

Protein Structure

Biochemistry Boot Camp 2021

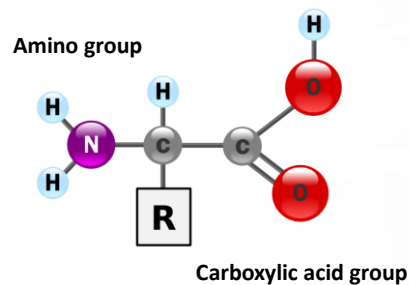
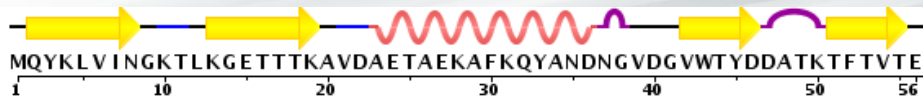
Session #1

Matt Thompson

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1

What is a Protein?

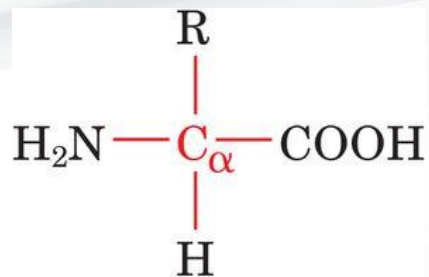


Cartoon Model

- **Answer:** Polymer of amino acids connected by peptide bonds
 - Multiple representations, including sequence, chemical structure, simplifying cartoons
- PyMOL Download: Staphylococcal Nuclease (sticks and cartoon)

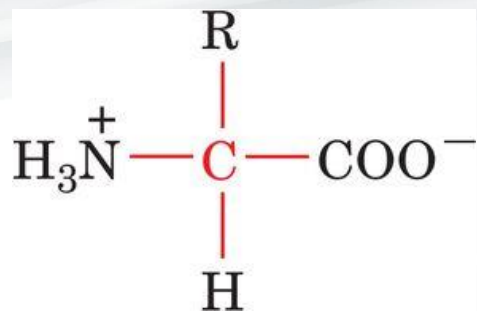
2

General Structure of α -Amino Acid



3

Dipolar Amino Acid: Zwitterion



4

Drawing Amino Acids 101

5

Structures of Standard Amino Acids

TABLE 4-1 Covalent Structures and Abbreviations of the "Standard" Amino Acids of Proteins, Their Occurrence, and the pK Values of Their Ionizable Groups

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula ^a	Residue Mass (Da) ^b	Average Occurrence in Proteins (%) ^c	pK _a α-COOH ^d	pK _a α-NH ₃ ⁺ ^e	pK _a Side Chain ^f
Amino acids with nonpolar side chains						
Glycine Gly G		57.0	7.1	2.35	9.78	
Alanine Ala A		71.1	8.2	2.35	9.87	
Valine Val V		99.1	6.9	2.29	9.74	
Leucine Leu L		113.2	9.7	2.33	9.74	
Isoleucine Ile I		113.2	6.0	2.32	9.76	
Methionine Met M		131.2	2.4	2.13	9.28	
Proline Pro P		97.1	4.7	1.85	10.64	
Phenylalanine Phe F		147.2	3.9	2.20	9.31	
Tryptophan Trp W		186.2	1.1	2.46	9.41	

^aThe ionic form shown are those predominating at pH 7.0 (except for that of histidine^h) although residue mass is given for the neutral compound. The C_α atom, as well as atoms marked with an asterisk, are chiral centers with configurations as indicated according to Fischer projection formulas (Section 4-2). The standard organic numbering system is provided for heterocycles.

^bThe residue masses are given for the neutral residues. For the molecular masses of the parent amino acids, add 18.0 Da, the molecular mass of H₂O, to the residue masses. For side chain masses, reference 56.0 Da, the formula mass of a peptide group, from the residue masses.

^cThe average amino acid composition in the complete SWISS-PROT database (<http://www.expasy.ch/spot/research/afdata.html>), Release 2013.13.

^dIndividual proteins may exhibit large deviations from these quantities.

^eData from Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, R.M., *Data for Biochemical Research* (3rd ed.), pp. 1-31, Oxford Science Publications (1986).

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Structures of Standard Amino Acids

TABLE 4-1 (Continued)

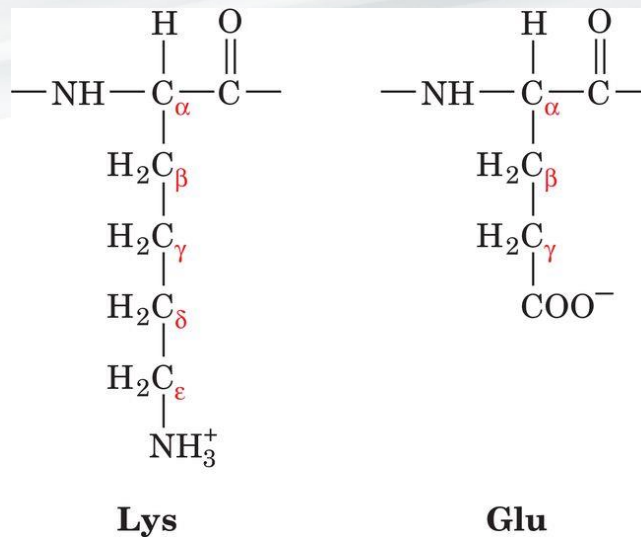
Name, Three-letter Symbol, and One-letter Symbol	Structural Formula ^a	Residue Mass (Da) ^b	Average Occurrence in Proteins (%) ^c	pK ₁ α-COOH ^d	pK ₂ α-NH ₃ ⁺ ^d	pK _a Side Chain ^e
Amino acids with uncharged polar side chains						
Serine Ser S		87.1	6.6	2.19	9.21	
Threonine Thr T		101.1	5.3	2.09	9.10	
Asparagine ^f Asn N		114.1	4.1	2.14	8.72	
Glutamine ^f Gln Q		128.1	3.9	2.17	9.13	
Tyrosine Tyr Y		163.2	2.9	2.20	9.21	10.46 (phenol)
Cysteine Cys C		103.1	1.4	1.92	10.70	8.37 (sulfhydryl)
Amino acids with charged polar side chains						
Lysine Lys K		128.2	5.9	2.16	9.06	10.54 (ε-NH3+)
Arginine ^f Arg R		156.2	5.5	1.82	8.99	12.48 (guanidino)
Histidine ^f His H		137.1	2.3	1.80	9.33	6.04 (imidazole)
Aspartic acid ^f Asp D		115.1	5.4	1.99	9.90	3.90 (β-COOH)
Glutamic acid ^f Glu E		129.1	6.8	2.10	9.47	4.07 (γ-COOH)

