

Fall Semester 2026-27

**“BABIT101: BIOCHEMISTRY”
(FRESHERS)**

Module 3. PROTEINS

☞ Structural Organization of Proteins

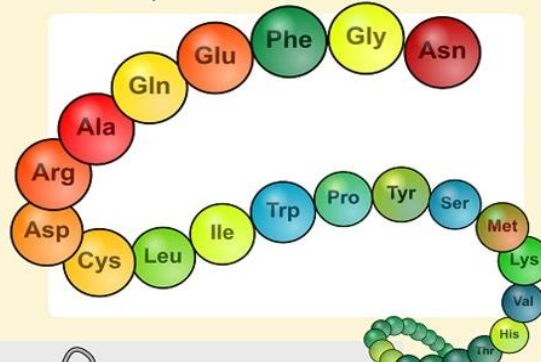
- ◆ **Secondary, Tertiary & Quaternary Structures of Proteins**
- ◆ **Disulfide Bonds in Peptides & Proteins**
- ◆ **Examples of some major proteins**
- ◆ **Molecular Masses of some proteins & number of constituting amino acids**

**Dr. V. Sabareesh (Emp. ID 13608)
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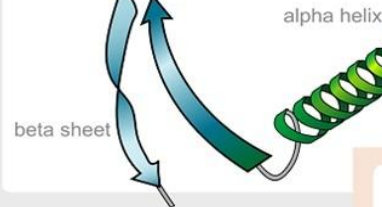
Definition of Different levels of PROTEIN STRUCTURES

1. Primary Structure

Primary structure
amino acid sequence

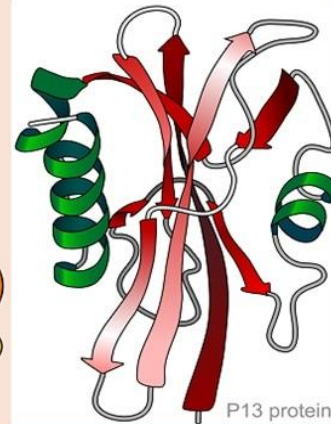


2. Secondary Structure



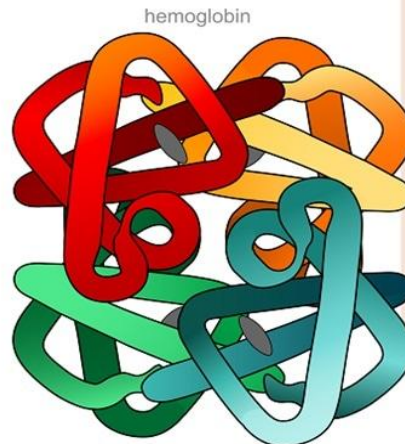
Secondary structure
regular sub-structures

3. Tertiary Structure



Tertiary structure
three-dimensional structure

4. Quaternary Structure



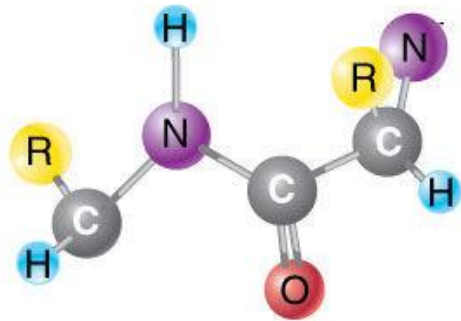
Quaternary structure
complex of protein molecules

(contd.)

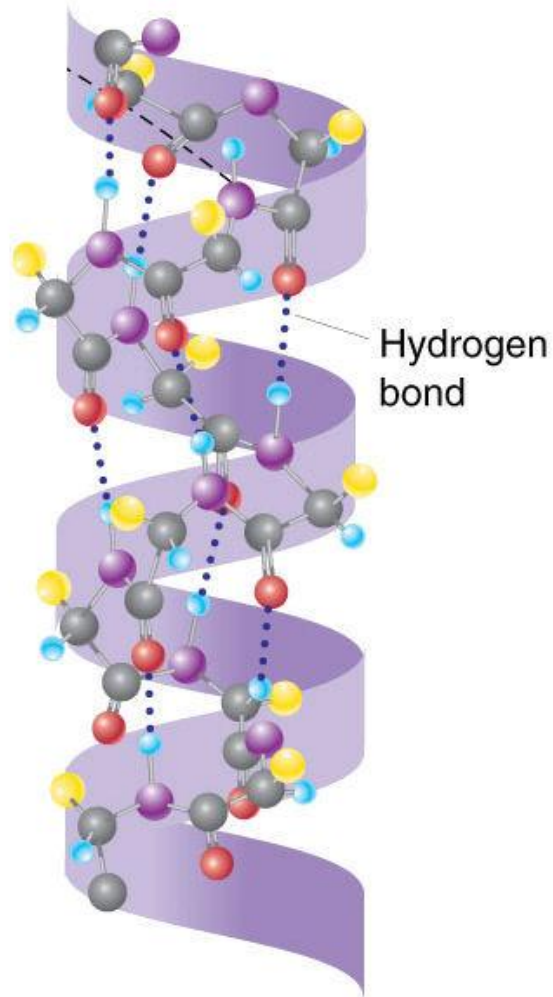
©LadyofHats/ commons.wikimedia.org

Definition of Different levels of **PROTEIN STRUCTURES**

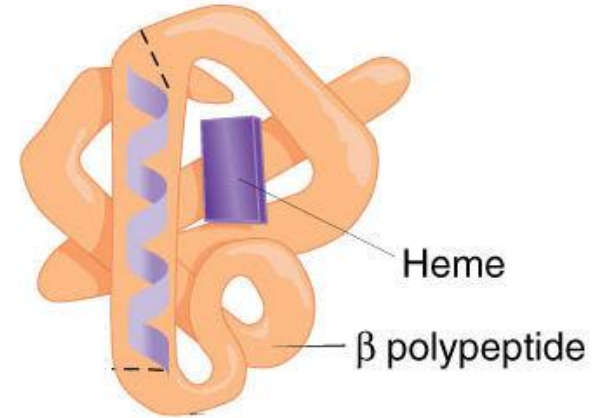
'Another View'



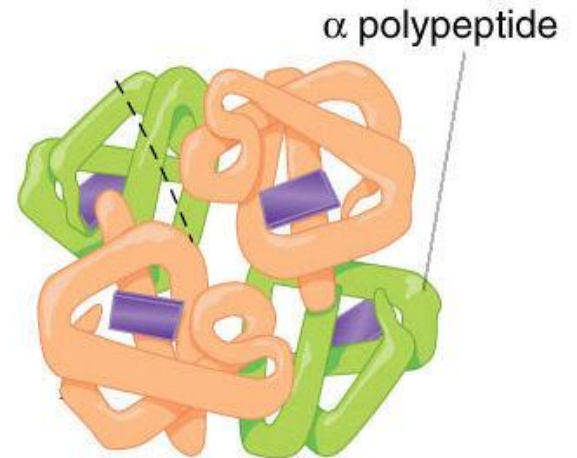
(a) Primary structure



(b) Secondary structure



c) Tertiary structure



(d) Quaternary structure—

PROTEINS' PRIMARY STRUCTURE

The order or '**Sequence**' of linkage of amino acids constituting a protein is referred as '**Primary Structure**'.

PROTEINS' SECONDARY STRUCTURE

- Folding of the polypeptide backbone in a periodic manner can result in the formation of different types well-ordered three-dimensional (3D) conformations or structures, called '**Secondary Structures**', which attains stability mainly by means of 'Hydrogen Bonds'.
- **α -Helix** and **β -Sheet** are two well-characterized 'Secondary Structures' that have been very commonly found in several 3D structures of proteins.
- Another 'secondary structure', which is prevalent in many proteins' 3D structures, is ' **β -Turn**'. **β -Turns** link two or more same or different types of secondary structural elements, viz., e.g., they link two or more **β -Sheets** or it can link an **α -Helix** and a **β -Sheet**.
- In most cases, secondary structural elements constitute certain portion(s) of the protein, i.e., form local region(s) at different parts within the protein's 3D structure.

In other words, different types of secondary structures occur as 'patches' at different parts of the protein's 3D structure. And the size of a secondary structural patch can be smaller or larger, depending on the number of constituent amino acids.

Primary Structure (or) Sequence

Sequence of the Human Serum Albumin shown in single-letter code

>sp|P02768|25-609

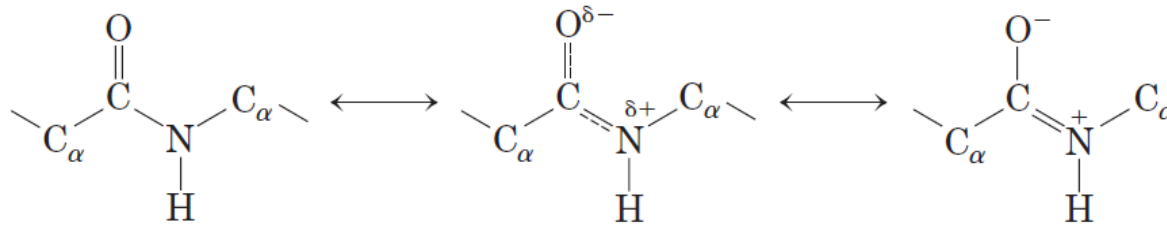
1	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAE NCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEV DVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLP KLDELRLDEGKASSAKQRLKCASLQKFGERAFAKAWAVARLSQRFPKAEFAEVSKLVTDLTK VHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLRLAKTYETTLK CAAADPHECYAKVFDEFKPLVEEPQNLIKQNCLEFEQLGEYKFQNALLVRYTKKVPQVST PTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTES LVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKAT KEQLKAVMDDFAAFVEKCKADDKETCFAEEGKKLVAASQAALGL	60
541		585

(Note: Slide Number 32 shows the same sequence, however with the Cysteines highlighted.)

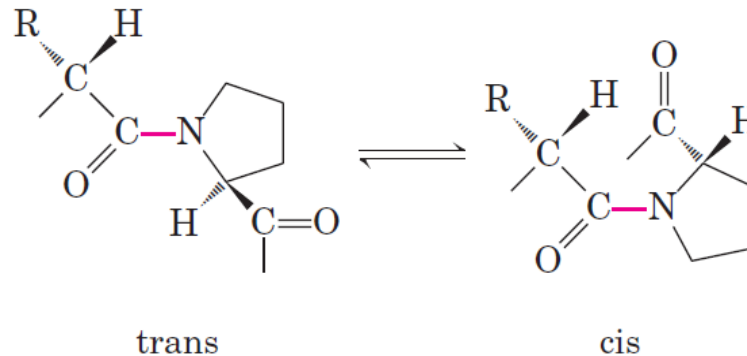
Source: <http://www.uniprot.org/uniprot/P02768> (Uniprot KB Database)

