Lecture #3

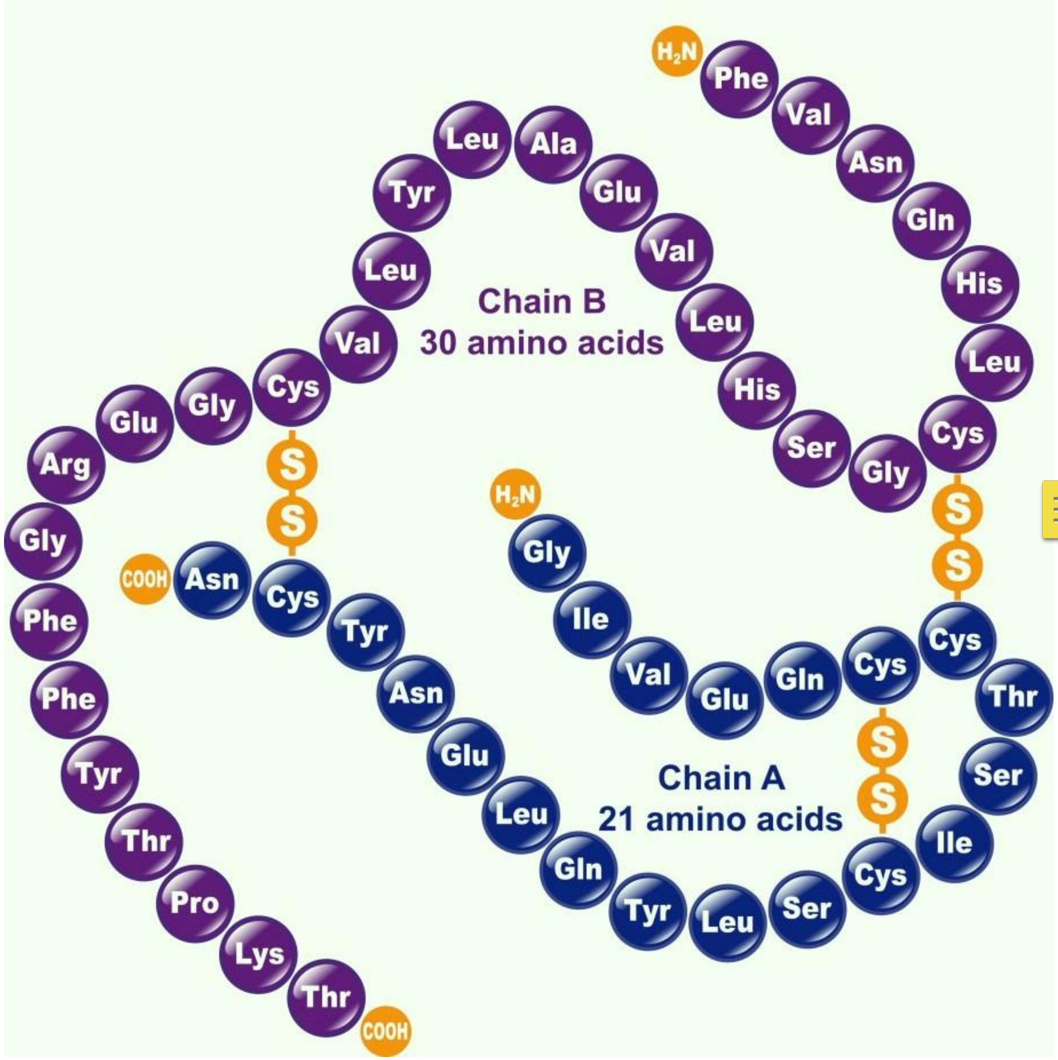
The four levels of protein structure:

- **1° Primary**
- **2° Secondary**
- **3° Tertiary**
- **4° Quaternary**

Levels of protein structure

- **Primary (1^{o}): the linear amino acid sequence**
- **Secondary (2^{o}): periodic, repetitive units (alpha-helix, beta-sheet, reverse turn)**
- **Tertiary (3^{o}): folding of secondary segments into a defined protein structure**
- **Quaternary (4^{o}): assembly of protein sub-units**

