

Introduction to Protein Structure with Chimera

EMBO Practical Course on Computational
analysis of protein-protein interactions:
From sequences to networks

28 September - 3 October 2014, UCT,
Cape Town, South Africa

Tuesday 30th September 2014

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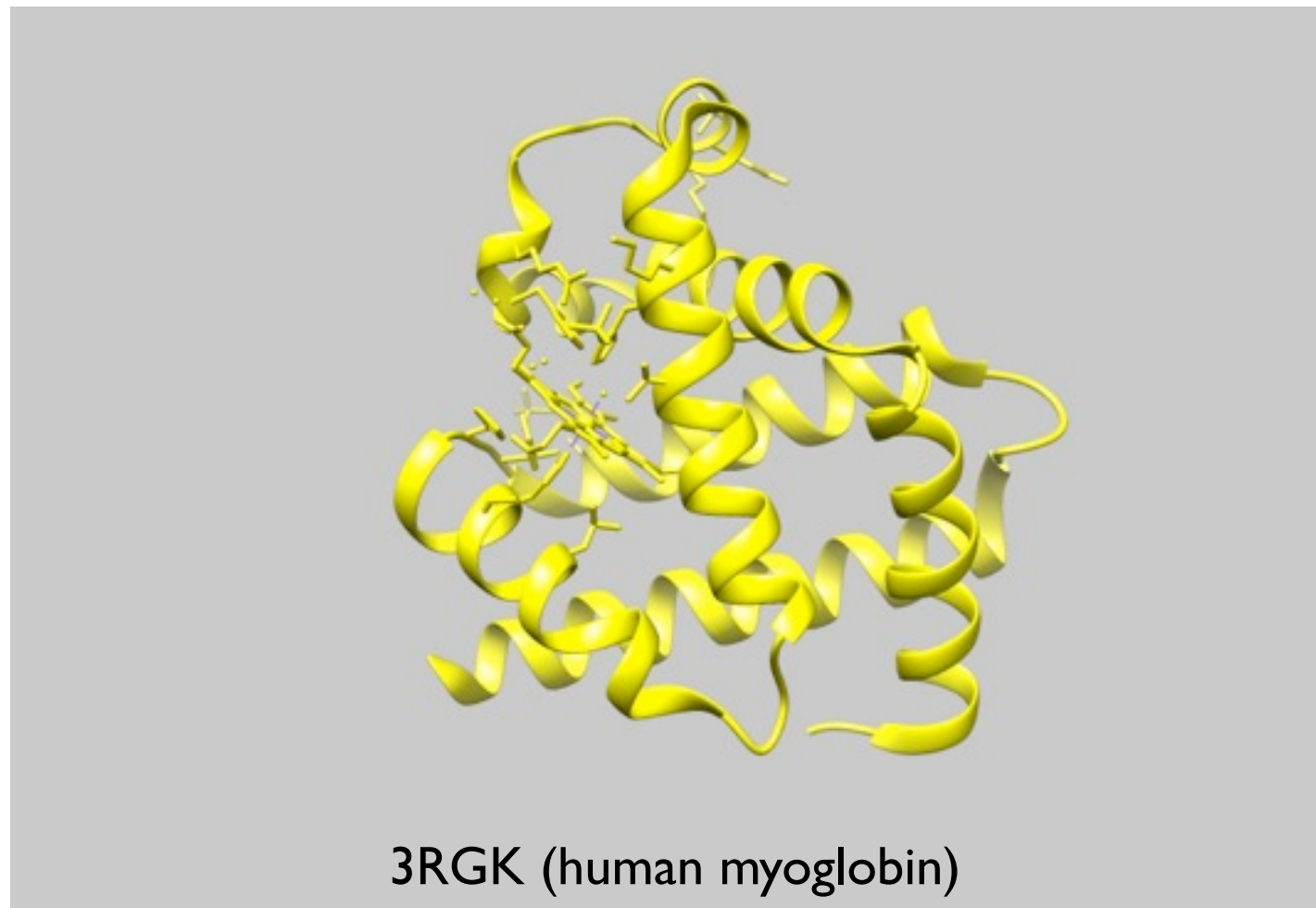
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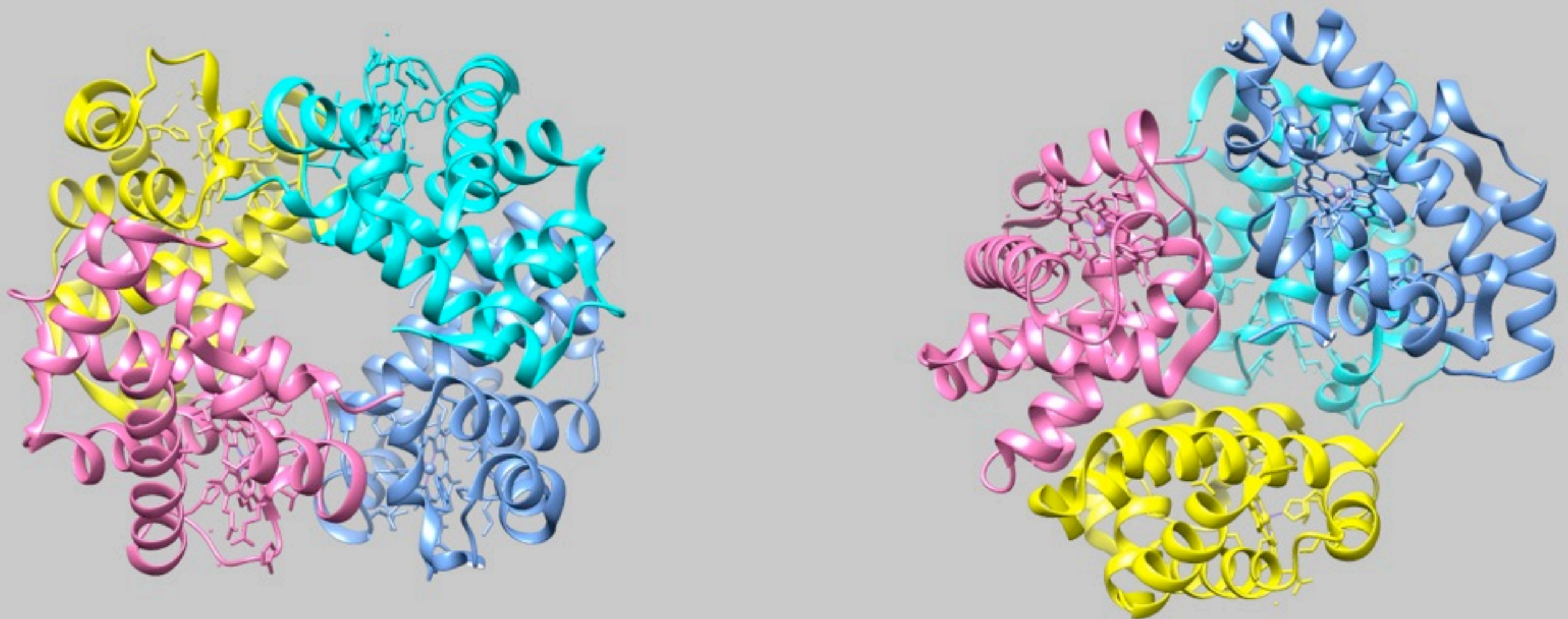
Protein Structure Basics

