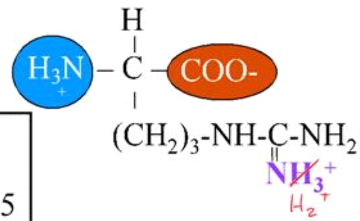
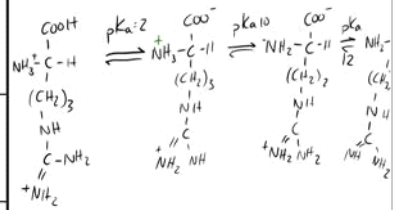
Notes 10/8

Monday, October 08, 2007
10:00 AM

Example pI calculation- Arginine (look this over on your own)



Ionizable group (HA) pK$_a$		pH 2	7	10	12.5
α-carboxyl (α-COO$^-$)	~2	-½	-	-	-
α-amino (α-H_3N^+)	~10	+	+	+½	0
Guanidinyl ((NHR)$_2$C=NH$_2$+)	12.5	+	+	+	+½
TOTAL CHARGE: (at each pH)		+1½	+1	+½	-½



pI will be half-way between these two pHs or ~11.3

Proteins: Secondary Structure

Oct. 8, 2007

- Turn in extra credit
- Answers to problem set #2 avail. online
- Problem set #3 avail.
- More practice problems available soon
- Quiz 1 this week (20 pt)!
- This Friday is the last day to drop
- Voet & Voet should be read to enhance your understanding, not to substitute for lecture
- Check VOH regularly, especially the ques. & answers section

Review

- Protein primary structure
- Peptide bond
- Torsional angles (phi, psi)
- Naming peptides

Rotation around bonds

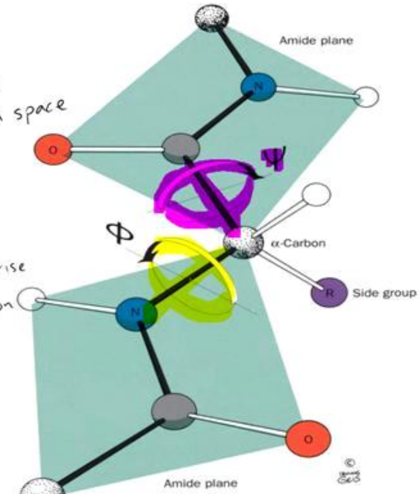
Ramachandran diagrams

Configuration: diff. geom due to orientation in space

D/L R/S

cis/trans

Confirmation: alternate arrangements that arise from molecular motion

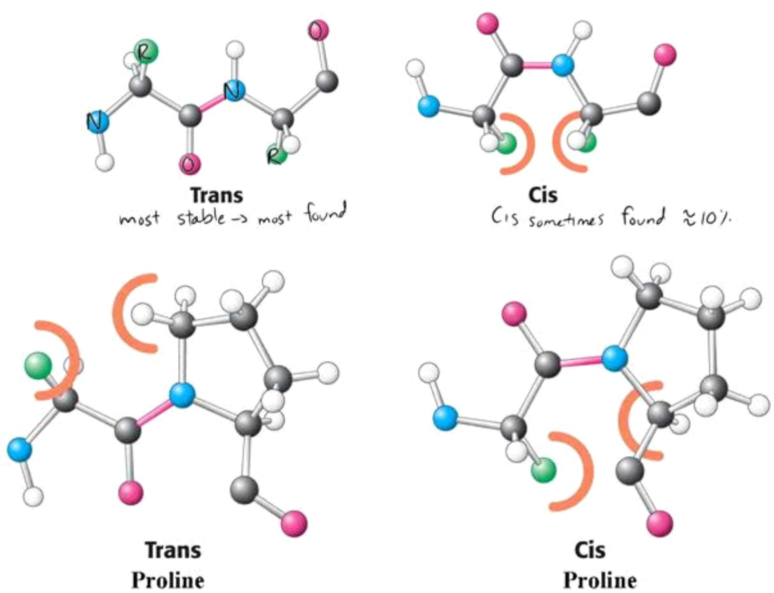


to determine + or - 180° look from perspective of α-carbon

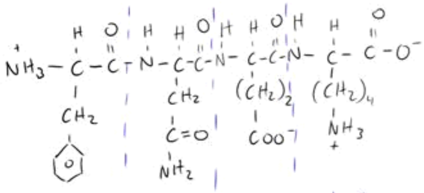
Phi, ϕ: Rotation about the $N\text{-}C_\alpha$ bond, +180 to -180°

