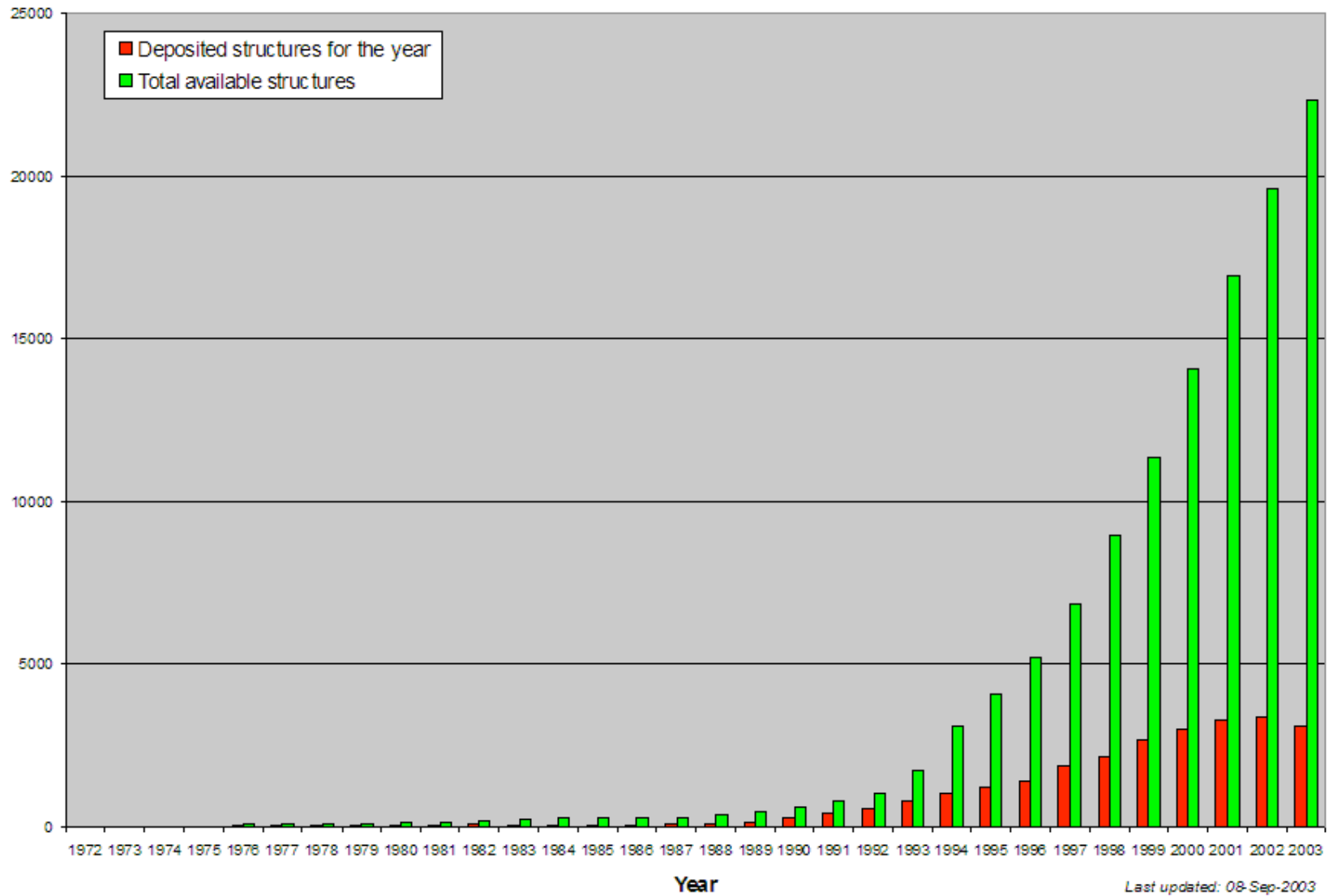
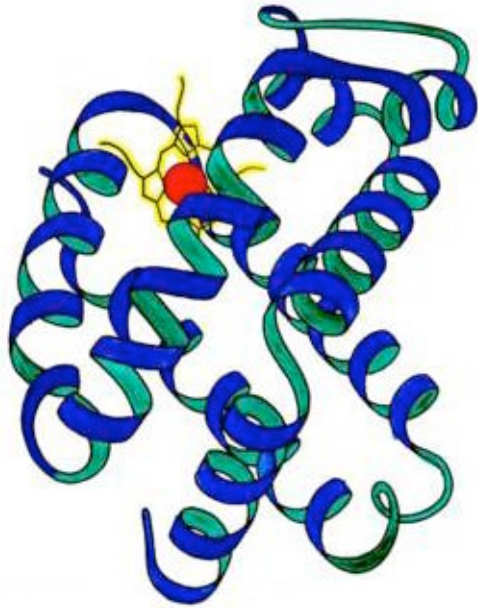


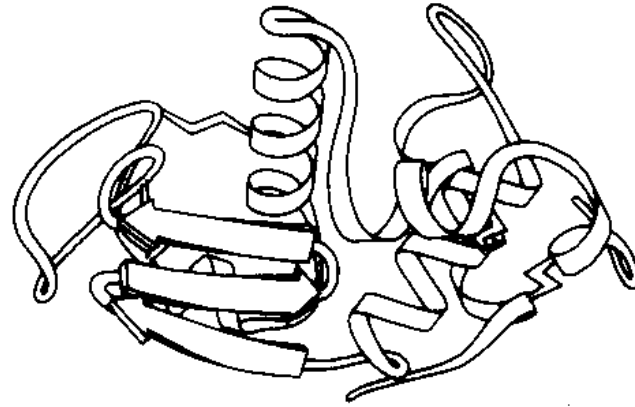
Protein Data Bank Structure (www.rcsb.org)



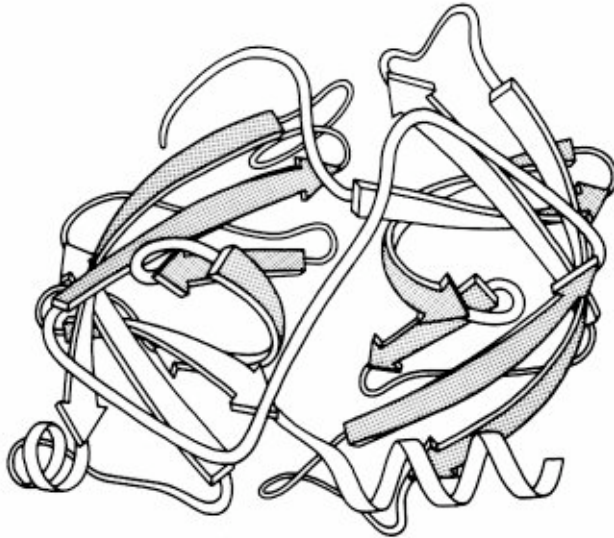
Early Structures



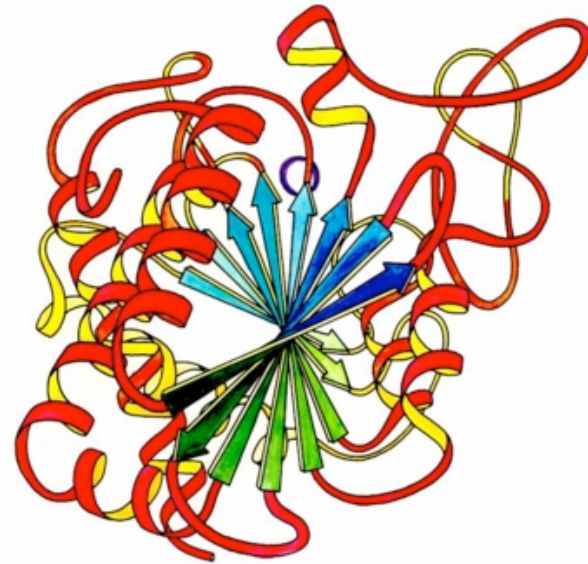
myoglobin



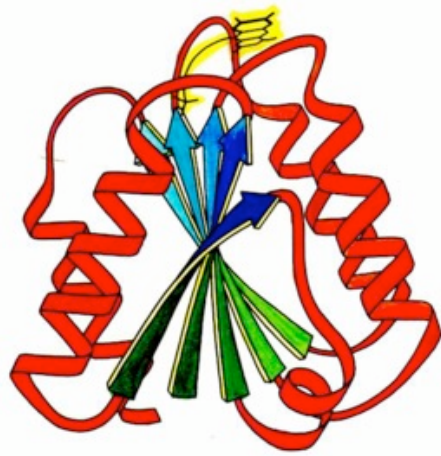
lysozyme



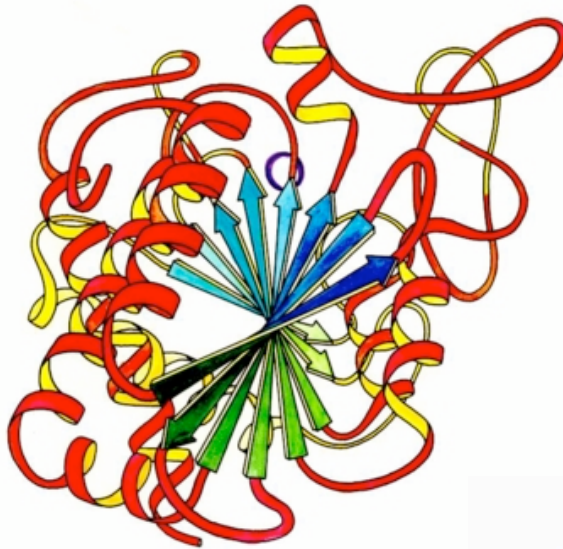
Serine protease



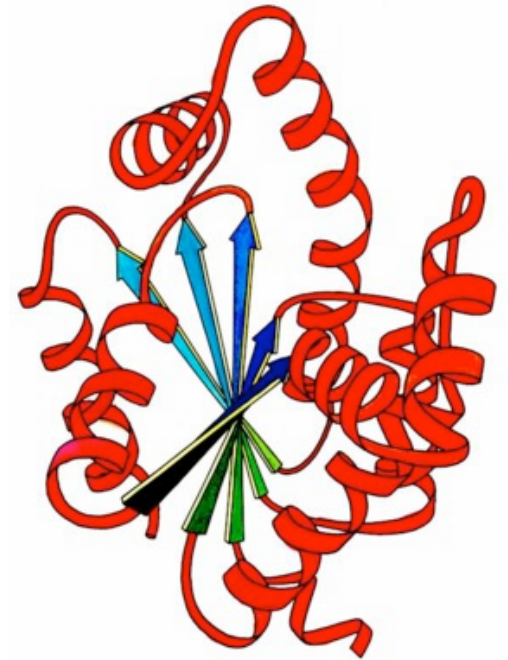
Carboxypeptidase



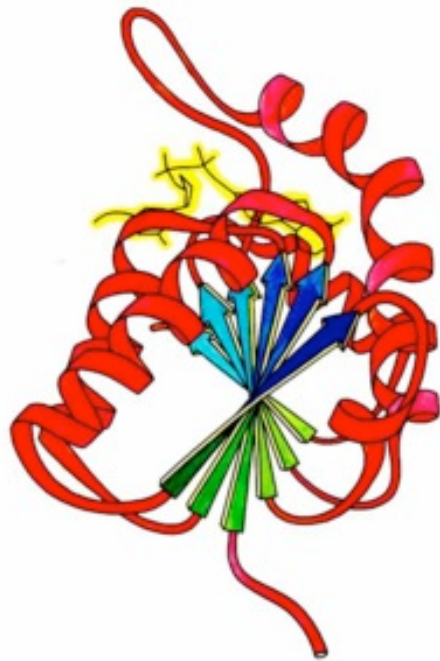
Flavodoxin



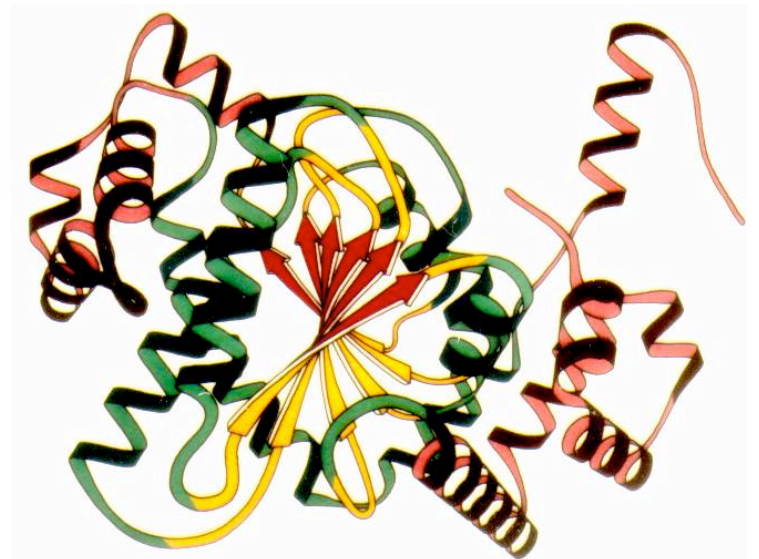
Carboxypeptidase

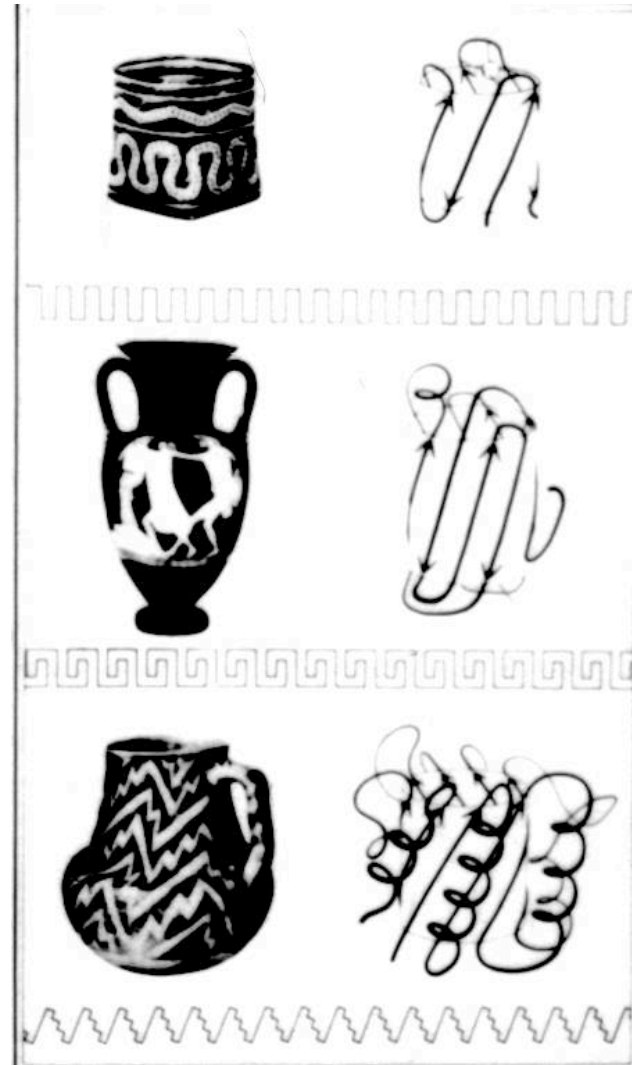
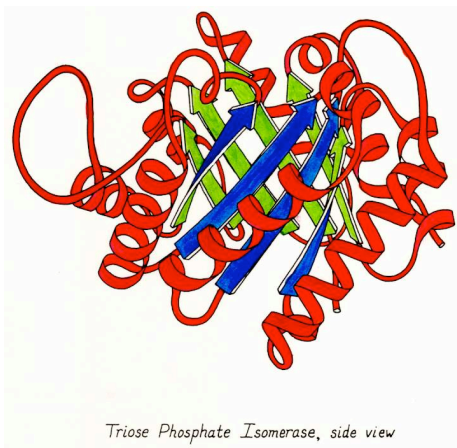
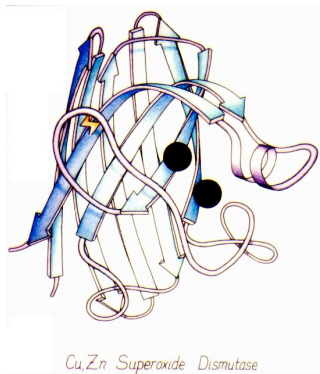
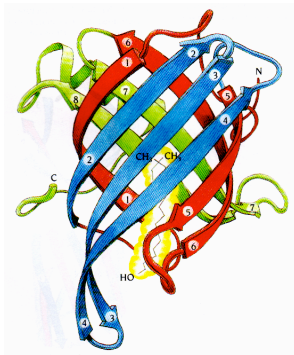