all proteins consist of one (or more) polypeptide chains



Protein Structure Basics

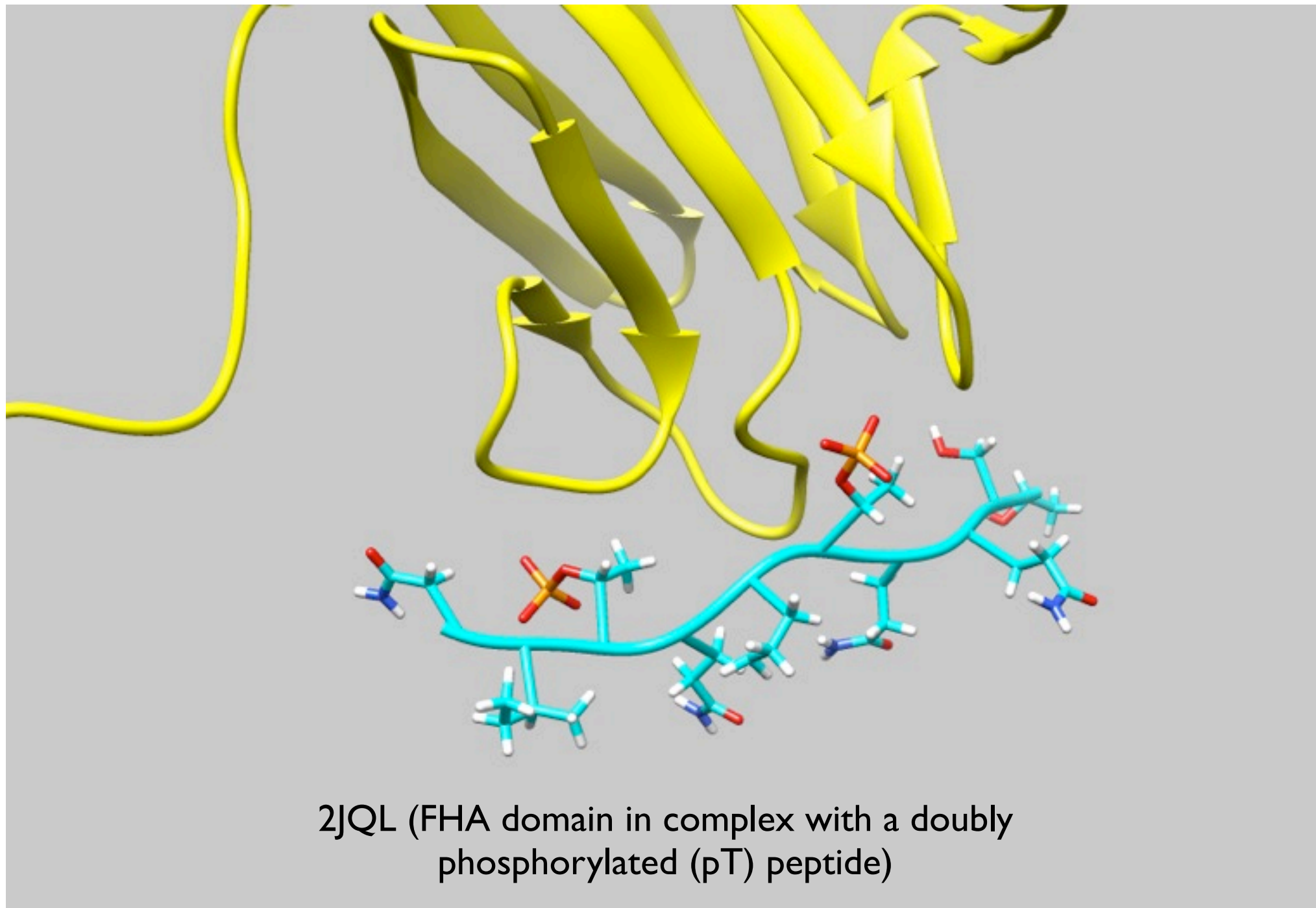
all proteins consist of one (or more) polypeptide chains