^aThe three- and one-letter symbols for asparagine or aspartic acid are Asn and As, whereas for glutamine or glutamic acid they are Gln and Glu. The one-letter symbol for an underlined or "nonstandard" amino acid is N.

^bBoth neutral and protonated forms of histidine are present at pH 7.0, since its pK_a is close to 7.0.

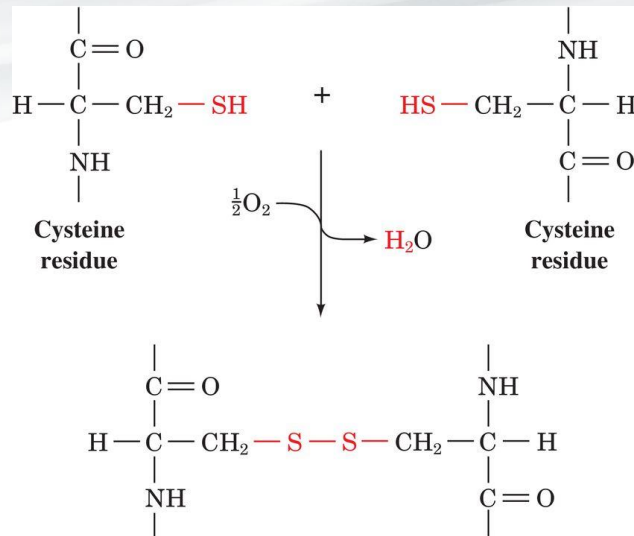
7

Amino Acid Nomenclature



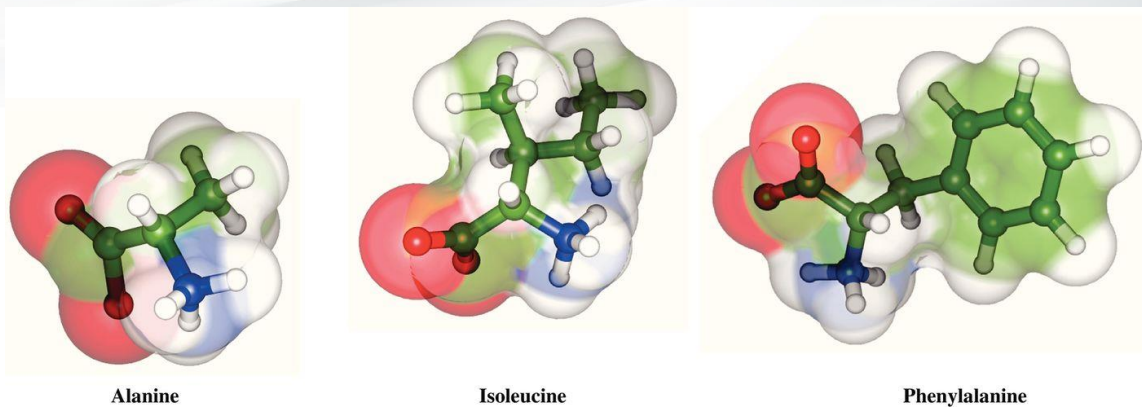
8

Cysteine Can Form Disulfide Bonds



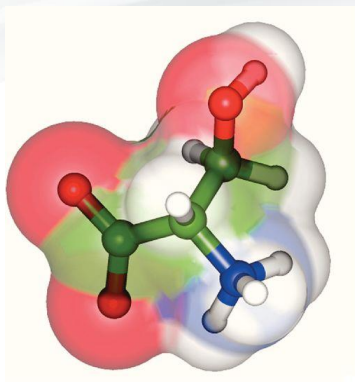
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Nonpolar Side Chains