Adenylate Kinase



Lactate Dehydrogenase domain 1, end view

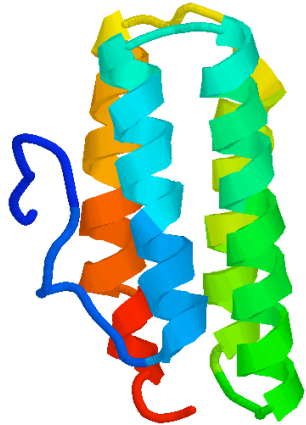




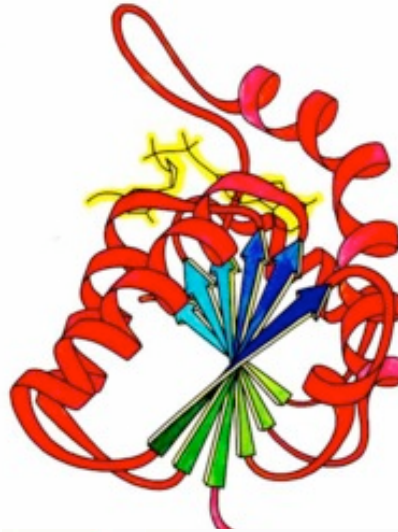
Proteins have recurring folding patterns.

The classical protein folding patterns

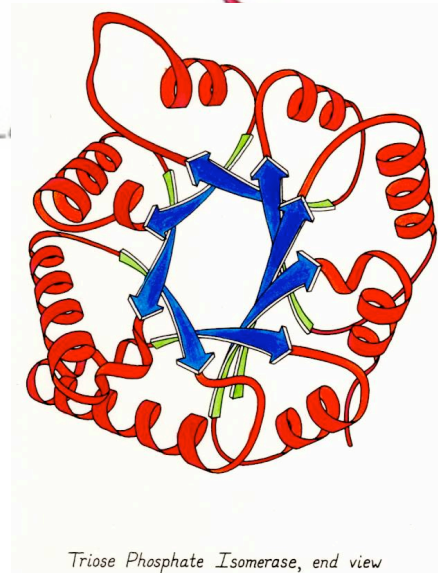
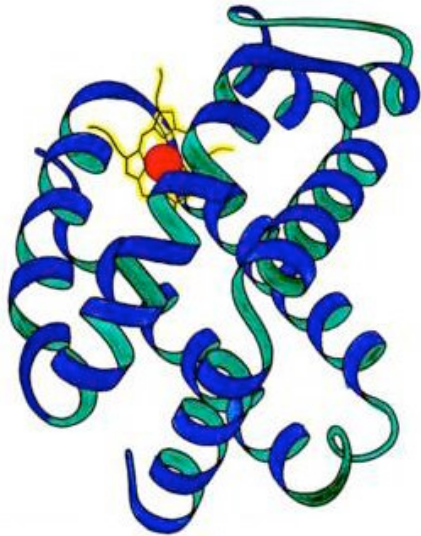
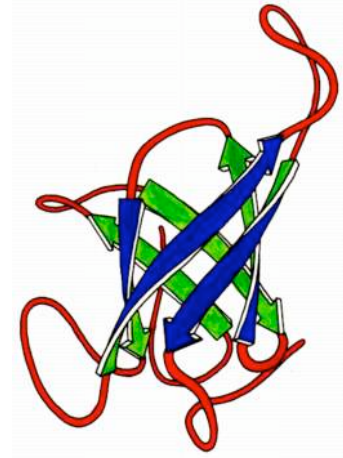
Antiparallel \square



Parallel \square/\square

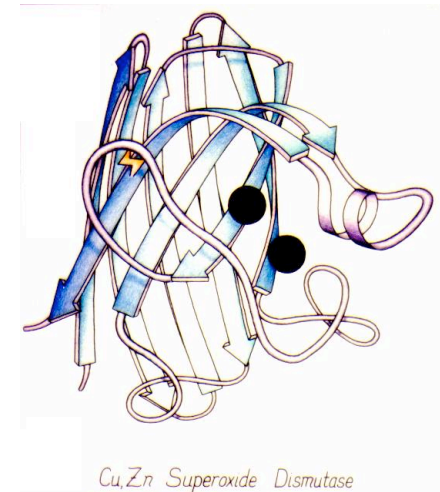


Antiparallel \square



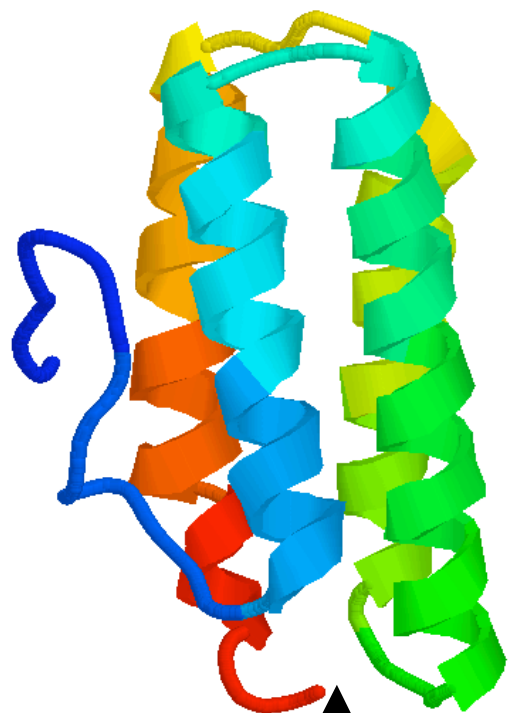
Triose Phosphate Isomerase, end view

(also, $\square+\square$)

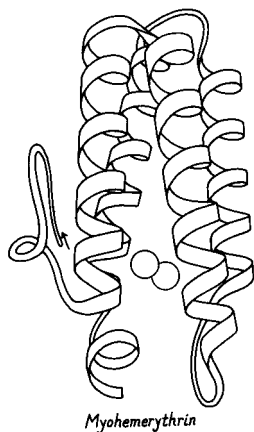


Cu,Zn Superoxide Dismutase

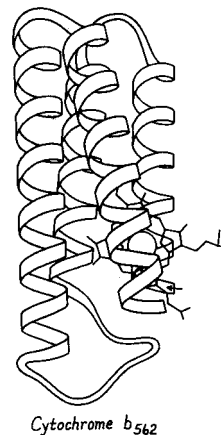
Antiparallel \square : 4-helix bundle



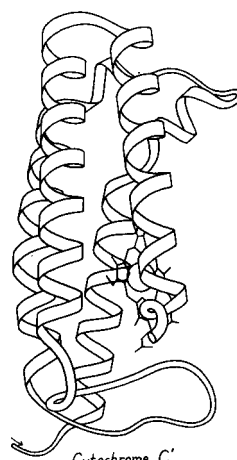
Hydrophobic interior



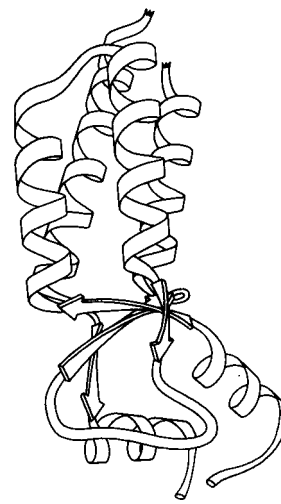
Myohemerythrin



Cytochrome b₅₆₂



Cytochrome C'



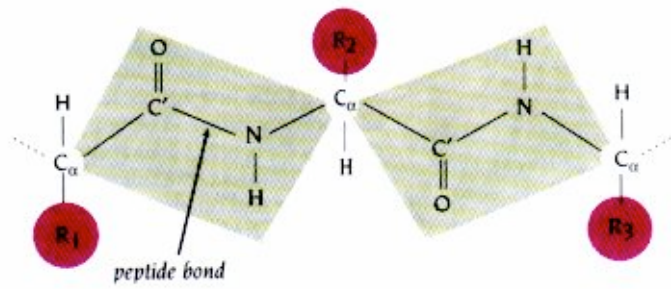
Tobacco Mosaic Virus Protein



Note the "packing angle" between helices

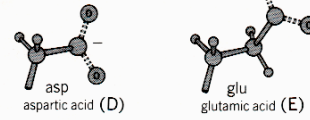
Amino acid side chains

Polypeptide backbone

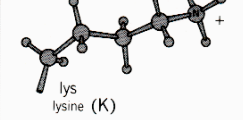


EXTERNAL

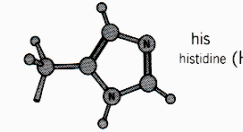
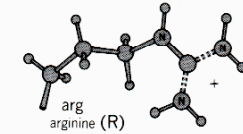
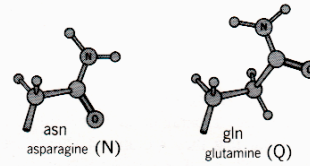
ACIDIC



BASIC

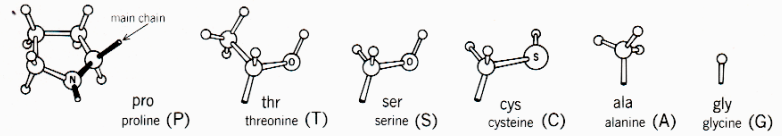


NEUTRAL

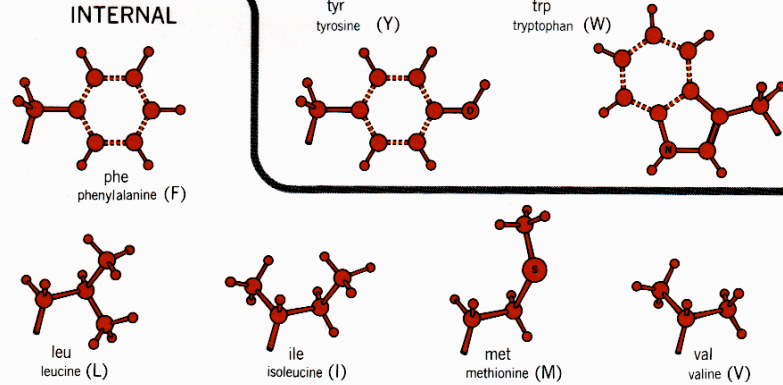


Asparagine and glutamine, although neutral, have very polar side chains that cause them to be generally on the outside of the molecule. In these side chain drawings, heavy double lines indicate double bonds, and dashed lines indicate resonance bonds intermediate between single and double bonds.

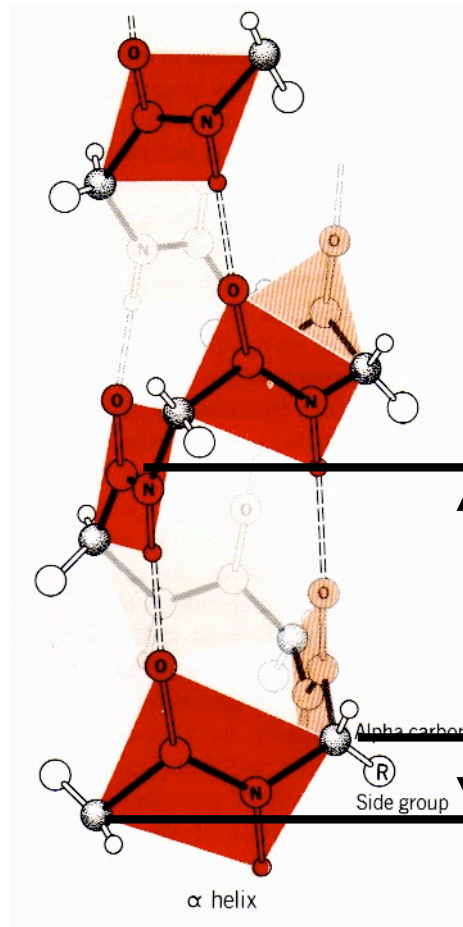
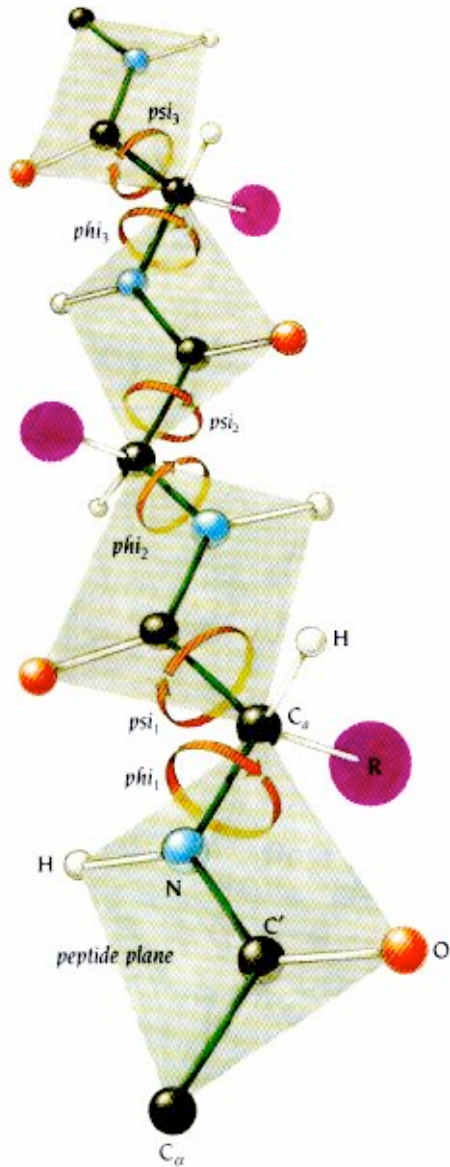
AMBIVALENT



