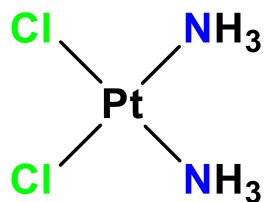
Covalently bonds 2 G bases together
(via substitution of the two Cl ligands)

Makes it impossible for
DNA to replicate

Anti-cancer drug

Side-effects?

**See theory
sheet TC5 &
video VC2**

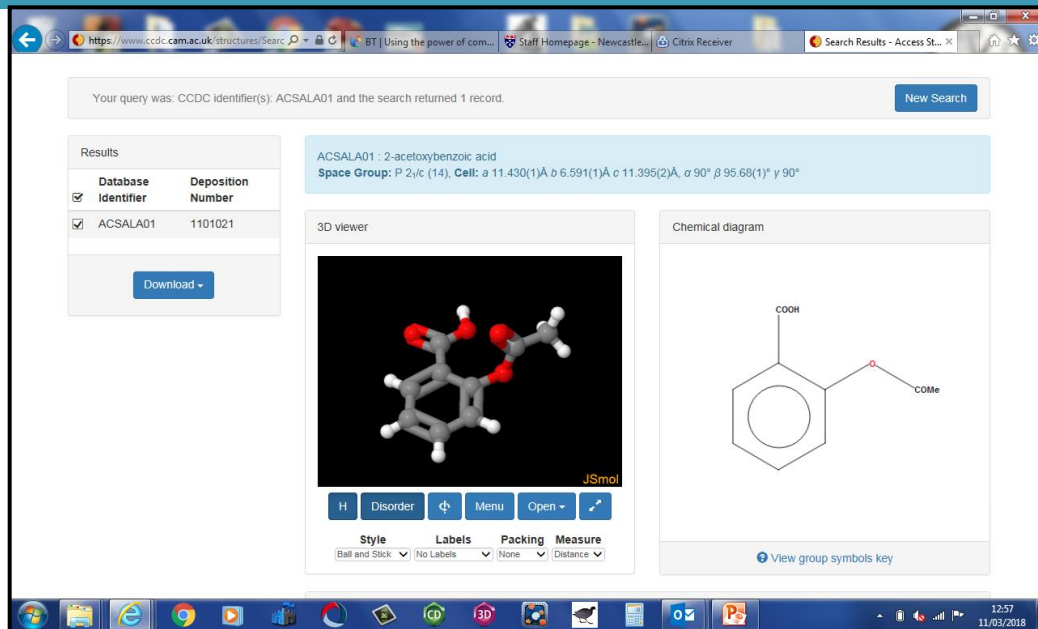


Learning Resources - Crystallography

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!



The screenshot shows a web browser window displaying the CSD Access Structures search results for ACSALA01. The search query is "CCDC Identifier(s): ACSALA01" and it returned 1 record. The results table shows the Database Identifier as ACSALA01 and the Deposition Number as 1101021. A "Download" button is visible. The 3D viewer shows a ball-and-stick model of the molecule, and the chemical diagram shows the 2D structure of 2-acetoxybenzoic acid. The chemical diagram labels the COOH group and the COMe group. The 3D viewer includes controls for "H", "Disorder", "Menu", "Open", "Style" (Ball and Stick), "Labels" (No Labels), "Packing" (None), and "Measure" (Distance). The chemical diagram includes a "View group symbols key" link.

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>

Thanks - PDBe Learning Resources Project

EMBL-EBI/PDBe:

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- Dr Ian Hardcastle, Reader in Medicinal Chemistry
- Adam Stubbs; Summer UG Research Placement student 2017 (currently doing PGCE)

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- 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

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!** 😊