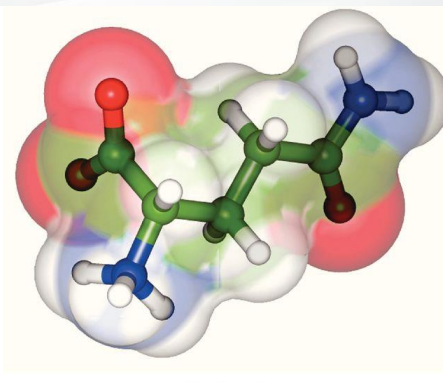


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Uncharged Polar Side Chains



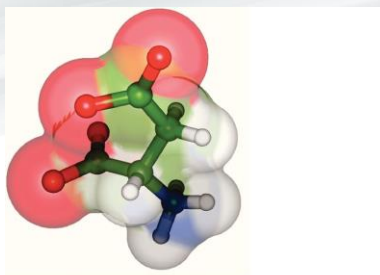
Serine



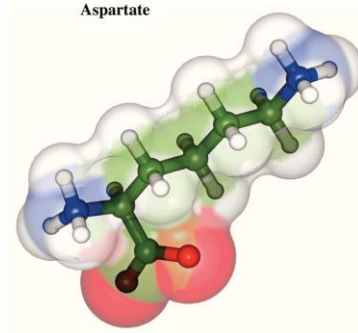
Glutamine

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Charged Polar Side Chains



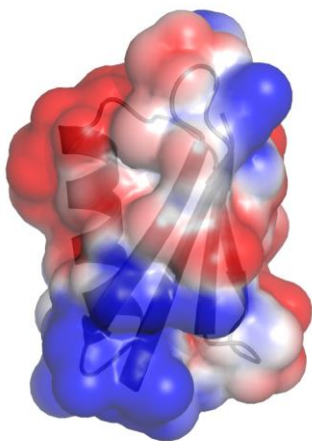
Aspartate



Lysine

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Electrostatic surface



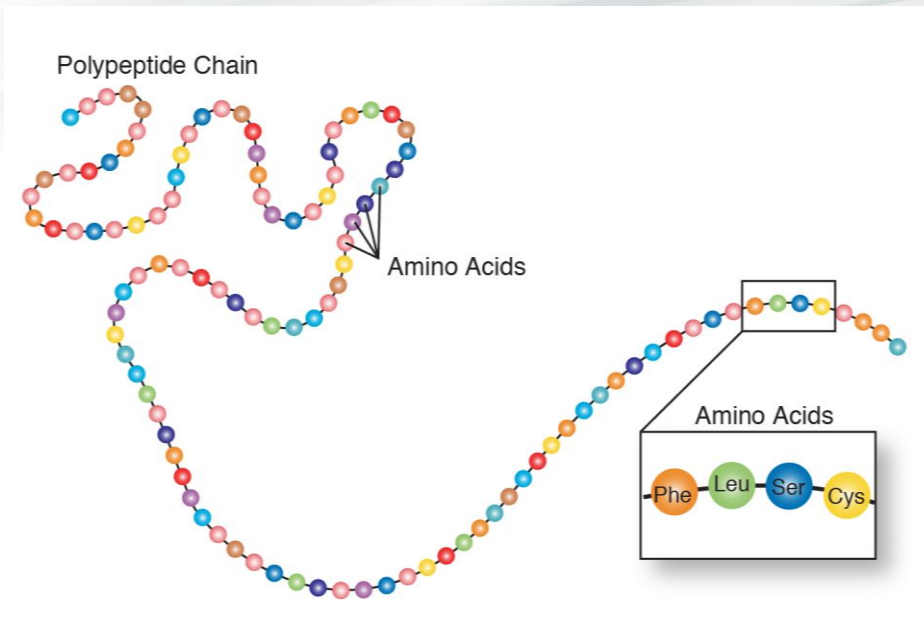
Red – negative charge

Blue – positive charge

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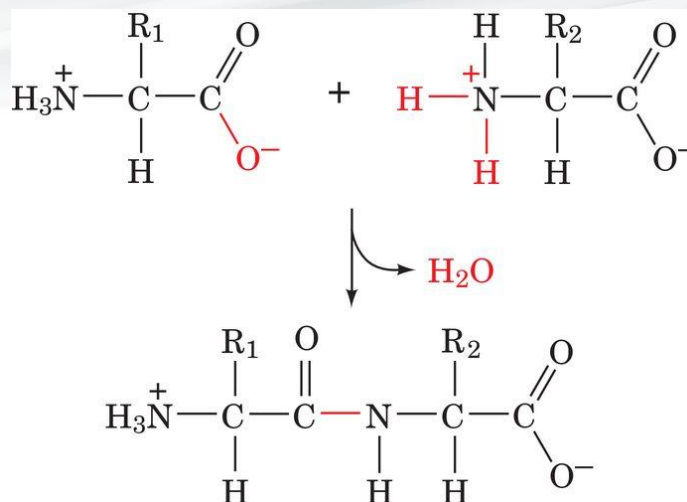
14

Proteins Are Composed of a “Chain” of Amino Acids



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Condensation of Two Amino Acids

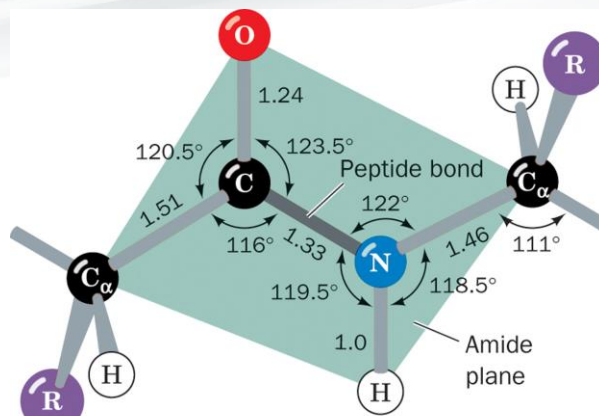


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Condensation of Two Amino Acids

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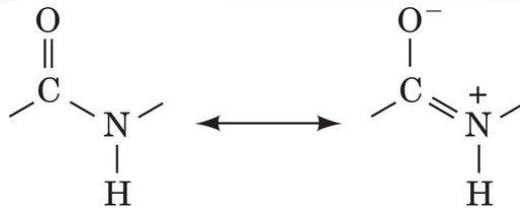
Peptide Bonds Assume Trans Conformation



After Marsh, R.E. and Donohue, J., Adv. Protein Chem. 22, 249 (1967).