Geometry of the Peptide Bond

Trans & Cis Peptide Configuration

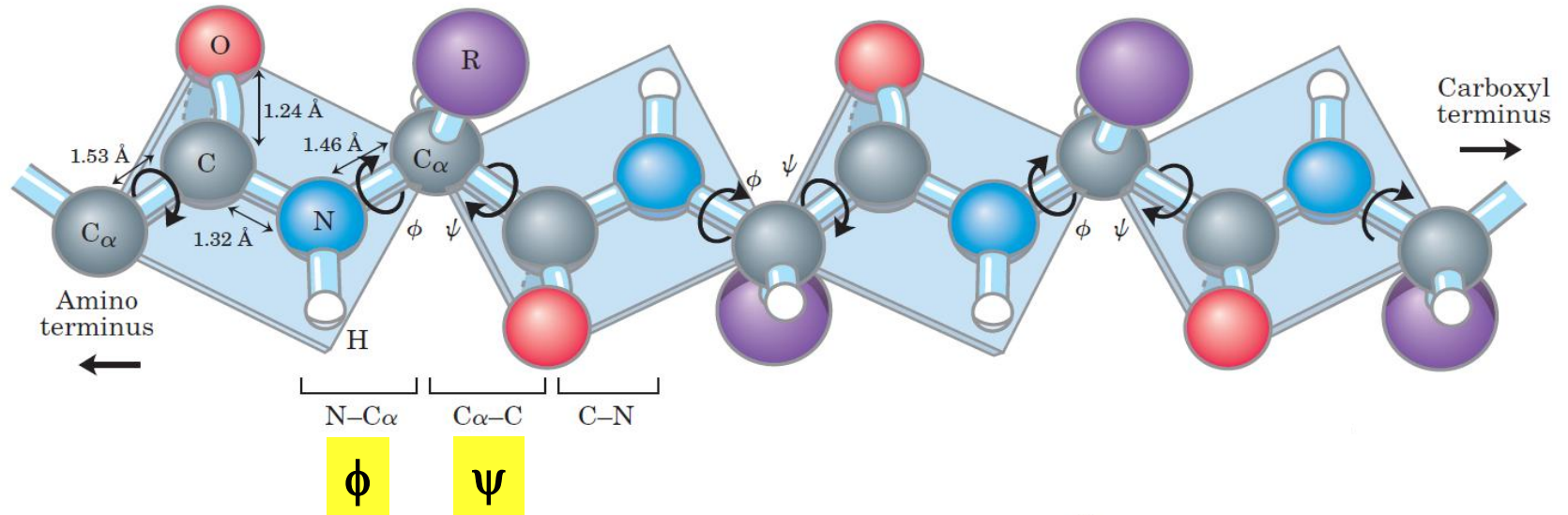


Cis-Pro Peptide Bond

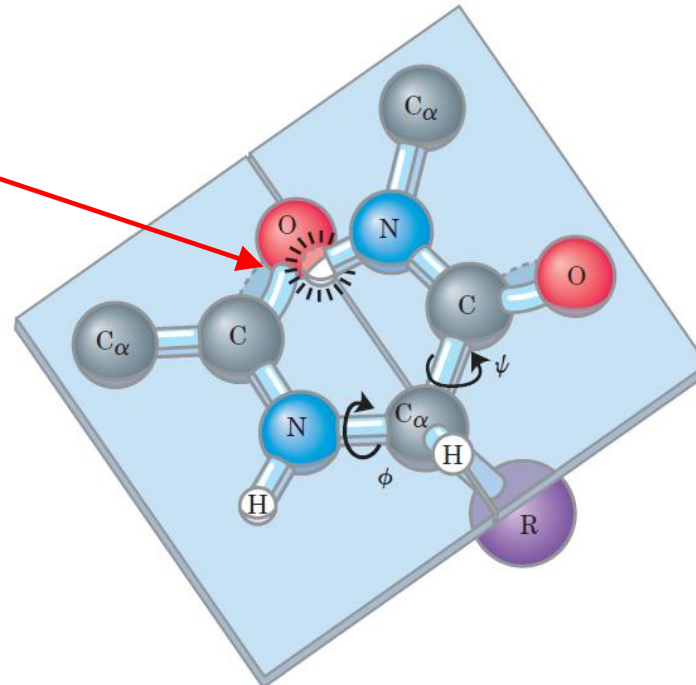


Note: Of the peptide bonds between amino acid residues other than Pro, over 99.95% are in the trans configuration. However, for peptide bonds involving the **imino nitrogen of Proline**, **about 6% are in the cis configuration** & many of these occur at β turns. **β turn is one type of secondary structure.**
(Refer slide number 22, to know about β turn.)

DIHEDRAL ANGLES - Ramachandran's Angles: ϕ , ψ



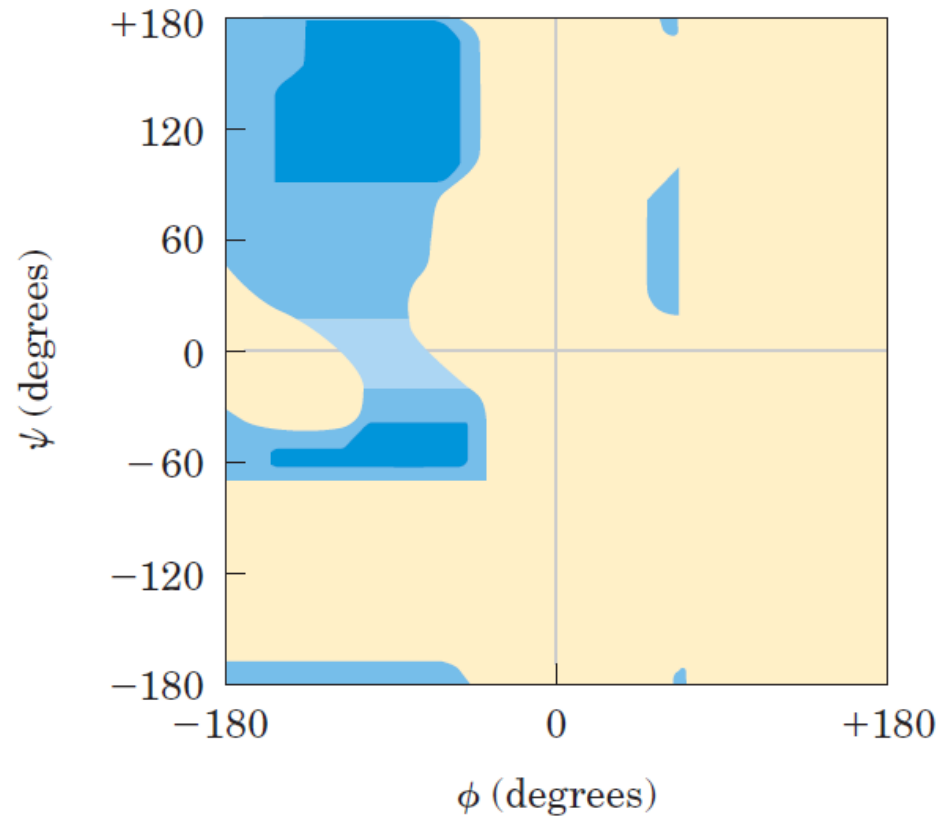
Steric Overlap between Carbonyl Oxygen and Amino Hydrogen Atoms, when $\phi = 0^\circ$ & $\psi = 0^\circ$



(contd.)

(contd.)

Ramachandran Plot for L-Ala residues in proteins



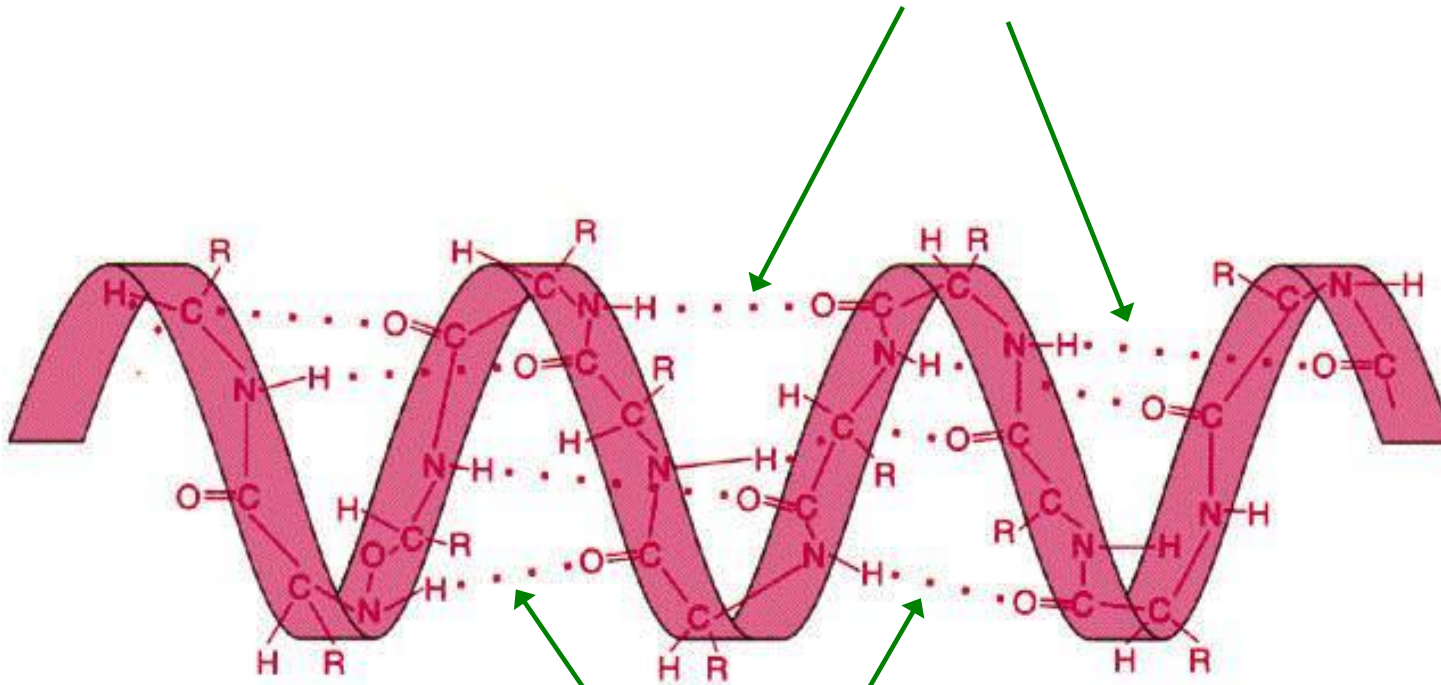
Source: Lehninger PRINCIPLES OF BIOCHEMISTRY by D.L. Nelson & M.M. Cox, 4th Ed., p. 119.

PROTEINS' SECONDARY STRUCTURE

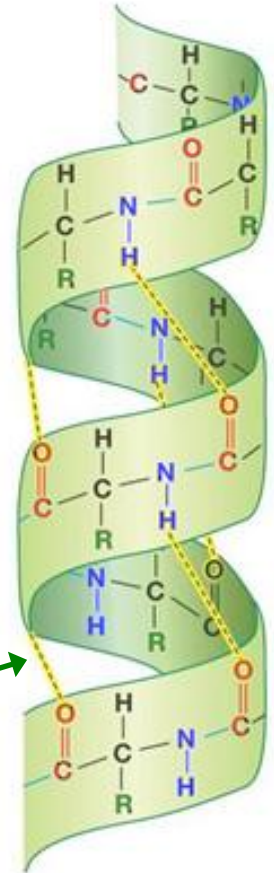
(I) HELIX

“Stabilization of Helix
by
Hydrogen Bonds”

HYDROGEN BOND



HYDROGEN BOND



Sources:

(1) http://www.cbs.dtu.dk/courses/genomics_course/roanoke/fig12_7b.jpg

(2) <http://cbm.msoe.edu/teachingResources/jmol/proteinStructure/assets/alphaHelix.jpg>

α - Helix : 3.6₁₃ Helix

Why α - Helix is called 3.6₁₃ Helix?

