

Lecture 4

Levels of Organization in Proteins

Secondary Structures of Protein

LAST LECTURE

- Beta Turn
 - Properties
- Alpha Helix
 - Structure
 - Shape
 - Properties
- 3_{10} , Pi, and polyproloine Helix
- Polyproloine Helix
- Triple Collagen Helix
- Dipole Helix
- Amphipathic Alpha Helix
- Coiled Coil Helix

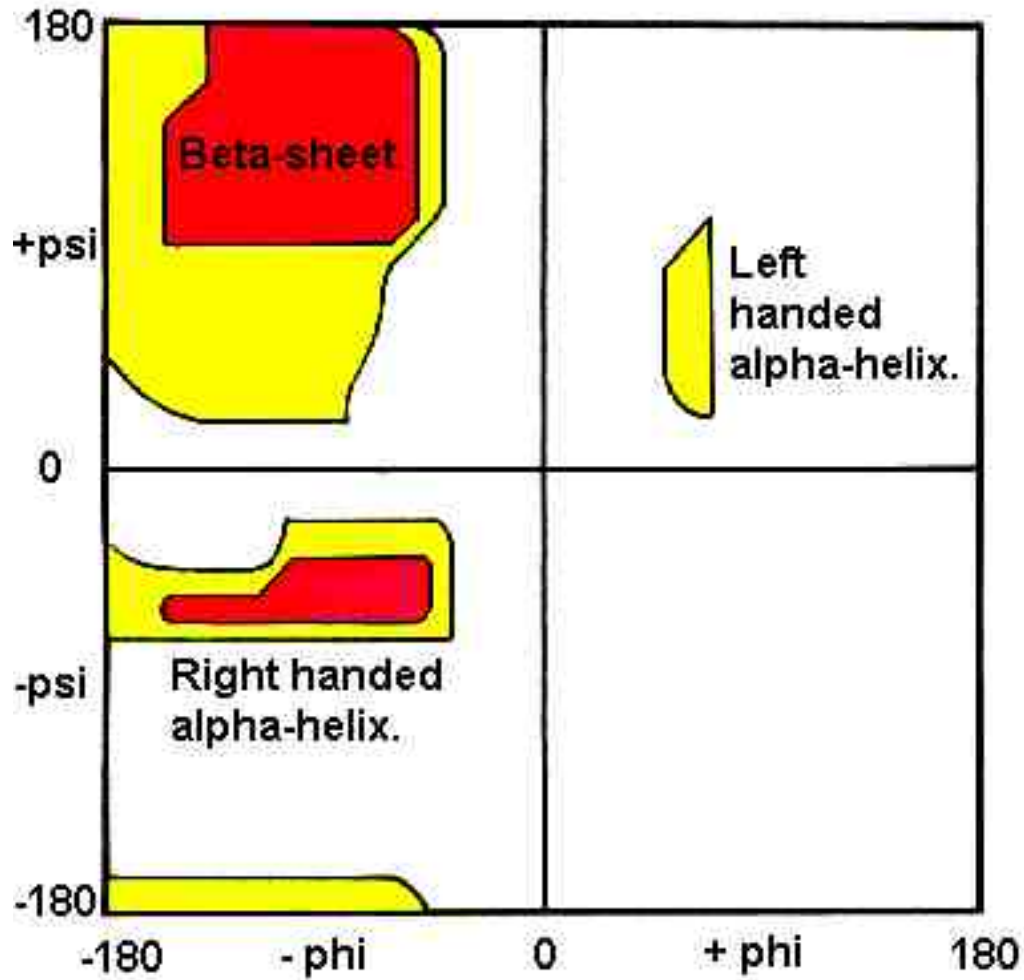


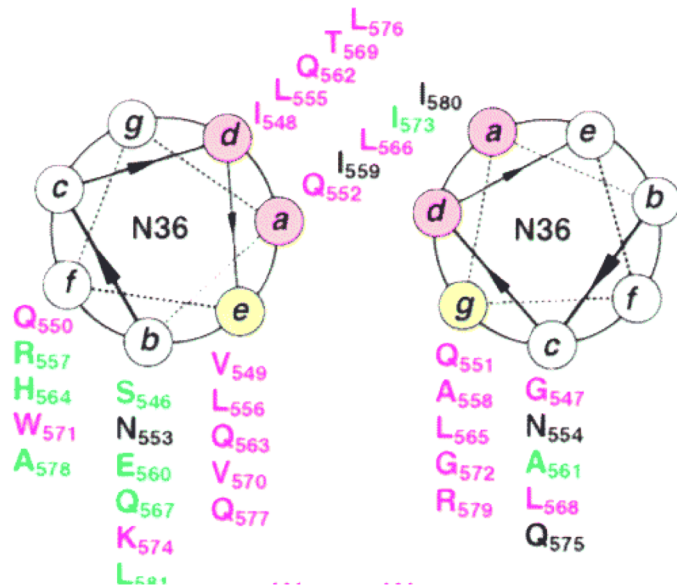
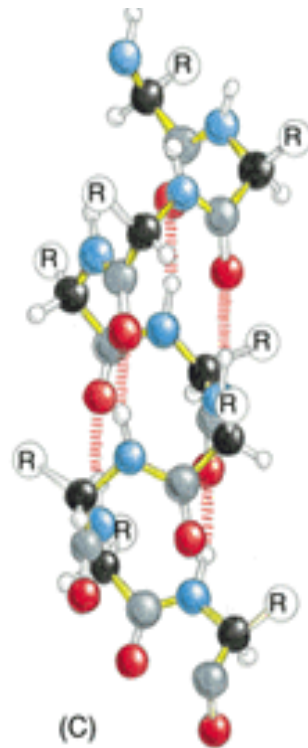
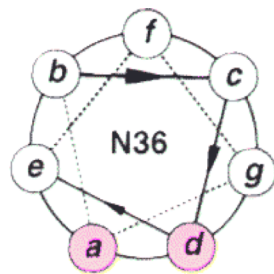
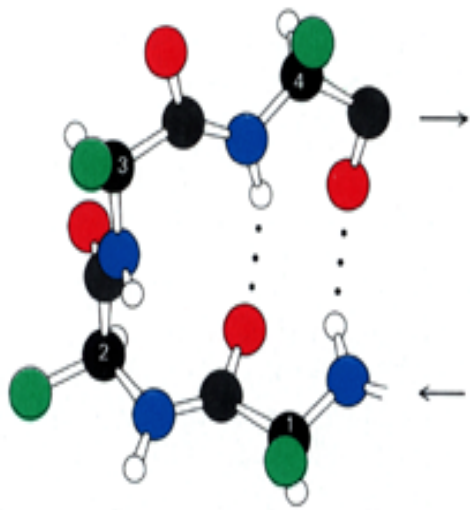
TODAY'S OUTLINE

- Beta sheets
 - Properties
- Motifs and Domains
- Folds
- Amino Acid preferences



The Ramachandran Plot.