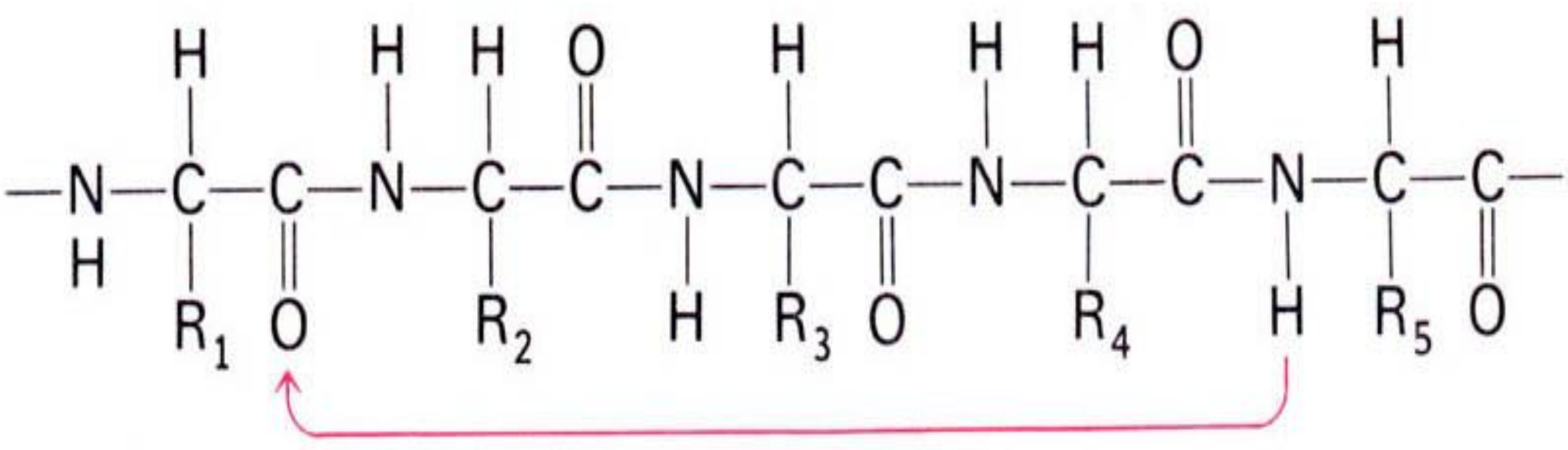
Primary structure (1^o) of insulin



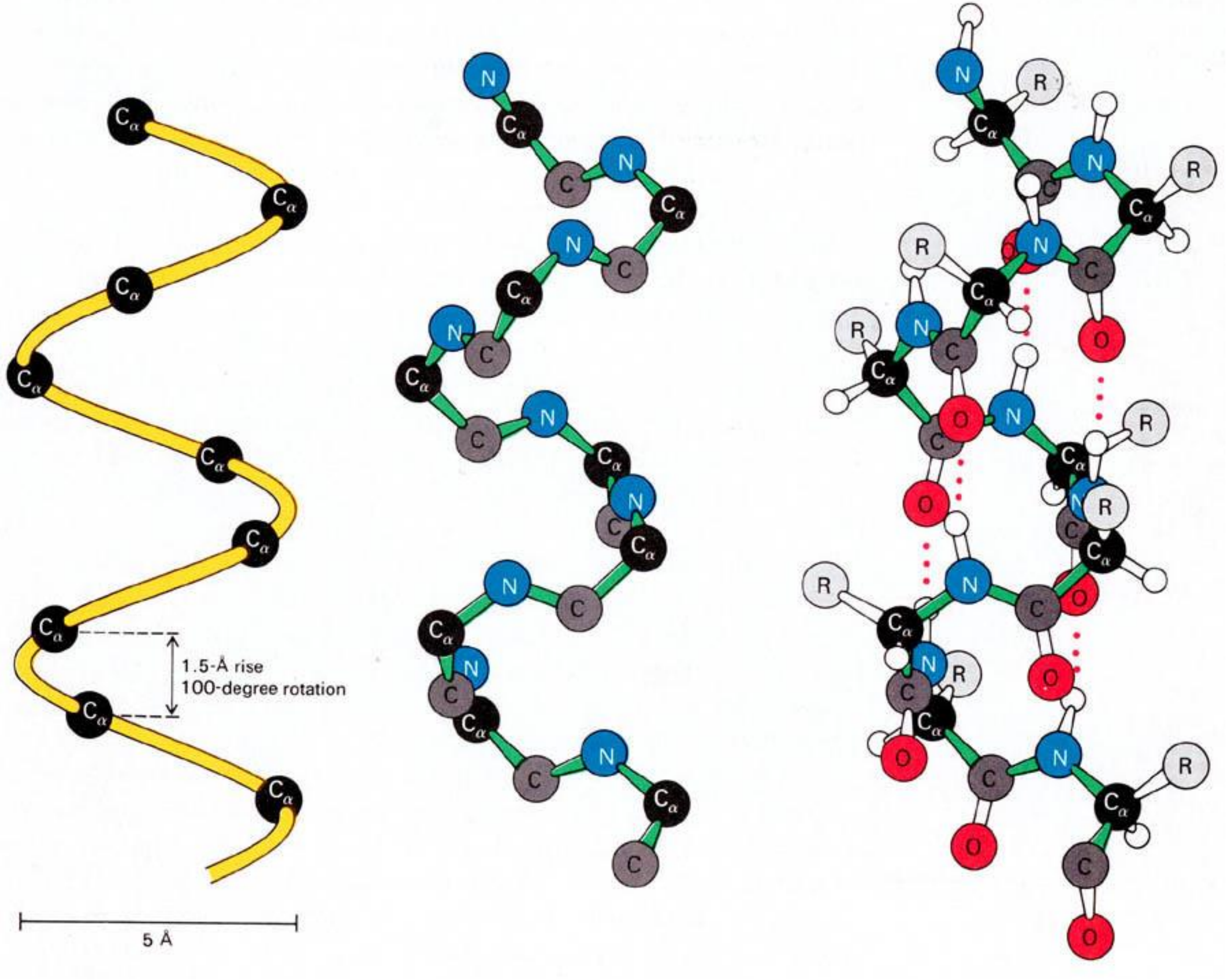
Secondary structure (2º): α-helix

- In the α-helix, the N-H group of residue i donates a H-bond back to the C=O group of residue i - 4
- Need to pack side chains and minimize side-chain steric clashes
- Right-handed helix

