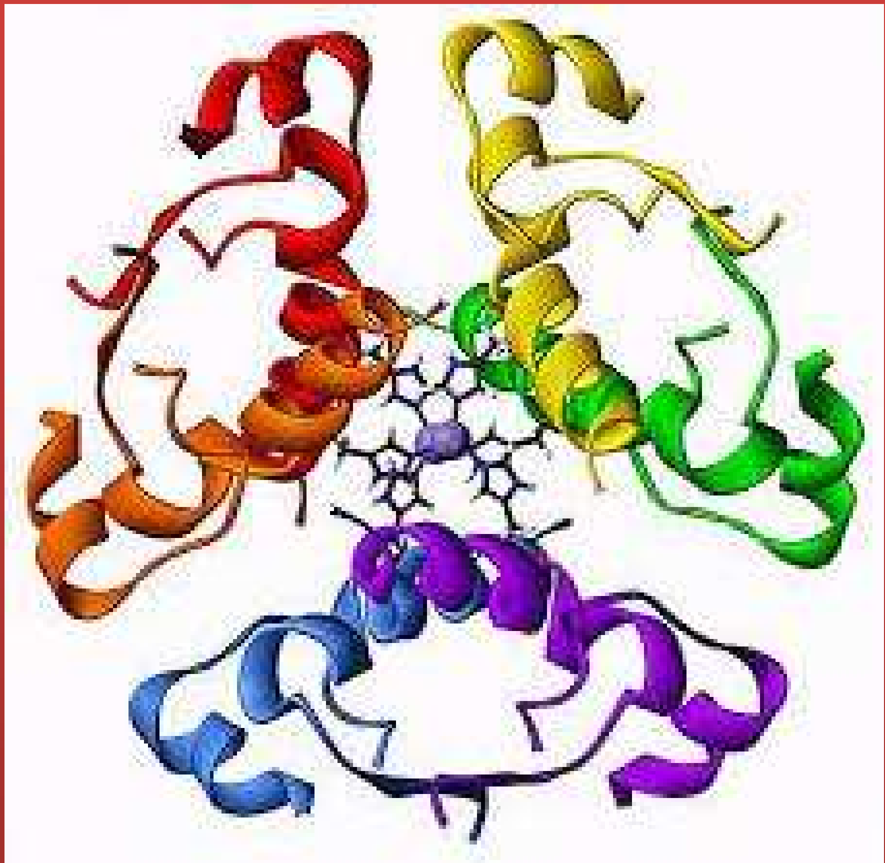


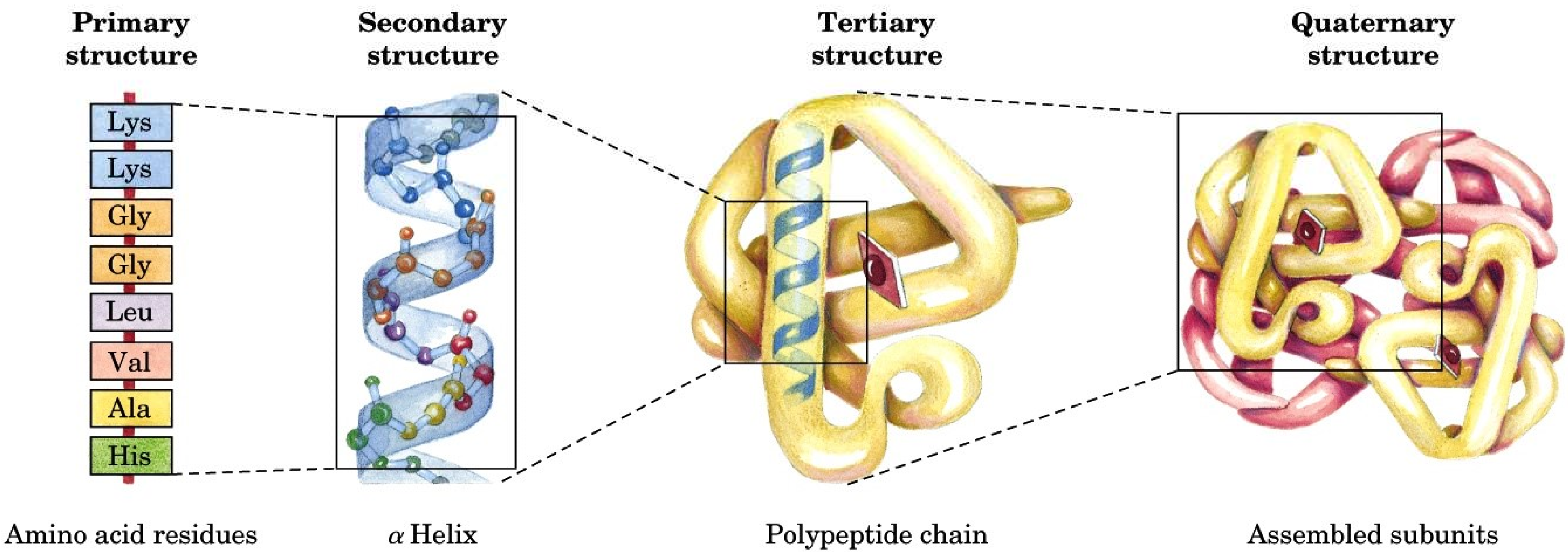
Proteins

By

S.K.Sinha , Kota

Levels of Protein Structure

Proteins show 4 levels of structural organisation:



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Levels of Protein Structure

Proteins show 4 levels of structural organisation:

1.Primary structure = amino acid sequence

- **Determined by the genetic code of the mRNA.**

2. Secondary structure = folding and twisting of a single polypeptide chain.

- **Result of weak H-bond and electrostatic interactions.**
- **e.g., α-helix (coiled) and β-pleated sheet (zig-zag).**

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Levels of Protein Structure

3. Tertiary structure = three dimensional shape (or conformation) of a polypeptide chain.
   - Function of R groups contained in the polypeptide.

4. Quaternary structure = association between polypeptides in multi-subunit proteins (e.g. hemoglobin).
   - Occurs only with two or more polypeptides.

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Peptide Bonds

–α-carboxyl of one amino acid is joined to α-amino of a second amino acid (with removal of water)

- only α-carboxyl and α-amino groups are used, not R-group carboxyl or amino groups.