β - SHEETS

- The first β sheet structure was proposed by William Astbury in the 1930s
- A refined version was proposed by Linus Pauling and Robert Corey in 1951

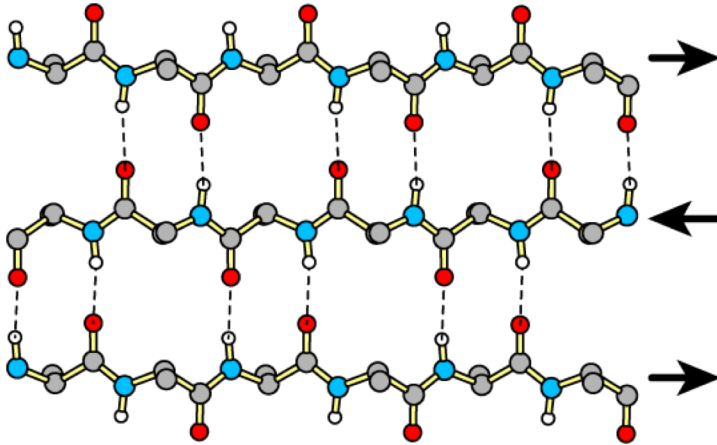


β - SHEET BASICS

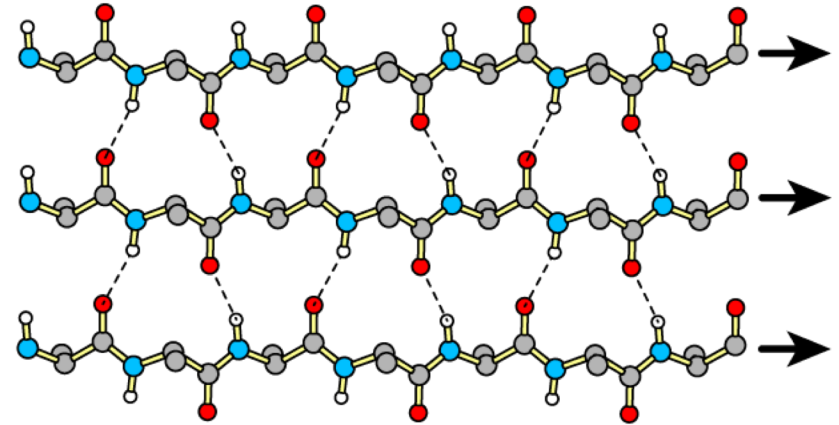
- Made up of β -Strands
- Diverse:
 - Parallel/Antiparallel
 - Edge/Interior Strands
 - Typically Twisted
 - Many Forms
 - β -sandwiches, β -barrels, β -helices, β -propellers, etc.



β -SHEETS



Antiparallel β -sheet



Parallel β -sheet

β -sheets fulfill the hydrogen bonding potential of the main-chain atoms, except at the edges. Adjacent strands are usually close in sequence.