Psi, ψ: Rotation about the $C_\alpha\text{-}C(O)$ bond, +180 to -180°

Proline's configuration about peptide bond



Name this peptide



gln glutaminyl
glu glutamyl
asp aspartyl

Phe-Asn-Glu-Lys

phenylalanyl-asparaginyl-glutamyl-lysine

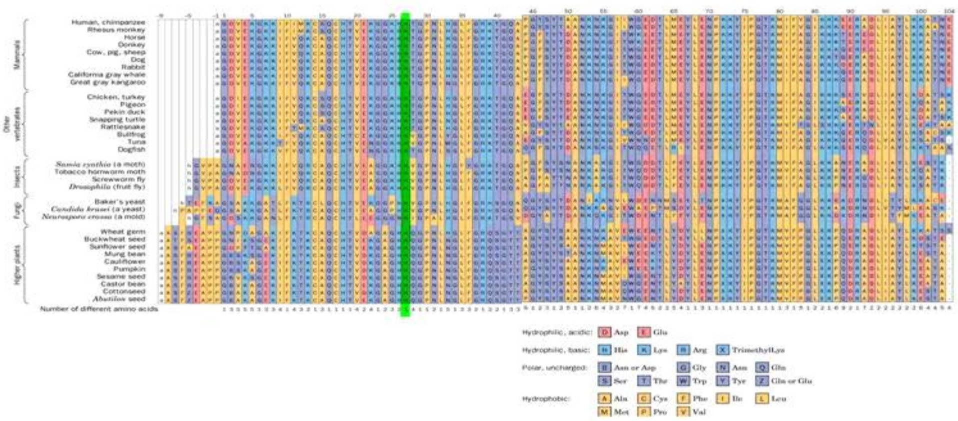
New Material Outline

- Amino acid primary structure homology
- Secondary protein structure
- Alpha helix
  - Collagen, keratin
- Beta helix
  - Fibroin
- Supersecondary structure
- Biological functions of proteins

What is the Nature of Amino Acid Sequences?

- Sequences and composition reflect the function of the protein
- Homologous proteins from different organisms have homologous sequences
- Evolutionary relatedness can be inferred from sequence homology
- e.g., cytochrome c is highly conserved

Amino Acid Sequences of Cytochromes *c* from 38 Species.



Amino Acid Difference Matrix for 26 Species of Cytochrome *c*

Average differences

	Man, chimpanzee	Rhesus monkey	Horse	Donkey	Pig, cow, sheep	Dog	Gray whale	Rabbit	Kangaroo	Chicken, turkey	Penguin	Pekin duck	Rattlesnake	Snapping turtle	Bullfrog	Tuna fish	Screw worm fly	Silkworm moth	Wheat	*Neurospora crassa*	Baker's yeast	*Candida krusei*
Man, chimpanzee	0																					
Rhesus monkey	1	0																				
Horse	12	11	0																			
Donkey	11	10	1	0																		
Pig, cow, sheep	10	9	3	2	0																	
Dog	11	10	6	5	3	0																
Gray whale	10	9	5	4	2	3	0															
Rabbit	9	8	6	5	4	5	2	0														
Kangaroo	10	11	7	8	6	7	6	6	0													
Chicken, turkey	13	12	11	10	9	10	9	8	12	0												
Penguin	13	12	12	11	10	10	9	8	10	2	0											
Pekin duck	11	10	10	9	8	8	7	6	10	3	3	0										
Rattlesnake	14	15	22	21	20	21	19	18	21	19	20	17	0									
Snapping turtle	15	14	11	10	9	9	8	9	11	8	8	7	22	0								
Bullfrog	18	17	14	13	11	12	11	11	13	11	12	11	24	10	0							
Tuna fish	21	21	19	18	17	18	17	17	18	17	18	17	26	18	15	0						
Screw worm fly	27	26	22	22	22	21	22	21	24	23	24	22	29	24	22	24	0					
Silkworm moth	31	30	29	28	27	25	27	26	28	28	27	27	31	28	29	32	14	0				
Wheat	43	43	46	45	45	44	44	44	47	46	46	46	46	46	48	49	45	45	0			
Neurospora crassa	48	47	46	46	46	46	46	46	49	47	48	46	47	49	49	48	41	47	54	0		
Baker's yeast	45	45	46	45	45	45	45	45	46	46	45	46	47	49	47	47	45	47	47	41	0	
Candida krusei	51	51	51	50	50	49	50	50	51	51	50	51	51	53	51	48	47	47	50	42	27	0

10.0 · 5.1 · 9.9 · 14.3 · 12.6 · 18.5 · 25.9 · 47.0

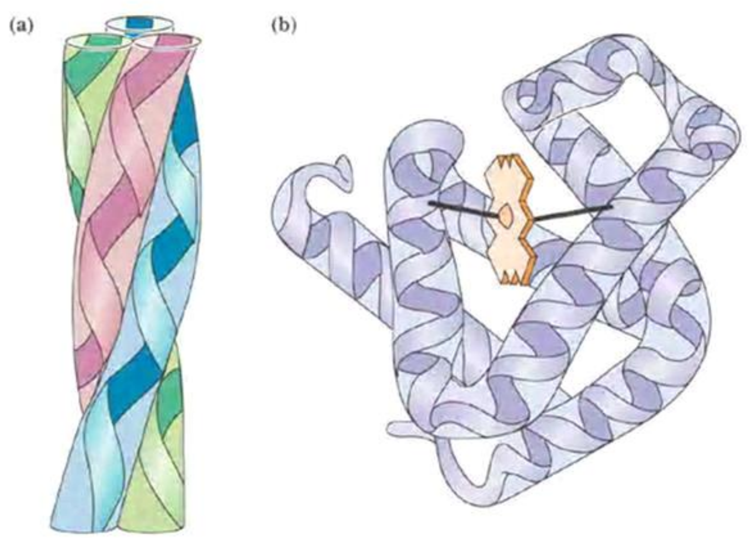
What Architectural Arrangements Characterize Protein Structure?