INTERNAL



α-helix



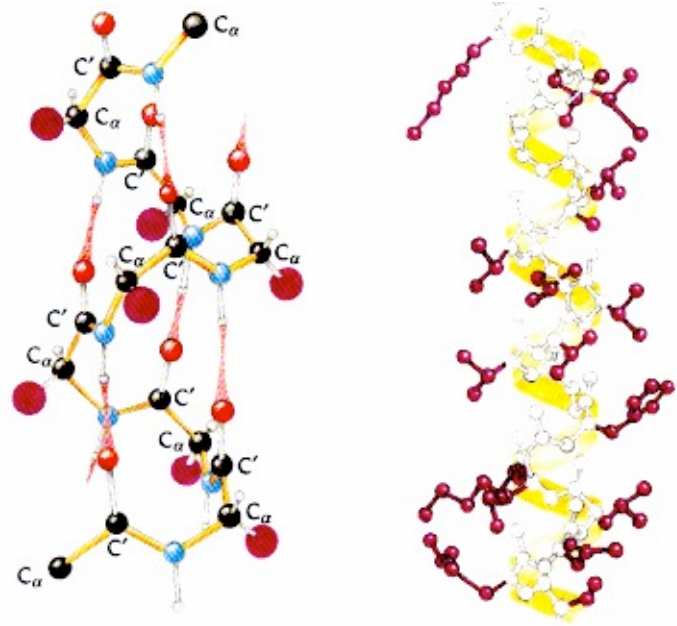
3.6 residues/turn

⇒ 5.4 Å helical repeat

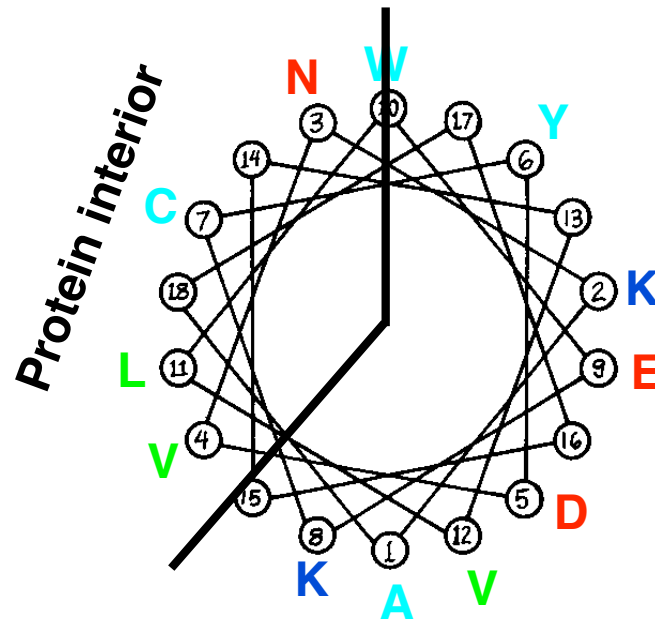
1.5 Å rise/residue

~10 Å packing diameter

α -helix side view

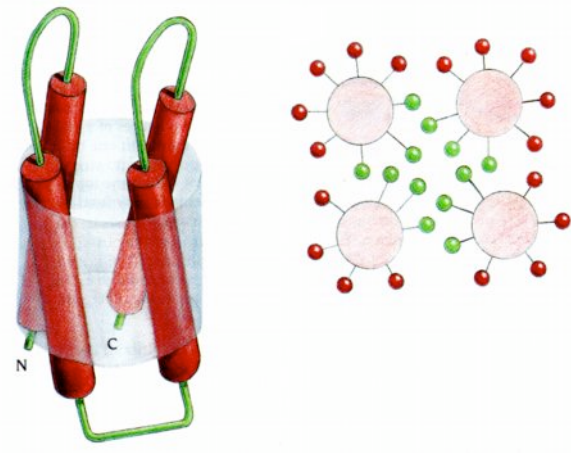


Top view: a residue every 100°
("helical wheel" construct)

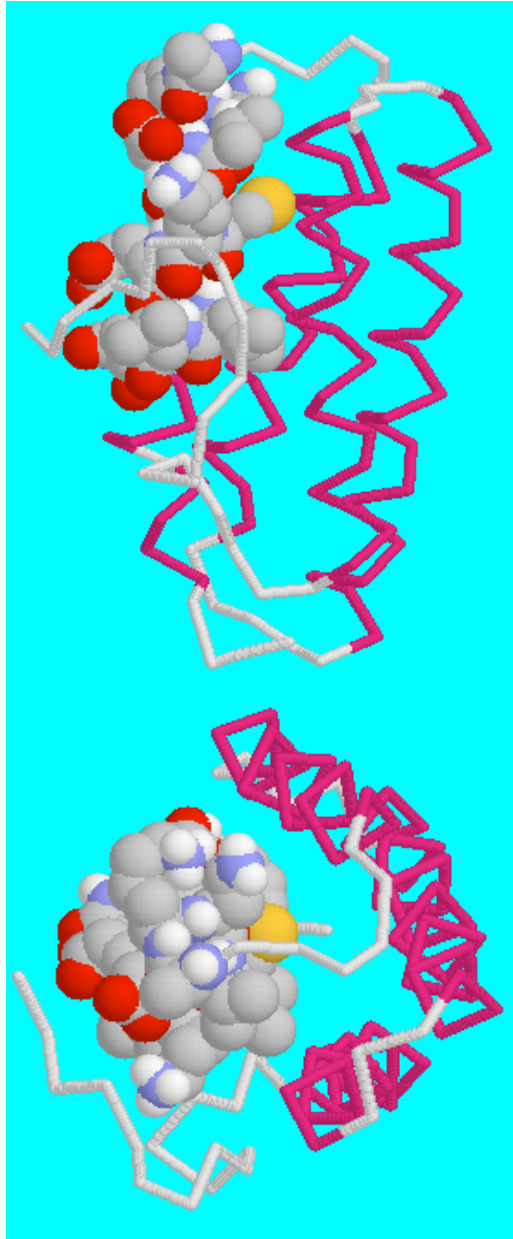


Sequence from one helix
of 4-helix bundle:

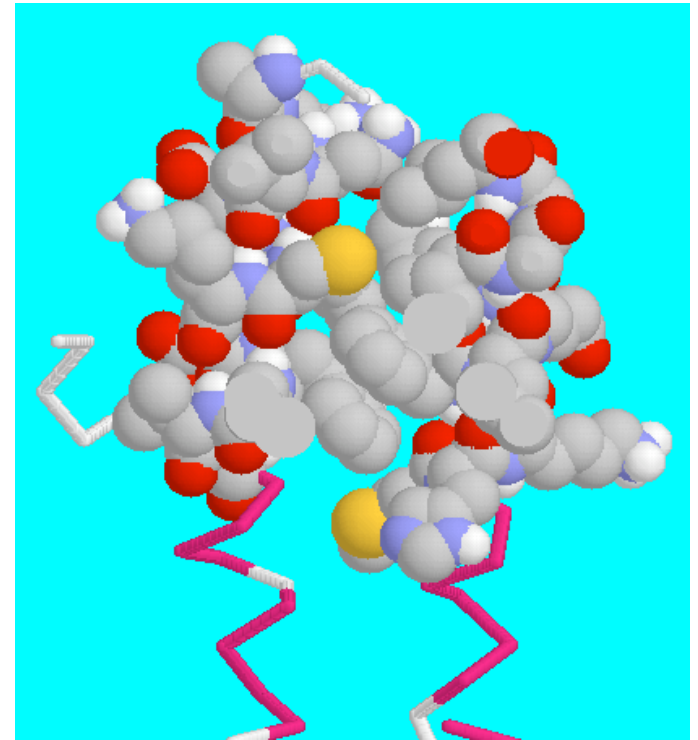
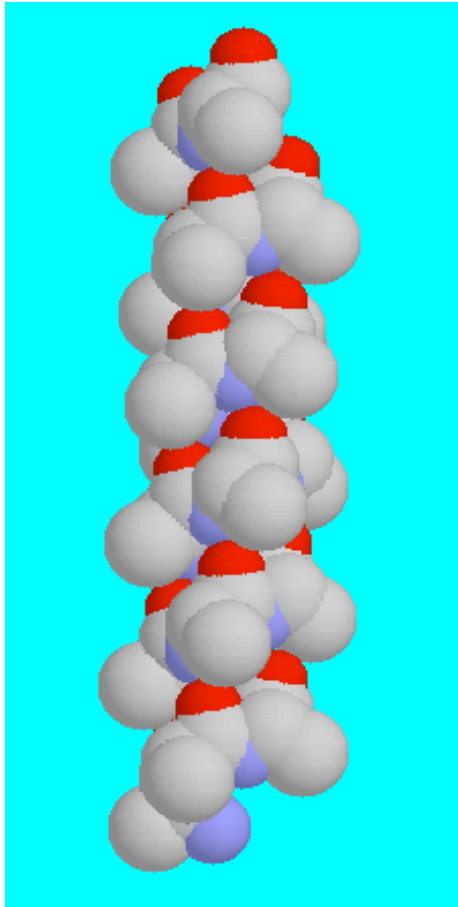
AKNVDYCKEWLIV



**Myohemerythrin
helix**

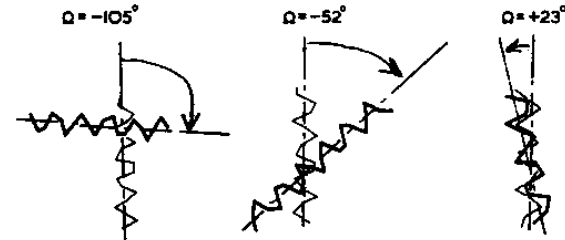
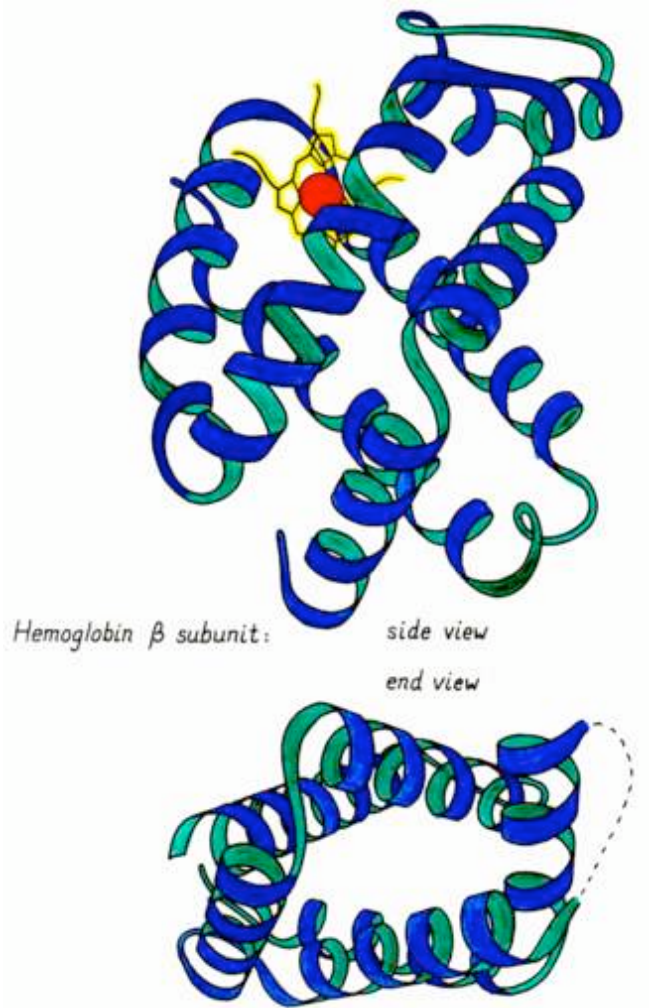


Poly-Ala

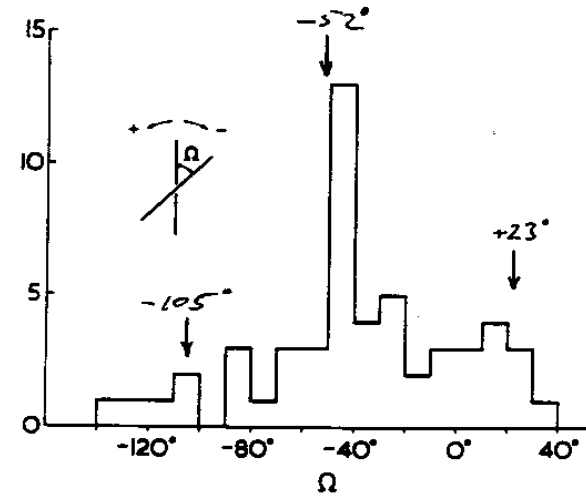


**"Tight packing" of
hydrophobic side chains
gives rise to helix packing
angle of $\sim 20^\circ$.**

Larger α -helical domain--
 Note that not all packing angles are $\sim 20^\circ$.