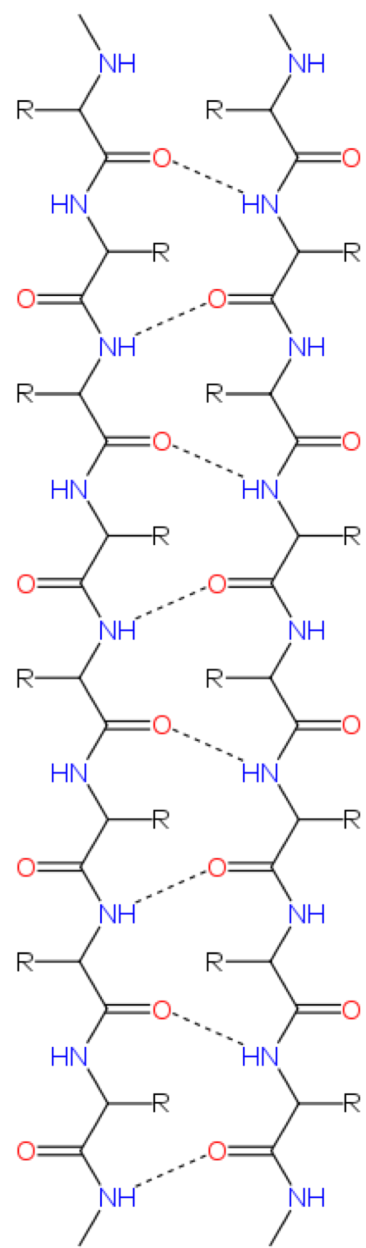
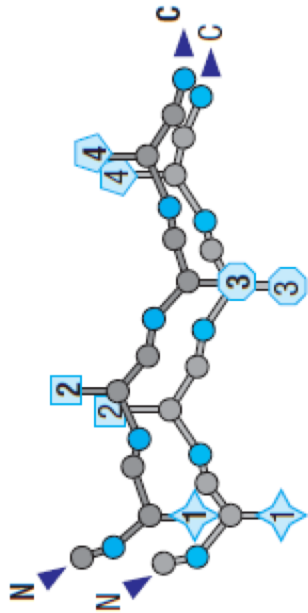
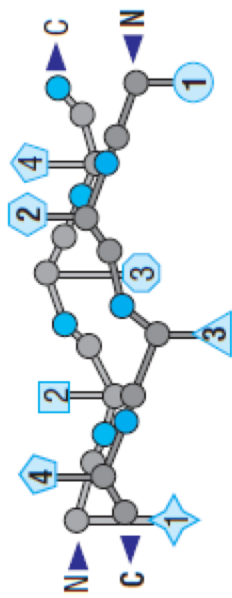
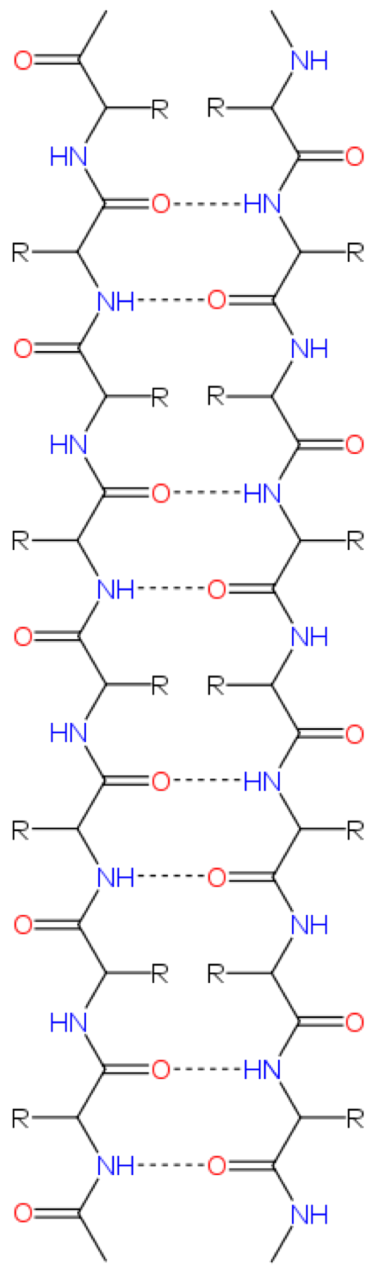
Properties:

Distance between $C\alpha$'s is $\sim 3.6 \text{ \AA}$ in an extended strand

Distance between strands $\sim 4.6 \text{ \AA}$

Strands are not flat. They have a characteristic right-handed twist



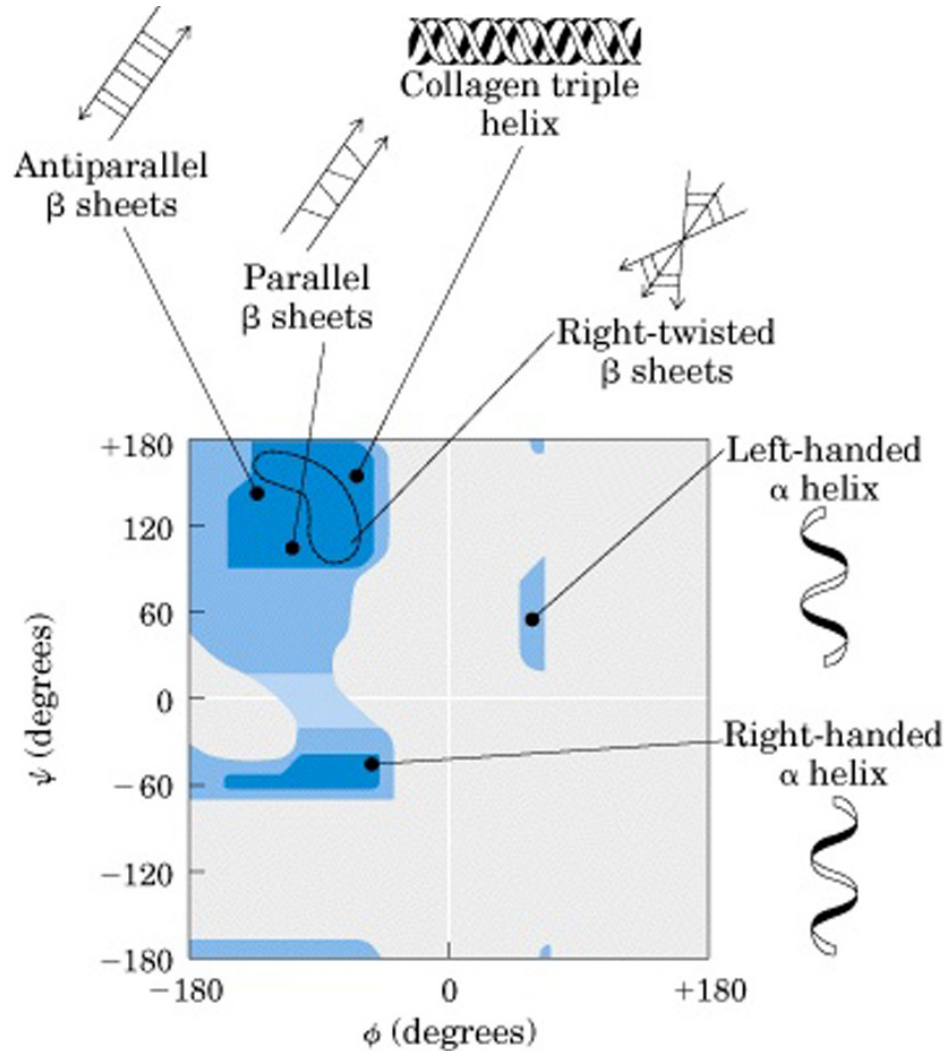


PROPERTIES OF BETA SHEETS

- Nearly all polar amide groups are hydrogen bonded to one another in a beta-sheet structure except for the N–H and C=O groups on the outer sides of the two edge strands.
- Parallel beta sheets containing fewer than five strands are rare.
- The polypeptide chain in a beta sheet is almost fully extended. The distance between consecutive residues is 3.3 Å
- The phi and psi angles for peptides in beta sheets are approximately -130° and $+125^\circ$ respectively.
- Beta strands usually have a pronounced right-handed twist due to steric effects arising from the L-amino acid configuration.
- Parallel strands are less twisted than antiparallel ones. The effect of the strand twist is that sheets consisting of several long strands are themselves twisted.



RAMACHANDRAN PLOT

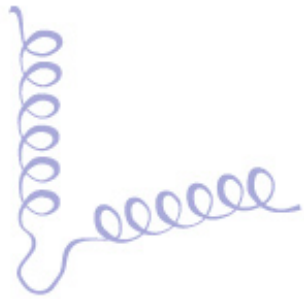


AMPHIPATHIC BETA SHEETS

- Nearly all peptide bonds are *trans*
- Stretch of sequence with alternating hydrophobic and hydrophilic residues could have one hydrophobic and one hydrophilic face
- Polypeptide chain in a beta sheet is extended
 - Valine
 - Isoleucine