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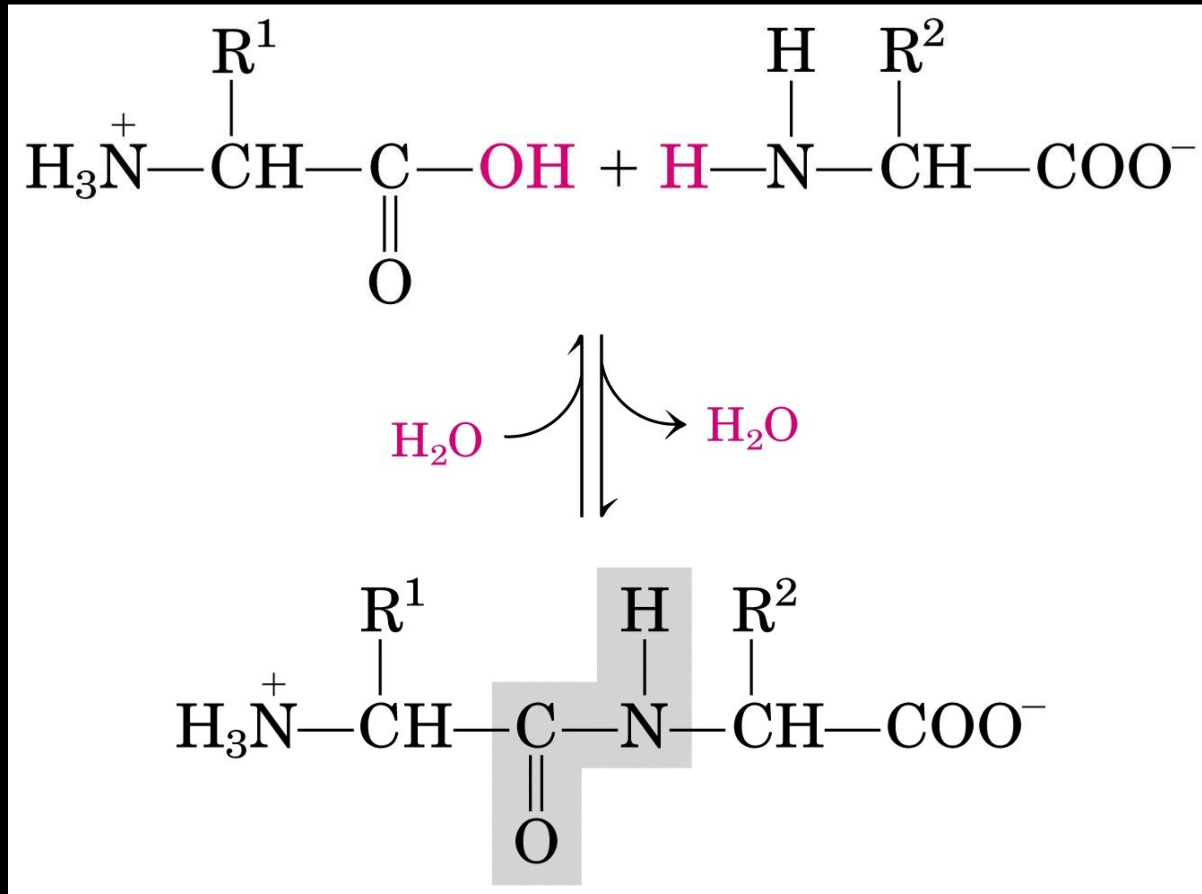
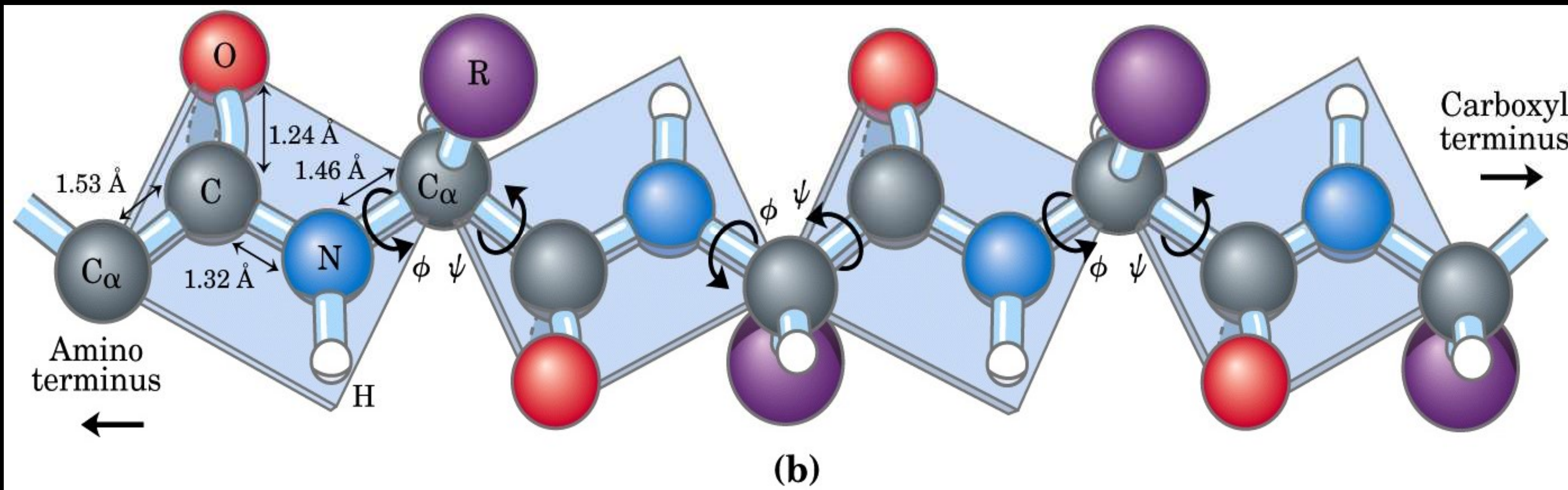
Peptide bond formation