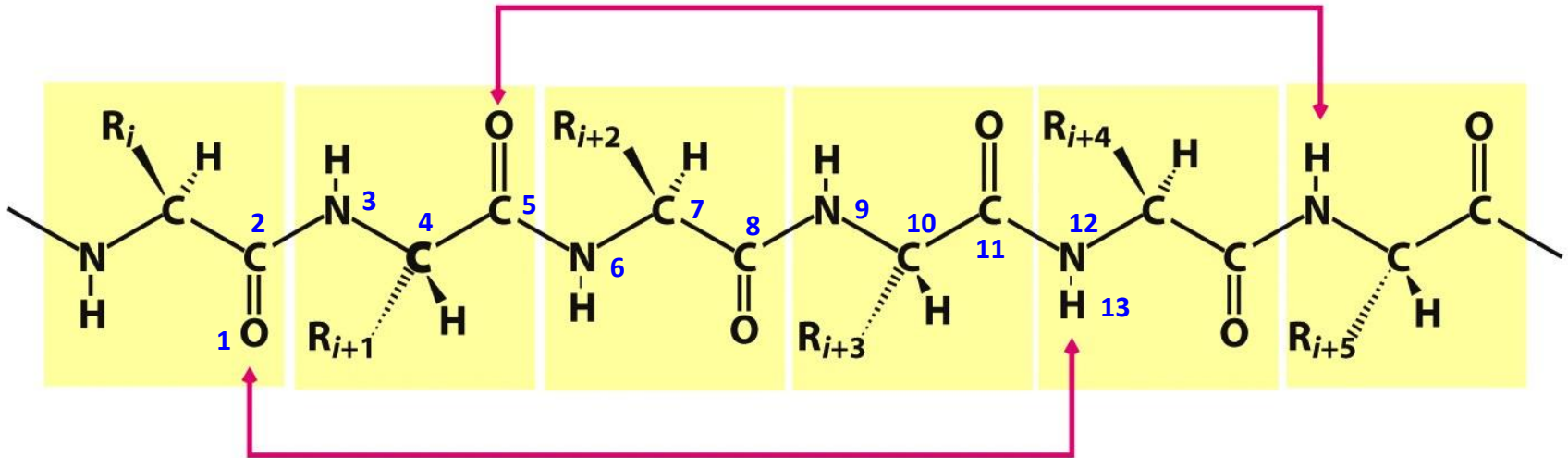
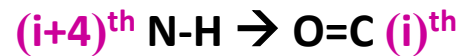


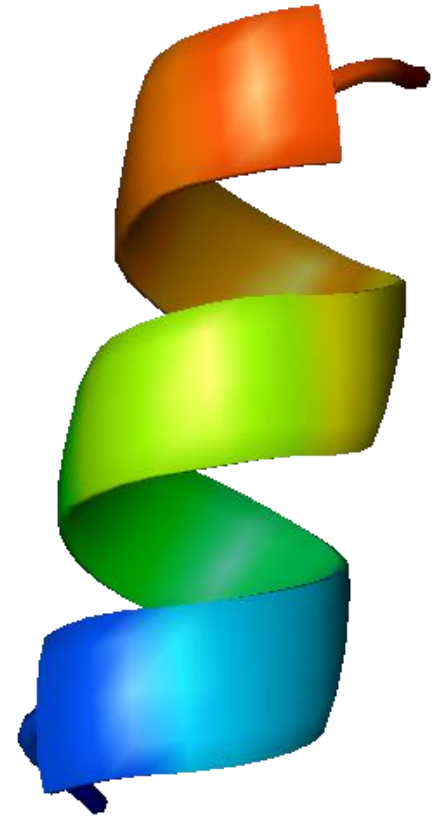
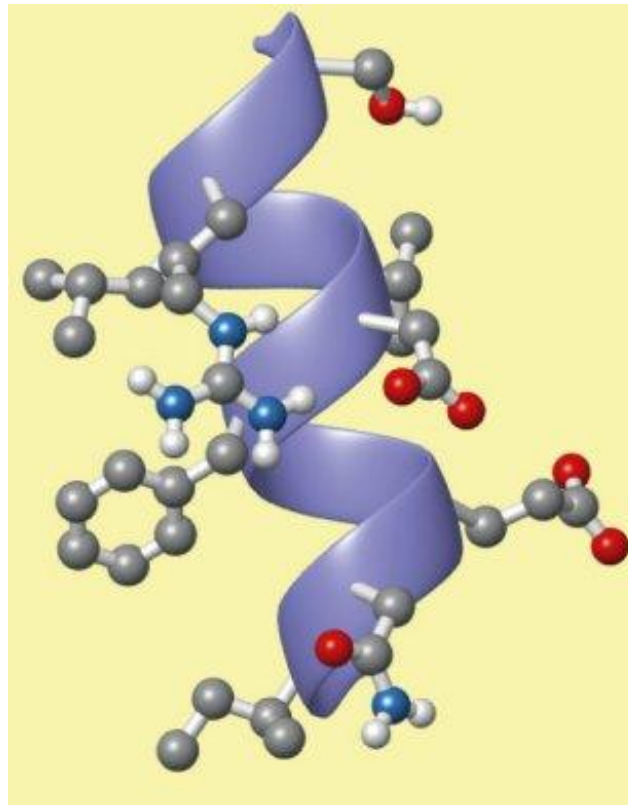
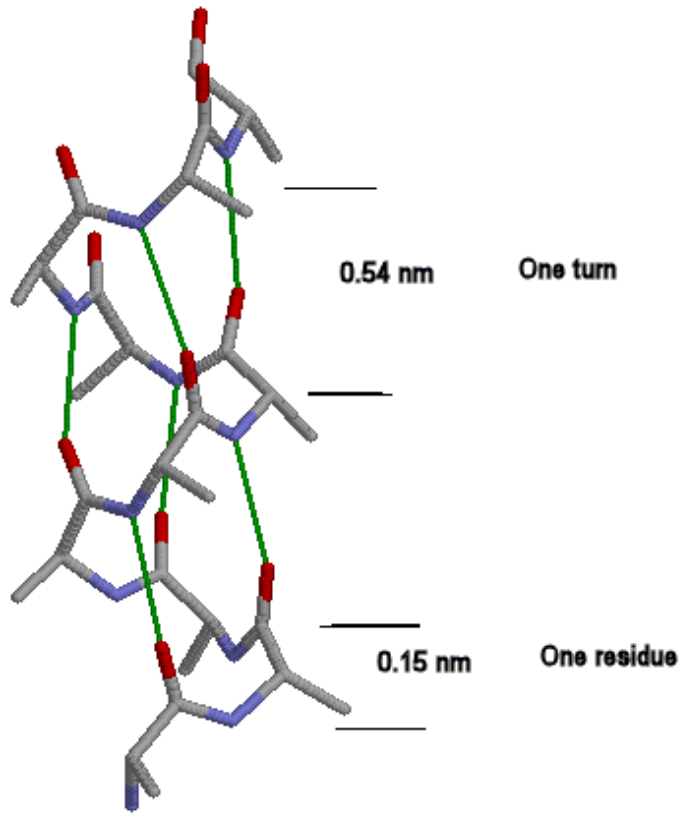
Figure 2.25
Biochemistry, Seventh Edition
 © 2012 W. H. Freeman and Company



Due to the hydrogen bonding interaction between $(i+4)^{\text{th}} \text{ N-H} \rightarrow \text{O=C } (i)^{\text{th}}$, a ring-like structure can be imagined, which is composed of 13 atoms of the polypeptide's backbone. This can be understood from the numbering shown above.

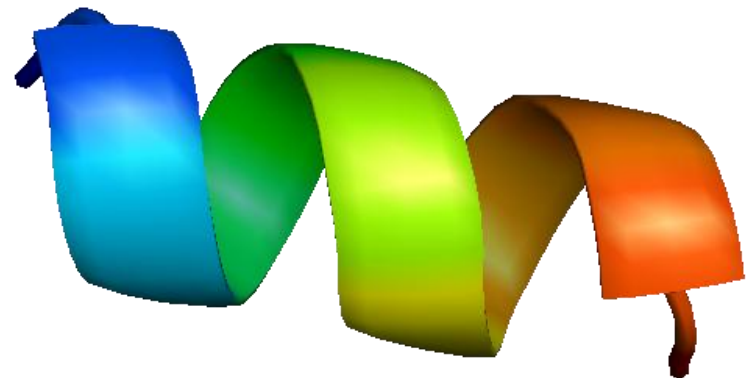
These 13-atoms, encompass 3 complete amino acid residues (viz., $i+1$, $i+2$, $i+3$), plus a C=O group of $(i)^{\text{th}}$ residue and a N-H group of $(i+4)^{\text{th}}$ residue. This means, one turn of this helical structure, contains more than 3 amino acid residues, but less than 4 amino acid residues. And thus, this is called as 3.6₁₃ helix.

Ribbon Diagram Representation of HELIX



Rise per residue = $1.5 \text{ \AA}$ (0.15 nm)
(height)

Note: Arrangement of only the backbone atoms are shown in the RIBBON diagram representation & sidechains are usually NOT shown.

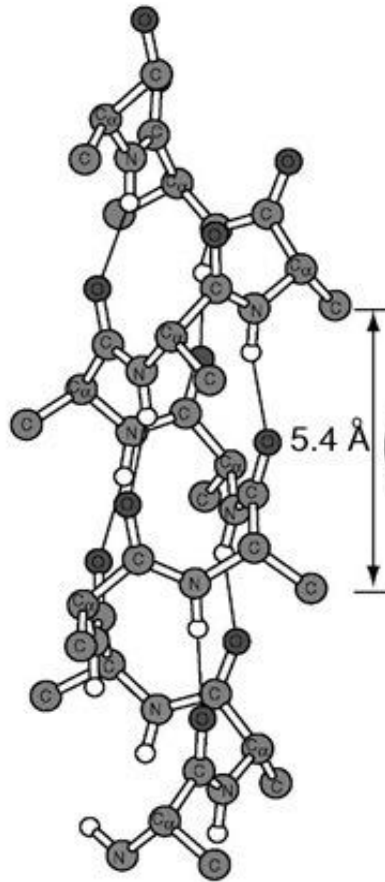
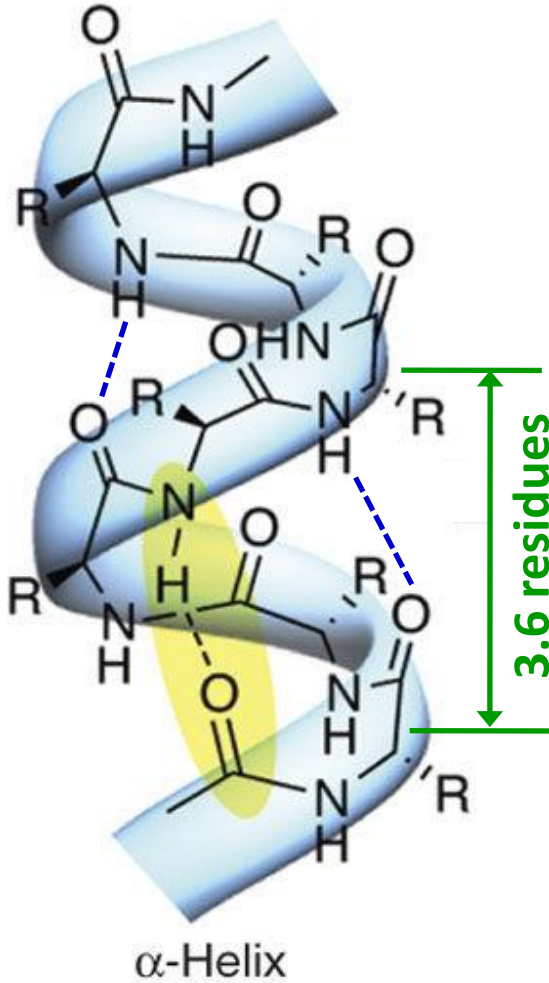


Sources: (1) <http://chemistry.umeche.maine.edu/MAT500/a-Helix.gif>
(2) <http://chemistry.umeche.maine.edu/MAT500/Proteins4.html>
(3) https://upload.wikimedia.org/wikipedia/commons/4/4e/Helix_ribbon.png

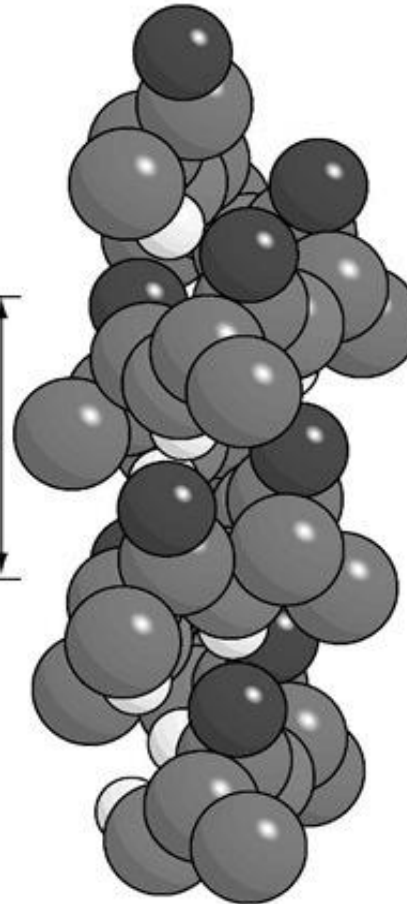
α - Helix : 3.6₁₃ Helix

This is the first 'SECONDARY STRUCTURE' to be predicted (by Corey & Pauling in 1951) & later identified experimentally.