(a) Helix-loop-helix



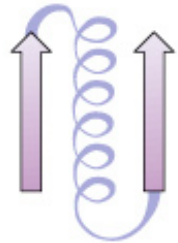
(b) Coiled coil



(c) Helix bundle



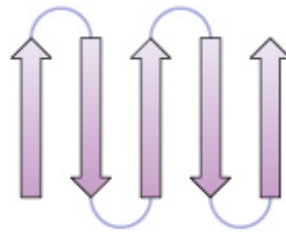
(d) $\beta\alpha\beta$ unit



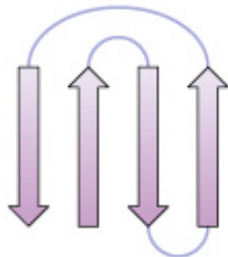
(e) Hairpin



(f) β meander



(g) Greek key



(h) β -sandwich



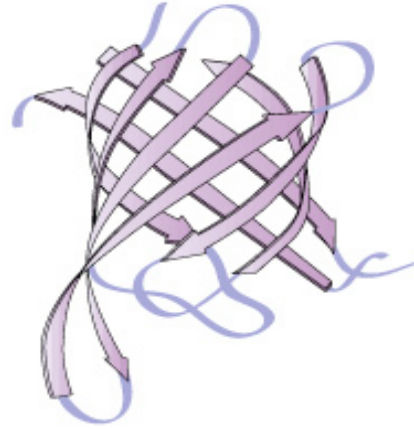
COMMON MOTIFS



(a) Parallel twisted sheet

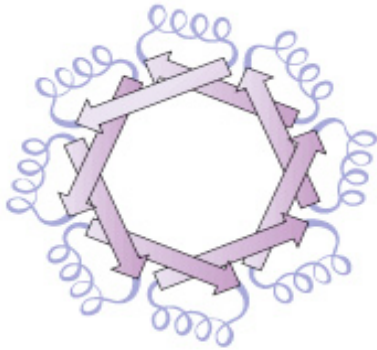


(b) β barrel

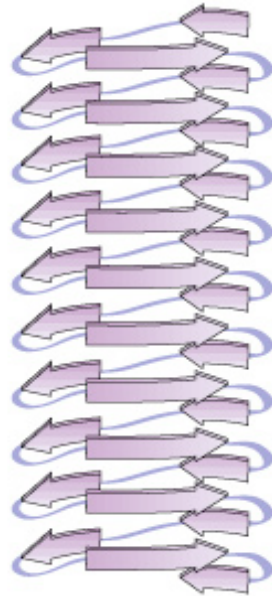


COMMON FOLDS

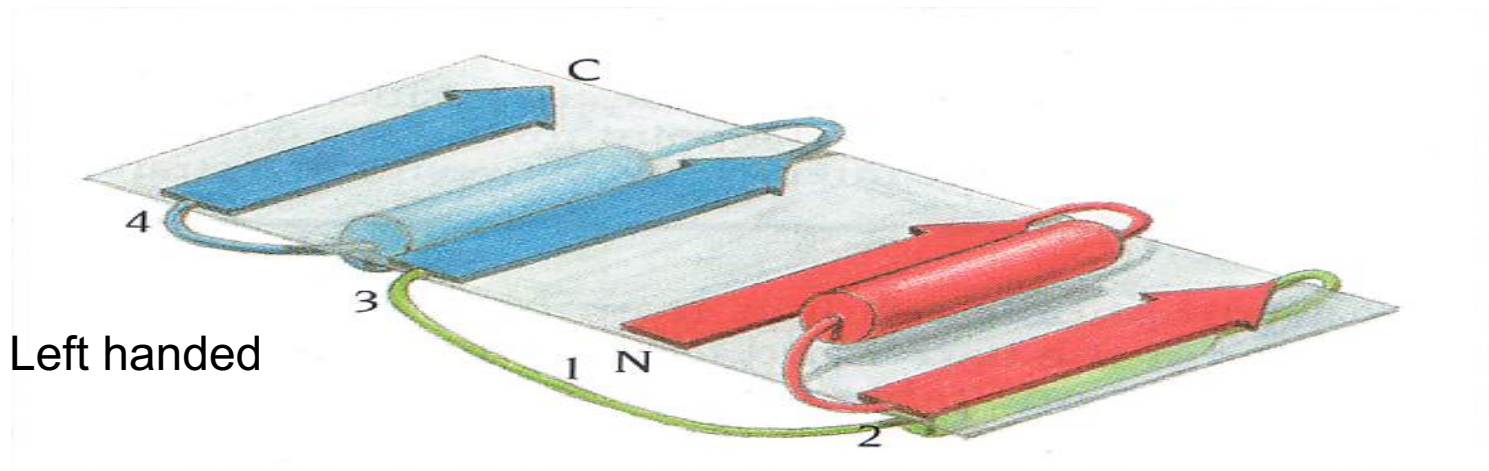
(c) α/β barrel



(d) β helix



Supersecondary structure: Crossovers in β - α - β -motifs



Left handed

Right handed

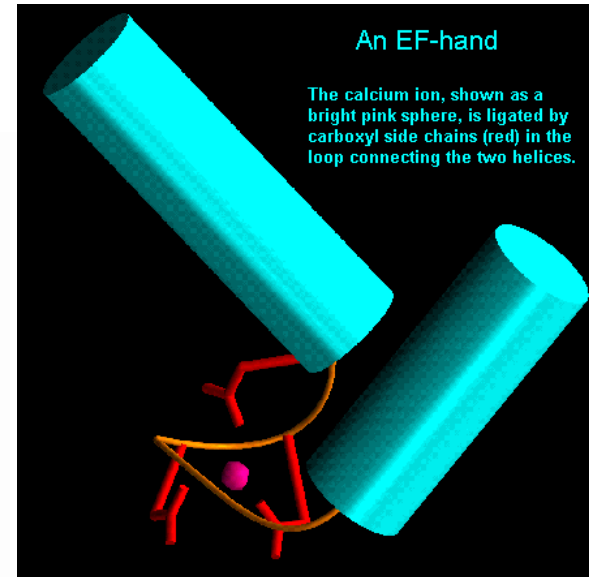


EF Hand

- Consists of two perpendicular 10 to 12 residue alpha helices with a 12-residue loop region.
- Form a single calcium-binding site (helix-loop-helix).
- Calcium ions interact with residues contained within the loop region.
- Each of the 12 residues in the loop region is important for calcium coordination.
- In most EF-hand proteins the residue at position 12 is a glutamate. The glutamate contributes both its side-chain oxygens for calcium coordination.