The peptide bond is planar



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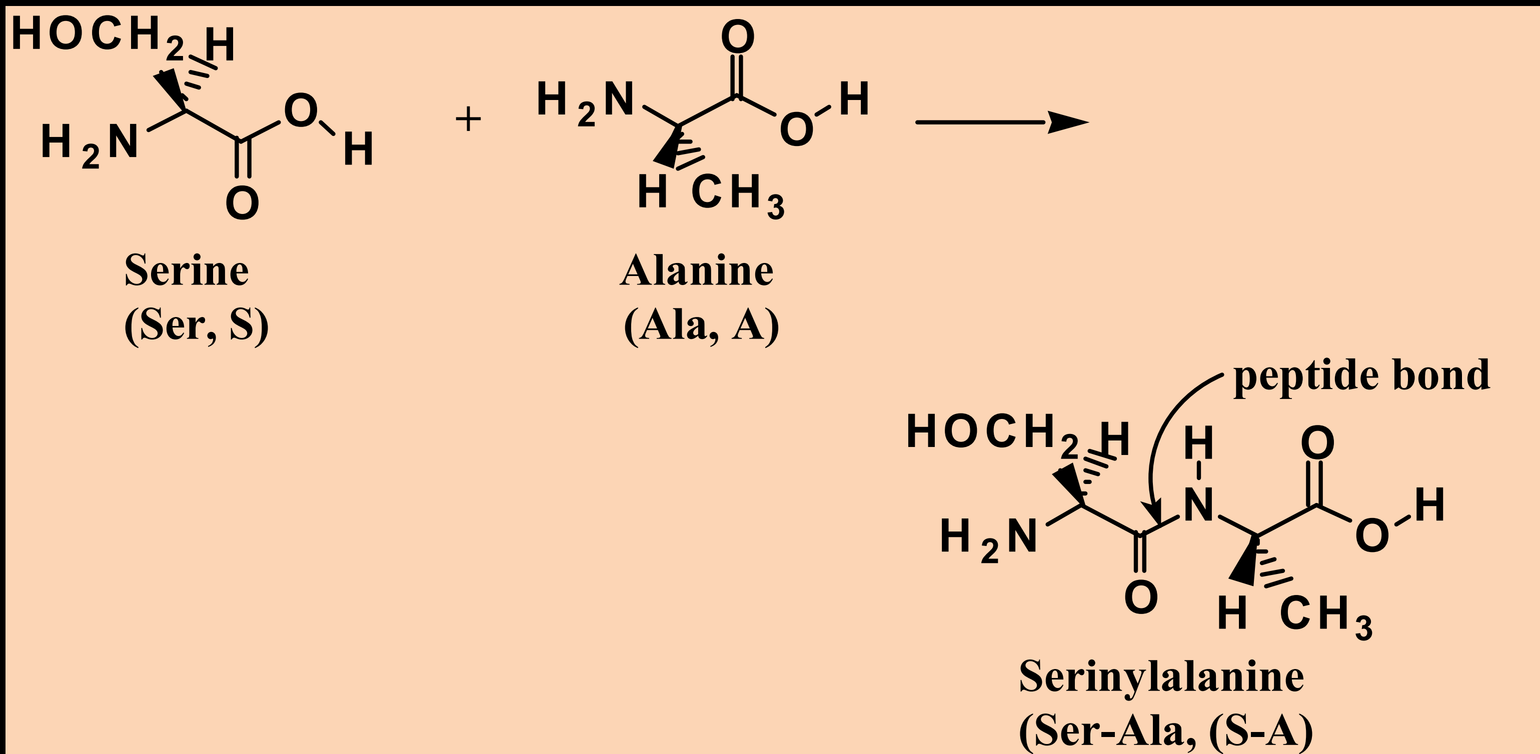
Peptide bond: The special name given to the amide bond between the α-carboxyl group of one amino acid and the α-amino group of another.

Serinylalanine (Ser-Ala)



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Dipeptide: A molecule containing two amino acids joined by a peptide bond.

Tripeptide: A molecule containing three amino acids joined by peptide bonds.

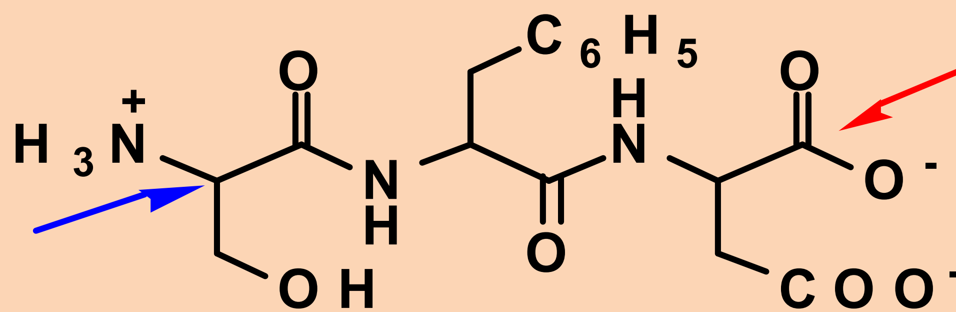
Polypeptide: A macromolecule containing many amino acids joined by peptide bonds.