- Proteins are classed according to shape and solubility
- Shape - globular or fibrous
- The four levels of protein structure
    - Primary - sequence (Oct. 5th)
    - Secondary - local structures - H-bonds
    - Tertiary - overall 3-D shape
    - Quaternary - subunit organization

Two Major Classes of Proteins

only found in animals (not plants)

1. Fibrous: this class of proteins are elongated molecules w/ well-defined secondary structures and function primarily in a structural role, I.e. they hold things together.
   - α- and β-keratins, fibroin, collagen, elastin
   - generally water insoluble
   - found to aggregate
2. Globular: most of the chemical work is done by this class of protein so named because of their compact 3-D fold.
   - Synthesizing, transporting, metabolizing, catalyzing,etc.
   - tend to be more round like shape



(a) Collagen, a fibrous protein

insoluble

(b) Myoglobin, a globular protein

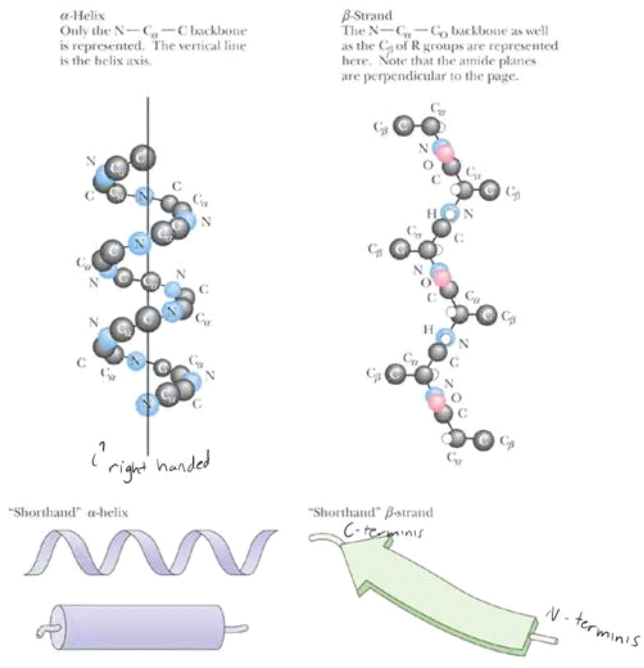
Soluble

Secondary Structure

Linus Pauling studied the crystal structures of the 20 amino acids, postulated 4 principles that a polypeptide structure should obey:

- Conserved bond lengths and angles with those of the free amino acids
- No two atoms should approach closer than their van der Waals radii would allow
- Amide group must remain planar & in the trans configuration
- Some kind of non-covalent bonding is necessary to stabilize a regular folding. The most obvious possibility being the H-bond between amide protons and carbonyl oxygens

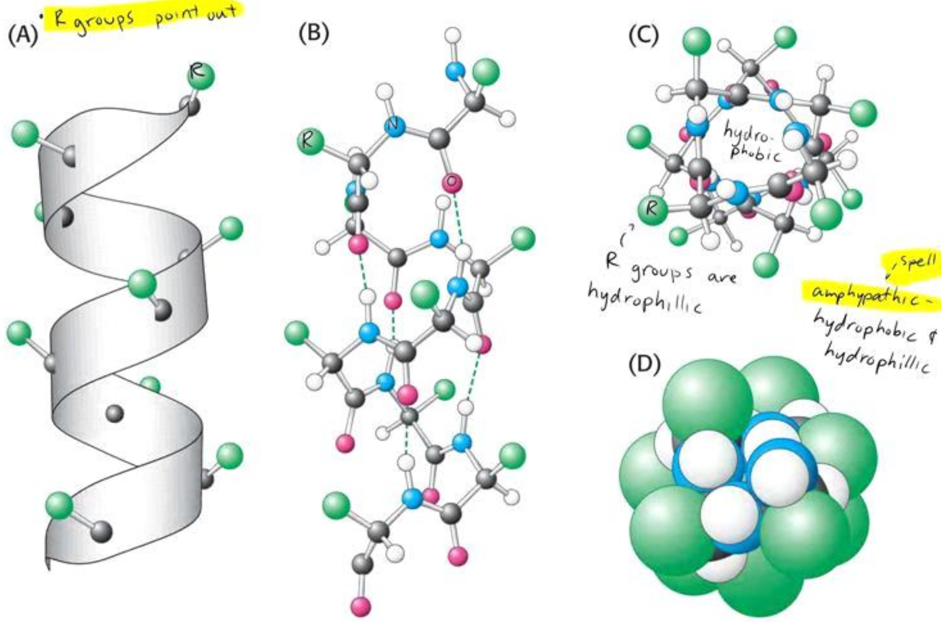
In the end, he came up with two possible structures: the α-helix and the β-sheet.