EF Fold

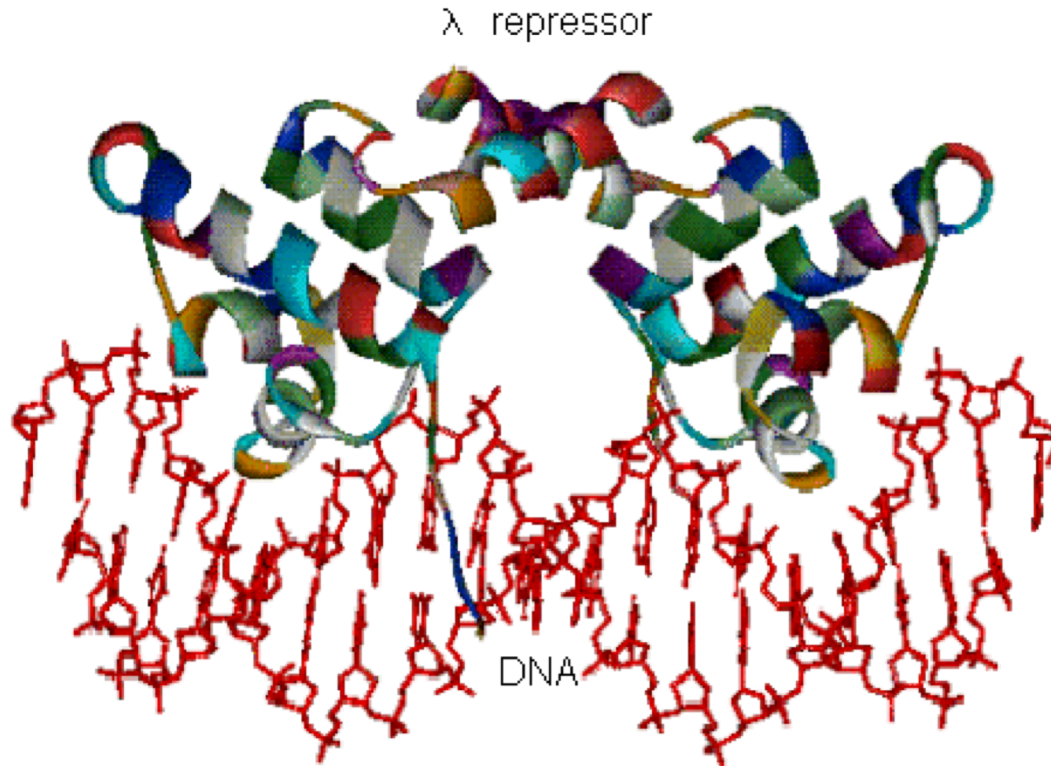


Found in Calcium binding proteins such as Calmodulin

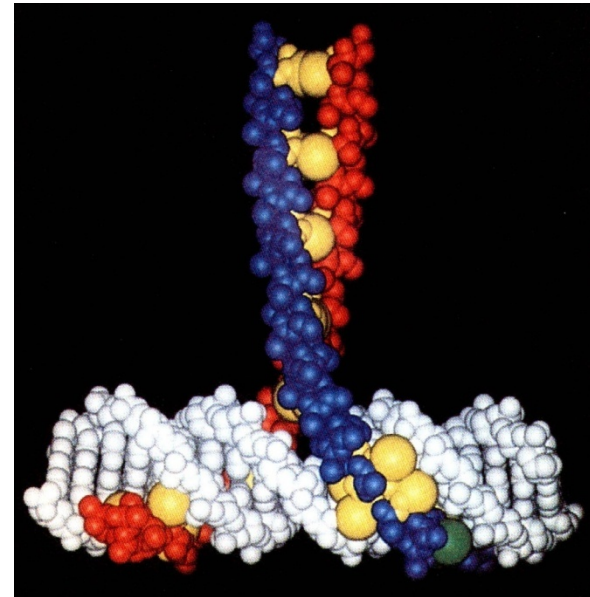
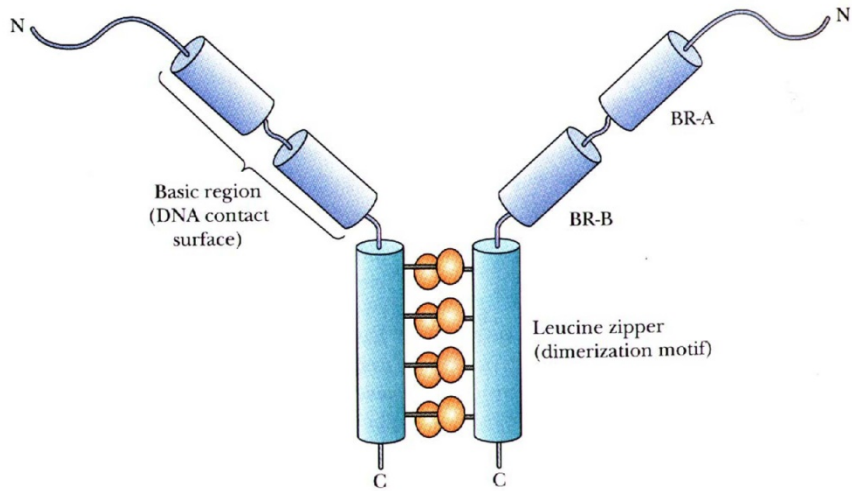


Helix Turn Helix Motif

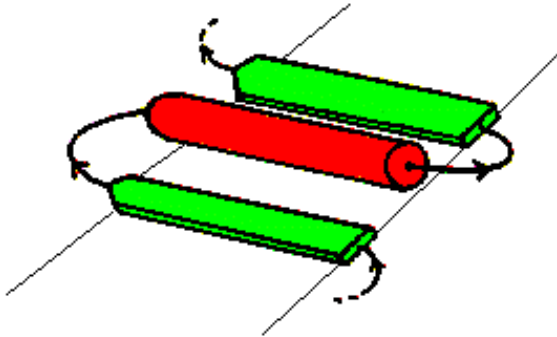
- Consists of two α helices and a short extended amino acid chain between them.
- Carboxyl-terminal helix fits into the major groove of DNA.