3VRE (wooly mammoth haemoglobin)

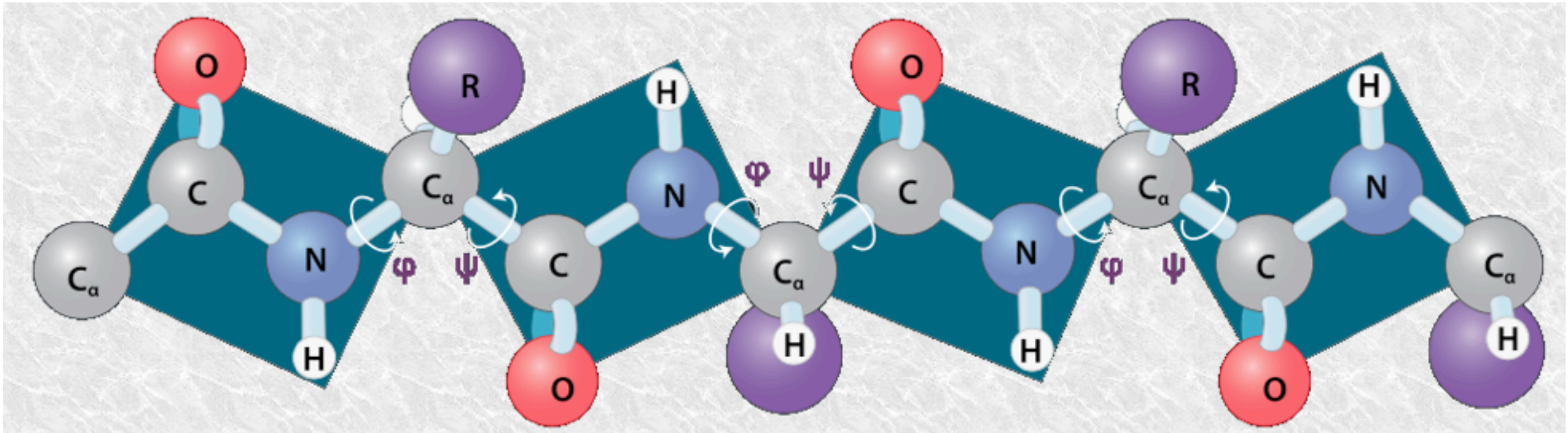
Protein Structure Basics

some proteins are post-translationally chemically modified



Protein Structure Basics

- peptide units are planar
- peptide backbone C_α carbon bound to backbone C and N atoms by bonds that can rotate (φ and ψ angles)



WikiMedia commons, attributed to Alejandro Porto

<http://upload.wikimedia.org/wikipedia/commons/3/3d/Enlace-peptidico-caracter-planar.png>