The α-helix

top view - looking down

• R groups point out

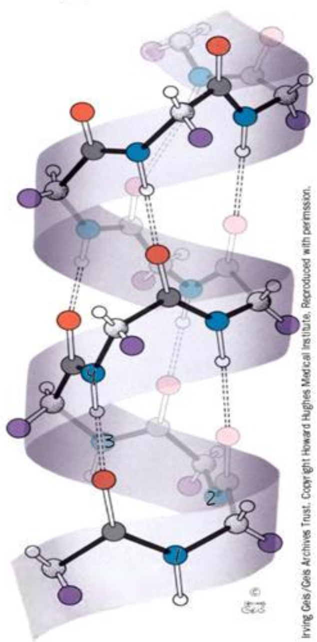


R groups are hydrophillic

amphypathic - spell?
hydrophobic & hydrophillic

The right-handed α-helix.

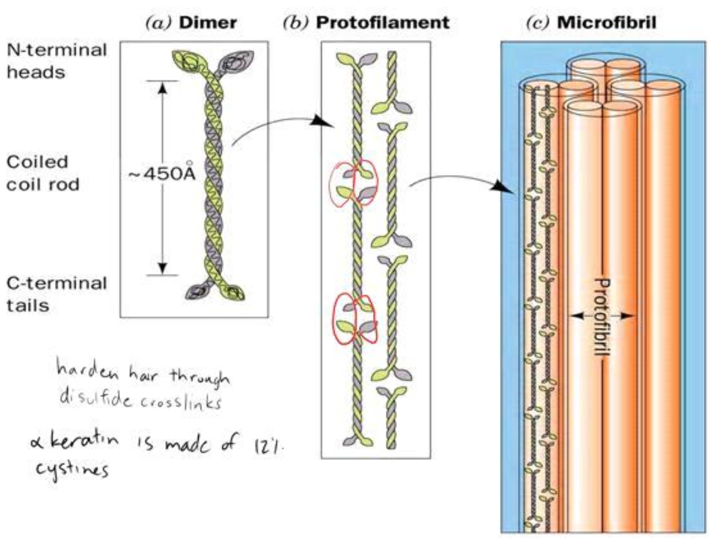
carbonyl is H-bonded to 4th nitrogen



in middle of helix, there are Van der Waals forces which stabalizes the helix.

The microscopic organization of hair.

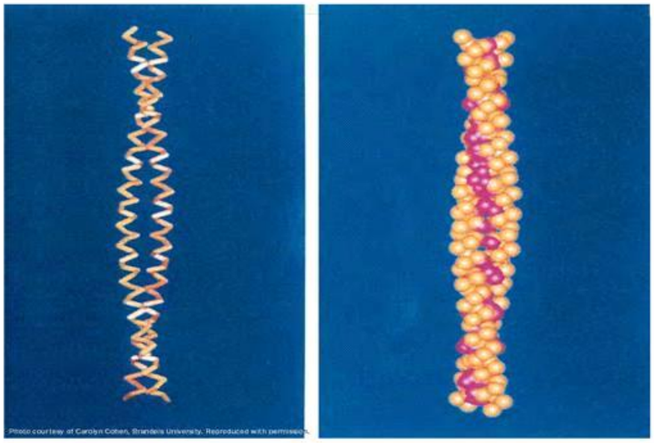
The structure of α keratin



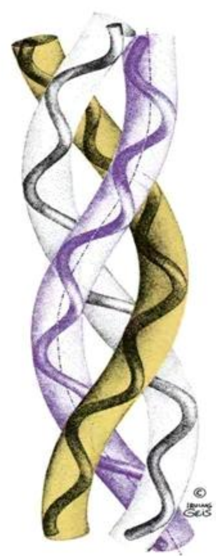
harden hair through disulfide crosslinks

α keratin is made of 12% cystines

The two-stranded coiled coil structure of tropomyosin



The triple helix of collagen



collagen - (kolla = glue, greek)

- found in skin, ligaments, bones, teeth
- responsible for elasticity
- where gellitan comes from
- has tripeptide repeat
  - -Gly-X-Y-Gly-X-Y-
  - X = Pro hdroxyproline

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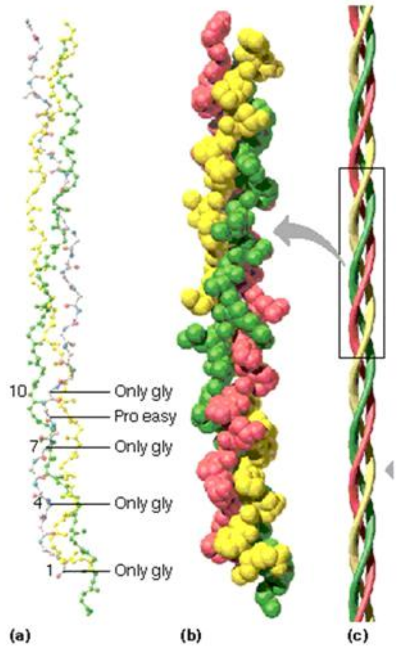
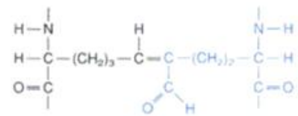
Vitamin C is precursor to collagen (scurvy)