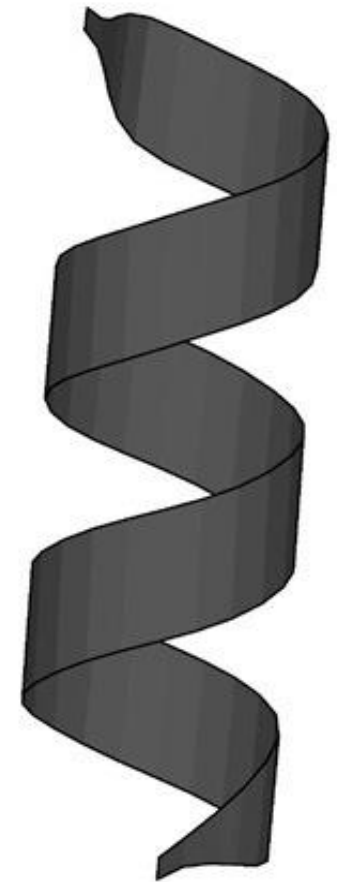
3.6 amino acid residues = 5.4 Å



**“BALL & STICK
MODEL”**

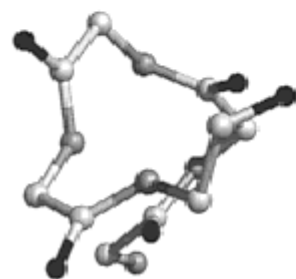
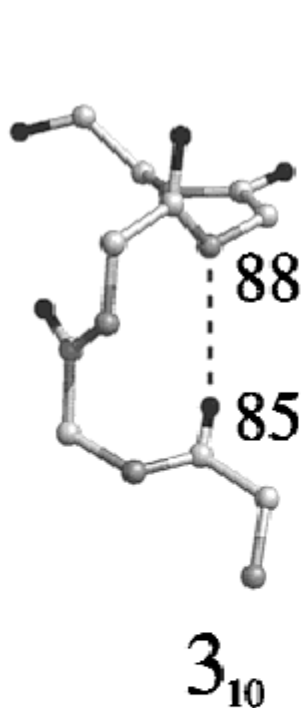


**“SPACE FILLING
MODEL”**



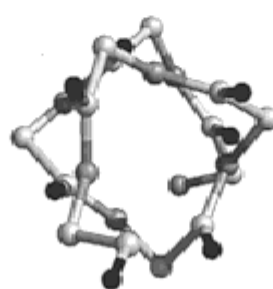
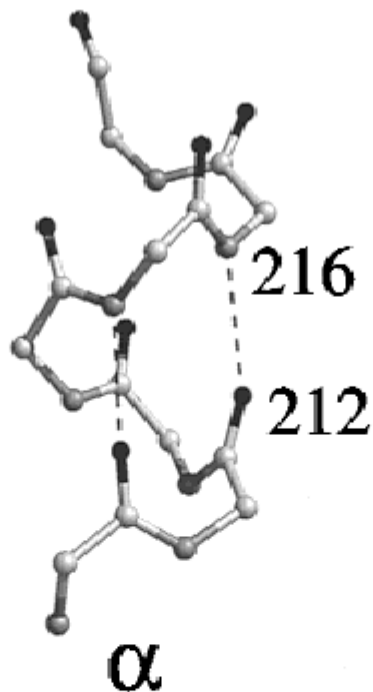
**“RIBBON
DIAGRAM”**

Different HELICAL STRUCTURES observed in Proteins' 3-dimensional structures: 3_{10} , α (3.6_{13}) and π HELICES



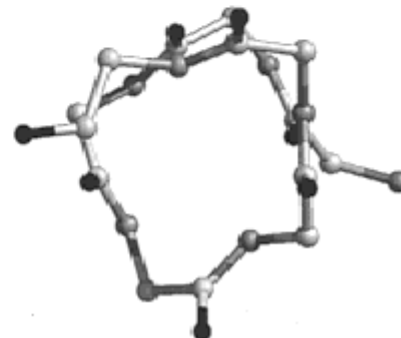
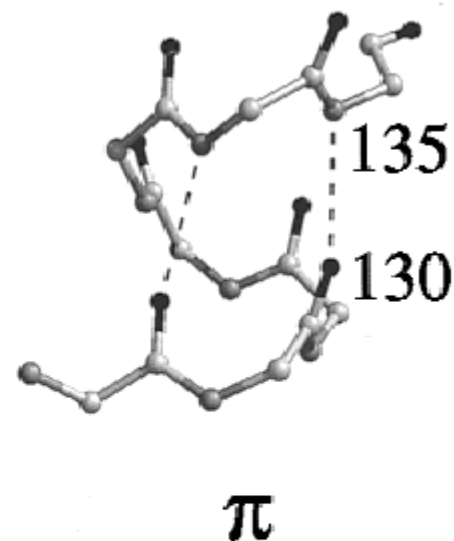
$(i+3)^{\text{th}}$ N-H $\rightarrow$ O=C $(i)^{\text{th}}$

88th N-H $\rightarrow$ O=C 85th



$(i+4)^{\text{th}}$ N-H $\rightarrow$ O=C $(i)^{\text{th}}$

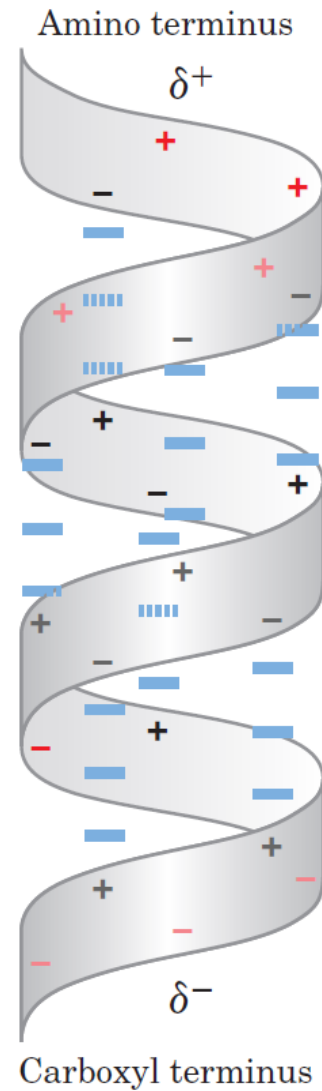
216th N-H $\rightarrow$ O=C 212th



$(i+5)^{\text{th}}$ N-H $\rightarrow$ O=C $(i)^{\text{th}}$

135th N-H $\rightarrow$ O=C 130th

HELIX DIPOLE



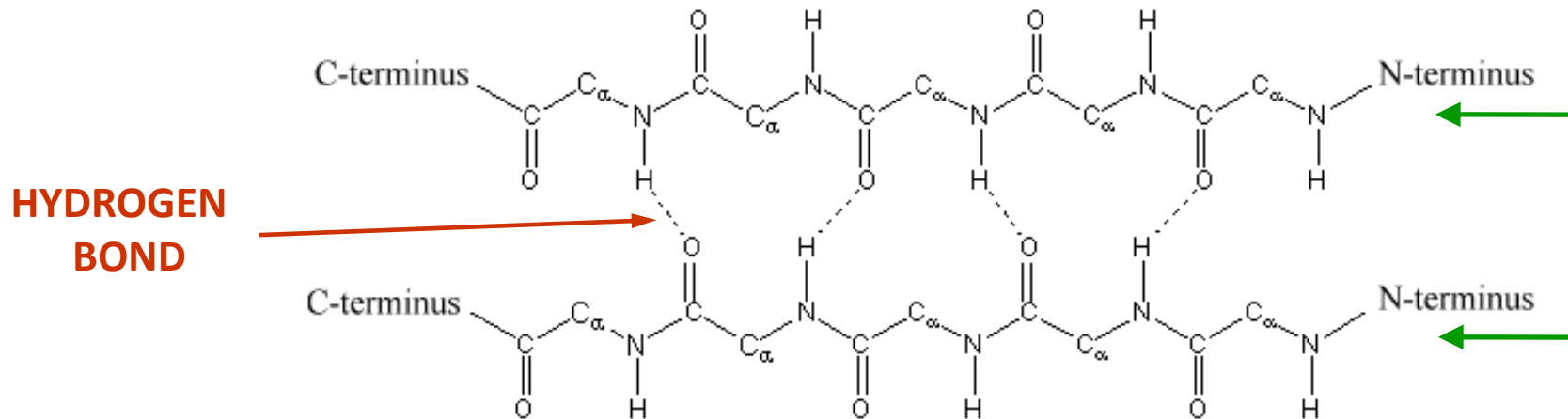
(contd.)

Five different kinds of constraints affect the stability of Helix

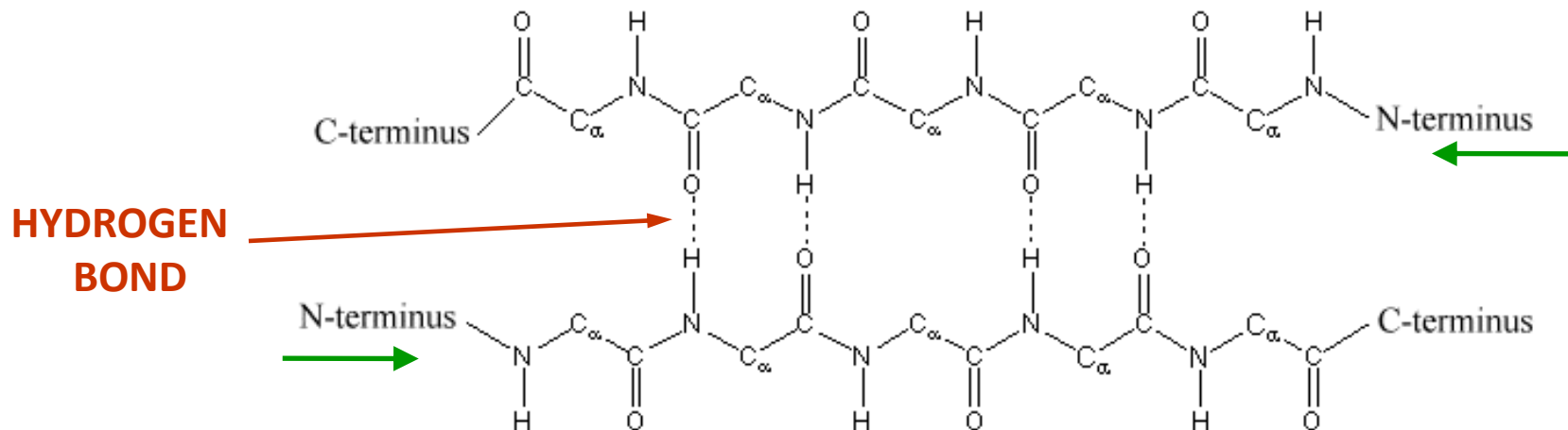
1. **Electrostatic repulsion (or attraction) between successive amino acid residues with charged sidechain groups,**
2. **Bulkiness of adjacent sidechain groups,**
3. **Interactions between sidechain groups spaced three (or four) residues apart,**
4. **Occurrence of Pro and Gly residues, and**
5. **Interaction between amino acid residues at the ends of the helical segment and the electric dipole inherent to the helix.**

“Stabilization of β -sheets
by
Hydrogen Bonds”

Parallel β Sheet



Antiparallel β Sheet



(contd.)