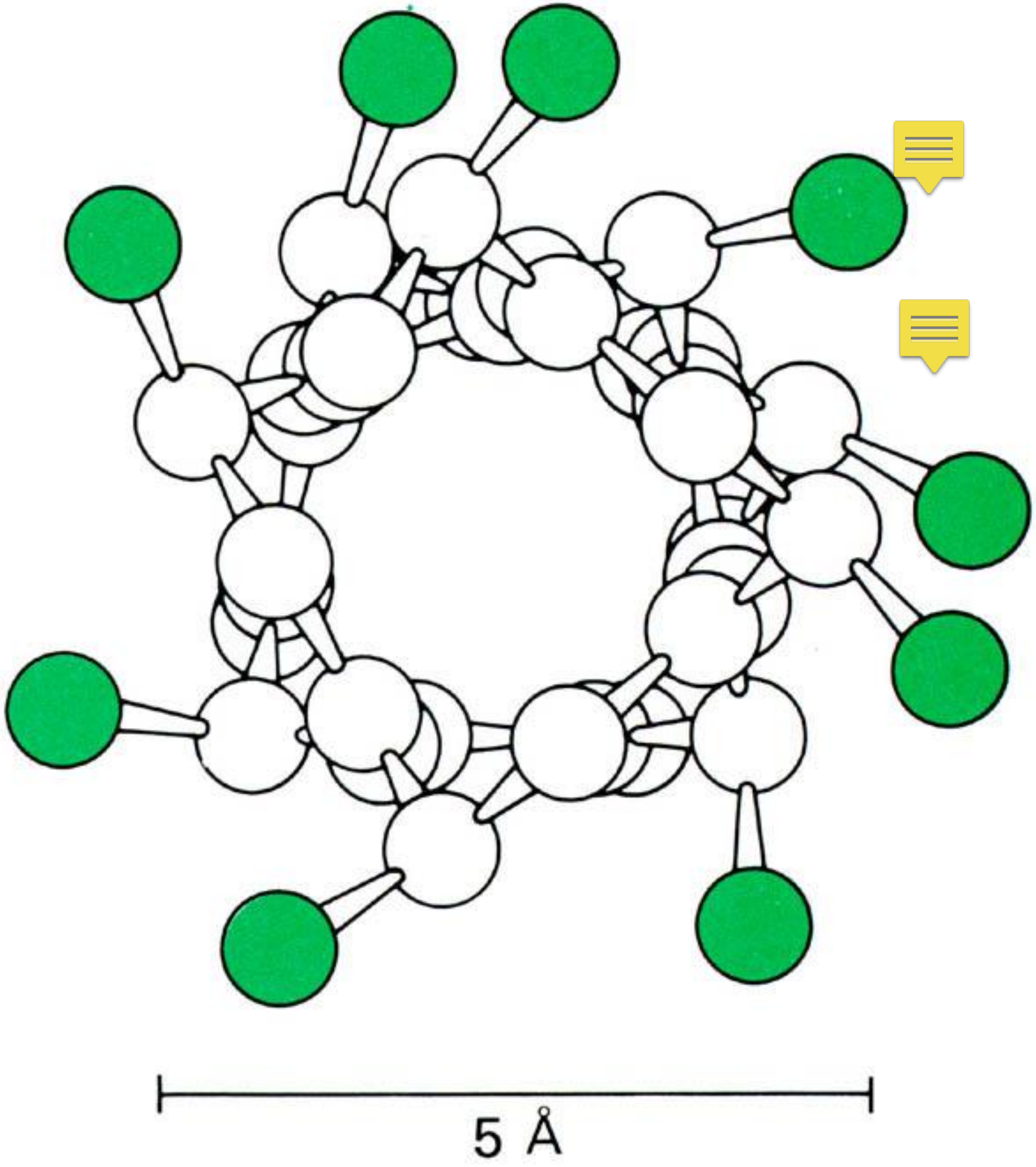
In the α-helix, the N-H group of residue i forms a hydrogen bond with the C=O group of residue i-4



α-helix



α-helix top view



Features of the α-helix

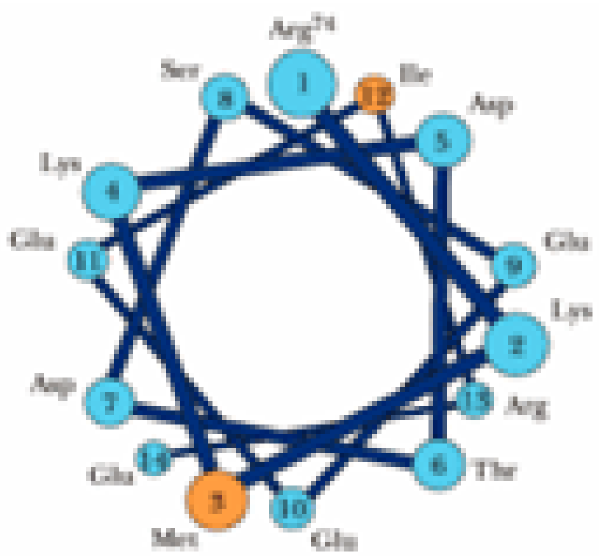
- Dimensions:
  - 3.6 residues per 360° turn
  - 100° between adjacent residues
  - 1.5 Å rise per residue
  - 5 Å across backbone

Features of the α-helix

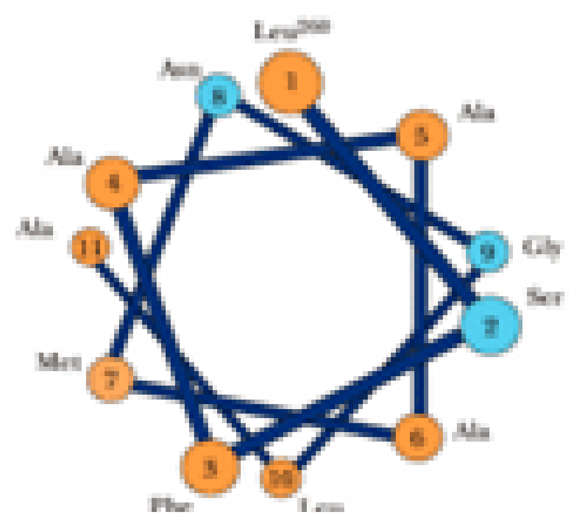
- Right-handed
- Hydrogen bonds face interior of helix
- Side chains exposed around the periphery of the structure
- Interact with the surrounding environment (water or protein)