- This motif is found in DNA-binding proteins, including λ repressor, tryptophan repressor, catabolite activator protein (CAP)



Leucine Zipper



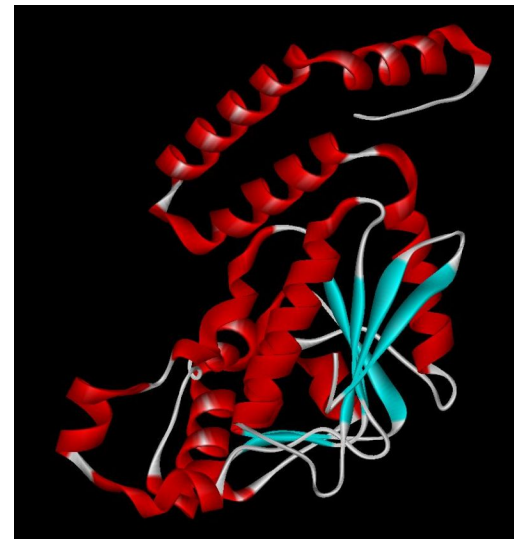
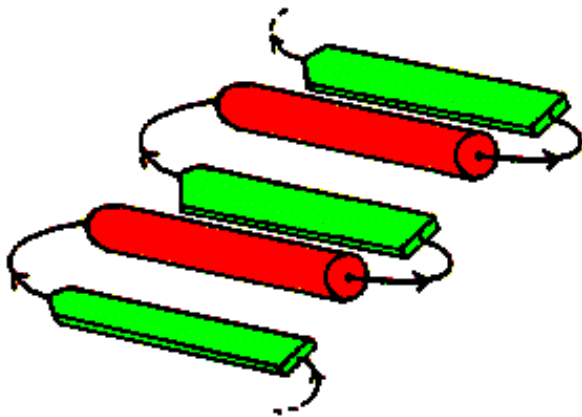
Rossman Fold



The right-handed beta-alpha-beta unit. The helix lies above the plane of the strands.

- The beta-alpha-beta-alpha-beta subunit
- Often present in nucleotide-binding proteins

The Rossman fold



What is a Protein Fold?