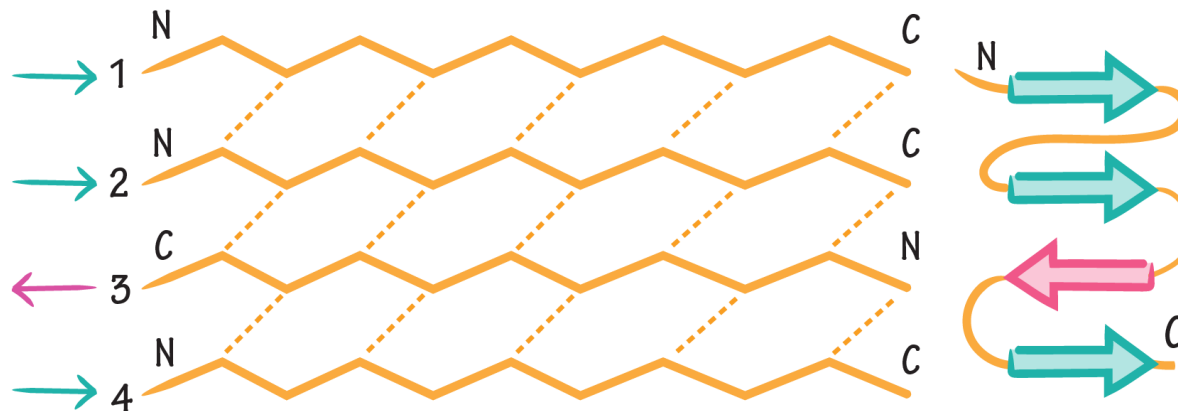
(contd.)

Simpler Representation of β - SHEETS

Beta Sheet

Beta sheet

Two or more beta strands (polypeptide chains connected by hydrogen bonds)



Note: Arrangement of only the backbone atoms are shown in the ARROW representation shown above & sidechains are NOT shown.

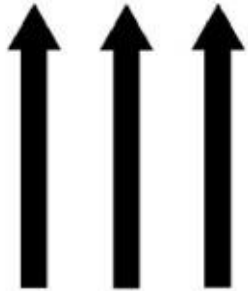
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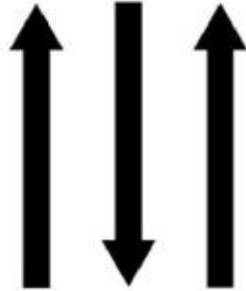
Simpler Representation of β - SHEETS

Each **ARROW** represents, or, is called as β - **strand**. The β - strands are connected by Hydrogen Bonds. But, in the Arrow representation, the Hydrogen Bonds between each strand are NOT shown.

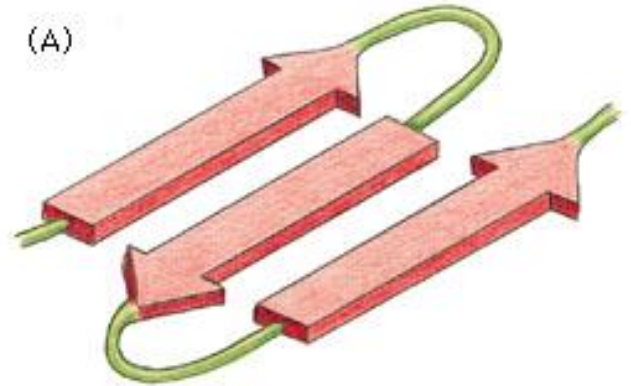
Parallel



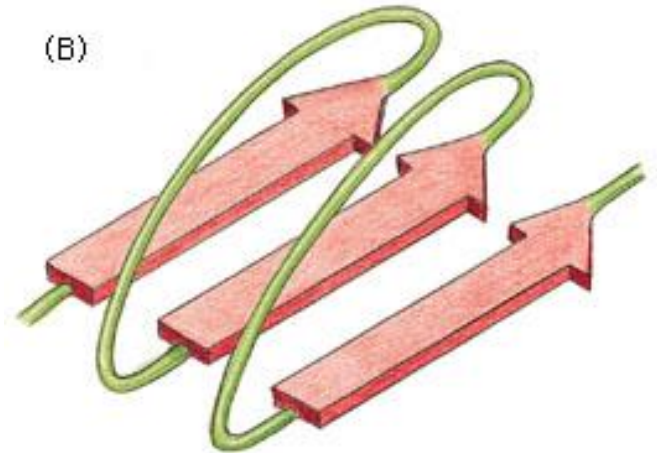
Antiparallel



(A)



(B)



©1998 GARLAND PUBLISHING

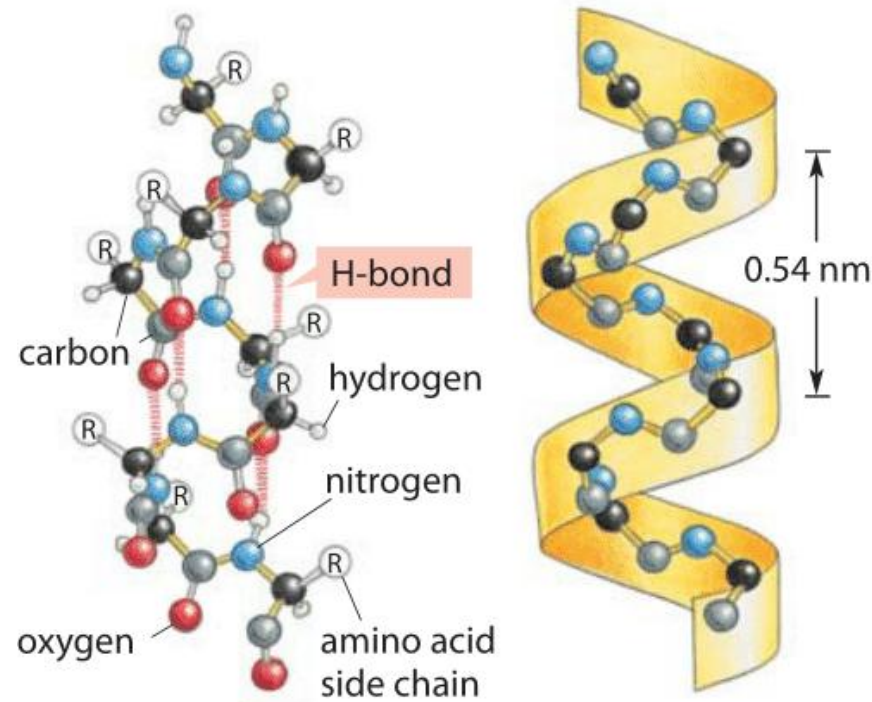
Source:

(1) http://what-when-how.com/wp-content/uploads/2011/05/tmpFD74_thumb.jpg

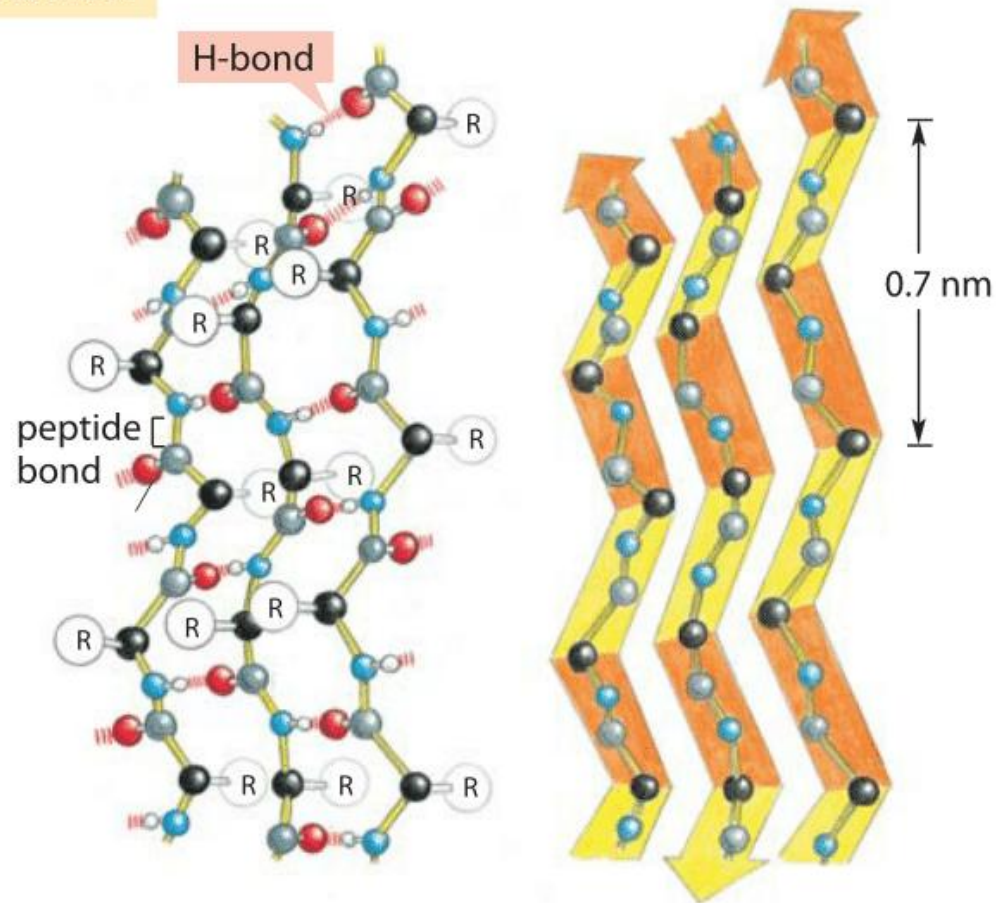
(2) http://www.bio.miami.edu/tom/courses/protected/ECB/CH05/5_10.jpg

Comparison of α -HELIX and β -SHEET

alpha helix



beta sheet



REMINDER: Protein secondary structures: α -helix and β -sheet, are stabilized by hydrogen bonds. But, in the ribbon diagram & in the arrow representations, hydrogen bonds are NOT shown for clarity. Further, the ribbon diagram & the arrow representations, show the arrangement of only the backbone atoms of the protein and NOT the sidechains.

Ramachandran Plot for different Secondary Structures

β -sheet

$$\phi = -140^\circ$$

$$\psi = +130^\circ$$

3_{10} Helix (Right-Handed)

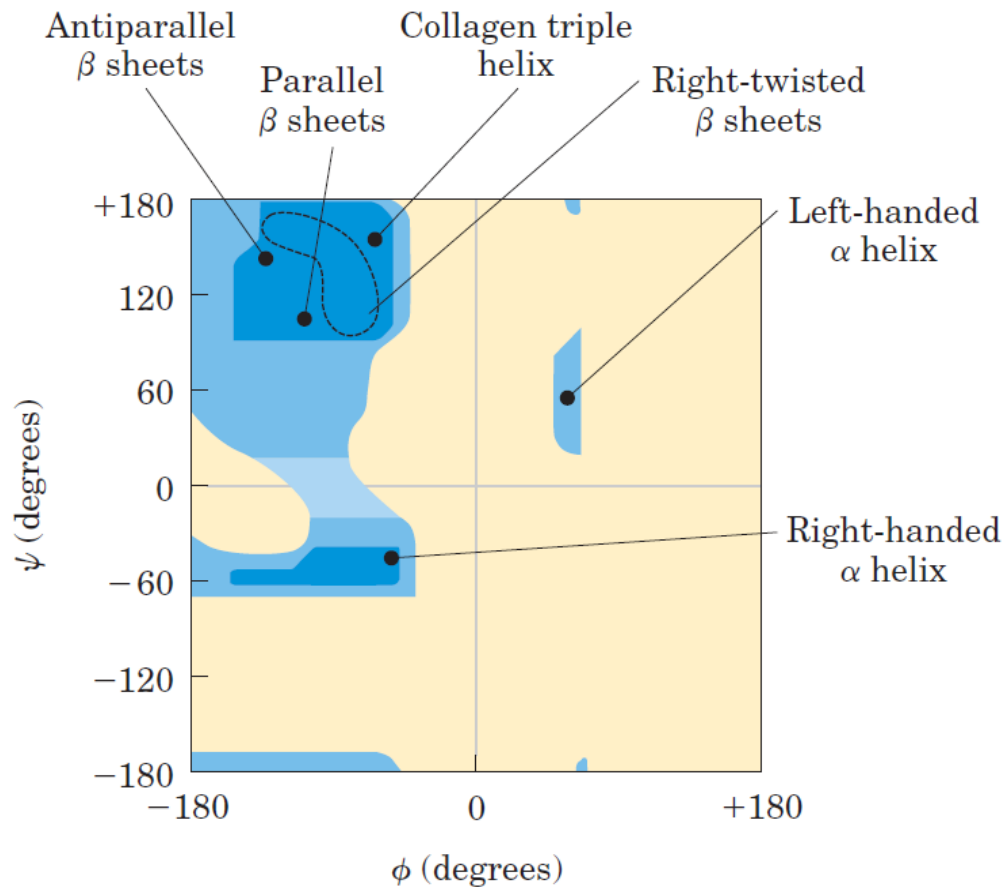
$$\phi = -60^\circ$$

$$\psi = -30^\circ$$

α -Helix (3.6_{13}) (Right-Handed)