Properties of α-helix depends on side chains

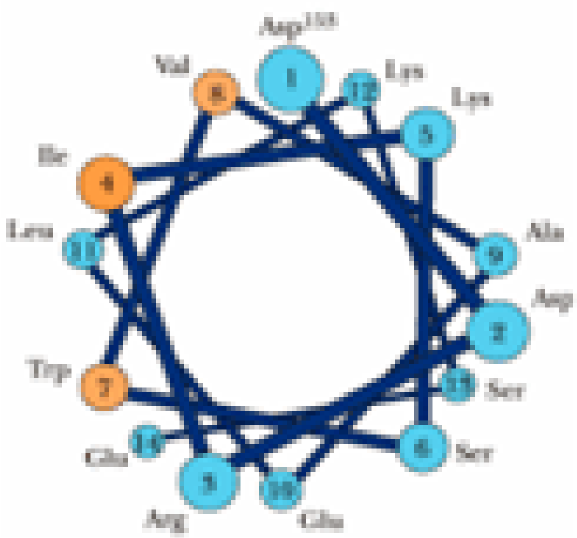
Polar



Hydrophobic

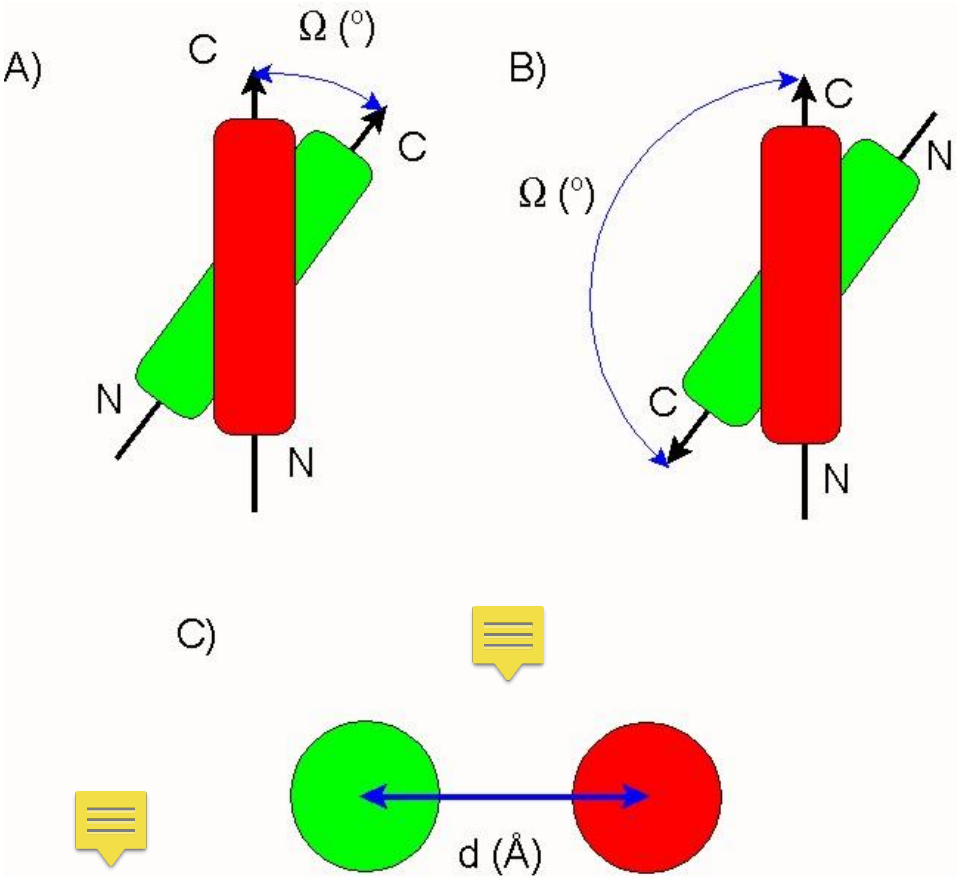


Amphipathic



Helix-helix interactions

- Typically anti-parallel
- 50° angle common
- Small residues at interface (Gly/Ala)