Protein: A biological macromolecule of molecular weight 5000 g/mol or greater, consisting of one or more polypeptide chains.

Writing Peptides

By convention, peptides are written from the left, beginning with the free -NH_3^+ group and ending with the free -COO^- group on the right.

N-terminal amino acid



Ser-Phe-Asn

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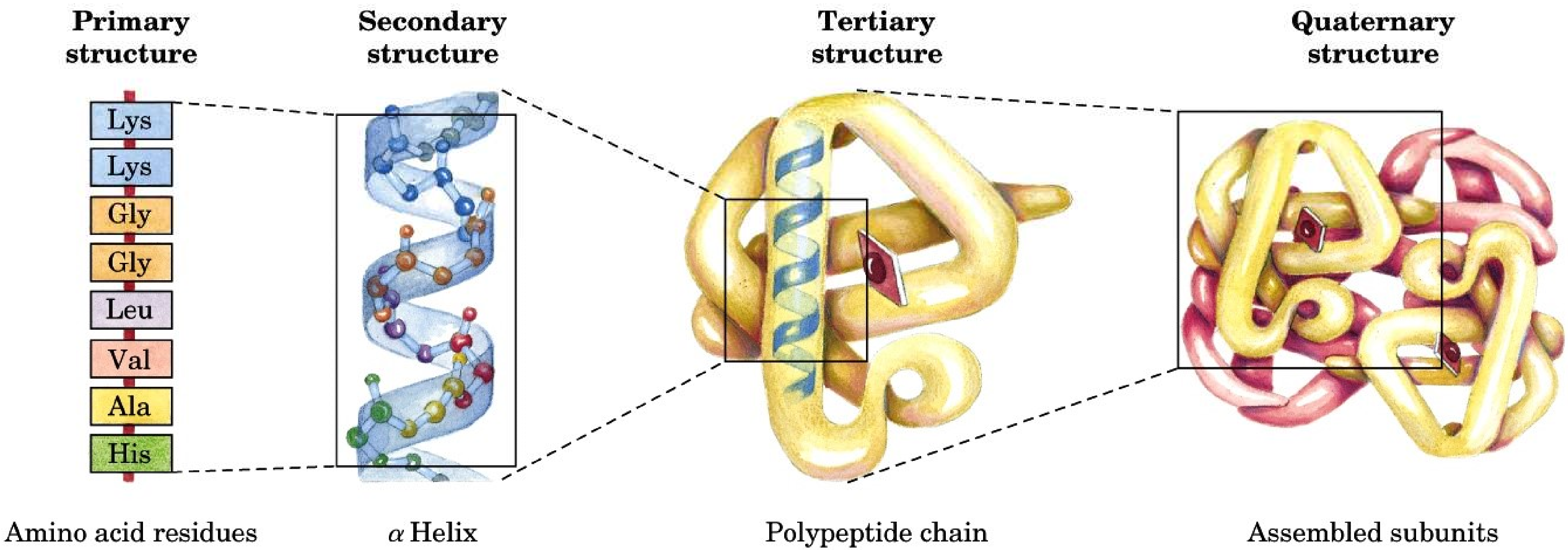
Secondary structure