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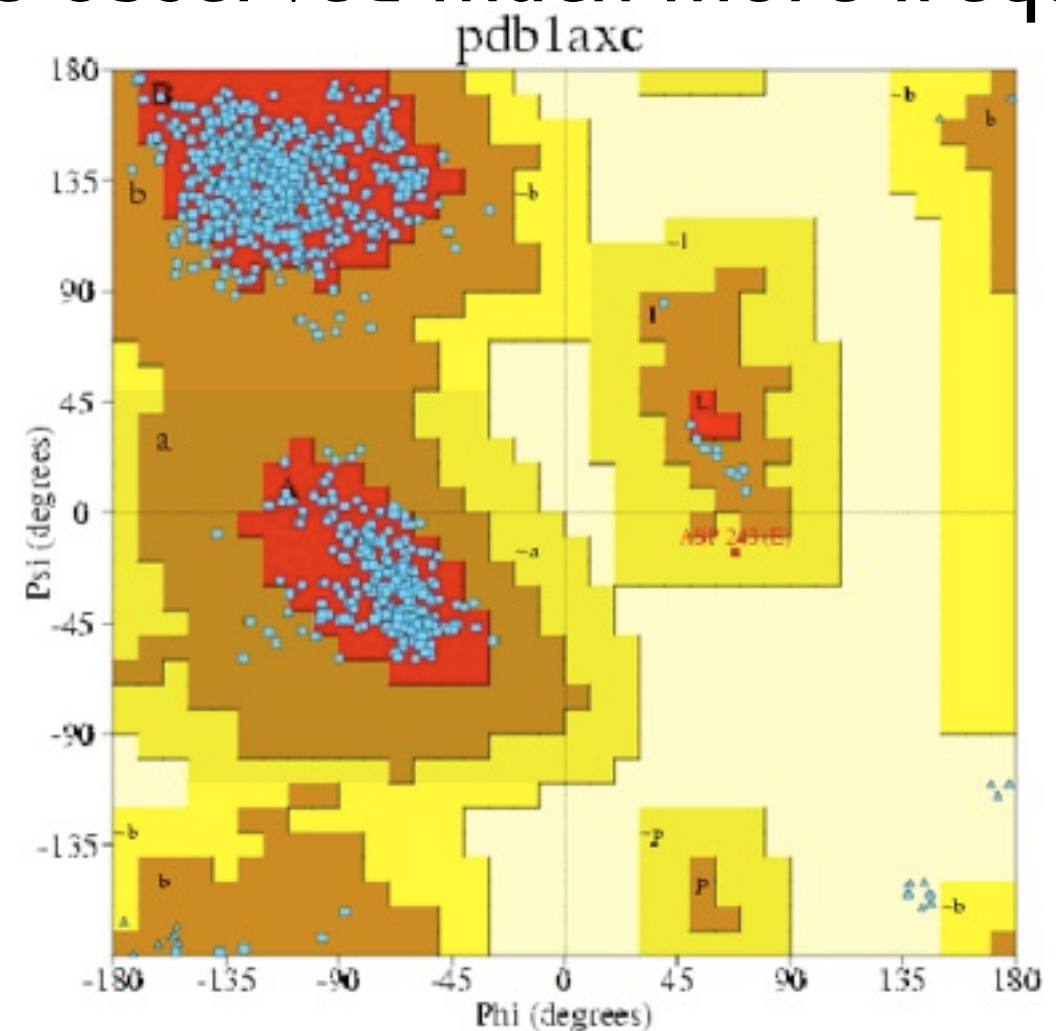
Protein Structure Basics

de novo prediction of 3D protein structure (even just the peptide backbone) is extremely difficult to do accurately, not least due to the huge number of different possible conformations of polypeptide chains

Protein Structure Basics

there are some commonly-observed patterns in protein structures

- certain φ/ψ angle combinations are observed much more frequently than others (ramachandran plot)



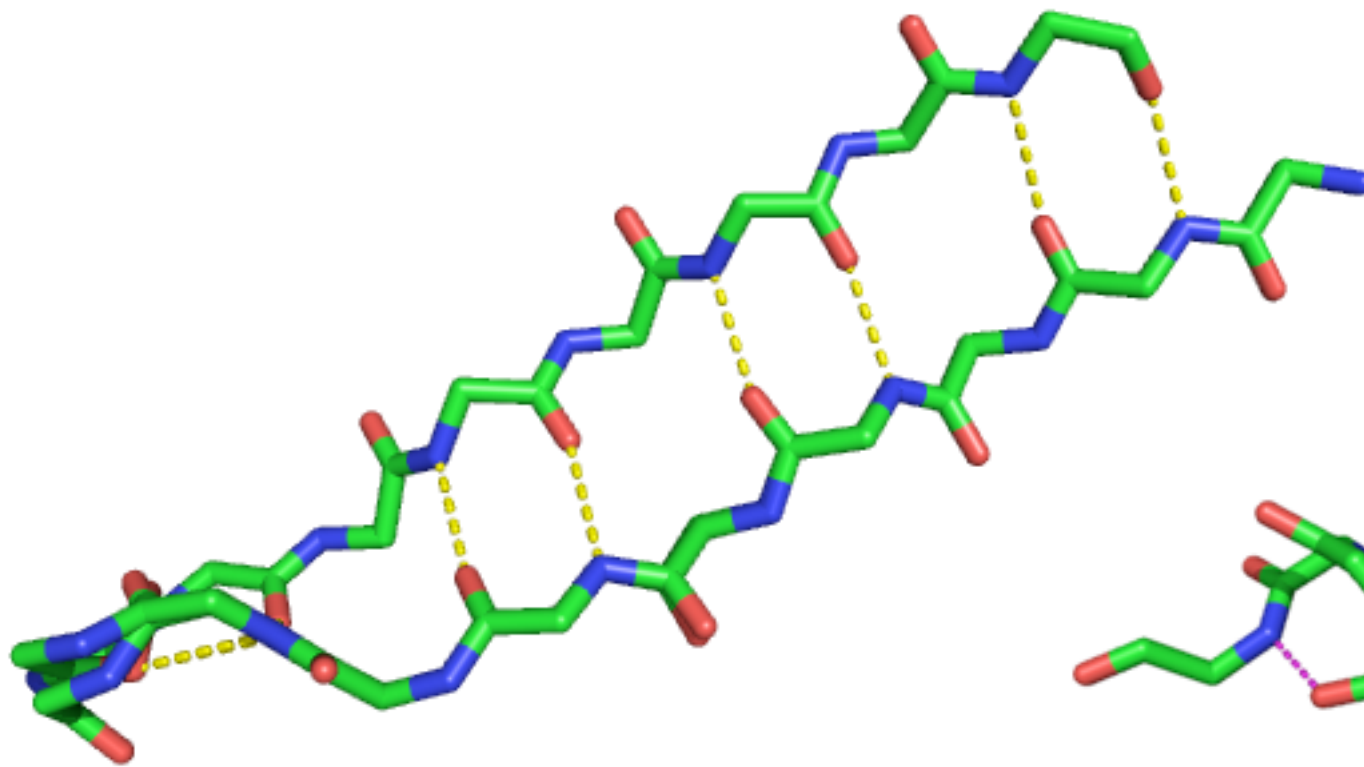
WikiMedia commons, attributed to Dcrrsr generated from human PCNA (PDB 1AXC) containing both β -sheets and α -helices http://en.wikipedia.org/wiki/File:1axc_PCNA_ProCheck_Rama.jpg