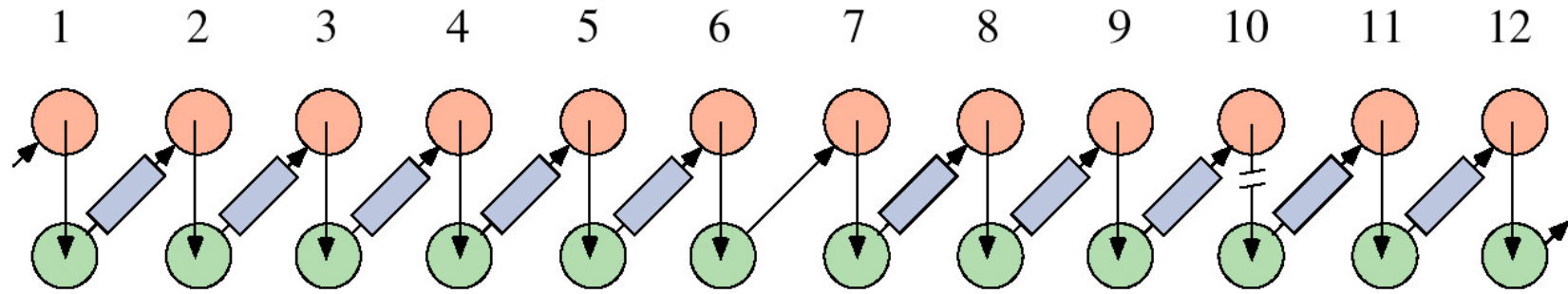


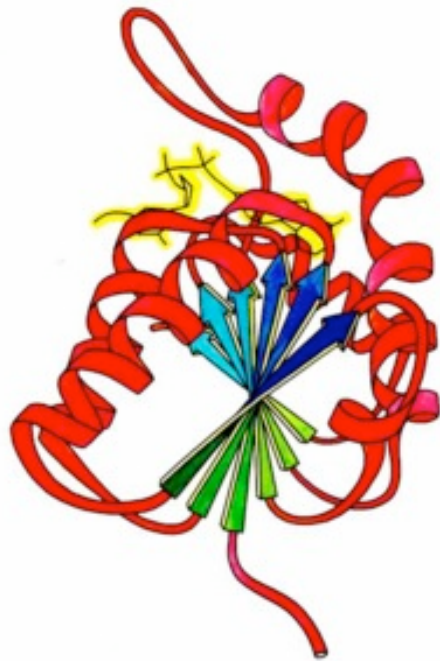
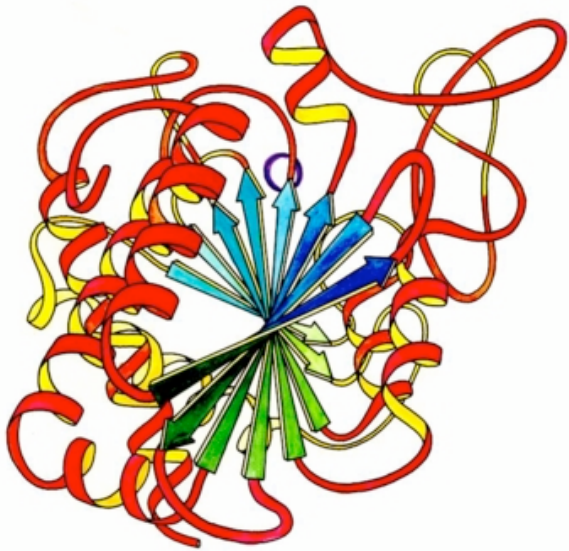
IDEALIZED HELIX PACKING ANGLES.



The relative orientations observed for packed α helices in proteins. The angle Ω describes the relative orientation of packed secondary structures. It is defined as the angle between the strands of β sheet and/or helix axes when projected onto their plane of contact.

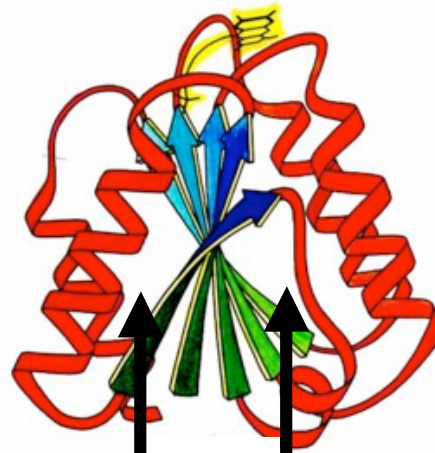
Armadillo repeats of β -catenin (Weis lab, Stanford)--lotsa β



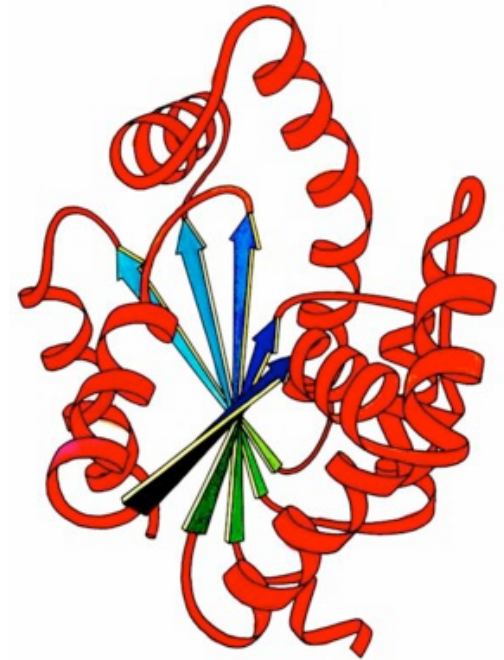


Lactate Dehydrogenase domain 1, end view

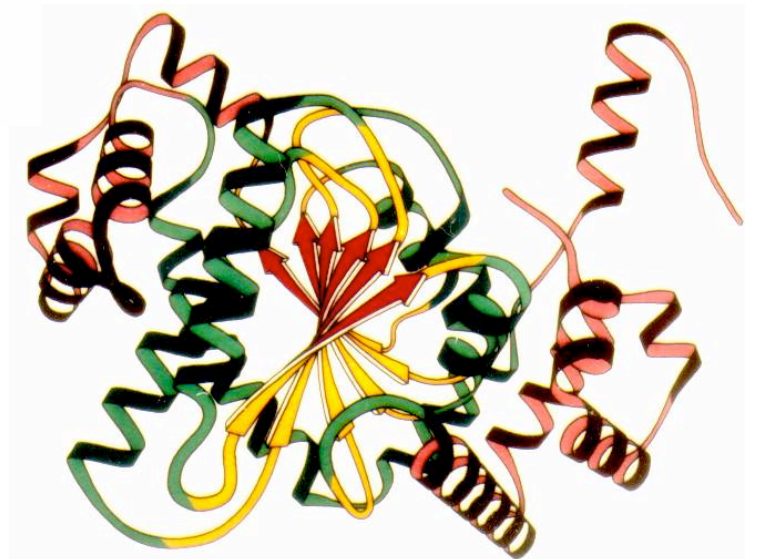
Parallel β/β domains

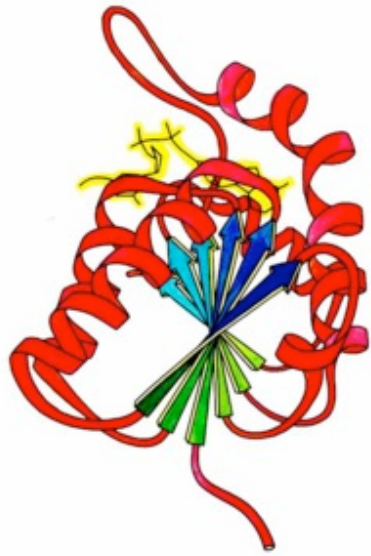


Hydrophobic interior

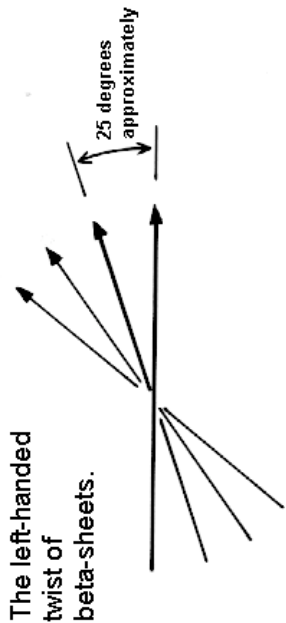


Adenylate Kinase

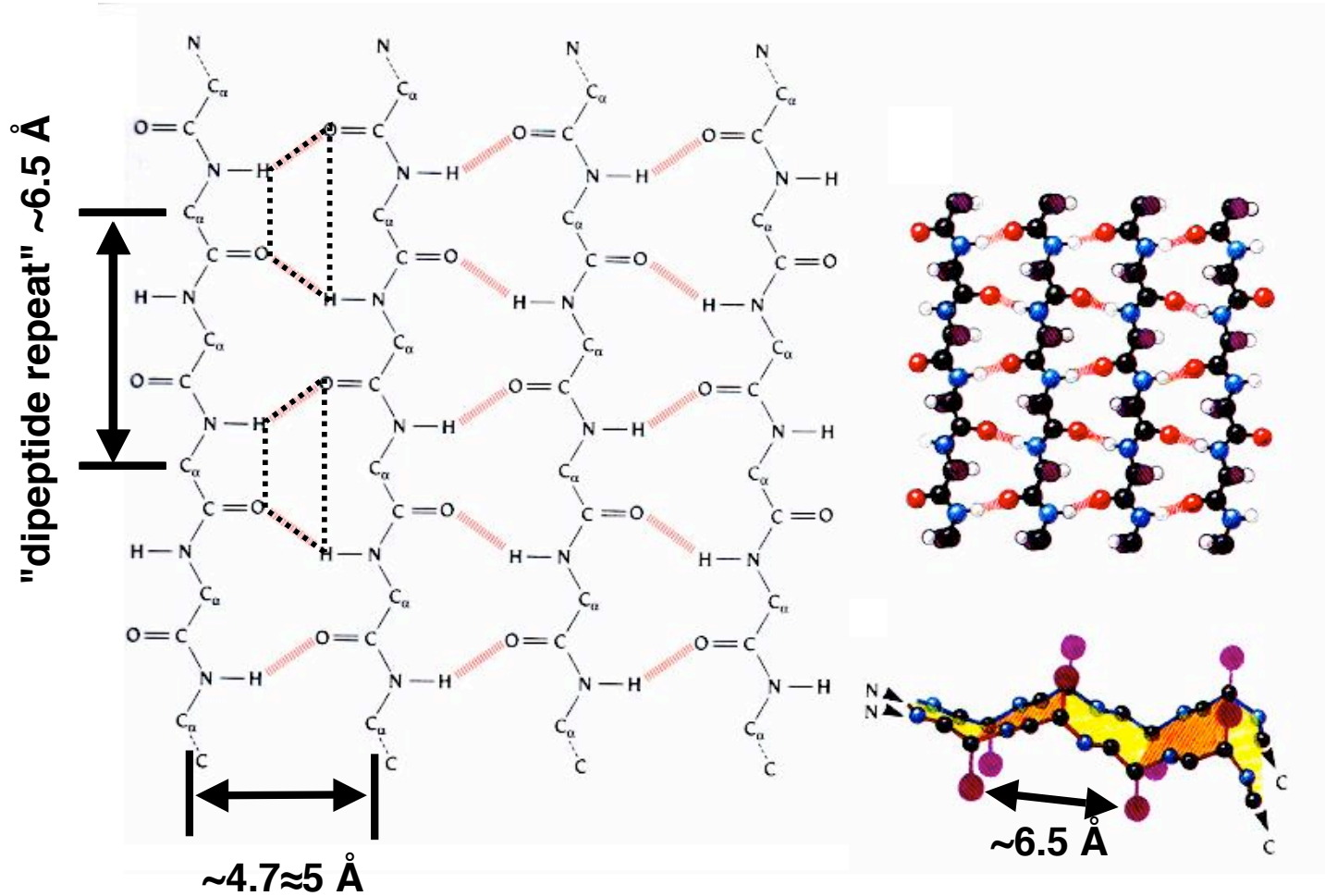




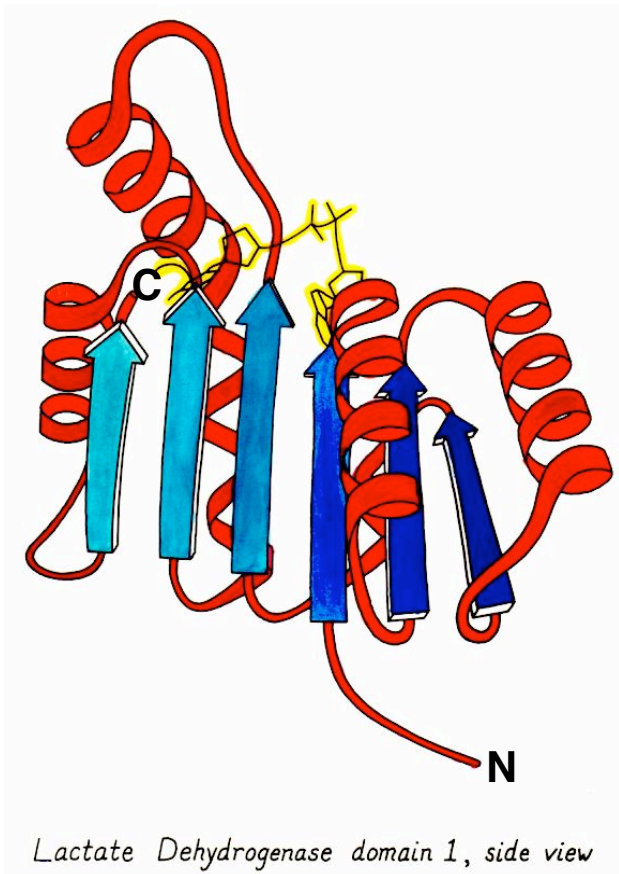
Lactate Dehydrogenase domain 1, end view



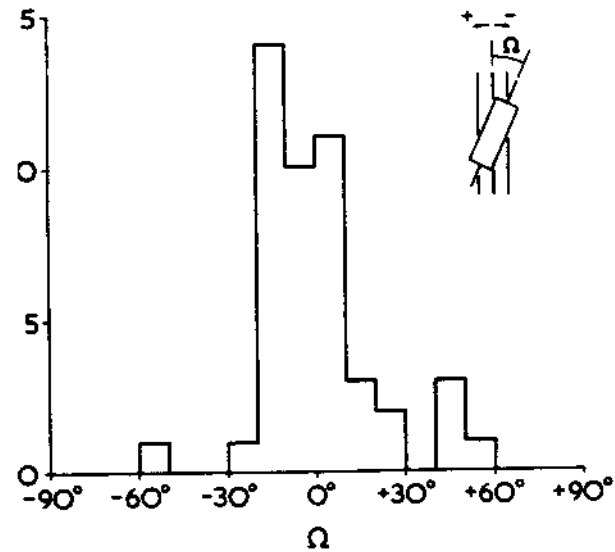
Parallel beta strands



The twist of the parallel β sheet is due to the intrinsic right-handed twist of the polypeptide backbone.