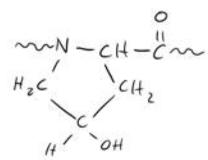
Collagen



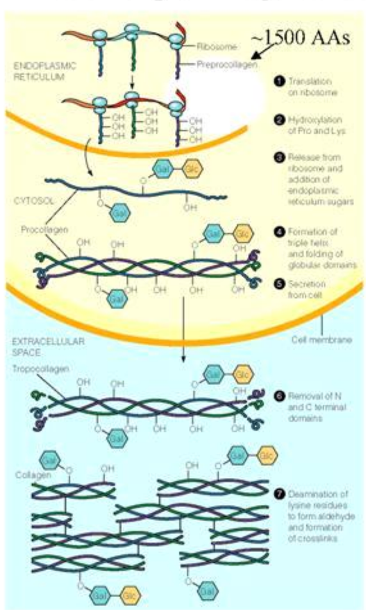


Oxidized LYS cross-links provide stiffness to collagen

4-hydroxyproline residue in collagen



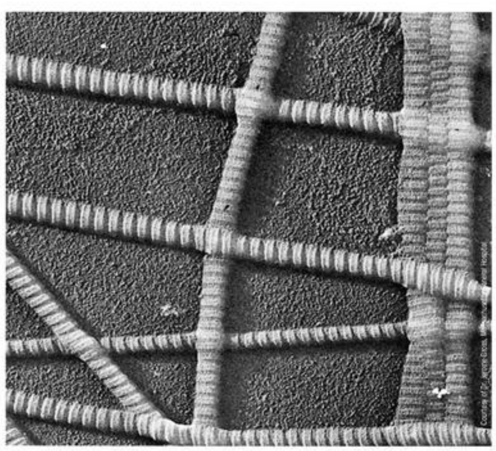
Collagen Synthesis - not time not covered



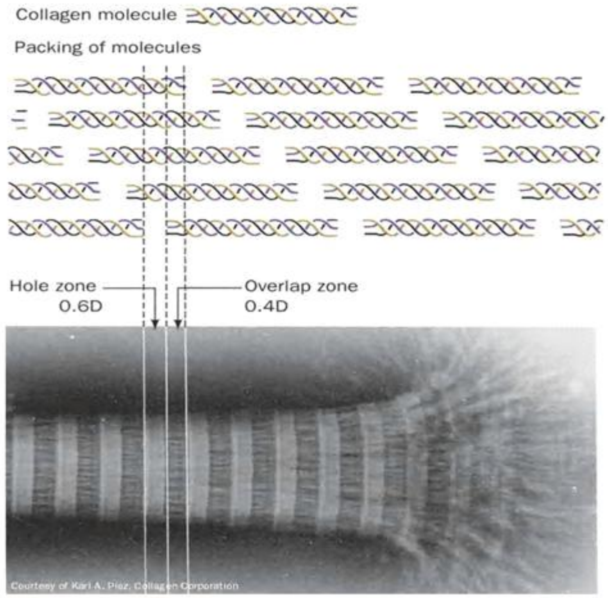
The Arrangement of Collagen Fibrils in Various Tissues

Tissue	Arrangement
Tendon	Parallel bundles
Skin	Sheets of fibrils layered at many angles
Cartilage	No distinct arrangement
Cornea	Planar sheets stacked crossways so as to minimize light scattering