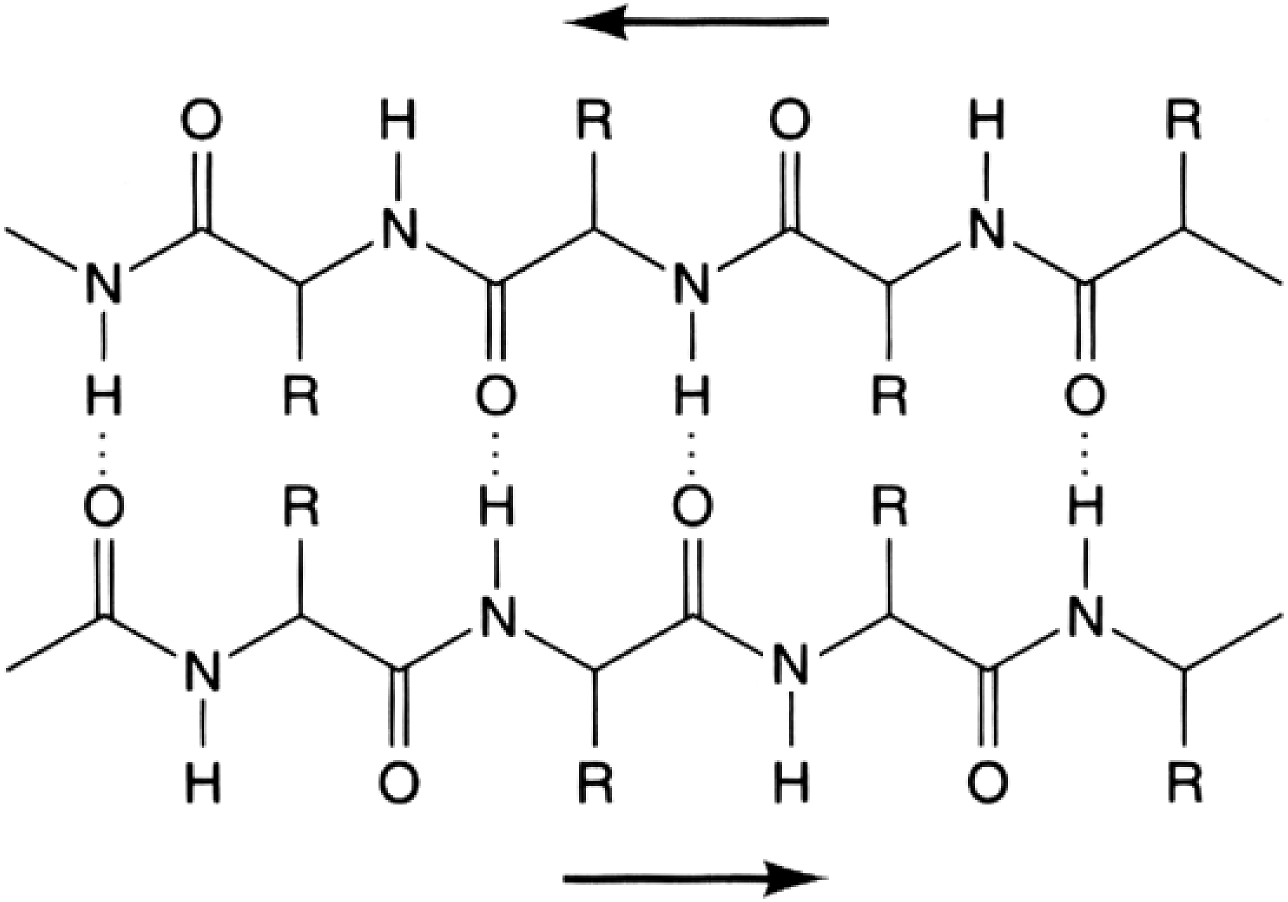
β-pleated sheet

- **Important feature of protein 2^o structure**
- **Formed from two or more extended β-strands of amino acids, bonded to each other through alternating intermolecular backbone H-bonds**