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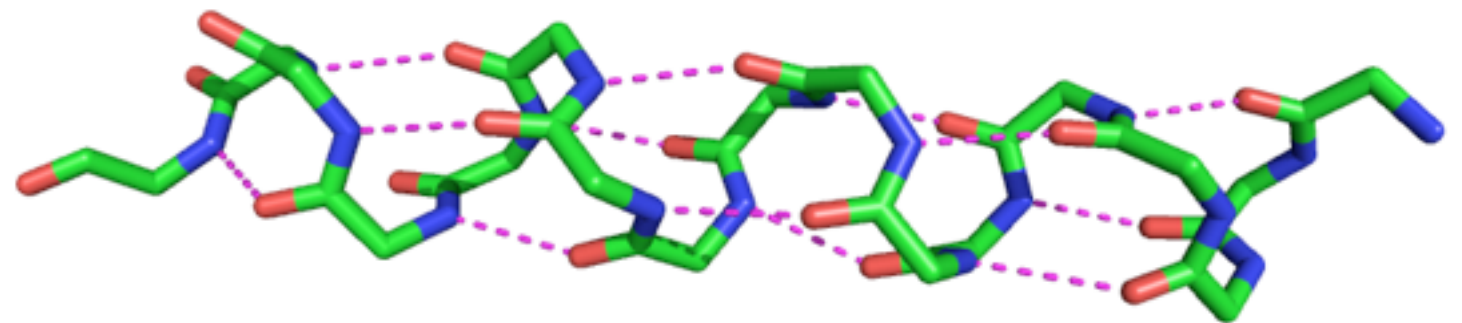
Protein Structure Basics

there are some commonly-observed patterns in protein structures

- secondary structure elements (helices and strands)