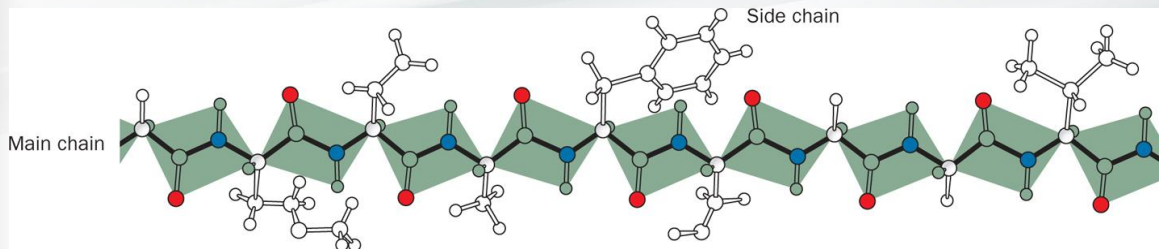
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Resonance of Peptide Bond

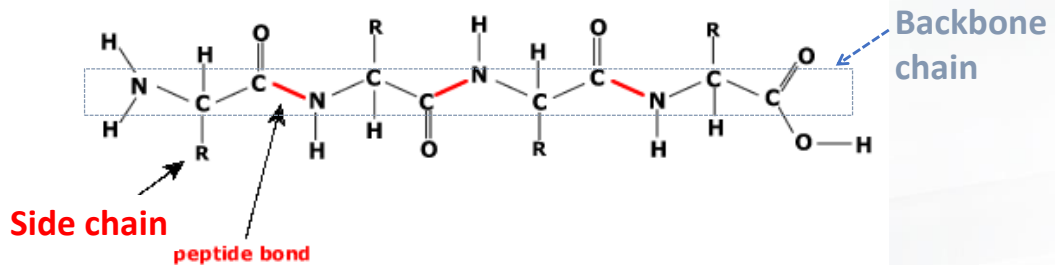


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Extended Conformation of Polypeptide The Protein “Backbone”

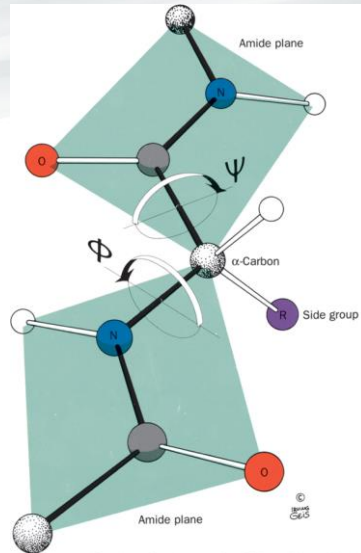


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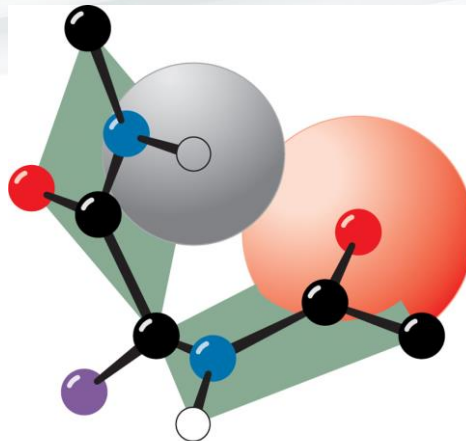
Torsion Angles of Polypeptide Backbone



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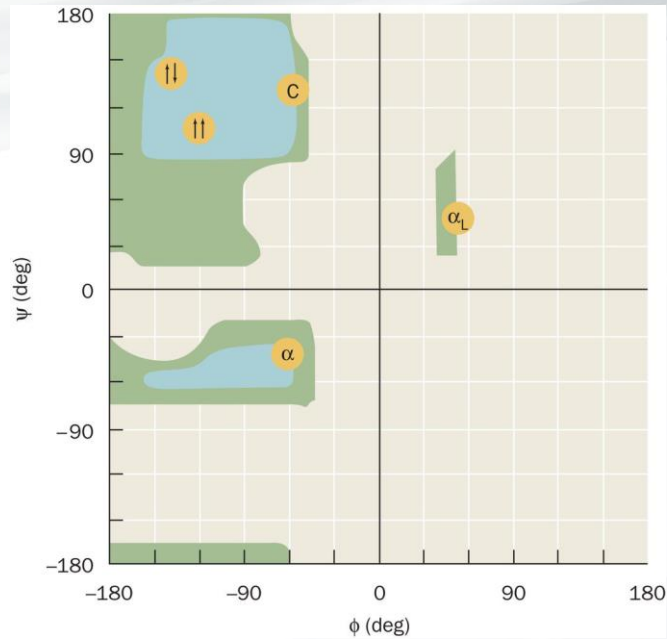
Steric Interference of Adjacent Peptide Groups



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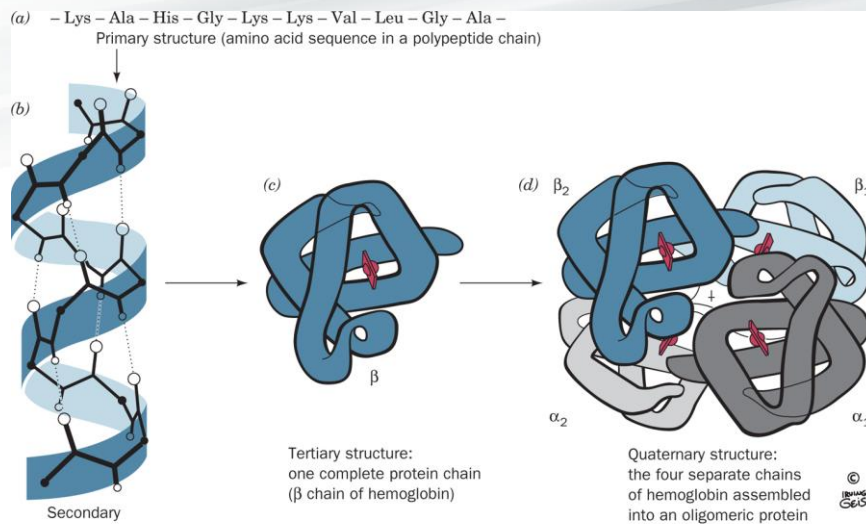
22