Electron micrograph of collagen fibrils from skin

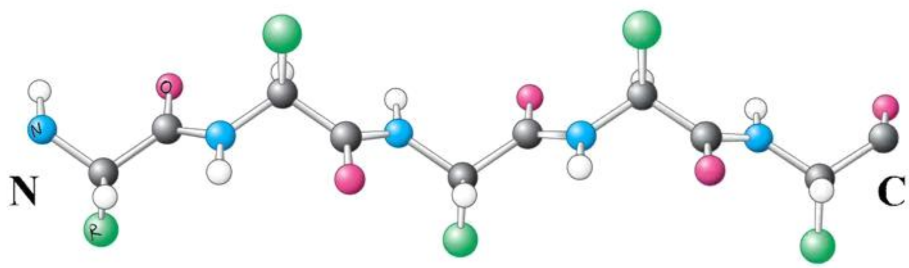


Banded appearance of collagen fibrils

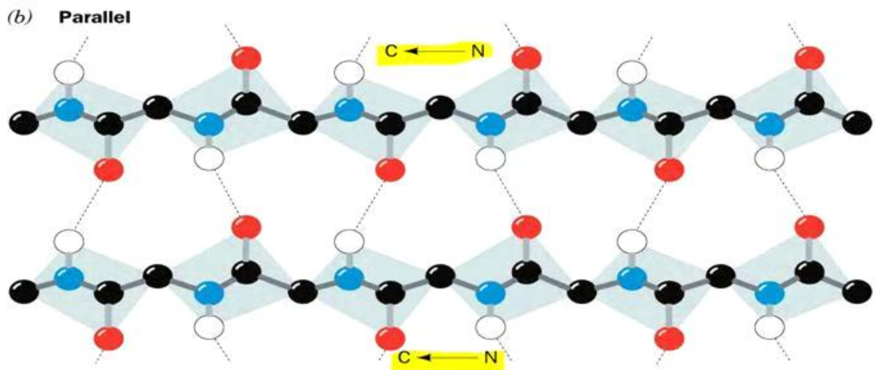


β-strand

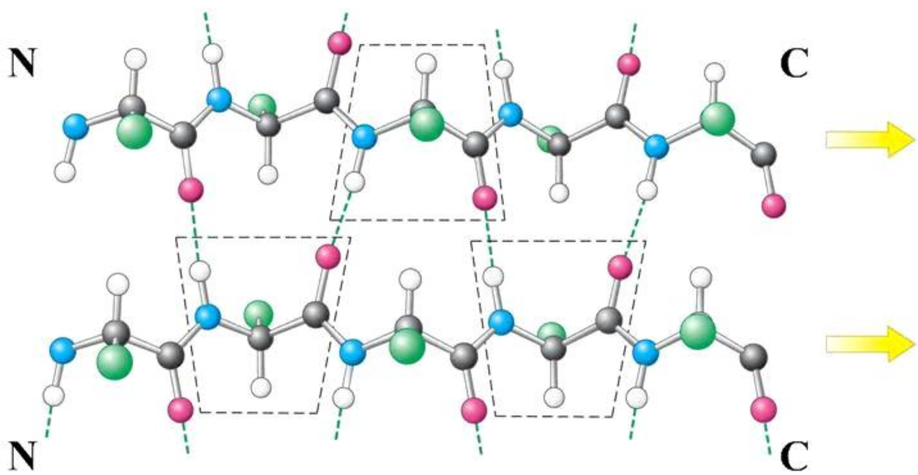
· trans R groups



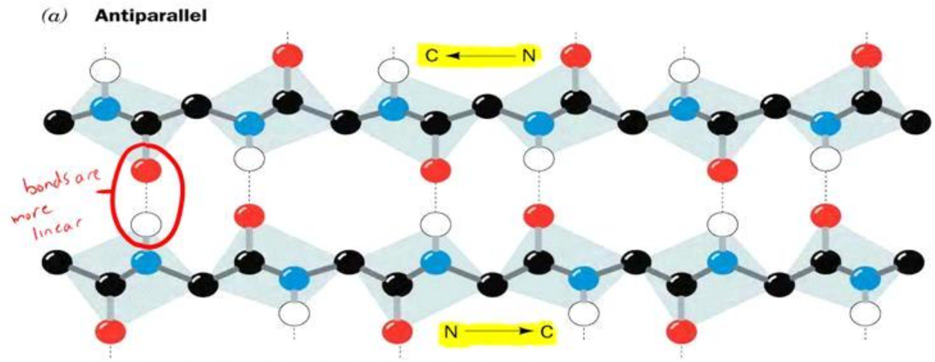
The parallel β pleated sheets



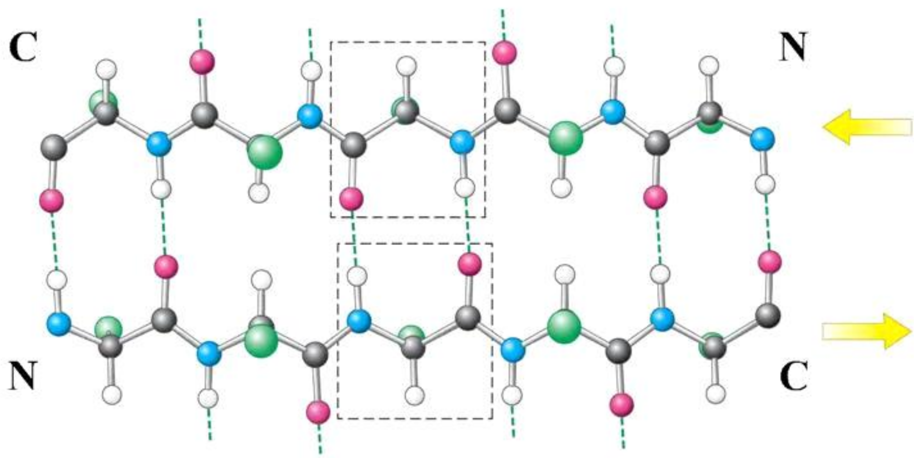
H-bonding in parallel β-sheet



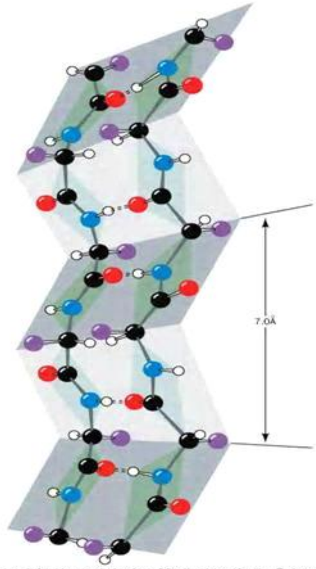