Strand from PDB 1V6P

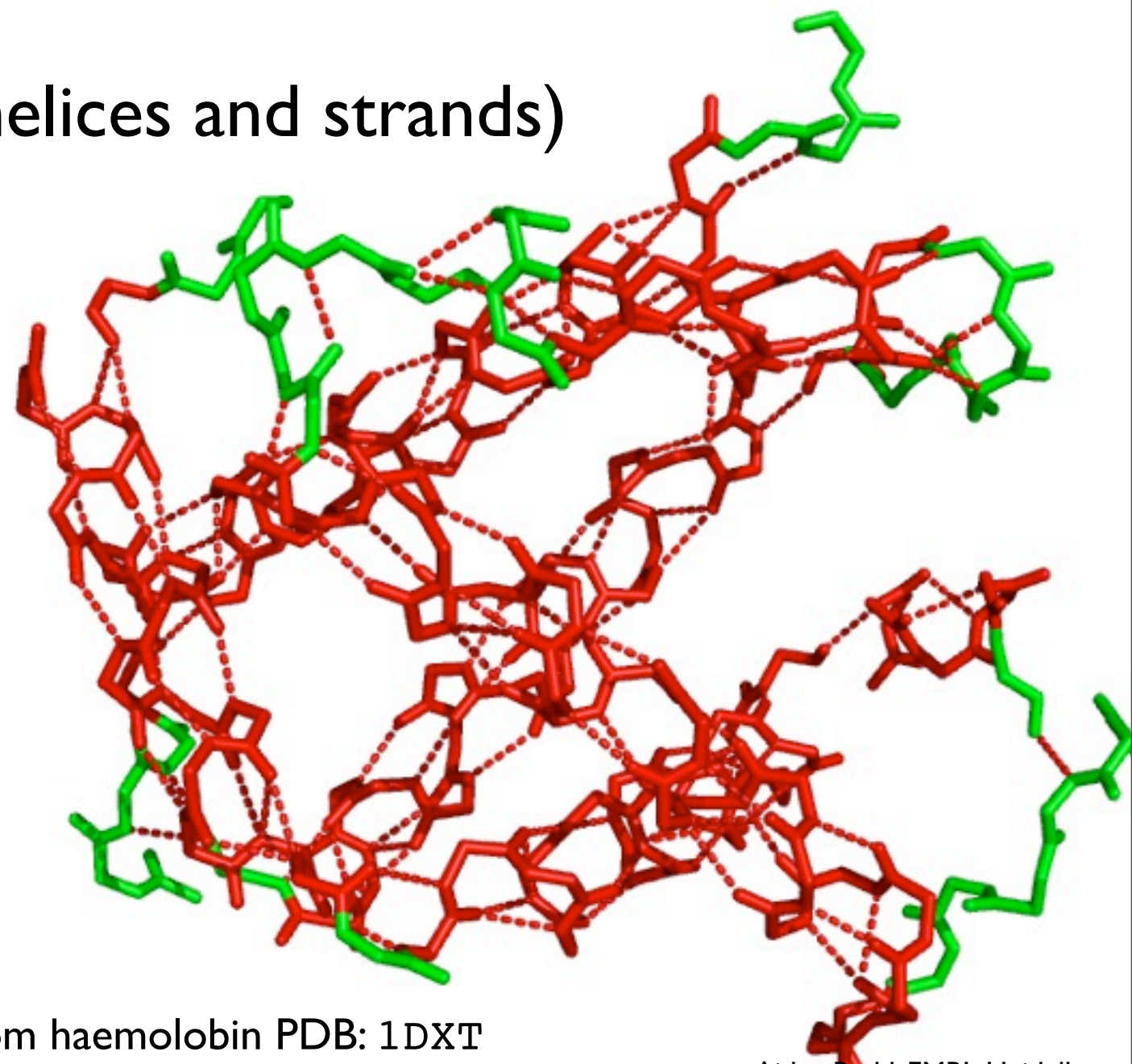


Helix from haemoglobin PDB: 1DXT

Protein Structure Basics

there are some commonly-observed patterns in protein structures

- secondary structure elements (helices and strands)



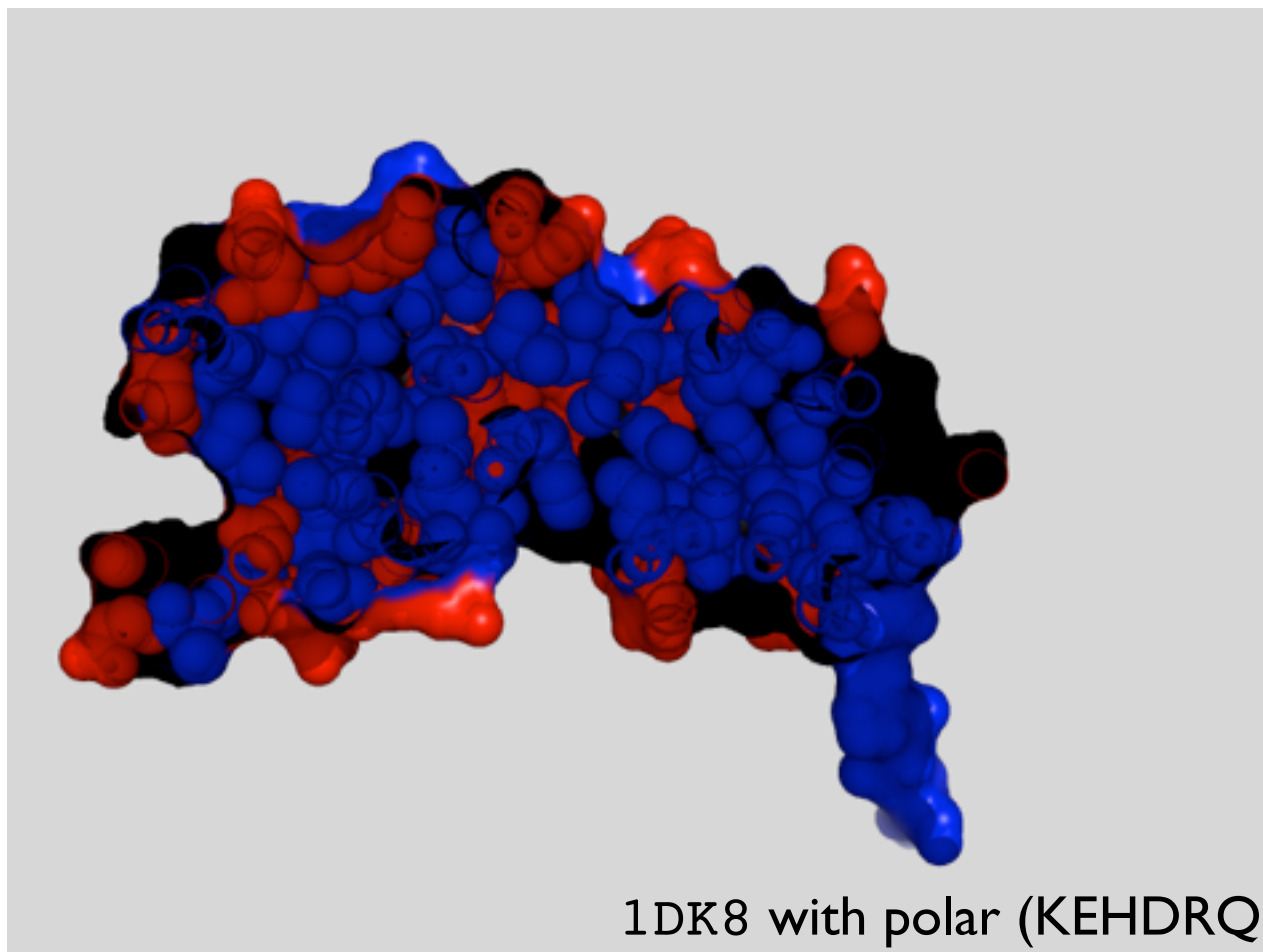
Peptide backbone H-bonds from haemoglobin PDB: 1DXT