Ramachandran Diagram



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Levels of Protein Structure



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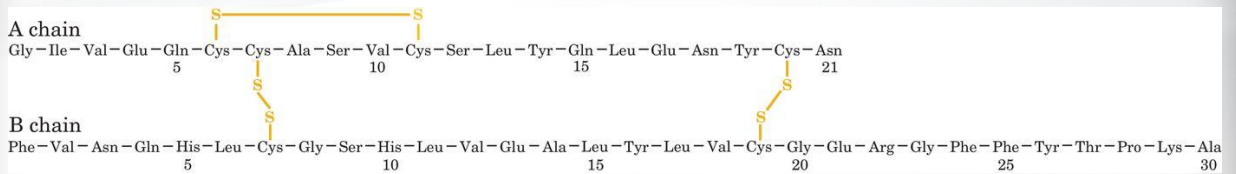
1° Structure

(a) – Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly – Ala –
Primary structure (amino acid sequence in a polypeptide chain)

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Bovine Insulin: 1° Structure



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1° & 2° Structure

(a) – Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly – Ala –
Primary structure (amino acid sequence in a polypeptide chain)



Secondary
structure
(helix)

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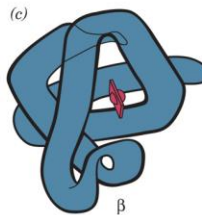
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1° , 2° , & 3° Structure

(a) – Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly – Ala –
Primary structure (amino acid sequence in a polypeptide chain)



Secondary
structure
(helix)

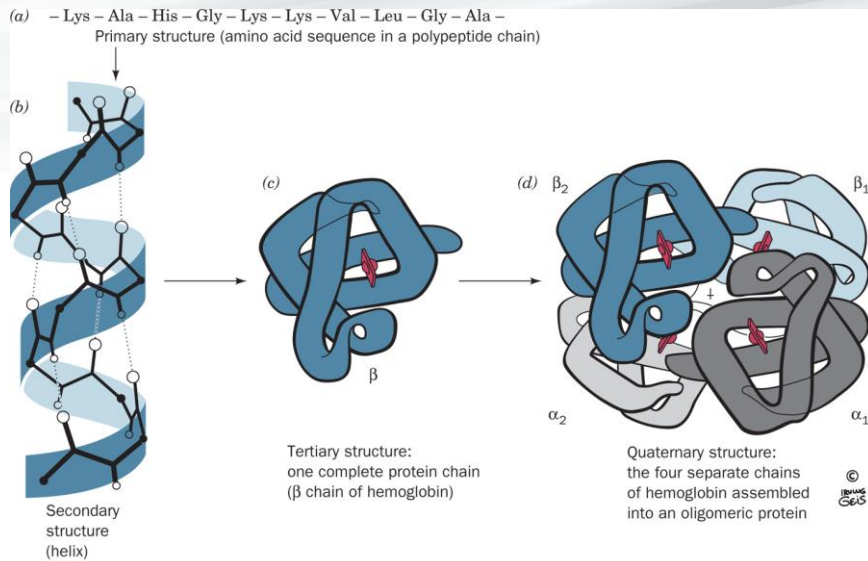


Tertiary structure:
one complete protein chain
(β chain of hemoglobin)

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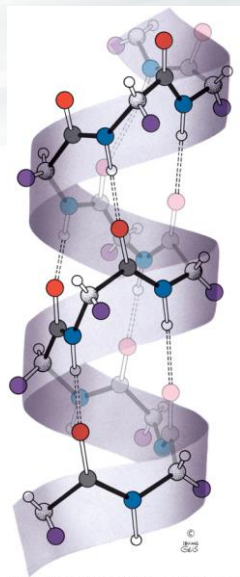
1°, 2°, 3° & 4° Structure



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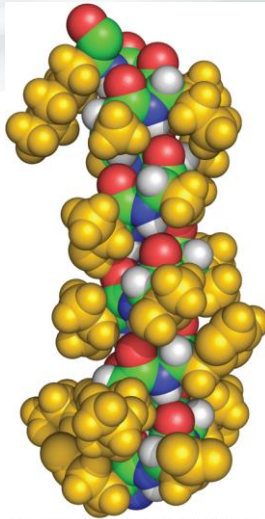
The α Helix



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The α Helix: Space Filling Model

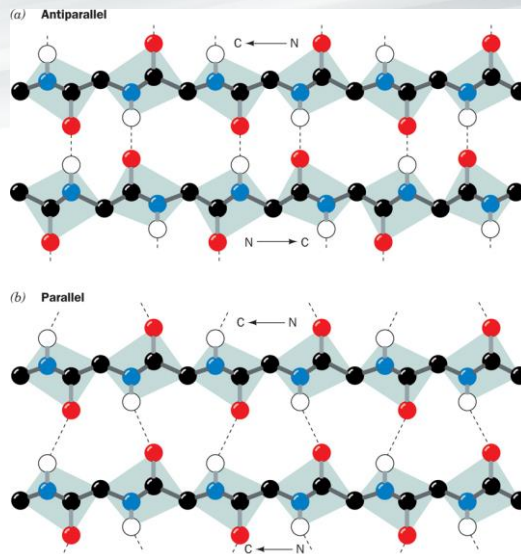


Based on an X-ray structure by Ilme Schlichting, Max Planck Institut für Molekulare Physiologie, Dortmund, Germany. PDBid 1A6M (for the definition of "PDBid" see Section 6-2E).