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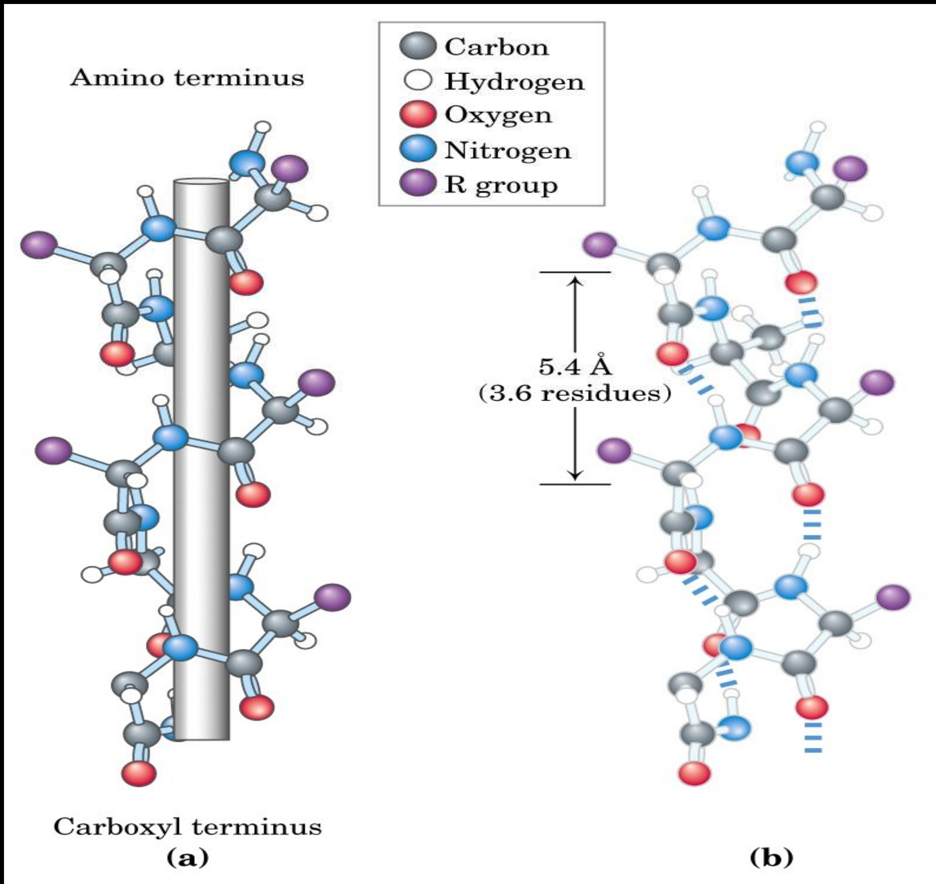
The α-helix



- In the α-helix, the carbonyl oxygen of residue "i" forms a hydrogen bond with the amide of residue "i+4".

- Although each hydrogen bond is relatively weak in isolation, the sum of the hydrogen bonds in a helix makes it quite stable.

- The propensity of a peptide for forming an α-helix also depends on its sequence.

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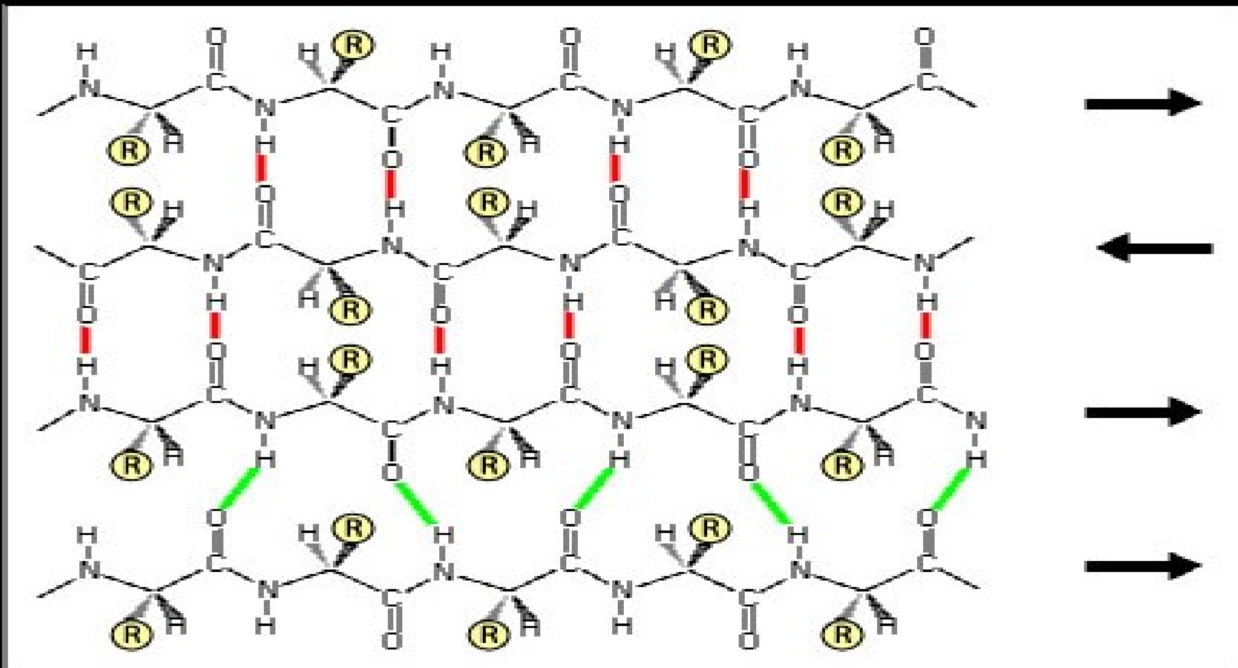
Protein structure: sheets