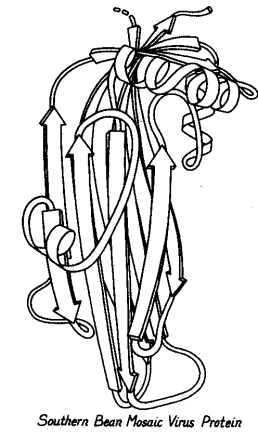
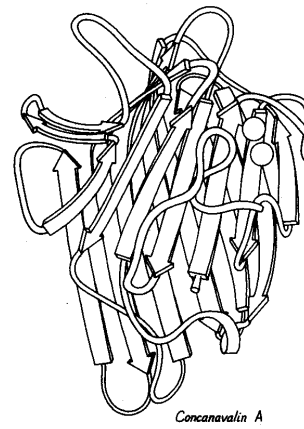
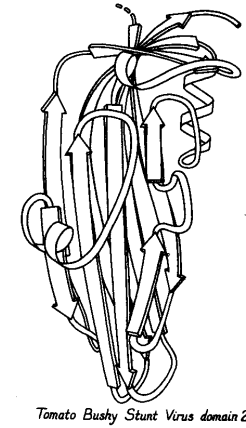
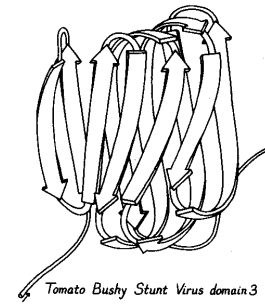
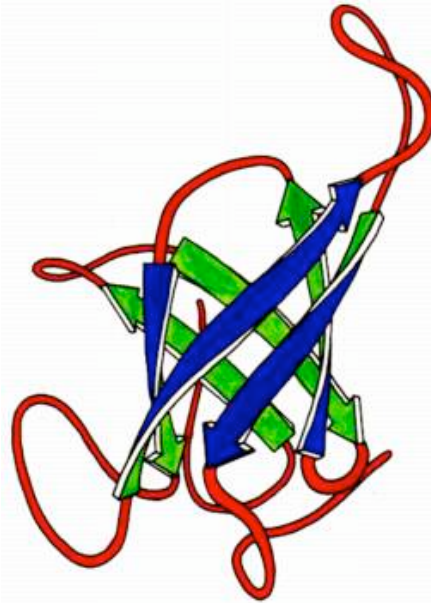
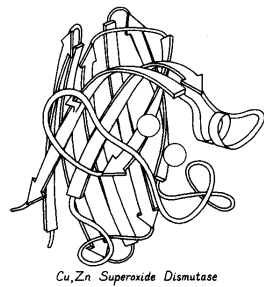
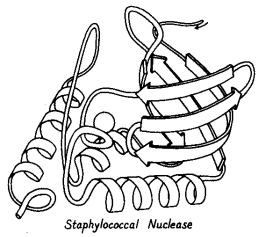
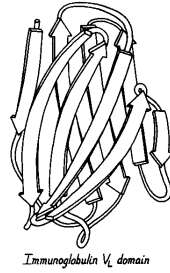
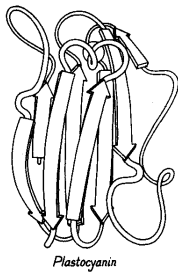
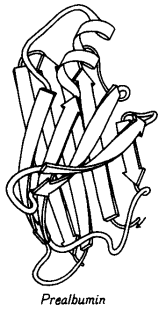
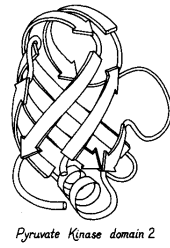
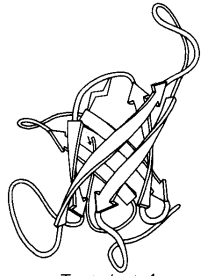


Close packing of hydrophobic side chains results in preferred angles of packing of helices on parallel beta sheets.

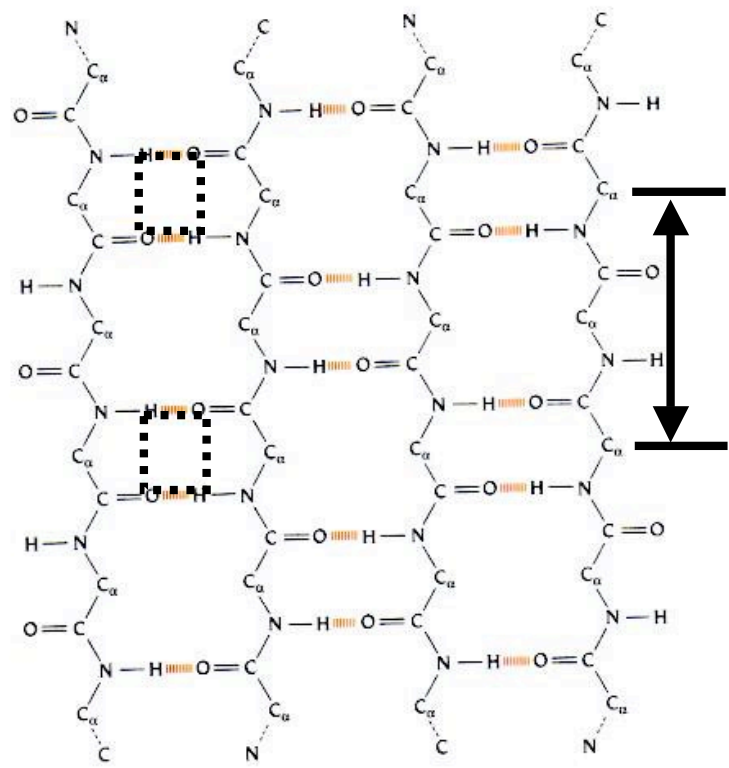
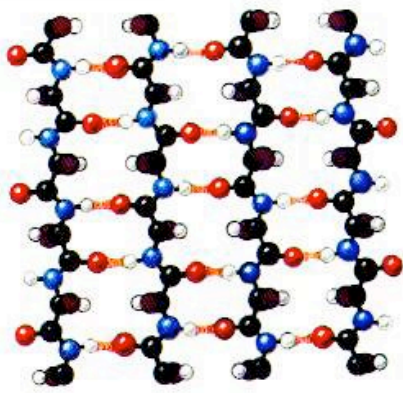
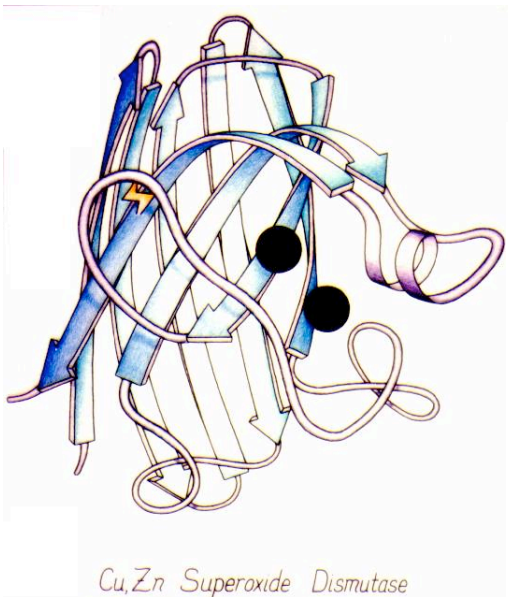


The relative orientations observed for α helices packed onto β sheets. The letter Ω is the angle between the helix axes and β strands,

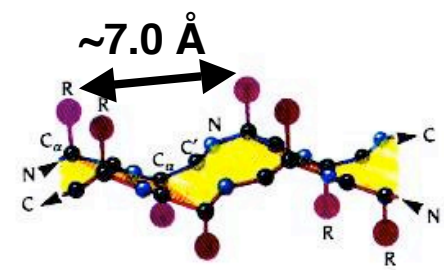
Antiparallel β domains

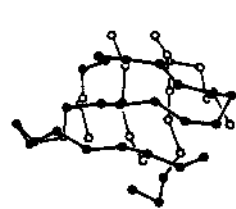
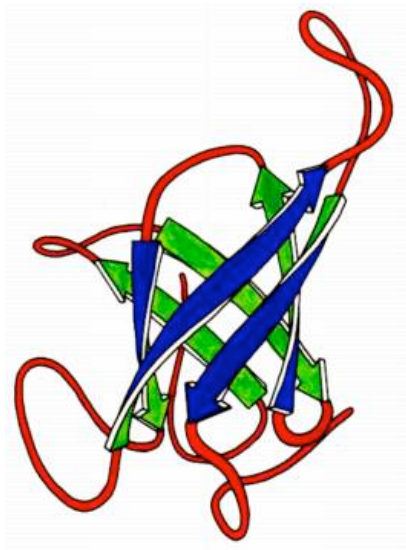


Antiparallel β sheets



"dipeptide repeat" $\sim 7.0 \text{ \AA}$

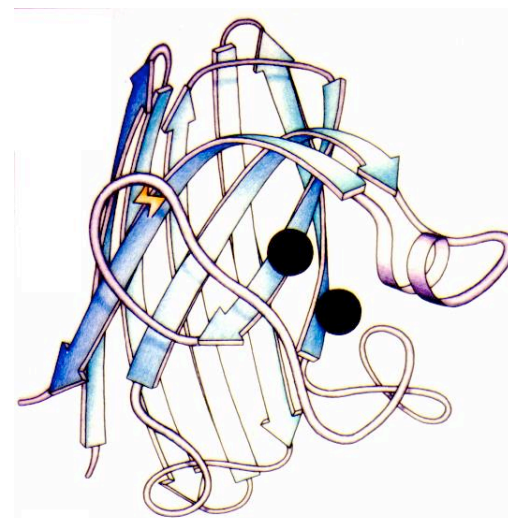
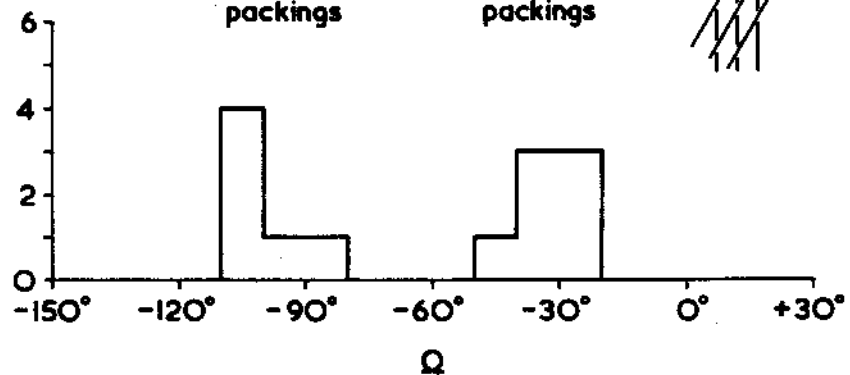




Orthogonal
β-sheet
packings



Aligned
β-sheet
packings

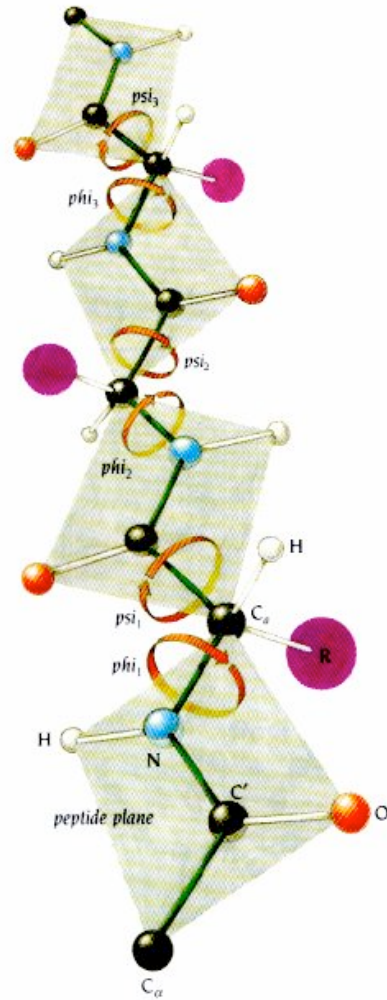


Cu,Zn Superoxide Dismutase

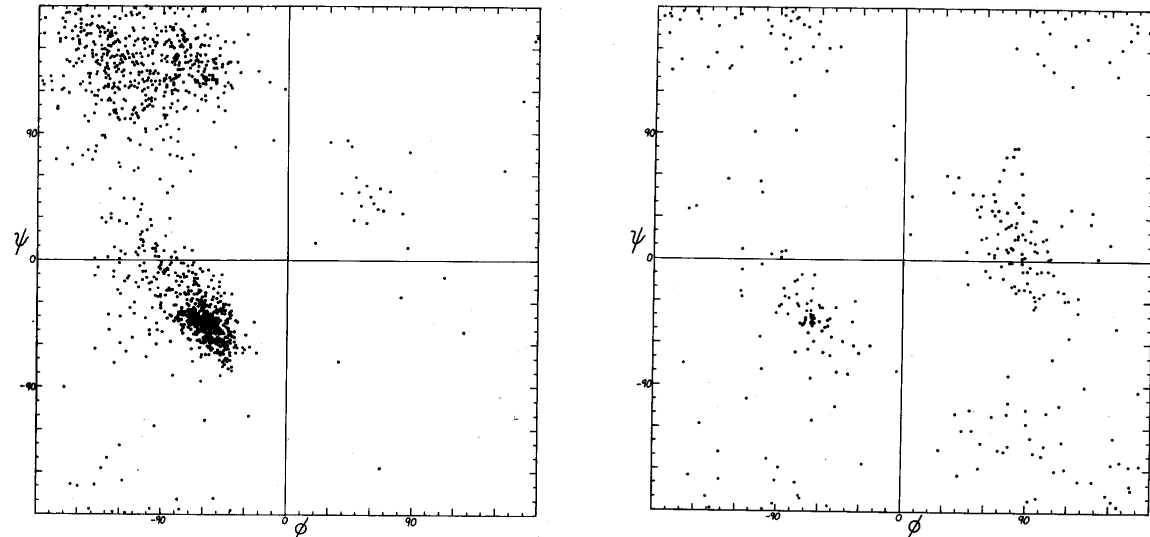
The relative orientation of packed β sheets in proteins in the aligned and orthogonal classes.

The upper part of the figure shows an example of each class. Circles, representing the Cα atoms of residues in β sheets, are closed for the β sheet above the plane of the page and are open for the β sheet below the plane. Note how in the orthogonal packing strands move from one β sheet to the next without interruption.

How much diversity in secondary structure?