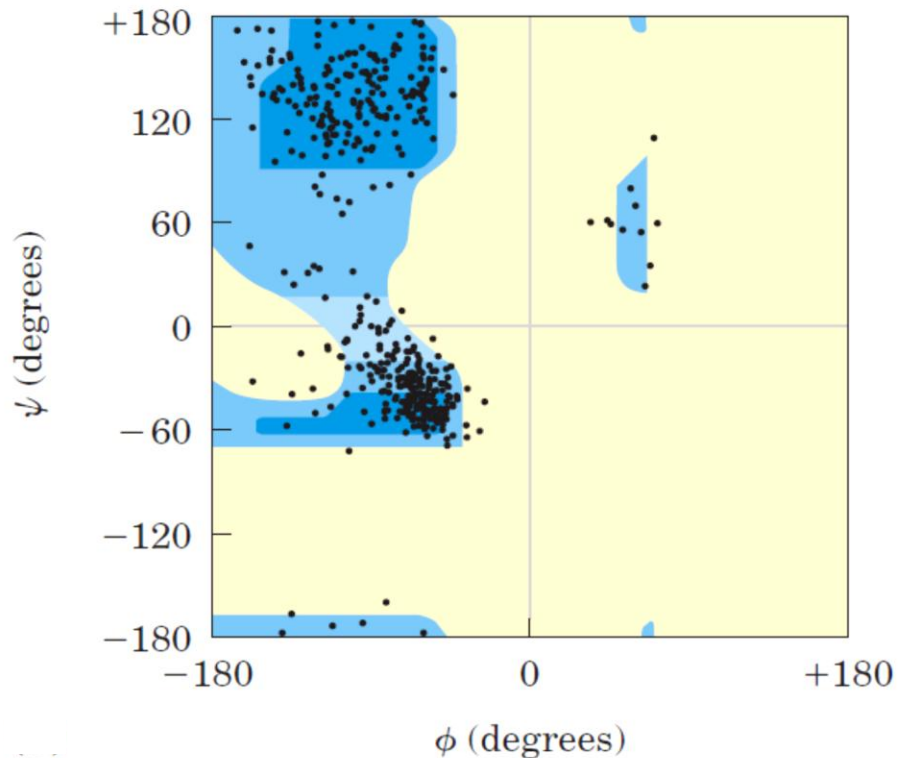
$$\phi = -57^\circ$$

$$\psi = -47^\circ$$



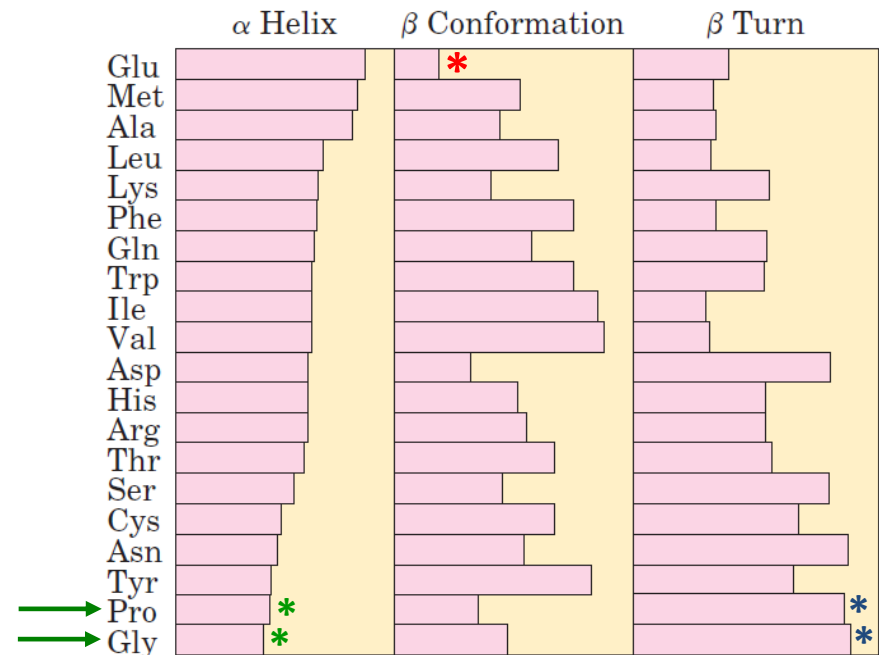
Left-Handed α -Helices do not occur widely, compared to Right-Handed α -Helices

Ramachandran Plot for Pyruvate Kinase (isolated from Rabbit)



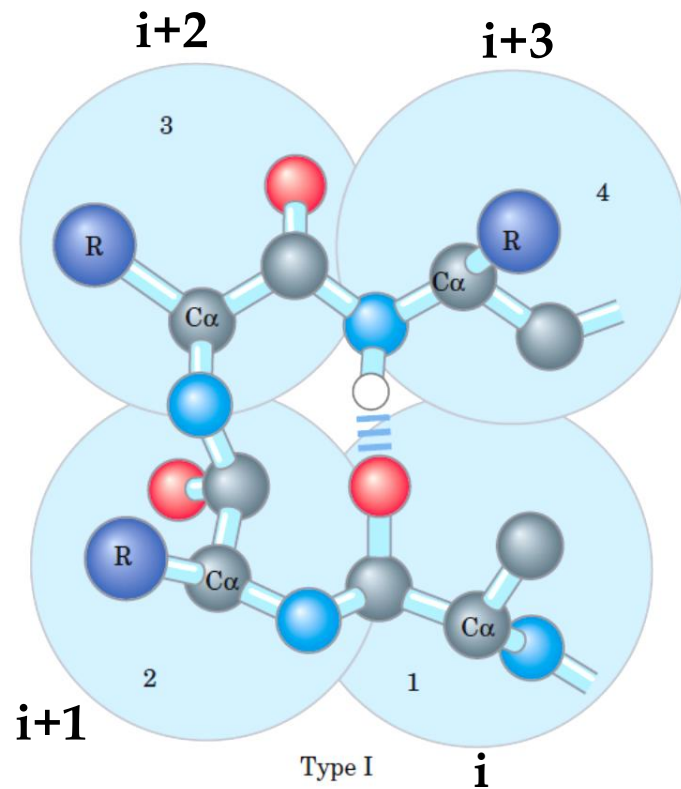
- The (ϕ, ψ) values of Glycine residues in this protein are not shown in the plot above, since these values frequently fall outside the allowed (blue) colored regions.

Relative Probabilities / Propensities of every amino acid occurring in three different Secondary structures

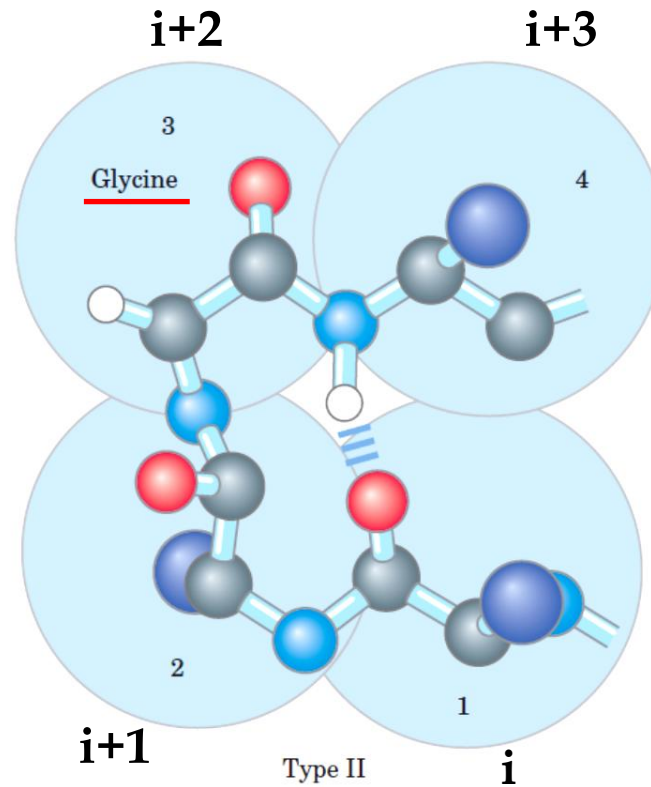


β - Turns

'Type I'



'Type II'



Glycine is the (i+2)th residue in most of the Type II turns

PROTEINS' TERTIARY STRUCTURE

- The **Tertiary Structure** of Proteins refers to, different **arrangements** of the **secondary structural elements** (viz., α -helix, β -sheet) and various **modes of connectivity** between those elements, in the three-dimensional (3D) space.

In other words, **Tertiary Structure** shows the '**topological arrangement**' of the constituent **secondary structural elements** in the **3D** space.

- The **arrangement & connectivity** of different secondary structural elements in the **3D**- space, depends on:
- (1) **Steric constraints**, which depends on the size of the atoms,
 - (2) Formation of **Hydrogen Bonds between the sidechain** functional groups of one amino acid with other;
 - (3) Formation of **Salt-Bridge interactions between the sidechain** functional groups of one amino acid with other;
 - (4) **van der Waals interactions between the sidechain groups** of one amino acid with other;
 - (5) **Hydrophobic interactions between the sidechain groups** of one amino acid with other

which are a few key factors that govern the formation of **tertiary structure** of proteins.

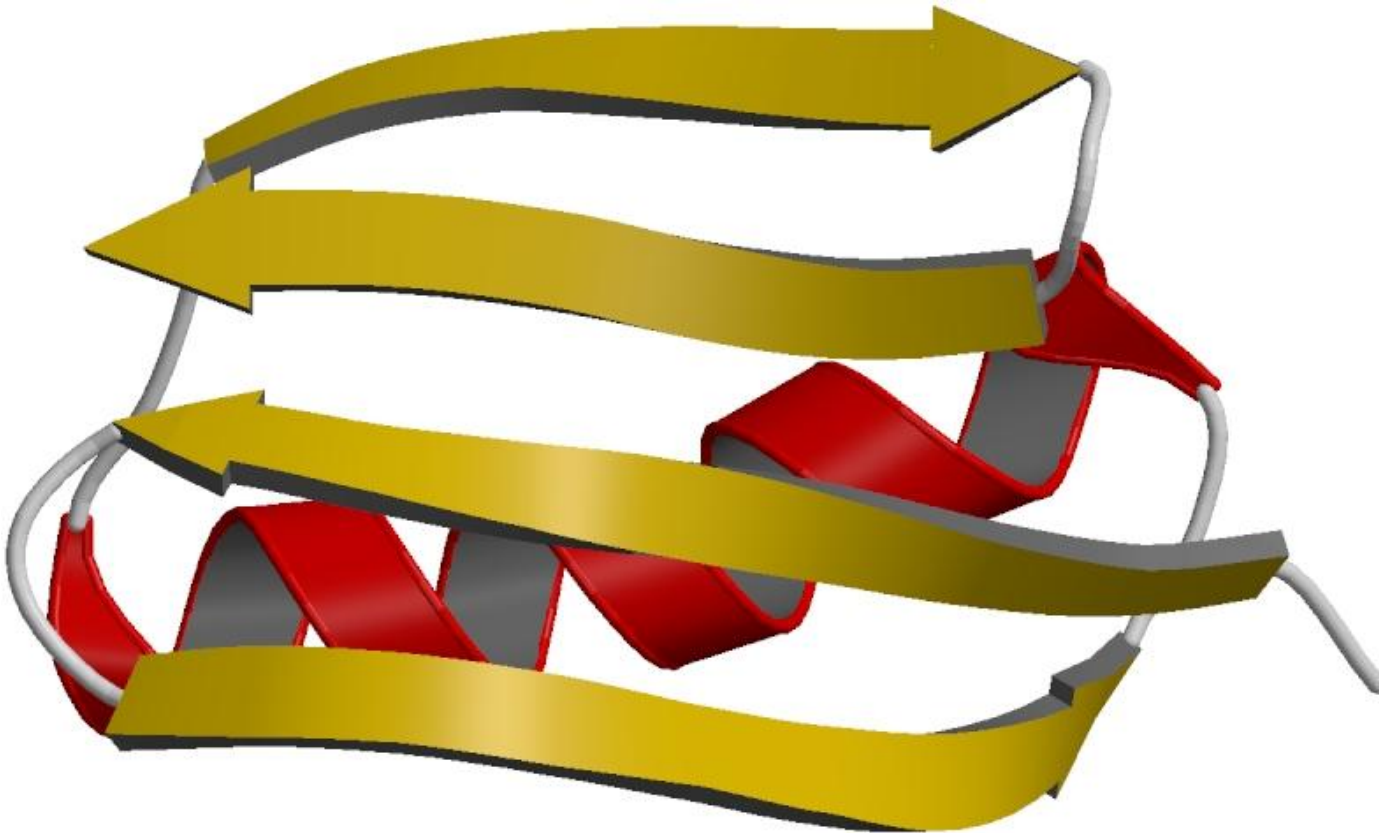
(contd.)