- notice the difference in H-bonding pattern between parallel and anti-parallel beta-sheets

- also notice orientation of side chains relative to the sheets

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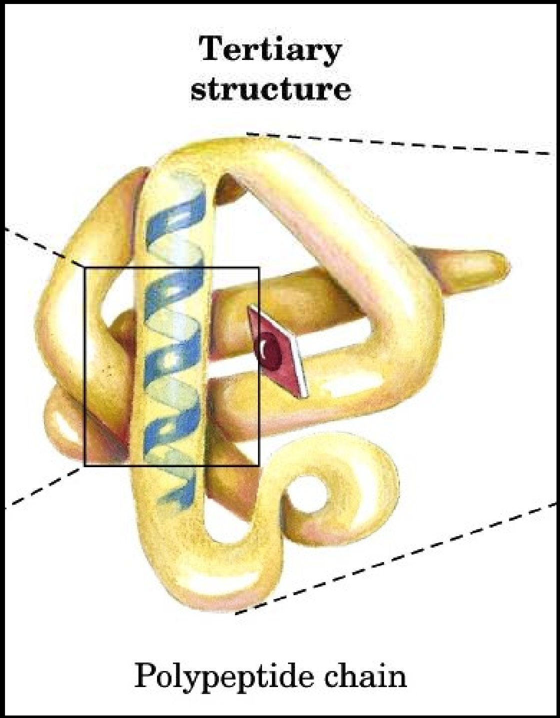
Tertiary structure



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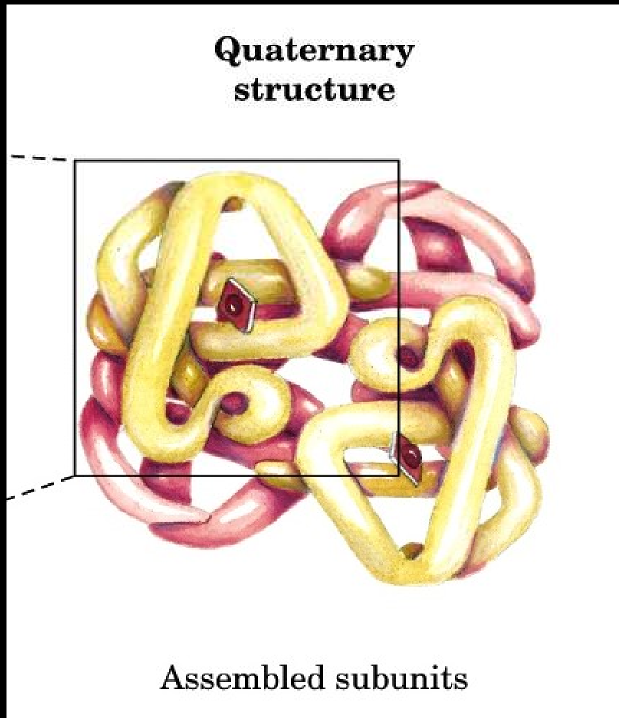
Quaternary structure



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Types of interactions

interaction	nature	bond length	"bond" strength	example
ionic (salt bridge)	electrostatic	1.8-4.0 Å (3.0-10 Å for like charges)	1-6 kcal/mol	positive: K, R, H, N-terminus negative: D, E, C-terminus
hydrophobic	entropy	-	2-3	hydrophobic side chains (M,I,L,V,F,W,Y,A,C,P)
H-bond	H-bonding	2.6-3.5	2-10	H donor, O acceptor
van der Waals	attraction/ repulsion	2.8-4.0	<1	closely-spaced atoms; if too close, repulsion
aromatic-aromatic	$\pi-\pi$	4.5-7.0	1-2	F,W,Y (stacked)
aromatic-amino group	H-bonding	2.9-3.6	2.7-4.9	N-H donor to F,W,Y