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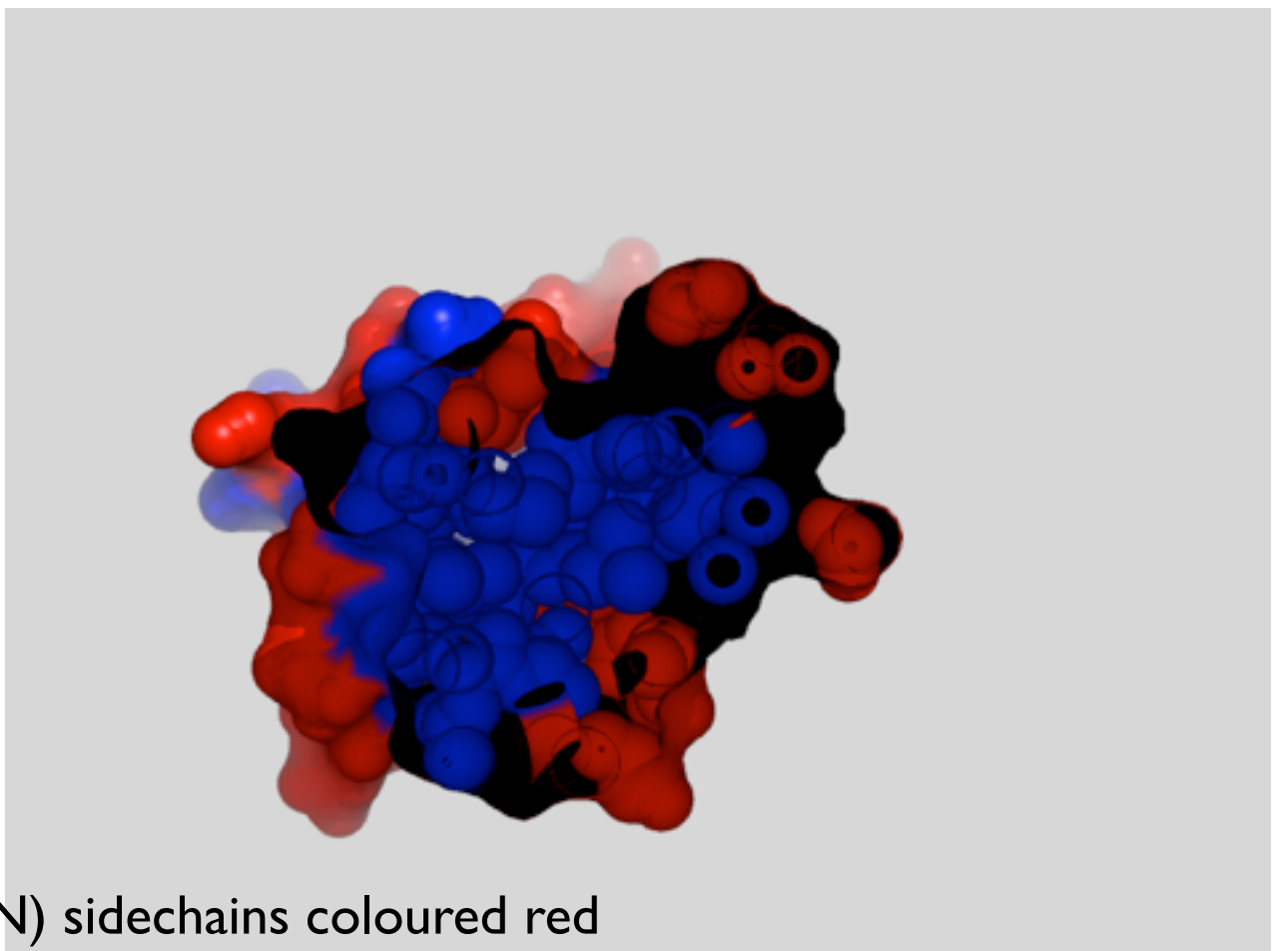
Protein Structure Basics

there are some commonly-observed patterns in protein structures

- buried sidechains aqueous proteins are almost all non-polar; exclusion of water from protein cores is a strong driver of folding



1DK8 with polar (KEHDRQN) sidechains coloured red



Protein Structure Basics

proteins are dynamic not rigid/static
- remember Natasha's videos!



Cytochrome C, wikimedia commons, By Richard Wheeler (Zephyris) 2006.
https://commons.wikimedia.org/wiki/File:Protein_Dynamics_Cytochrome_C_2NEW_smaller.gif

PDB files describe models of the 3D structure of biological macromolecules, typically locations of atoms of polypeptide chains

ATOM	153	CD2	HIS	A	20	-3.794	29.136	-14.141	1.00	46.06	C
ATOM	154	CE1	HIS	A	20	-3.858	28.728	-16.297	1.00	47.85	C
ATOM	155	NE2	HIS	A	20	-3.557	29.647	-15.395	1.00	48.51	N
ATOM	156	N	ALA	A	21	-6.982	26.053	-10.725	1.00	40.49	N
ATOM	157	CA	ALA	A	21	-7.210	24.945	-9.774	1.00	39.81	C
ATOM	158	C	ALA	A	21	-8.255	23.937	-10.274	1.00	39.47	C
ATOM	159	O	ALA	A	21	-8.042	22.722	-10.221	1.00	39.52	O
ATOM	160	CB	ALA	A	21	-7.569	25.474	-8.385	1.00	39.47	C