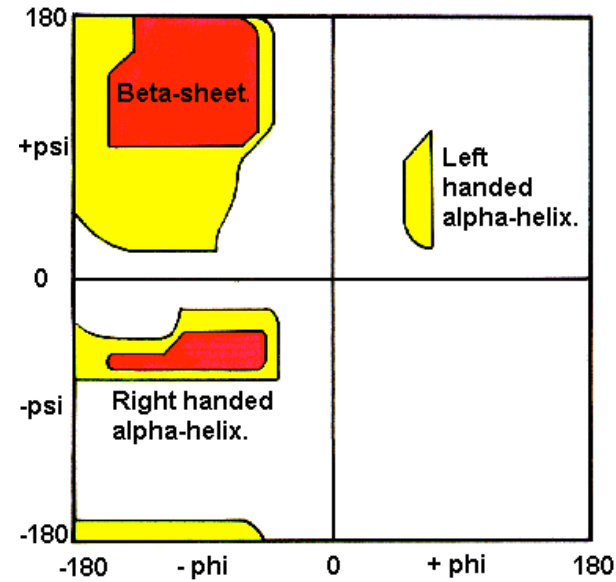
Ramachandran Plots



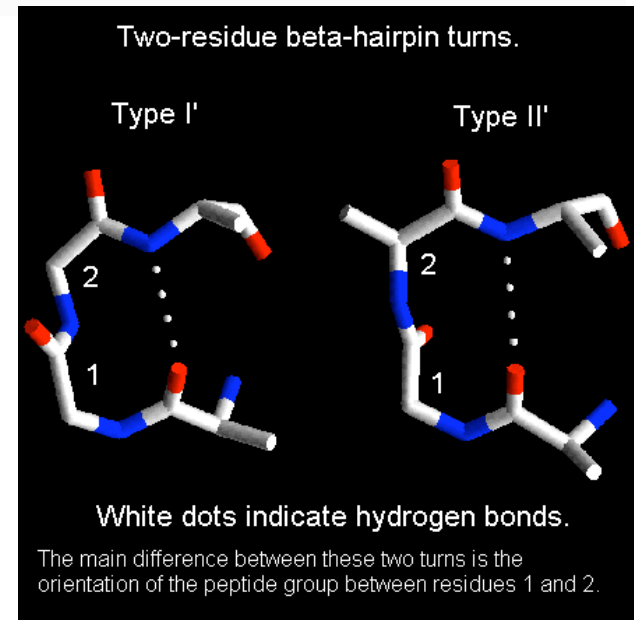
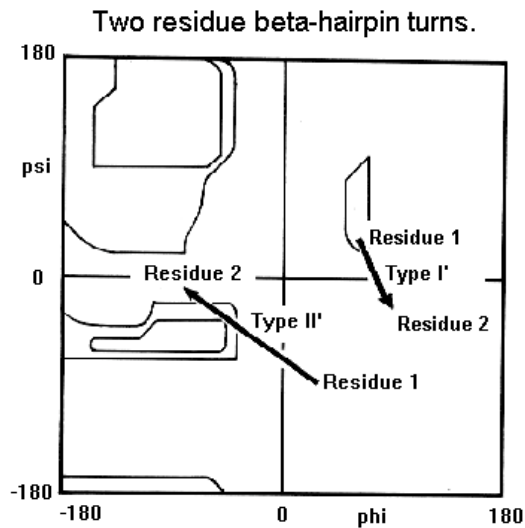
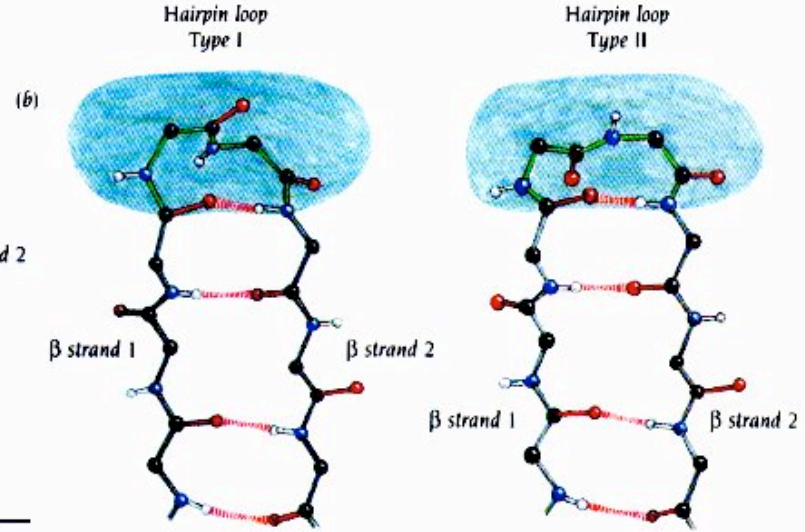
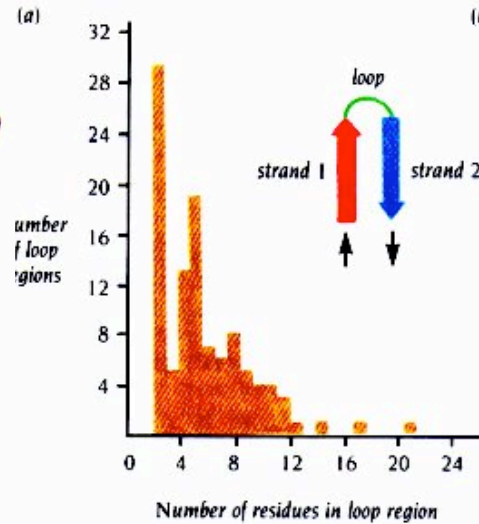
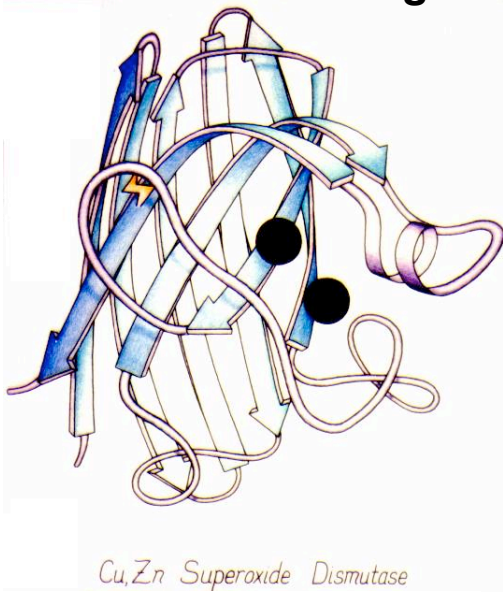
Non-glycine

Glycine

The Ramachandran Plot.

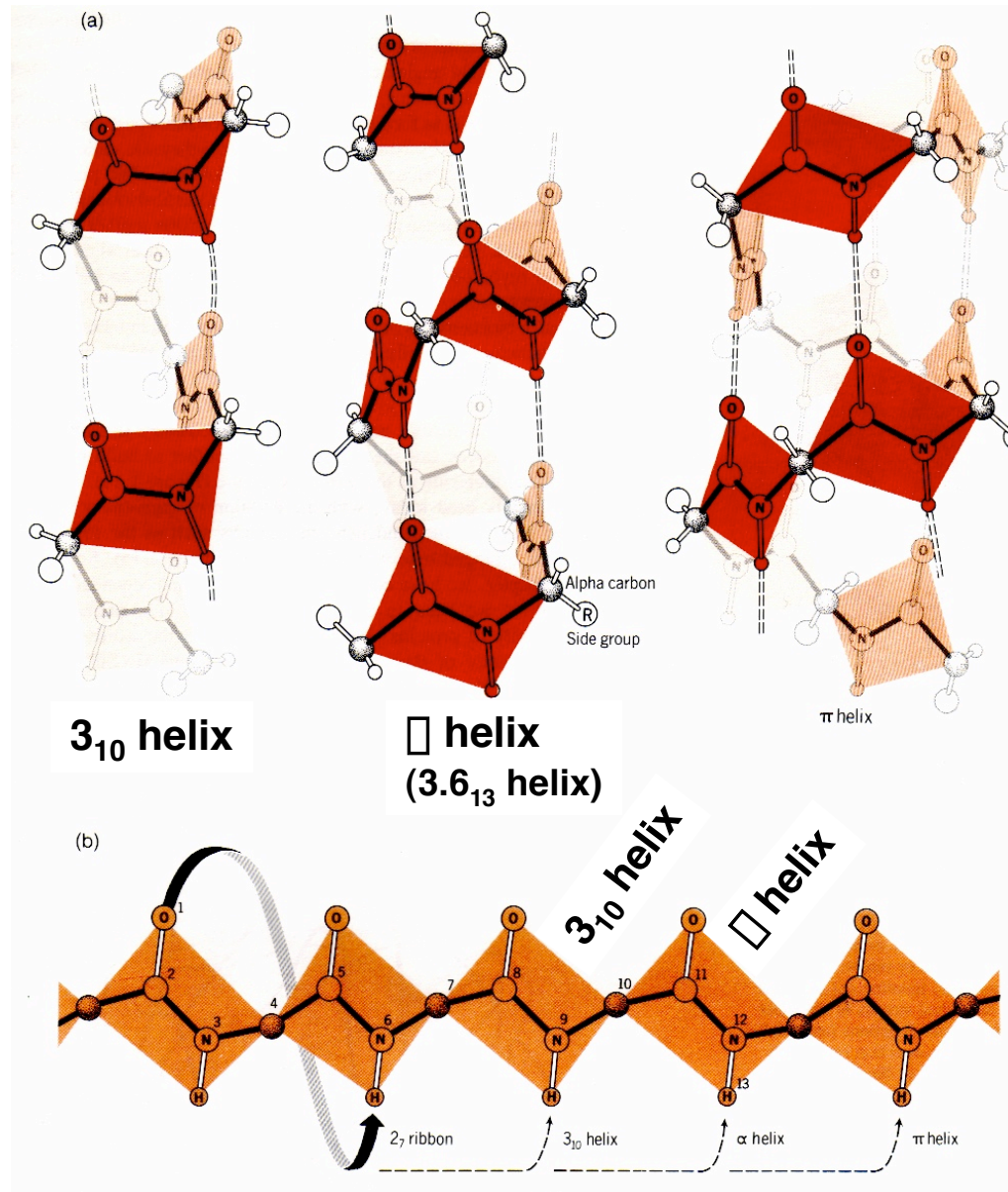


"Tight turns" are common connections between β strands

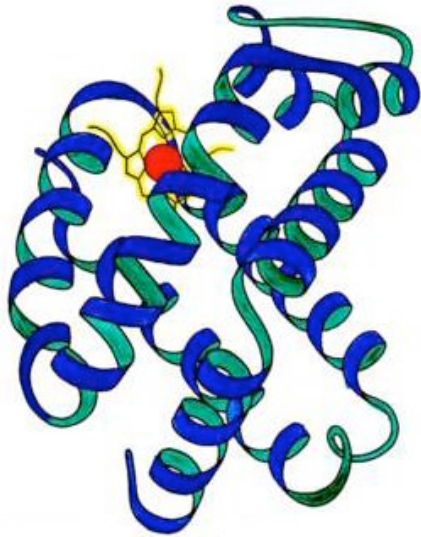
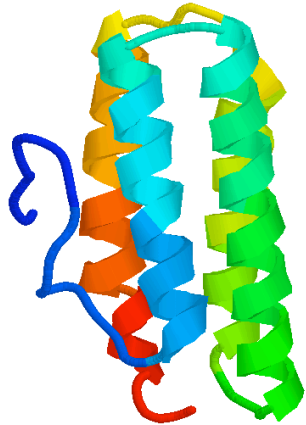


Type I' turns, residue 2 is always glycine
Type II' turns, residue 1 is always glycine.

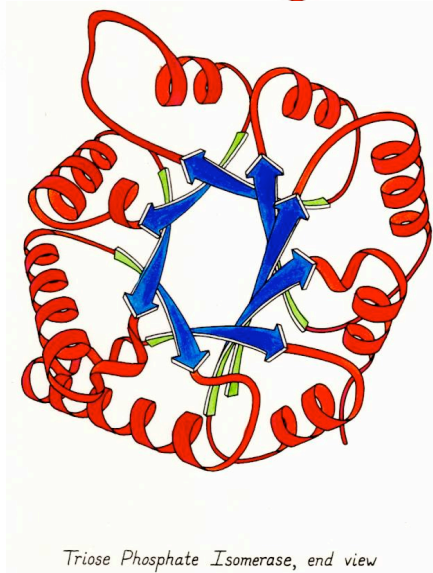
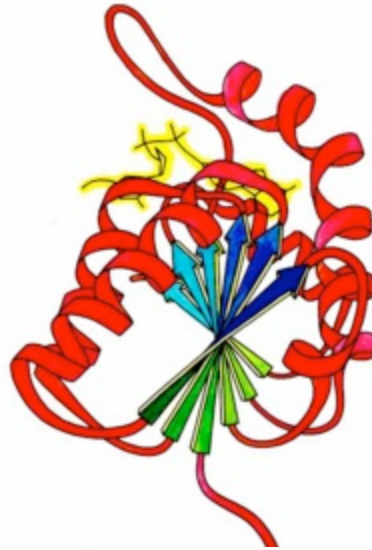
In addition to α helices, 3_{10} helices are occasionally found in proteins



Antiparallel \square



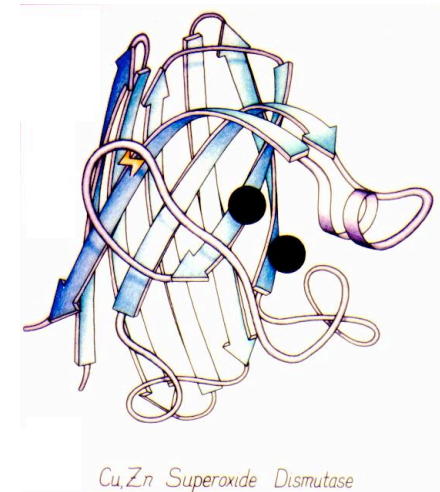
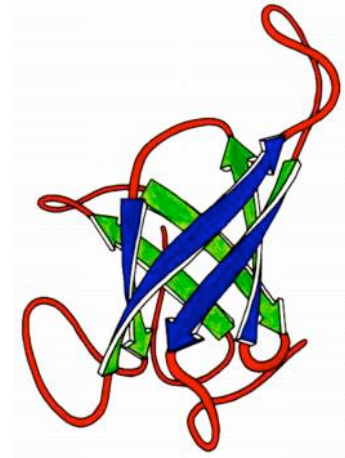
Parallel \square/\square



Triose Phosphate Isomerase, end view

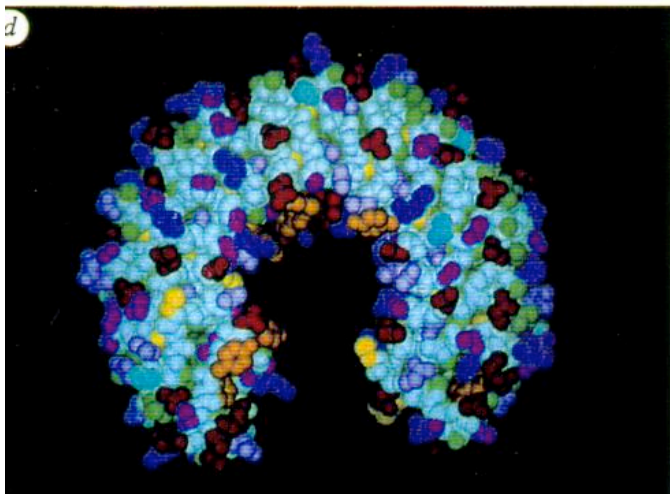
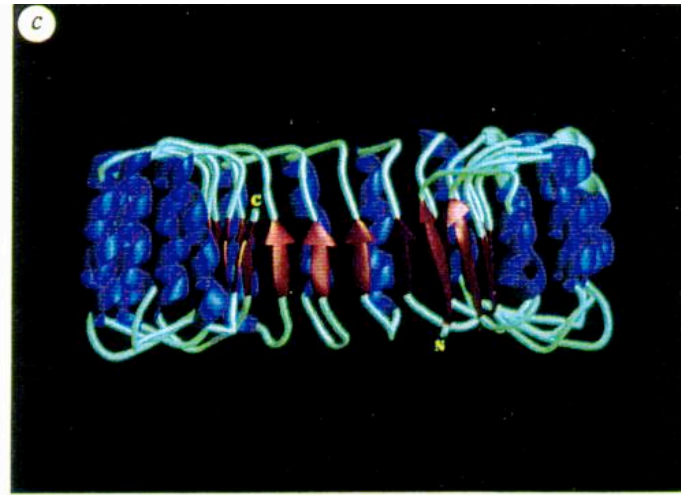
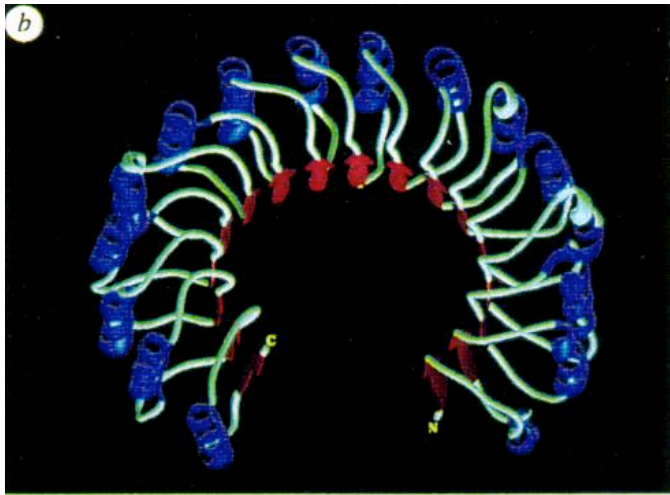
(also, $\square+\square$)