- ◆ Compact, globular folding arrangement of the polypeptide chain
- ◆ Chain folds to optimise packing of the hydrophobic residues in the interior core of the protein



AMINO ACID PREFERENCES

- long side chains such as those of leucine, methionine, glutamine and glutamic acid are often found in helices.
 - extended side chains can project out away from the crowded central region
- Residues whose side chains are branched at the beta carbon, such as valine, isoleucine and phenylalanine, are more often found in beta sheets
 - Every other side chain in a sheet is pointing in the opposite direction



Conformational Preferences of the Amino Acids

Amino acid	Preference		
	α -helix	β -strand	Reverse turn
Glu	1.59	0.52	1.01
Ala	1.41	0.72	0.82
Leu	1.34	1.22	0.57
Met	1.30	1.14	0.52
Gln	1.27	0.98	0.84
Lys	1.23	0.69	1.07
Arg	1.21	0.84	0.90
His	1.05	0.80	0.81
Val	0.90	1.87	0.41
Ile	1.09	1.67	0.47
Tyr	0.74	1.45	0.76
Cys	0.66	1.40	0.54
Trp	1.02	1.35	0.65
Phe	1.16	1.33	0.59
Thr	0.76	1.17	0.90
Gly	0.43	0.58	1.77
Asn	0.76	0.48	1.34
Pro	0.34	0.31	1.32
Ser	0.57	0.96	1.22
Asp	0.99	0.39	1.24



CHOU AND FASMAN PROTEIN STRUCTURE PREDICTION

- Partially Valid Assumption
- Prediction of Stretch Structure
- The methods take proteins of known three-dimensional structure
- Tabulate the preferences of individual amino acids for various structural elements
- By comparing these values with what might be expected randomly, conformational preferences can be assigned to each amino acid.
- A moving window of about five residues is scanned along a sequence, and the average preferences are tallied.



- Proline is disfavored in both helices and sheets
 - no backbone N–H group
- Glycine is also less commonly found in helices and sheets.
 - lacks a side chain
 - can adopt a much wider range of phi, psi torsion angles in peptides
- strongly associated with beta turns
- Pro–Gly and Gly–Pro



- Proline, for instance, is sometimes found in alpha helices; when it is, it simply interrupts the helical hydrogen-bonding network and produces a kink in the helix
- secondary structure formation is driven by the burial of peptide groups when hydrophobic side chains associate with each other.
- A few sequences form semistable helices in water, especially at reduced temperatures, and it has been suggested that these might serve as nucleation sites for protein folding.



SECONDARY STRUCTURE PREDICTION

	10	20	30	40	50	60	70
UNK_7585500	MTKNESYSGIDYFRFIAALLIVAIHTSPLFSFSETGNFIFTRIVAPVAVPFFFMTSGFFLISRYTCNAEK						
DPM	cccttttctccchhhhhhhheehcccccccttceeeeeehceheceeehcccccccccthhc						
DSC	ccccccccccchhhhhhhheeeeeccccccccccccccccccccccccccccccccccccchhh						
GOR4	ccccccccccchhhhhhhhhhhhhhhcccccccccccccccccccccccccccccccccccc						
HNNC	ccccccccchhhhhhhhhhhhhhhhhhhccccceccccccccccccccccccccccccchhh						
PHD	ccccccccccchhhhhhhhhhhhhhhhhhhccccceccccccccccccccccccccccccchhh						
Predator	ccccccccccchhhhhhhhhhhhhhhhhhhccccccccccccccccccccccccccccccccchhh						
SIMPA96	ccccccccchhhhhhhhhhhhhheccccccccccccccccccccccccccccccccccccchhh						
SOPM	hccttccttchhhhhhhhhheeeccccceecttceeeeecccccccccccccccccccccttceeehccccchhh						
Sec. Cons.	ccccccccccchhhhhhhhhhh??h?ccccccccccccccccccccccccccccccccccccchhh						
	80	90	100	110	120	130	140
UNK_7585500	LGAFIKKTTLIYGVAILLYIPINVYNGYFKMDNLLPNIKDIVFDGTLYHLWYLPASIIGAAIAWYLVKK						
DPM	hchhhhhccceeeeeeeeeeecectccccchccccccccccccccccccccccccccccchhhhhhehh						
DSC	hhhhhccchhhhhhhhh						
GOR4	ccccccccchhhhcceeeeeccccceccccccccccccccccccccccccccccccccccccchhhhhhhhhhhhh						
HNNC	hhhhhhhhhhhhhhhhhhheeeccccccccceehchhhhhhhhhhhheccccchhhhccccchhhhhhhhhhhhhhh						
PHD	hhhhhceeeeeccccccccccccccccccccccccccccccccchhhhhhhhhhhhhhhhhhhhhhhhhhhhhhh						
Predator	hhhhhccccccccccccccccccccccccccccccccccccchhhhhccccccccccccccccchhhhhhhhhhhhhhh						
SIMPA96	hhhhhhhhhhhhhhhhheeeeeccccccccccccccccccccchhhhhhhccccccccccccchhhhhhhhhhhhhhh						
SOPM	hhhhhhhhheeeeeeeeecccccttcchhhhtcchhhhhhhheettceeeeeccccchhhhhhhhhhhhhhh						
Sec. Cons.	hhhhh?h??eecccccccccccc?cccccccccccc?hhhhhecccc?eeeecccc?hhhhhhhhhhhhhh						



- Transmembrane proteins
 - single alpha helix
 - 20 hydrophobic residues