Oxy-Myoglobin
PDBid [1A6M](#)

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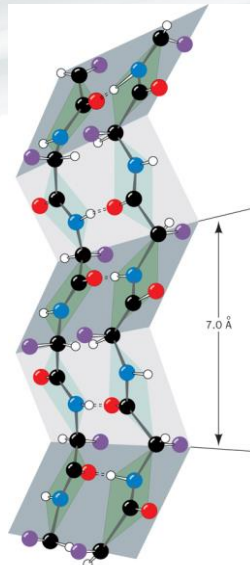
β Sheets



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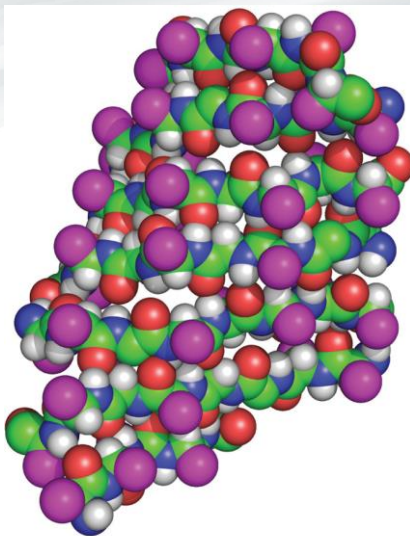
Pleating of β Sheet



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β Sheet: Space Filling Model

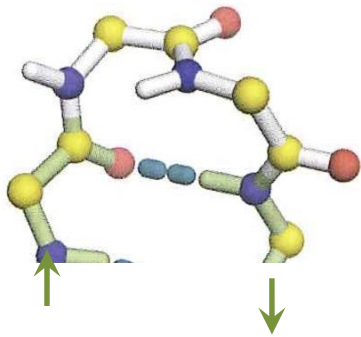


Based on an X-ray structure by Gerald Edelman, The Rockefeller University. PDBid 2CNA.

Concanavalin A
PDBid [2CNA](#)

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Connecting Adjacent β Strands Beta Turns Reverse the Direction of the Backbone



(a)



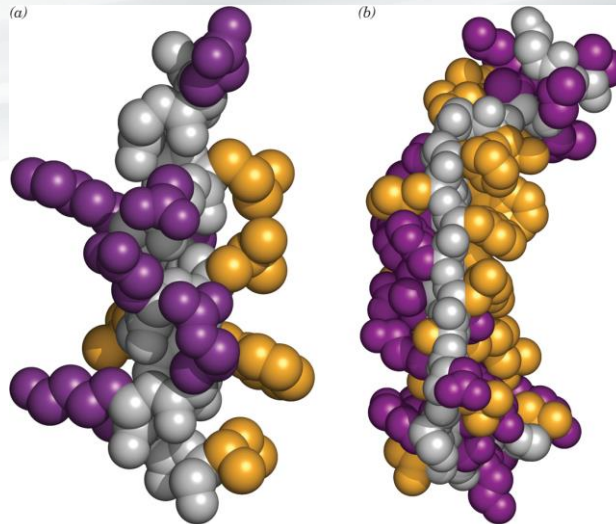
(b)



After Richardson, J.S., *Adv. Protein Chem.* 34, 196 (1981)

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Side Chain Location

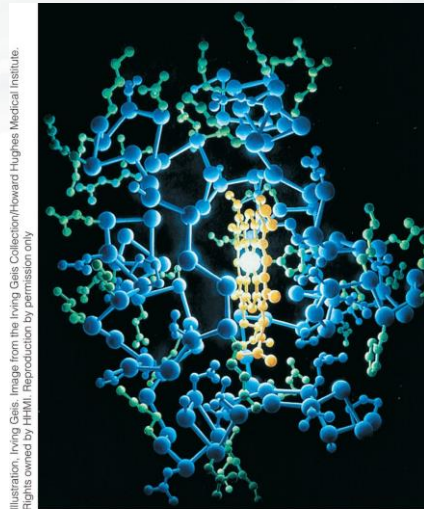


Based on X-ray structures by Ilme Schlichting, Max Planck Institut für Molekulare Physiologie, Dortmund, Germany, and Gerald Edelman, The Rockefeller University, PDBids 1A6M and 2CNA.

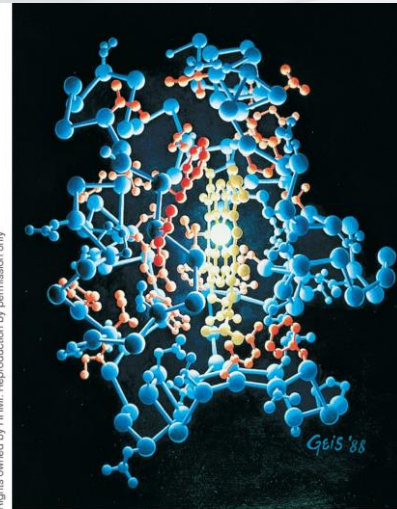
Oxy-Myoglobin and Concanavalin A
PDBids [1A6M](#) and [2CNA](#)

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Side Chain Distribution in Cytochrome



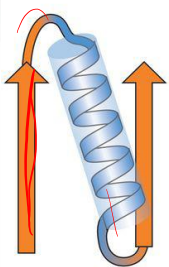
(a)



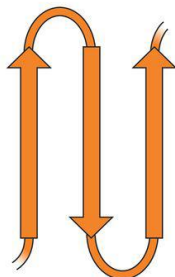
(b)

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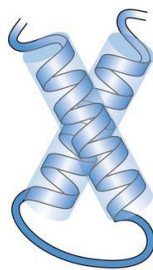
Motifs: Supersecondary Structures



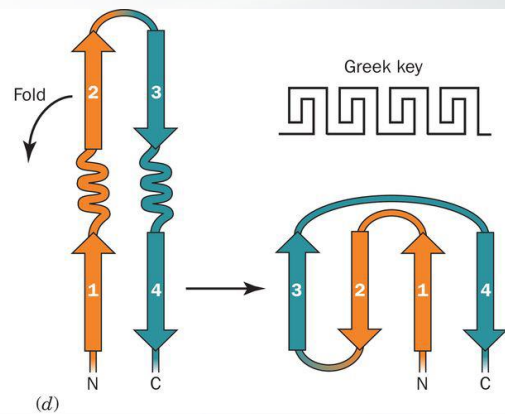
(a)