Antiparallel \square

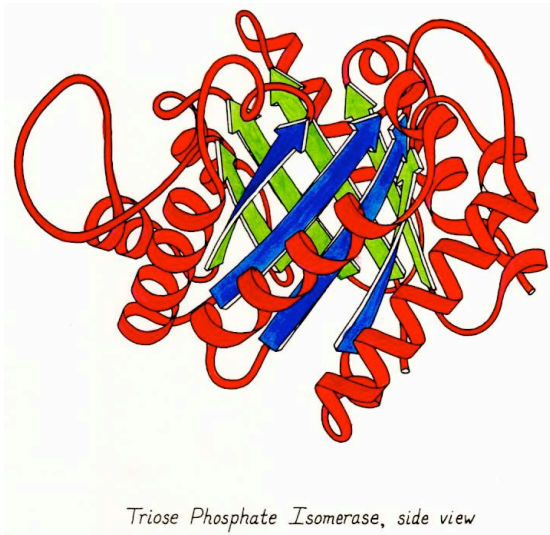


Cu,Zn Superoxide Dismutase

Unusual β/α structure: RNase inhibitor



Protein Domains



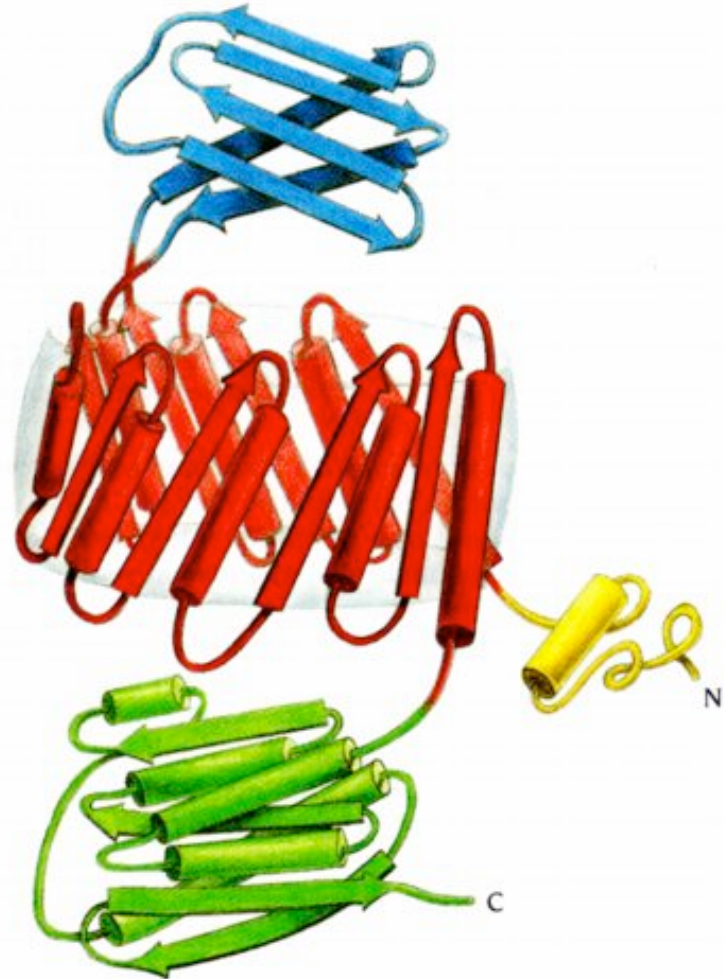
Triose Phosphate Isomerase (TIM)

One domain

Antiparallel β

β/β barrel

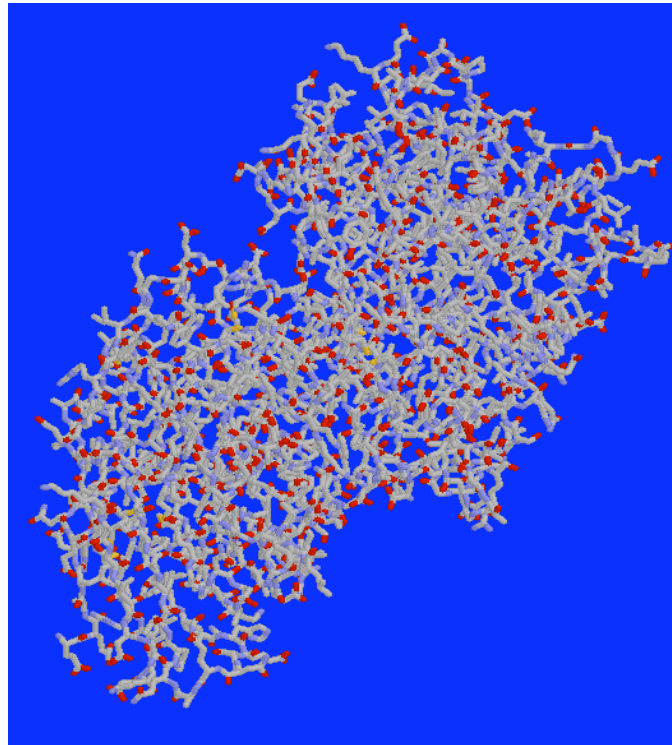
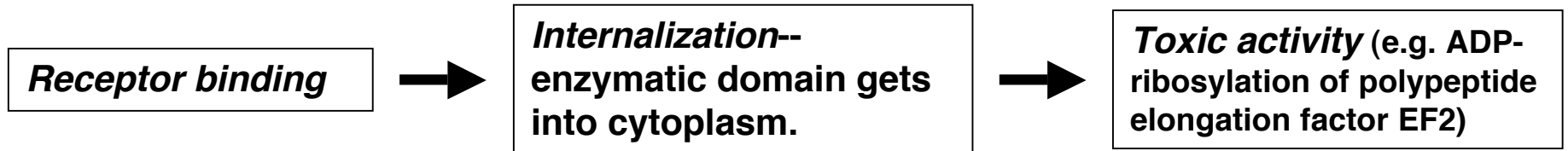
Parallel β/β



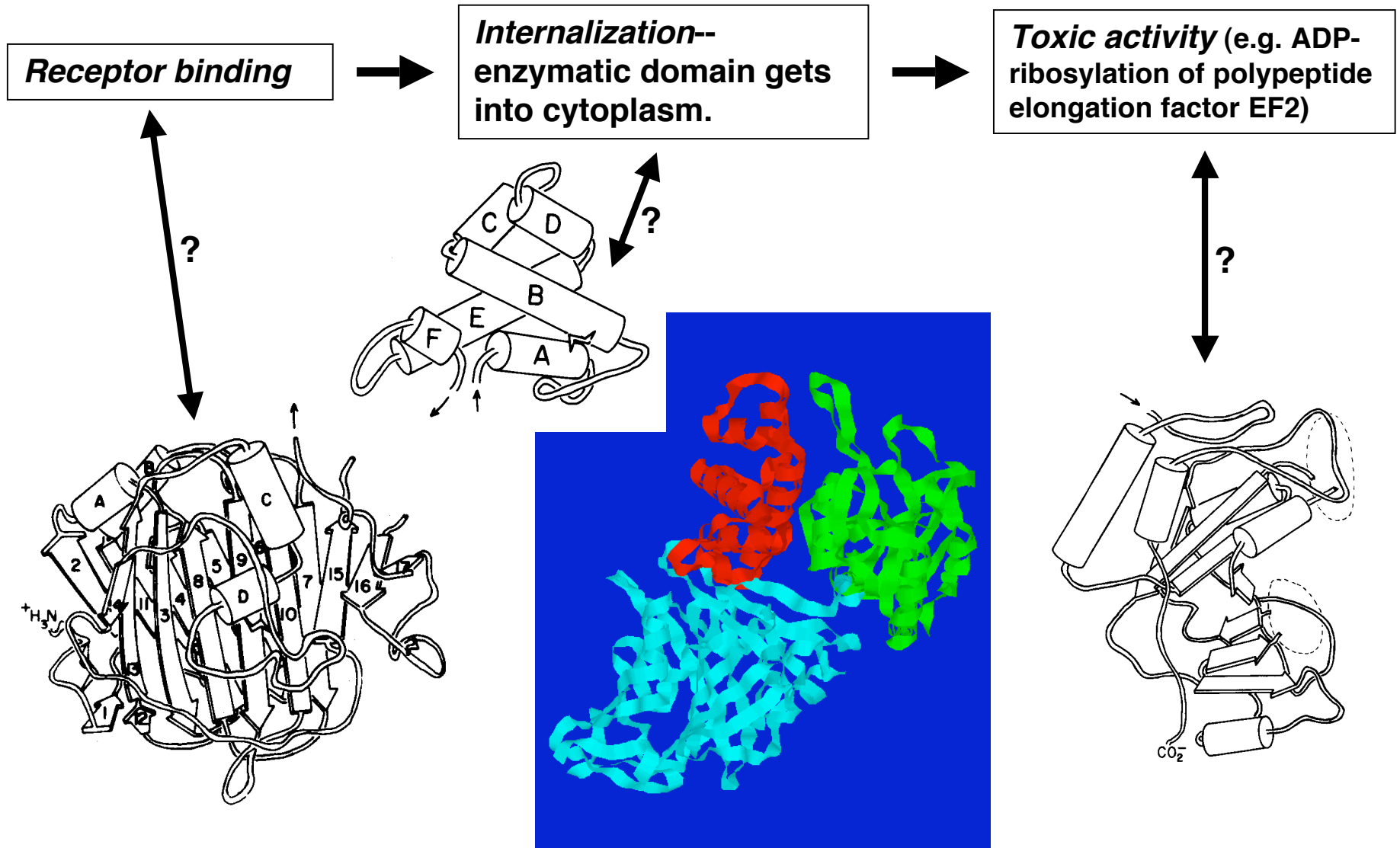
Pyruvate Kinase

**Three domains
(plus an N-terminal bit)**

Pathogenic Pathway of Bacterial Exotoxins (e.g. *Pseudomonas aeruginosa* exotoxin A)

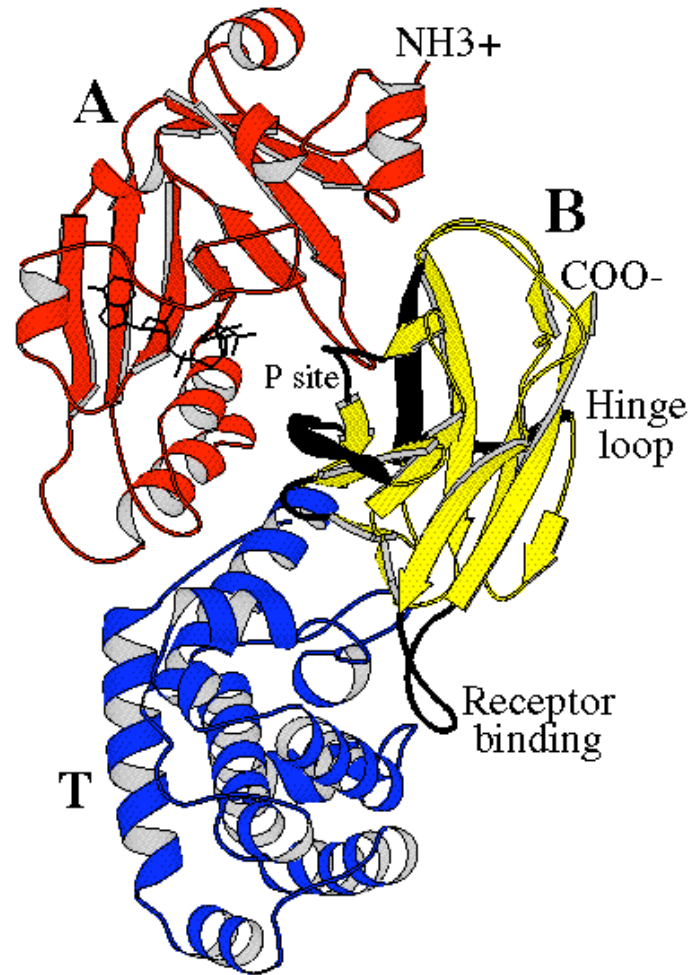
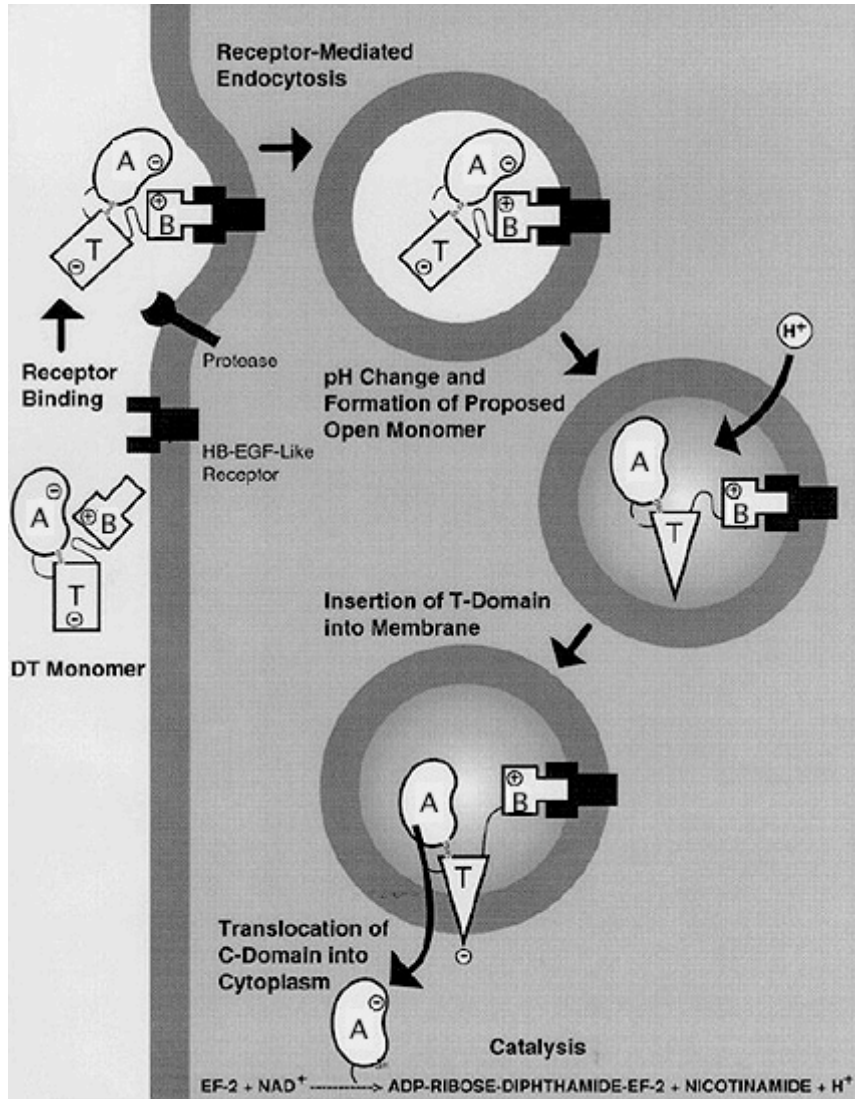