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PROTEINS' TERTIARY STRUCTURE

Ribbon Diagram Representation of 3-Dimensional Structure of Proteins

Shown here is '**TERTIARY STRUCTURE**' of the **Protein**, depicting the manner, by which different secondary structural elements are connected and arranged.

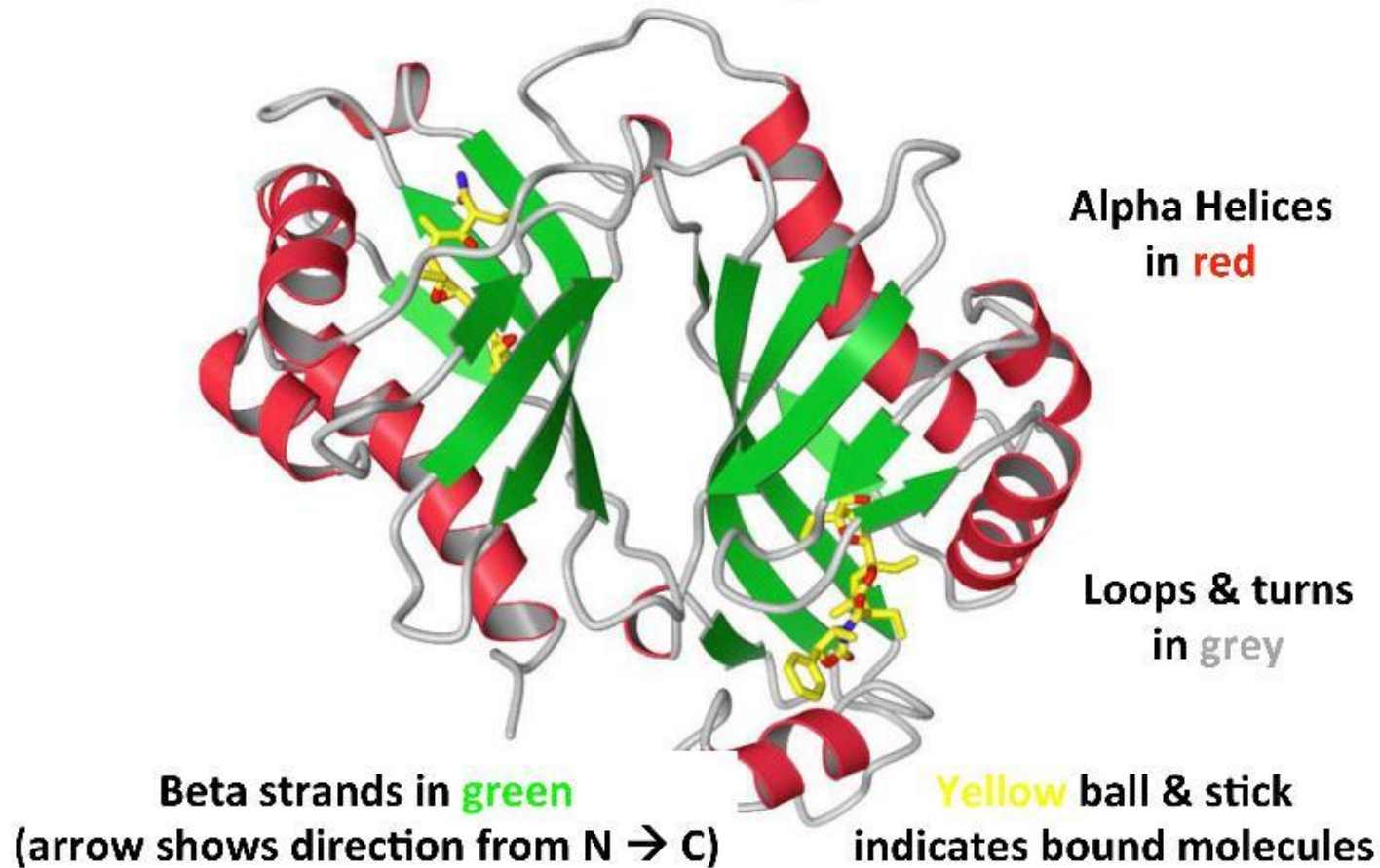


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PROTEINS' TERTIARY STRUCTURE

Ribbon Diagrams



(contd.)

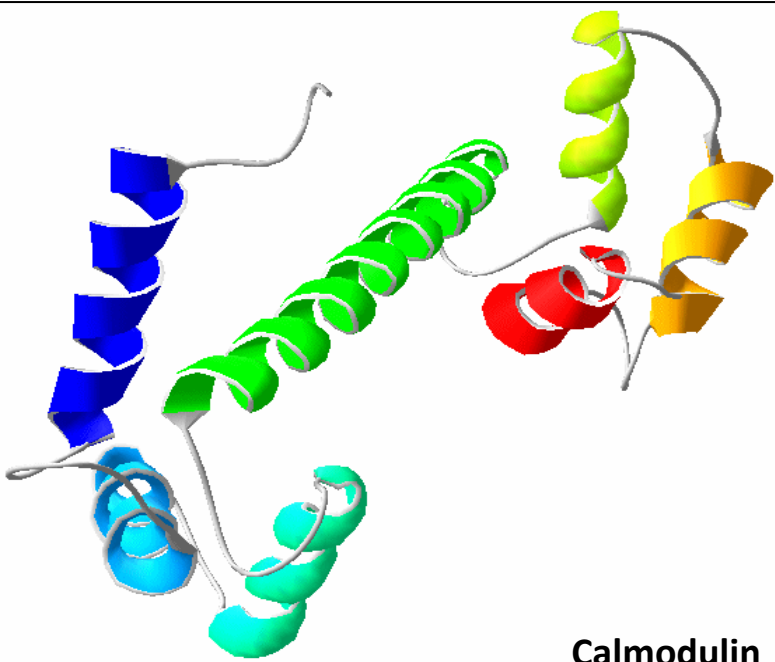
Source:

https://comis.med.uvm.edu/VIC/coursefiles/MD540/MD540-Protein_Organization_10400_574581210/Protein-org/Protein_Organization_print.html

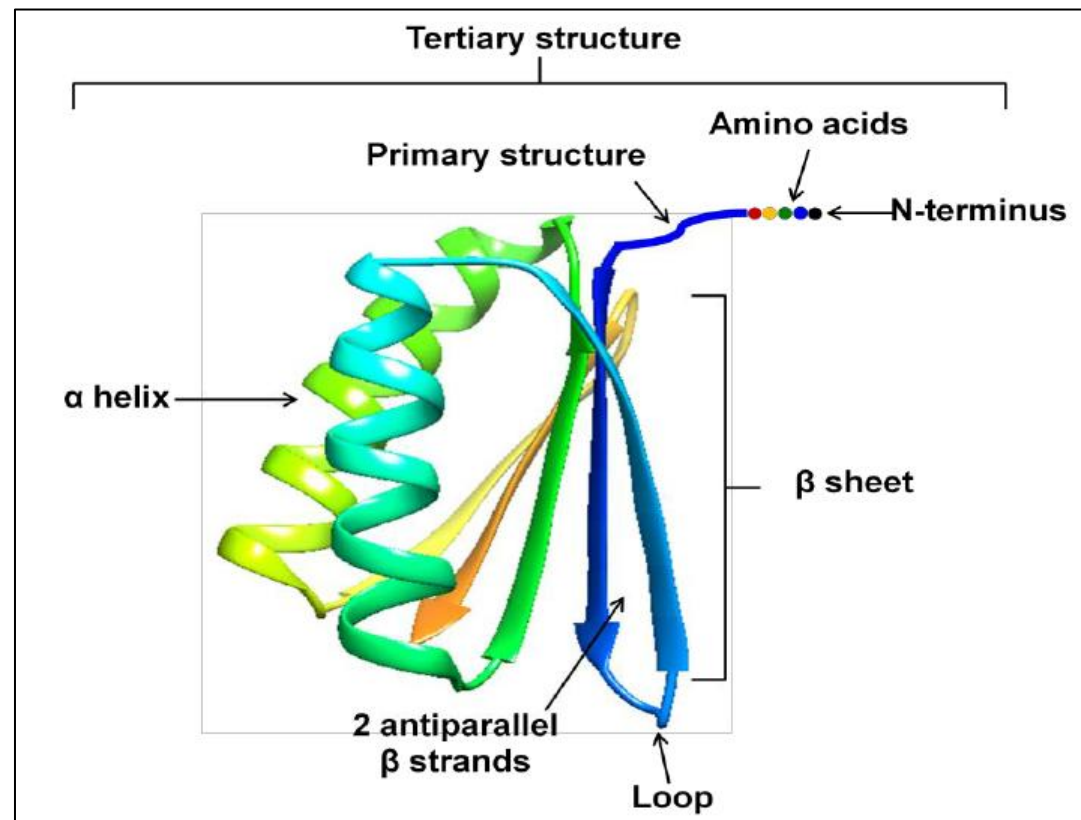
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PROTEINS' TERTIARY STRUCTURE

An example of a Tertiary Structure
composed of only α -helical elements



Calmodulin



(contd.)

PROTEINS' TERTIARY STRUCTURE

TABLE 4-2 Approximate Amounts of α Helix and β Conformation in Some Single-Chain Proteins

<i>Protein (total residues)</i>	<i>Residues (%)*</i>	
	<i>α Helix</i>	<i>β Conformation</i>
Chymotrypsin (247)	14	45
Ribonuclease (124)	26	35
Carboxypeptidase (307)	38	17
Cytochrome c (104)	39	0
Lysozyme (129)	40	12
Myoglobin (153)	78	0

*Portions of the polypeptide chains that are not accounted for by α helix or β conformation consist of bends and irregularly coiled or extended stretches. Segments of helix and conformation sometimes deviate slightly from their normal dimensions and geometry.