The antiparallel β pleated sheets



H-bonding in anti-parallel β-sheet

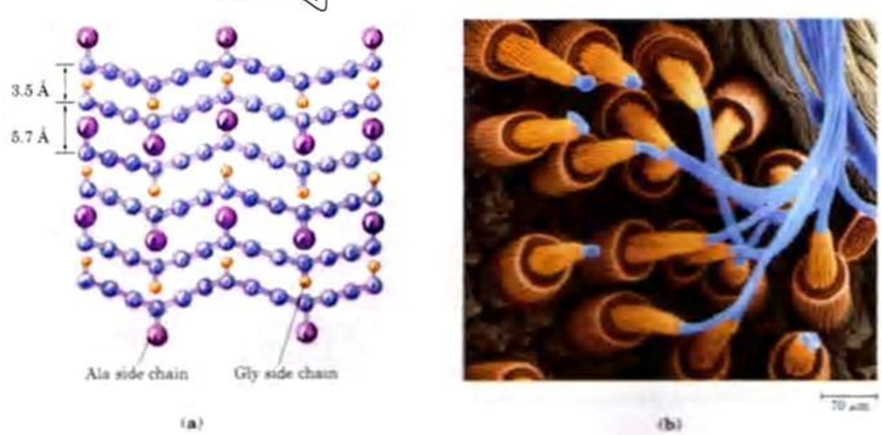


A two-stranded β antiparallel pleated sheet drawn to emphasize its pleated appearance

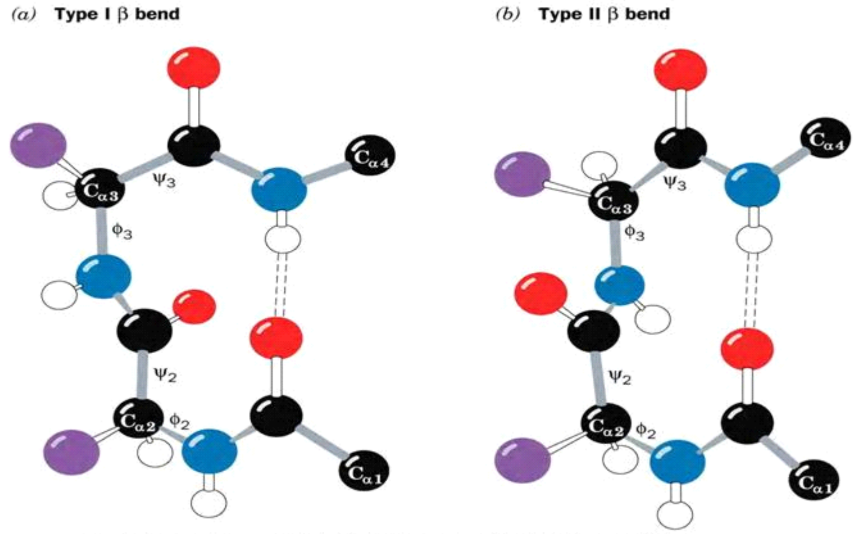


Fibroin

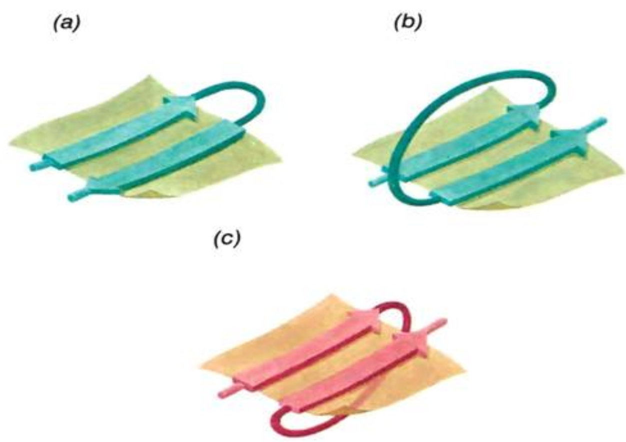
Ran out of time here ↓



Reverse turns in polypeptide chains



Connections between adjacent polypeptide strands in β pleated sheets.