Pathogenic Pathway of Bacterial Exotoxins (e.g. *Pseudomonas aeruginosa* exotoxin A)

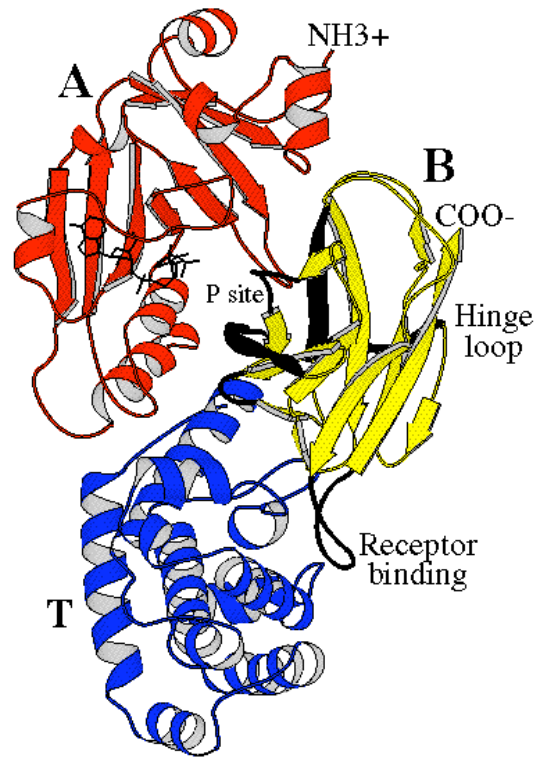


| Toxin | Subunits/MW | Function |
|--|--|---|
| Pseudomonas exotoxin A | Single polypeptide 66 kDa | ADP-ribosylation of EF-2 =>Inhibit protein synthesis |
| Diphtheria toxin | Single polypeptide 58 kDa | ADP-ribosylation of EF-2 =>Inhibit protein synthesis |
| Cholera toxin & <i>E. coli</i> heat-labile toxin (LT) | AB₅ A = 27; B= 11.6 kDa | ADP-ribosylation of G_n |
| Shiga toxin; <i>E. coli</i> verotoxins | AB₅ | N-glycosidase; removes single adenine from 28S RNA of 60S ribosome |
| Pertussis toxin | S₁S₂S₃2S₄S₅ S₁ = 26.2 kDa S₂ = 21.9 S₃ = 21.9 S₄ = 12.1 S₅ = 11.8 | ADP-ribosylation of G_i |

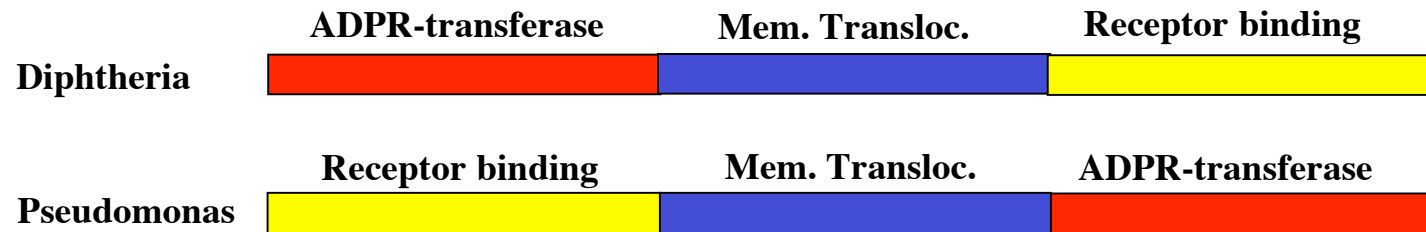
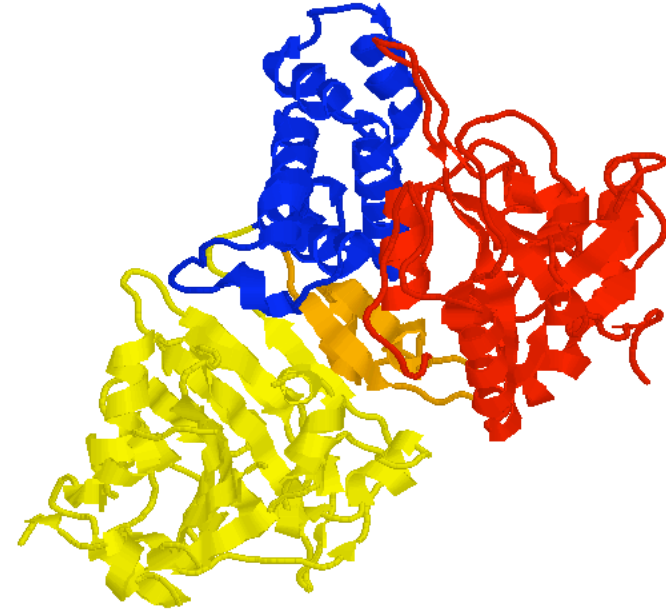
Diphtheria Toxin



Diphtheria Toxin

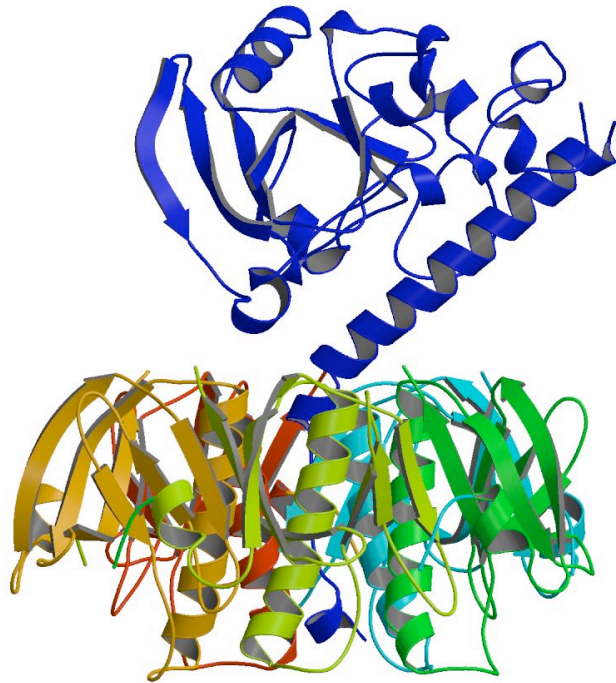


Pseudomonas Toxin

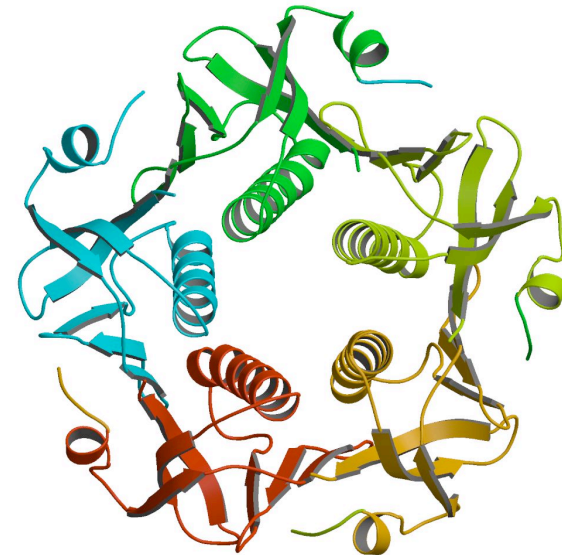


Diphtheria and Pseudomonas toxins have similar ADPR-transferase domains (low but significant seq. identity), but other domains are different; order of domains is different.

***E. coli* heat-labile toxin (~ 80% ID to cholera toxin)
ADP-ribosylates a G-protein**



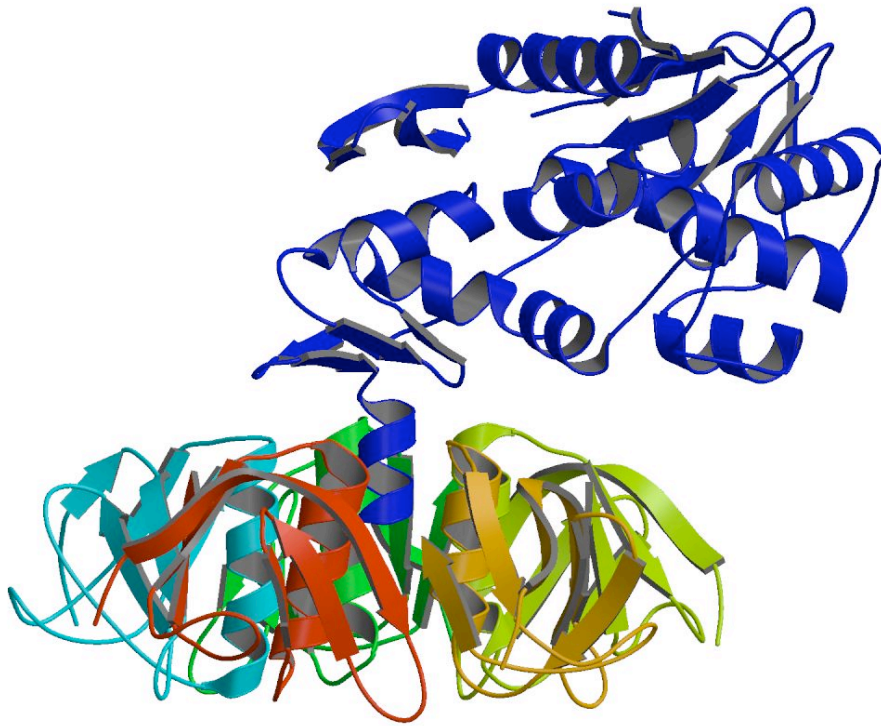
AB5 whole molecule



B5 cell binding pentamer

First surprise: Catalytic domain of heat-labile toxin is similar in structure to those of pseudomonas and diphtheria toxins; only a single amino acid (required for catalysis) is conserved between them.

Shiga toxin
a very specific ribonuclease

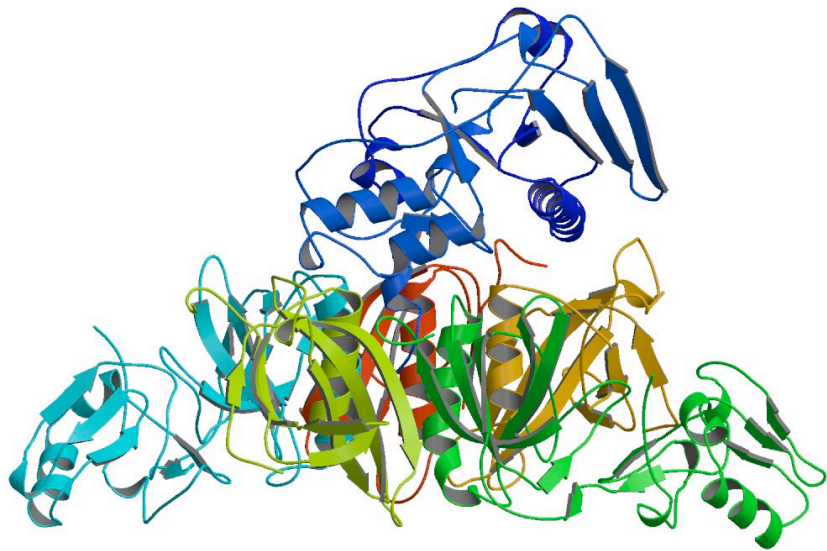


AB5 whole molecule

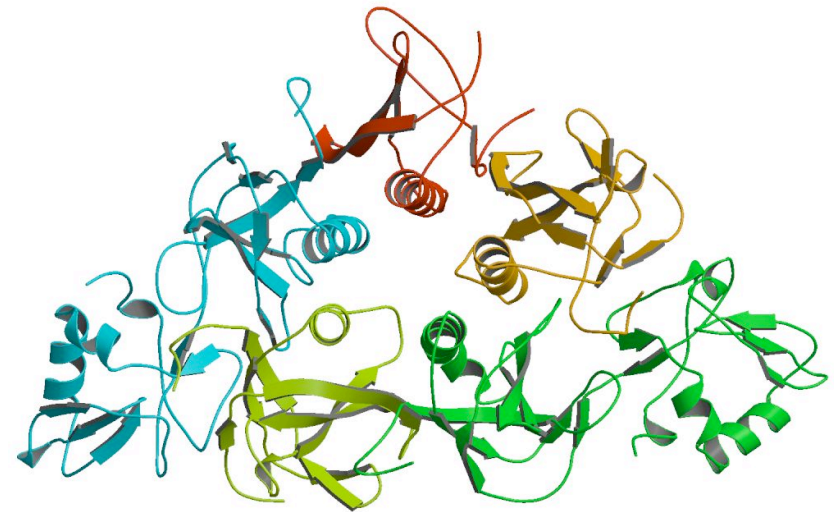


B5 cell binding pentamer

Pertussis toxin



$S_1-S_2S_32S_4S_5$ whole molecule



$S_2S_32S_4S_5$ cell binding pentamer

Second surprise: Receptor binding domains of pertussis toxin have a similar core structure to those of heat-labile toxin and shiga toxin, despite lack of obvious sequence similarity.

Mosaic structure of bacterial exotoxins