FIBROUS & GLOBULAR PROTEINS

FIBROUS PROTEINS

- Long & Narrow
- Structural Role

Examples: Keratin, Collagen

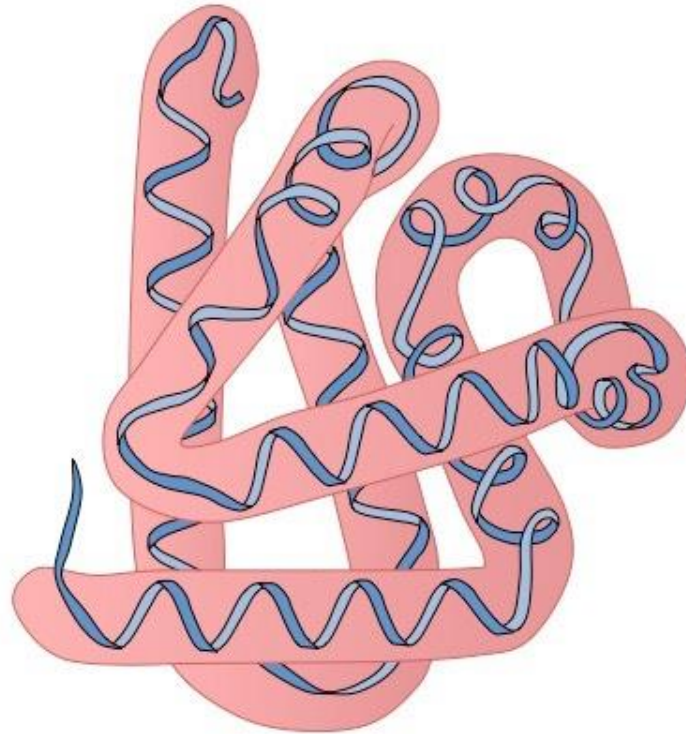


Fibrous Protein

GLOBULAR PROTEINS

- Round & Spherical
- Functional Role

Examples: Hemoglobin, Immunoglobulin, Enzymes



Globular Protein

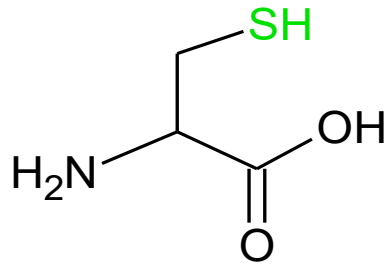
FIBROUS PROTEINS

TABLE 4-1 Secondary Structures and Properties of Fibrous Proteins

<i>Structure</i>	<i>Characteristics</i>	<i>Examples of occurrence</i>
α Helix, cross-linked by disulfide bonds	Tough, insoluble protective structures of varying hardness and flexibility	α -Keratin of hair, feathers, and nails
β Conformation	Soft, flexible filaments	Silk fibroin
Collagen triple helix	High tensile strength, without stretch	Collagen of tendons, bone matrix

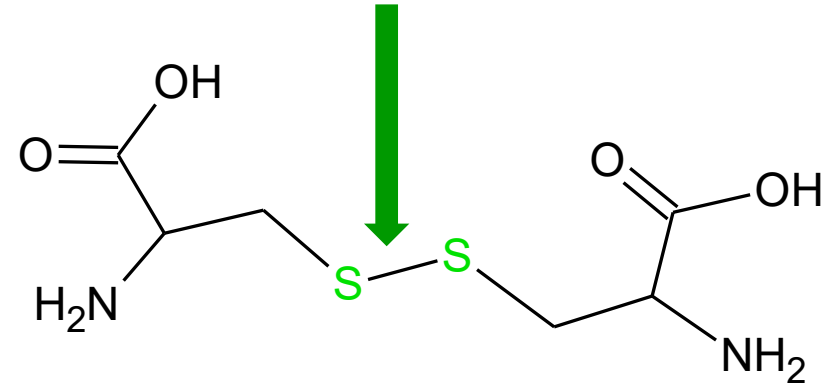
Disulfide Bonds in Peptides & Proteins

Cysteine (Cys; C)

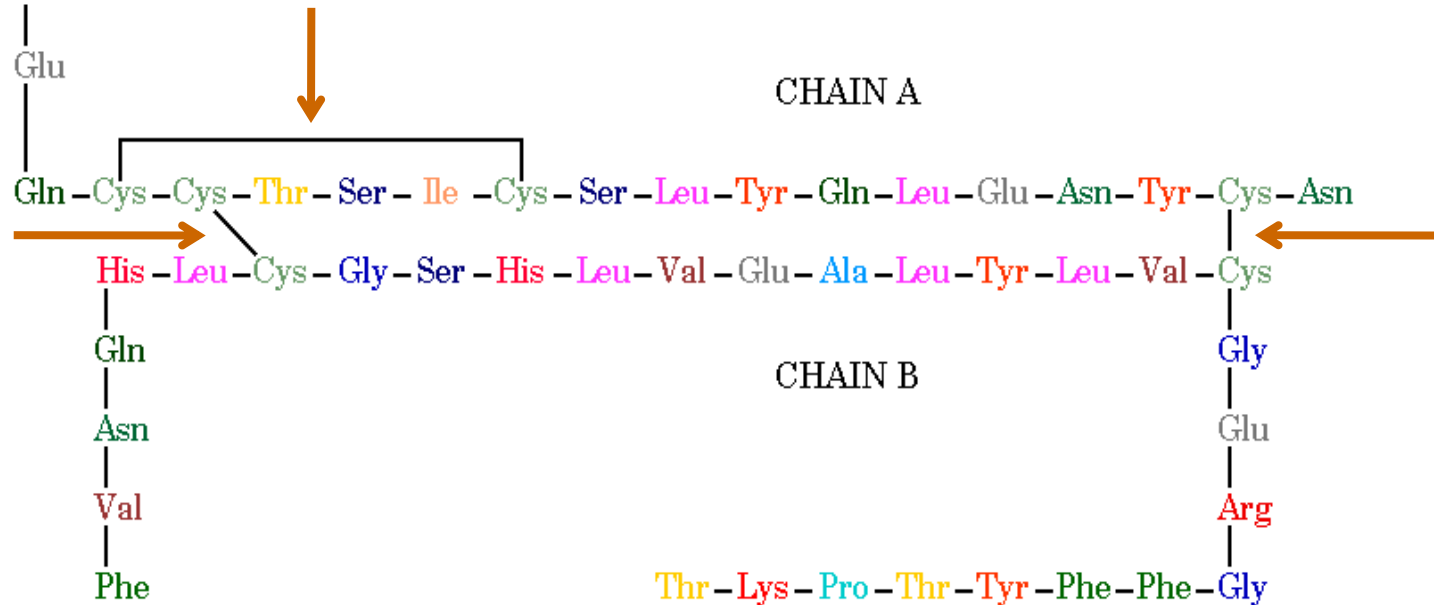


“Formation of Disulfide Bond is
a ‘POST-TRANSLATIONAL MODIFICATION (PTM)’

The sidechains of Two Cysteines
join to form ‘disulfide bond’.



human insulin

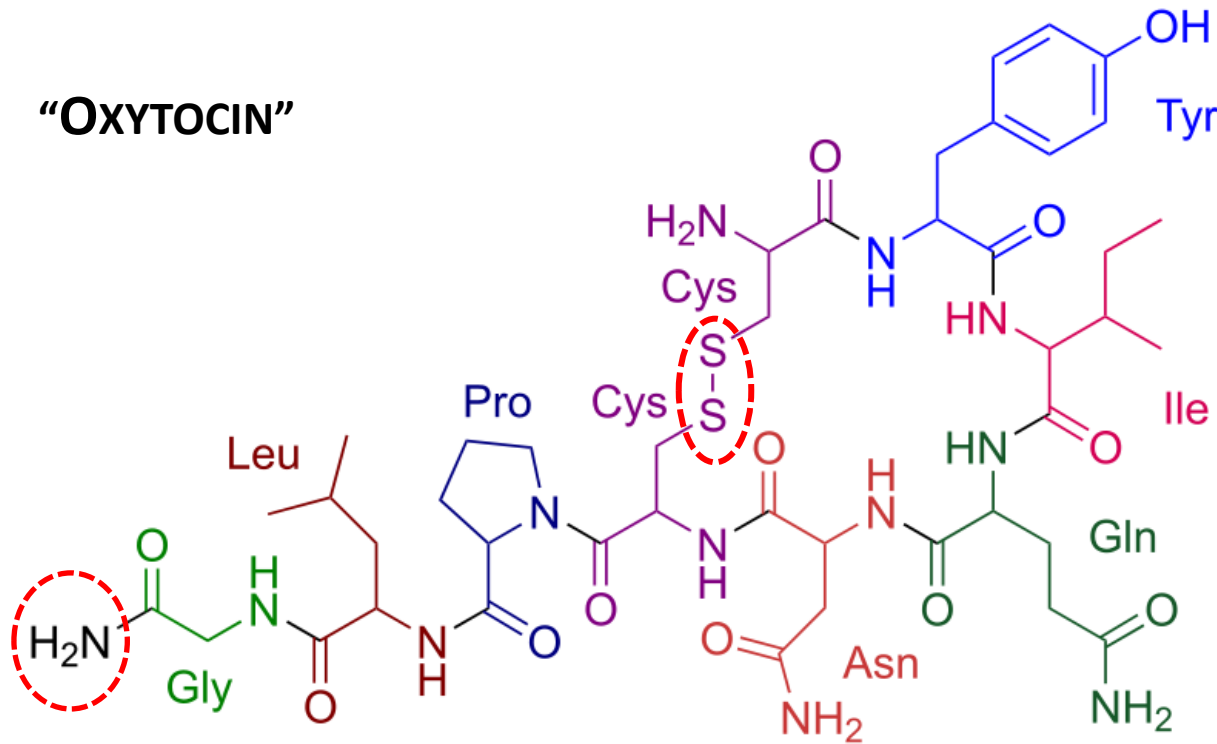


Example

Disulfide Bonds in Peptides (Intra-molecular Disulfide Bond)

- Peptide Hormones:
Oxytocin, Vasopressin - One Disulfide Bond

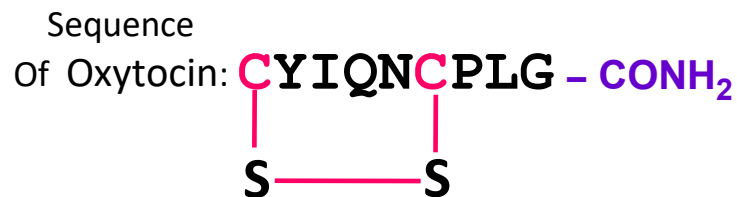
“OXYTOCIN”



‘Post-Translation Modifications (PTMs)’
2 PTMs in Oxytocin

- (i) S-S bond (intramolecular)
- (ii) C-terminus Amidation

(Source: https://commons.wikimedia.org/wiki/File:Oxytocin_color.svg)



Post-Translational Modification:

Amidation of C- terminus

Or

C-terminus Amidation

Disulfide Bonds in Proteins

“Human Serum Albumin” has **17 Disulfide Bonds (Intra molecular S-S bonds)**

This protein is in human plasma and serum (blood).

Sequence of the protein is shown in single-letter code

>sp|P02768|25-609

1

60

DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAE
 NCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEV
 DVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTCCQAADKAACLLP
 KLDELRLDEGKASSAKQRLKCASLQKFGERAFAKAWAVARLSQRFPKAEFAEVSKLVTDLT
 VHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA
 DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLRLRLAKTYETTLKC
CAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVST
 PTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTES
 LVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKAT
 KEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL

541

585

No. of Cysteines: 35

Source: <http://www.uniprot.org/uniprot/P02768> (Uniprot KB Database)

Examples of Some Major Proteins , Peptides & their Functions

- **HEMOGLOBIN:** Major component in Human's Blood → Essential for O₂ transport all over the body.
- **MYOGLOBIN:** Major component in Human's Muscles → Essential for O₂ Storage.
- **CASEIN:** Major component in Milk, e.g., Cow's Milk.
- **OVALBUMIN:** Major Protein in Egg White.
- **COLLAGEN:** Major Protein in Human's & Animal's Skins.
- **KERATIN:** Major Protein component in Human's & Animal's Hair.
Also present in Nails, Claws, Feathers, Horns of several animals.
- **INSULIN:** Peptide Hormone implicated in regulating blood glucose level.
- **GLUCAGON:** Peptide Hormone involved in increasing the blood glucose level, whenever required.

Molecular Mass of Proteins & Number of constituting amino acid residues

	<i>Molecular weight</i>	<i>Number of residues</i>	<i>Number of polypeptide chains</i>
Cytochrome c (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (chicken egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (<i>E. coli</i>)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (<i>E. coli</i>)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

Average mass of an amino acid residue = ~ 110 Daltons (Da)