3VRE (wooly mammoth haemoglobin)

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Protein Structure Basics

Important distinction between intrinsically structured (globular) & intrinsically unstructured/disordered proteins



1DEV **SARA** (intrinsically disordered) binding via induced fit to **SMAD** (globular)

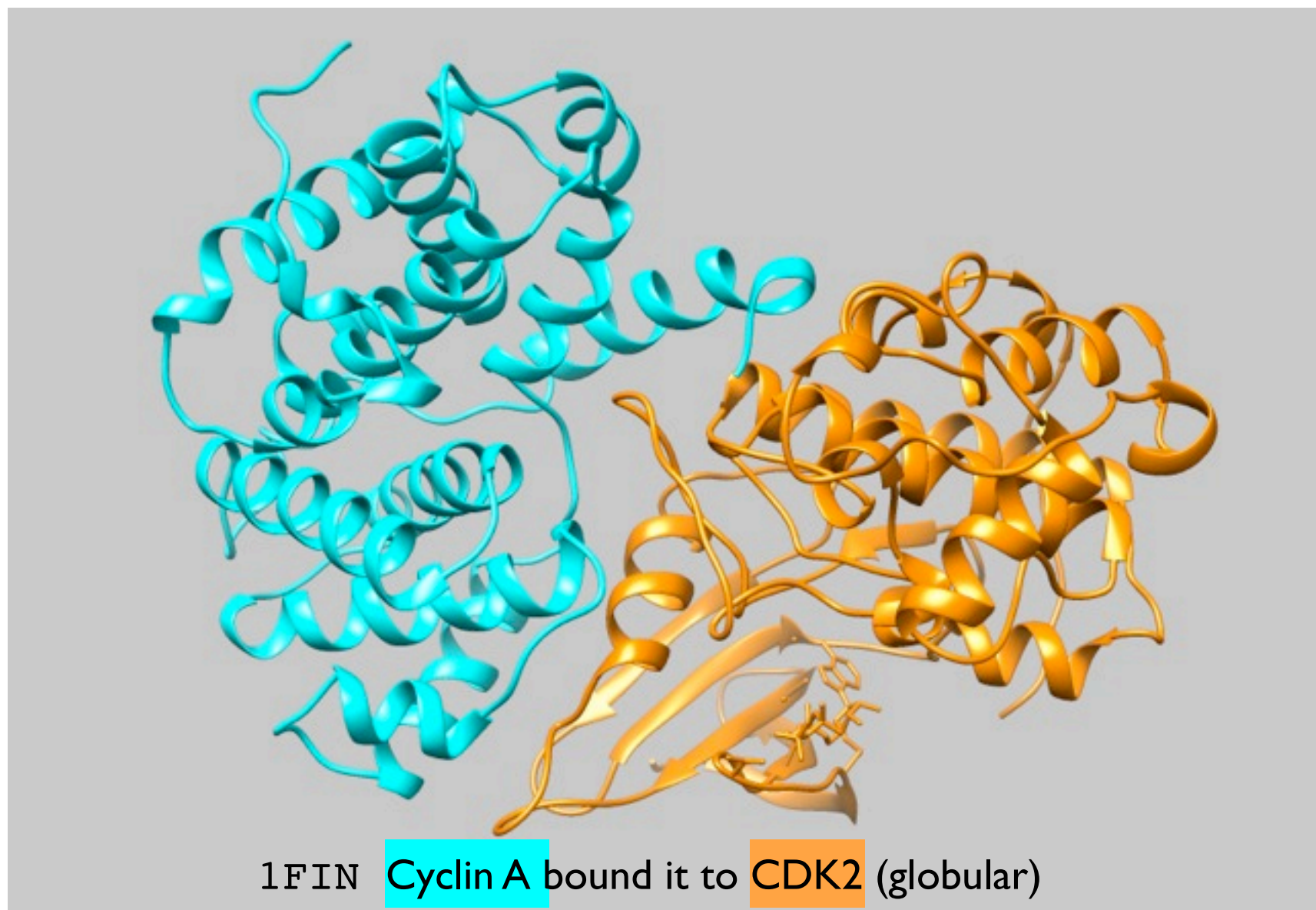
Protein Structure Basics

look through the slides so far with your neighbour

- decide if you agree with/understand the statements
- can you think of exceptions to the statements?
- are there words/concepts that are unclear in them?
- if you do have questions/problems, try and solve them together, or ask a trainer for help
- any unresolved questions/problems, share with everyone after your discussions

Linking Protein Structure to PPIs

- Analysing PPI 3D structures helps predict residues/regions important for the interaction



Linking Protein Structure to PPIs

- Analysing PPI 3D structures helps predict residues/ regions important for the interaction
- these are good candidates for residues that, if changed, would disrupt the interaction
 - useful for guiding experiments
 - more specifically, for example, useful for interpreting effects of mutations e.g. in genetic disease

Linking Protein Structure to PPIs

- thus: examining and analysing PPI 3D structures can help build more accurate predictive models of the system
- Chimera is a good **free** tool for such analyses
- Scooter will now teach an introduction to molecular visualisation using Chimera