(b)



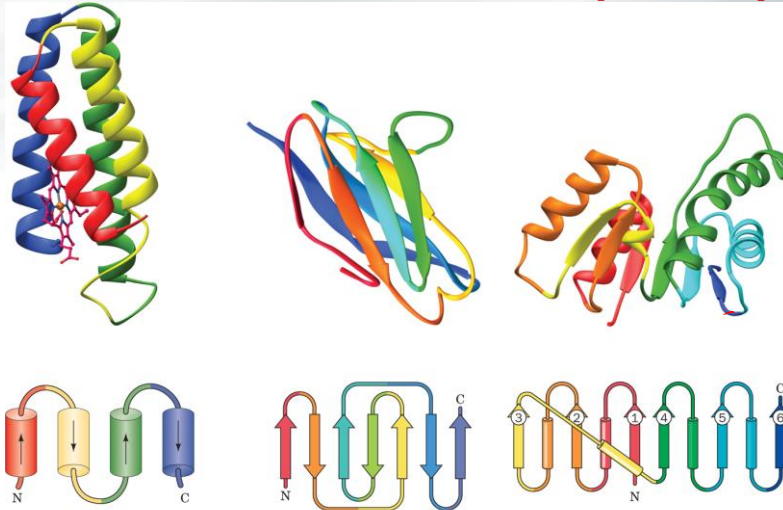
(c)



(d)

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Protein Classification: α , β , or α/β



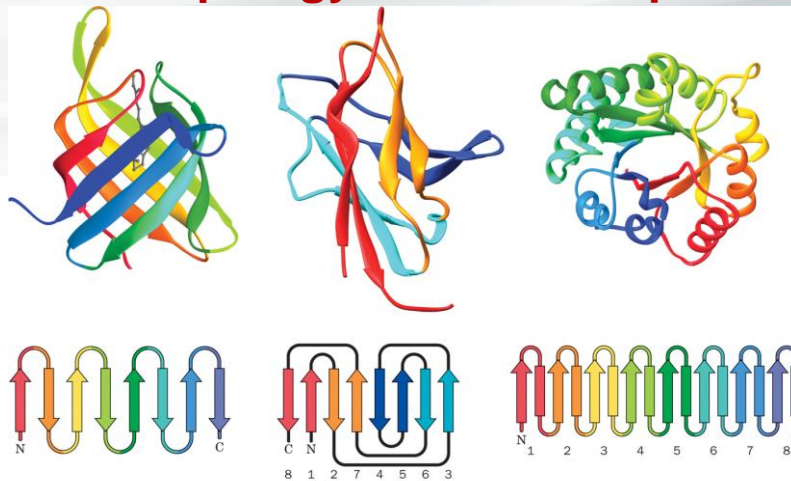
Cytochrome *b*562
PDBid [256B](#)

Human immunoglobulin fragment
PDBid [7FAB](#)

Dogfish lactate dehydrogenase
PDBid [6LDH](#)

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Protein Topology: 8-Stranded β Barrels

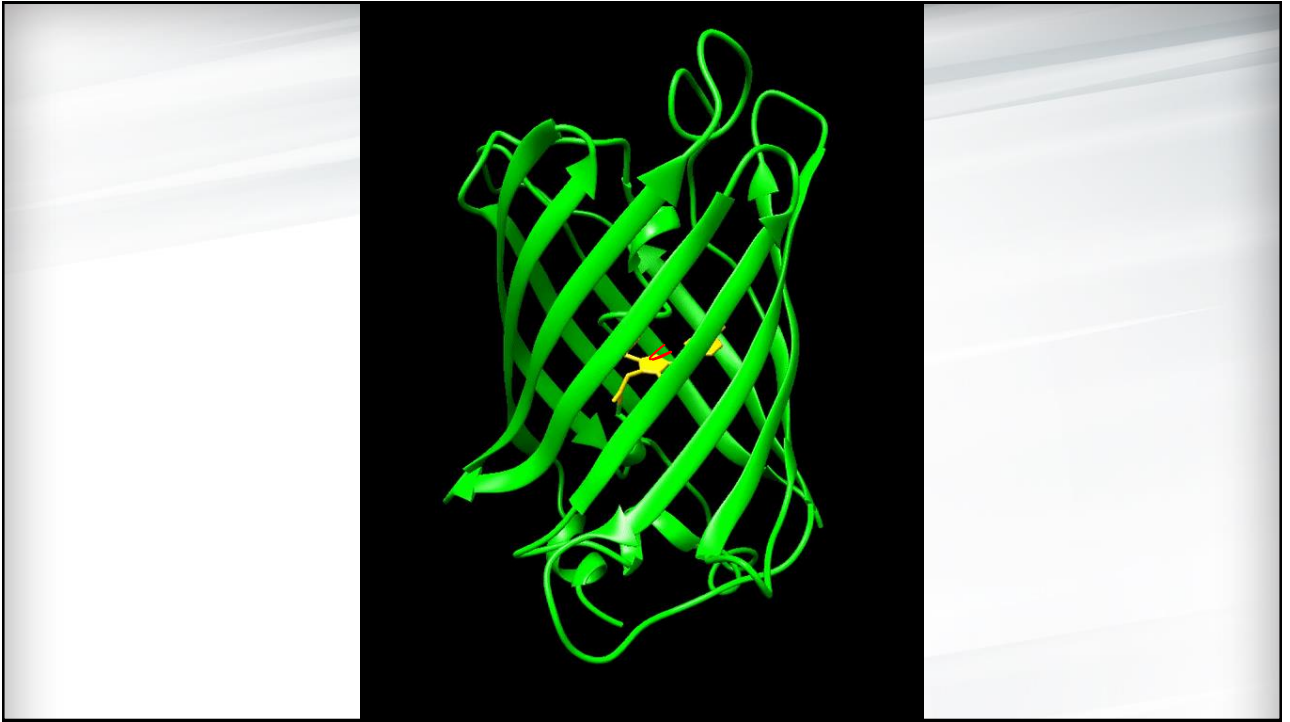


Human retinol binding protein
PDBid [1RBP](#)