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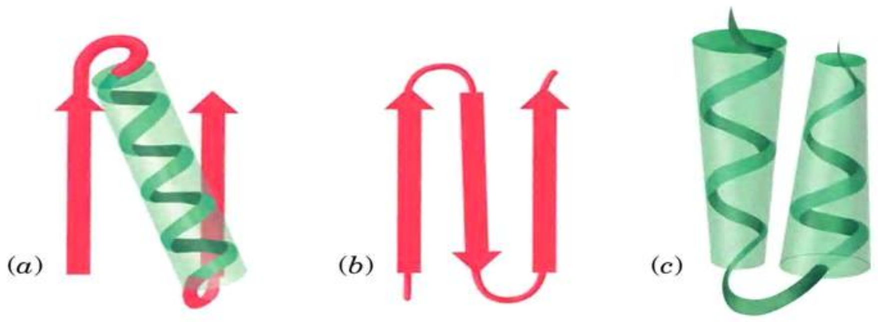
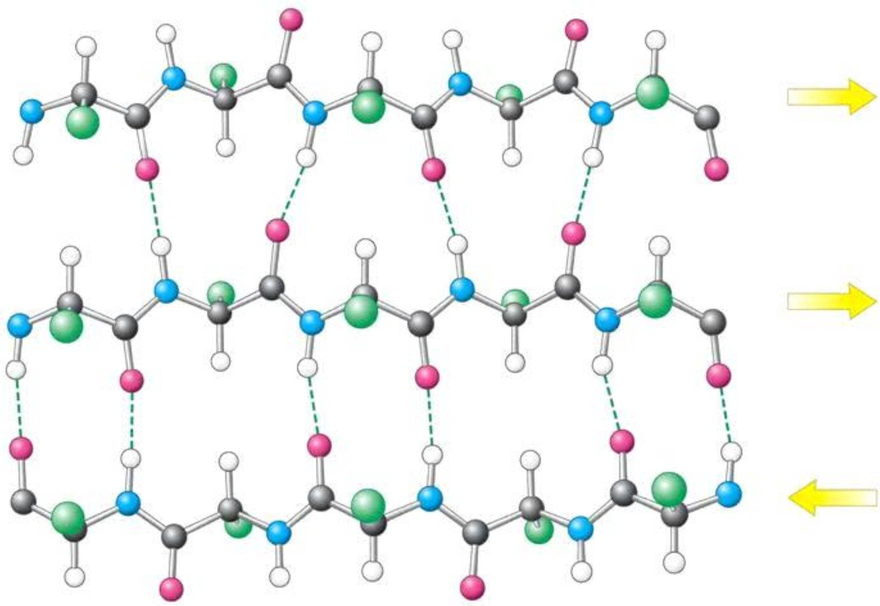
Protein Folding Patterns

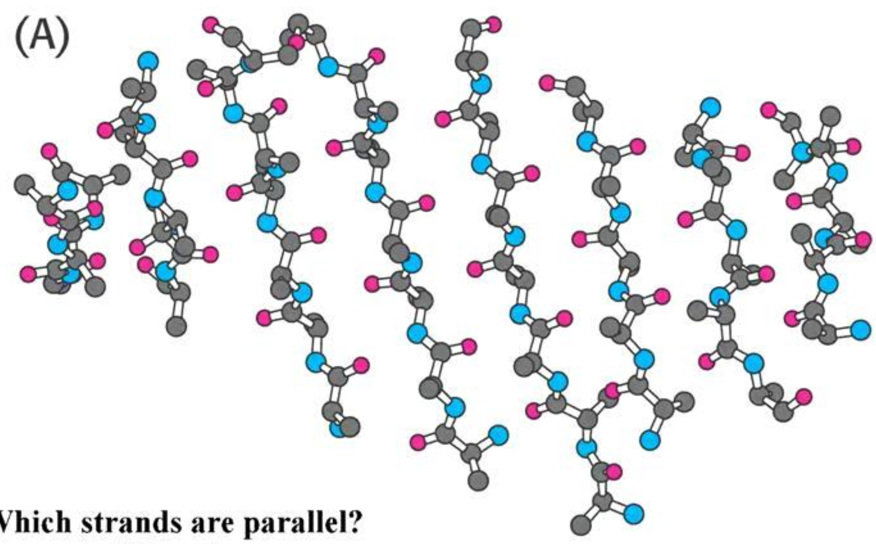
- Hairpin β- 2 antiparallel β-strands joined by a loop.
- βαβ motif- two parallel β strands connected by an α-helix
- Greek Key- Two sequentially adjacent hairpin motifs
- EF- hand- helix-loop-helix

Schematic diagrams of supersecondary structures



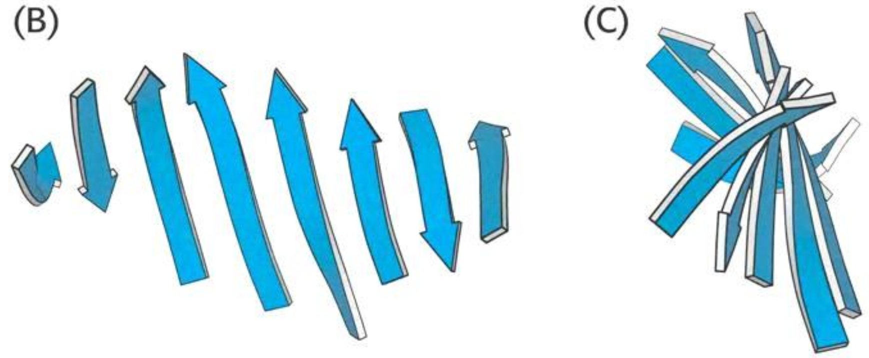


Test yourself



Which strands are parallel?
Draw the H-bonds.
Identify the amino-termini and carboxyl termini.

β-sheet Proteins



What Are the Many Biological Functions of Proteins?

- Many proteins are enzymes
- Regulatory proteins control metabolism and gene expression
- Many DNA-binding proteins are gene-regulatory proteins
- Transport proteins carry substances from one place to another
- Storage proteins serve as reservoirs of amino acids or other nutrients

What Are the Many Biological Functions of Proteins?

- Movement is accomplished by contractile and motile proteins
- Many proteins serve a structural role
- Proteins of signaling pathways include scaffold proteins (adapter proteins)
- Other proteins have protective and exploitive functions
- A few proteins have “exotic” functions