Protein-solvent interactions

hydrophilic amino acids

- these amino acids tend to interact extensively with solvent in context of the folded protein; the interaction is mostly ionic and H-bonding

Protein-solvent interactions

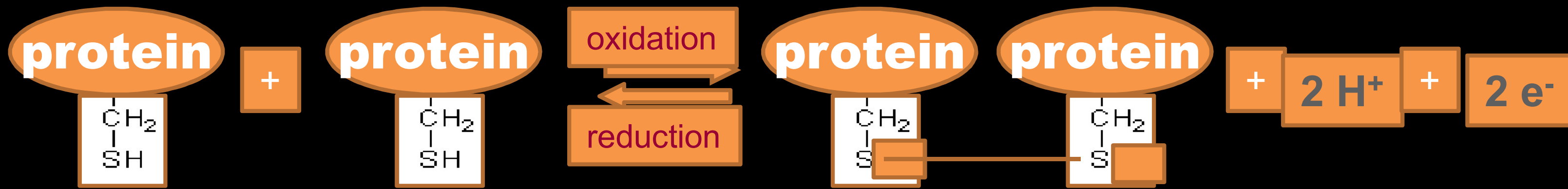
hydrophobic amino acids

-these tend to form the 'core' of the protein, *i.e.*, are buried within the folded protein; some hydrophobic residues can be entirely (or partially) exposed

small neutral amino acids

- less preference for being solvent-exposed or not

The disulfide bond



- **Disulfide bond formation is a covalent modification; the oxidation reaction can either be intramolecular (within the same protein) or inter-molecular (within different proteins)**

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Protein denaturants

- **high temperatures**
  - *cause protein unfolding, aggregation*

- **low temperatures**
  - *some proteins are sensitive to cold denaturation*

- **heavy metals (*e.g.*, lead, cadmium, etc.)**
  - *highly toxic; efficiently induce the 'stress response'*

Protein denaturants

- proteotoxic agents (*e.g.*, alcohols, cross-linking agents, etc.)

- oxygen radicals, ionizing radiation
  - cause permanent protein damage

- chaotropes (urea, guanidine hydrochloride, etc.)
  - highly potent at denaturing proteins; often used in protein folding studies

Classes of proteins

Functional definition:

Enzymes: Accelerate biochemical reactions

Structural: Form biological structures

Transport: Carry biochemically important substances

Defense: Protect the body from foreign invaders

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Classes of proteins

Structural definition:
Globular: Complex folds, irregularly shaped tertiary structures
Fibrous: Extended, simple folds - generally structural proteins

Cellular localization definition:
Membrane: In direct physical contact with a membrane; generally water insoluble.
Soluble: Water soluble; can be anywhere in the cell.

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Classes of proteins

Conjugated Proteins

	Prosthetic group	Example
Lipoproteins	Lipids	β_1-Lipoprotein of blood
Glycoproteins	Carbohydrates	Immunoglobulin G
Phosphoproteins	Phosphate groups	Casein of milk
Hemoproteins	Heme (iron porphyrin)	Hemoglobin
Flavoproteins	Flavin nucleotides)	Succinate dehydrogenase
Metalloproteins	Iron	Ferritin
	Calcium	Calmodulin
	Copper	Plastocyanin

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Use of Amino Acids

Aspartame (aspartyl-phenylalanine-1-methyl ester) is an artificial sweetener.

5-HTP (5-hydroxytryptophan) has been used to treat neurological problems associated with PKU (phenylketonuria), as well as depression.

L-DOPA (L-dihydroxyphenylalanine) is a drug used to treat Parkinsonism.

Monosodium glutamate is a food additive to enhance flavor.

Classification of Proteins

Proteins can be classified into two types on the basis of their molecular shape.

(a) Fibrous proteins :

(b) Globular proteins :

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Use of Amino Acids

(a) Fibrous proteins : The polypeptide chains run parallel and are held together by hydrogen and disulphide bonds, then fibre– like structure is formed.

Such proteins are generally insoluble in water. Examples:

1. keratin (present in hair, wool, silk)
2. Myosin (present in muscles),

Use of Amino Acids

(b) Globular proteins:

This structure results when the chains of polypeptides coil around to give a spherical shape. These are usually soluble in water.

Examples:

1. Insulin
2. albumins