Peptide- N^4 -(N-acetyl- β -D-glucosaminyl) asparagine amidase
PDBid [1PNG](#)

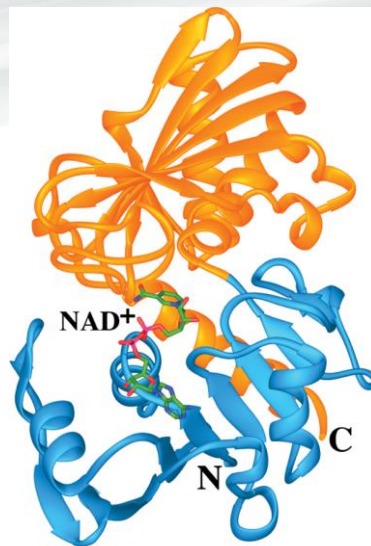
Triose phosphate isomerase
PDBid [1TIM](#)

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2-Domain Protein : GAPDH



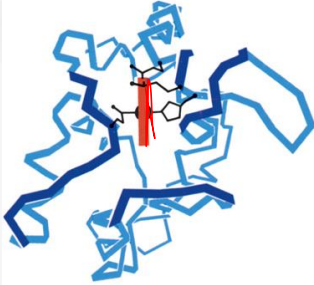
Based on an X-ray structure by Alan Wonacott, Imperial College, London, U.K. PDBid 1GD1.

Glyceraldehyde-3-phosphate dehydrogenase
PDBid [1GD1](#)

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Structure Conserved More Than Sequence

(a) *Paracoccus c₅₅₀*
134 amino acid residues



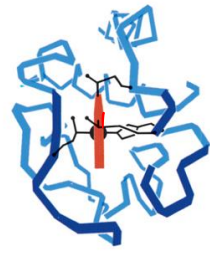
(b) *Rhodospirillum c₂*
112 amino acid residues



(c) Tuna *c*
103 amino acid residues



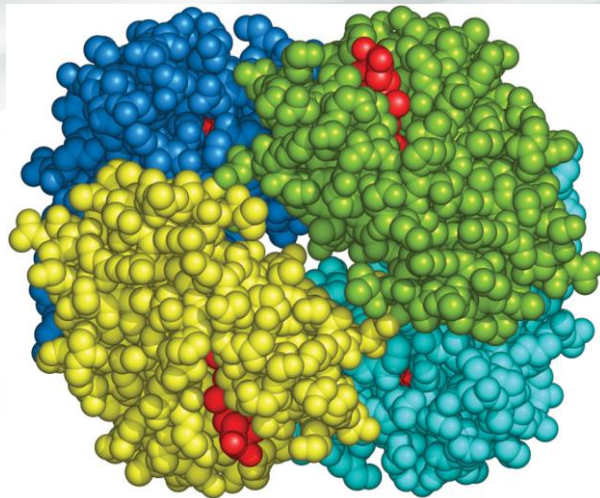
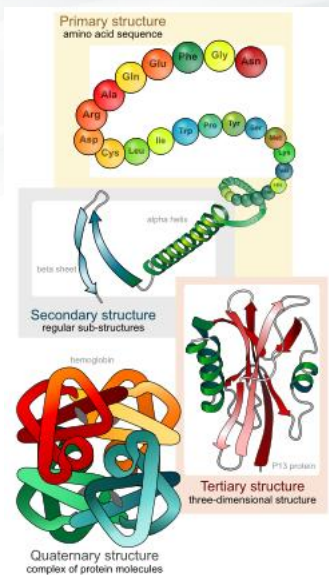
(d) *Chlorobium c₅₅₅*
86 amino acid residues



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4^o Structure of Hemoglobin

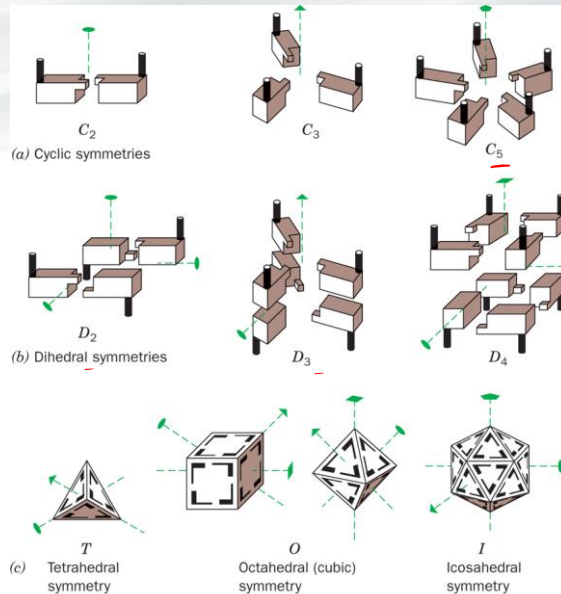


Based on an X-ray structure by Max Perutz, MRC Laboratory of Molecular Biology, Cambridge, U.K. PDBid 2DHB.

Deoxyhemoglobin
PDBid [2DHB](#)

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Symmetries of Oligomeric Proteins



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Summary

- Proteins are chemical chains made up of 20 different amino acids
- The chemical structure of the backbone has consequences: helices, sheets, and turns
- Protein structure is classified into a four-level hierarchy

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