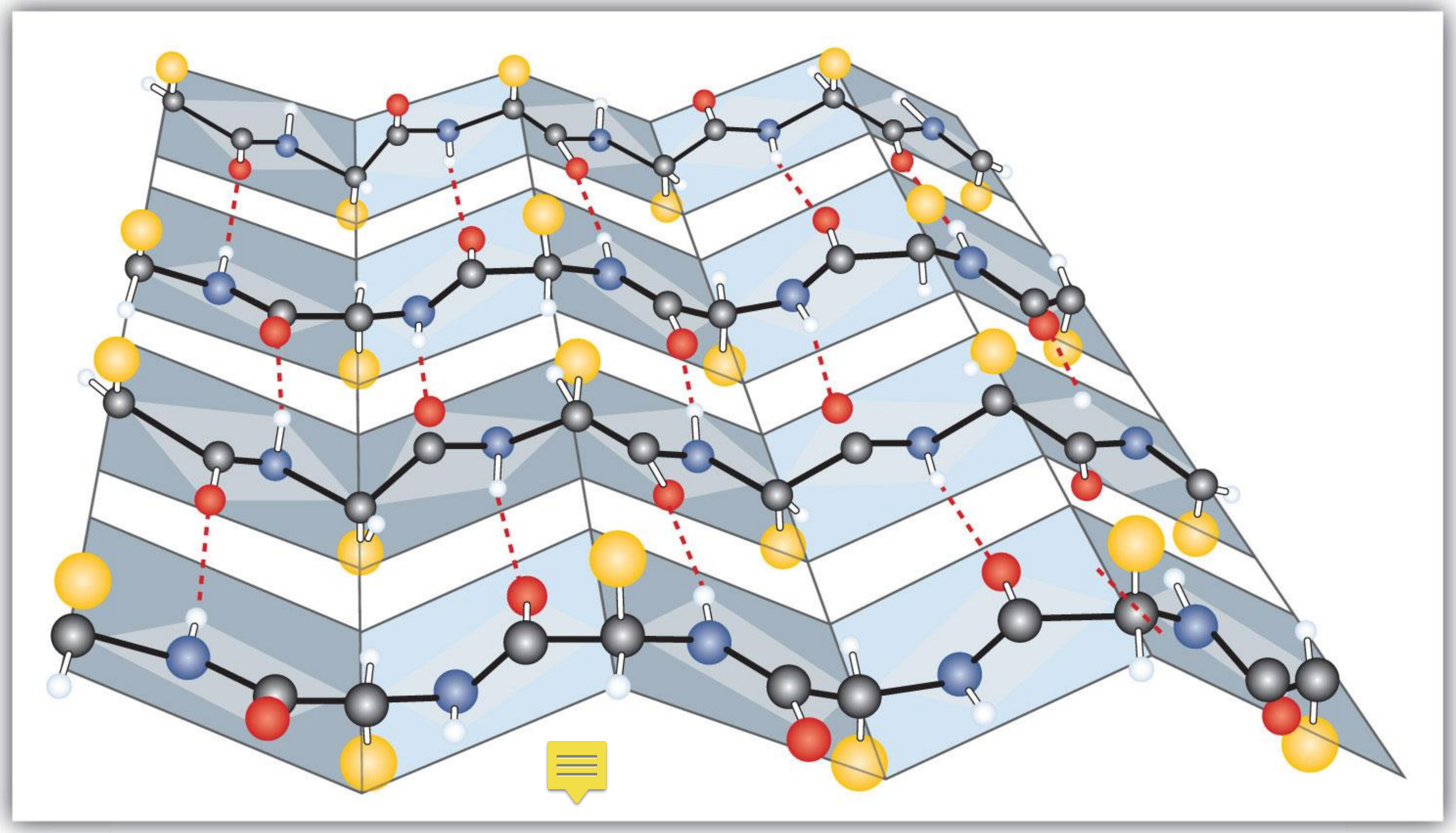
β-pleated sheet

- Adjacent extended strands of the β-sheet can be parallel or anti-parallel
- Can bring distant strands of a protein into proximity

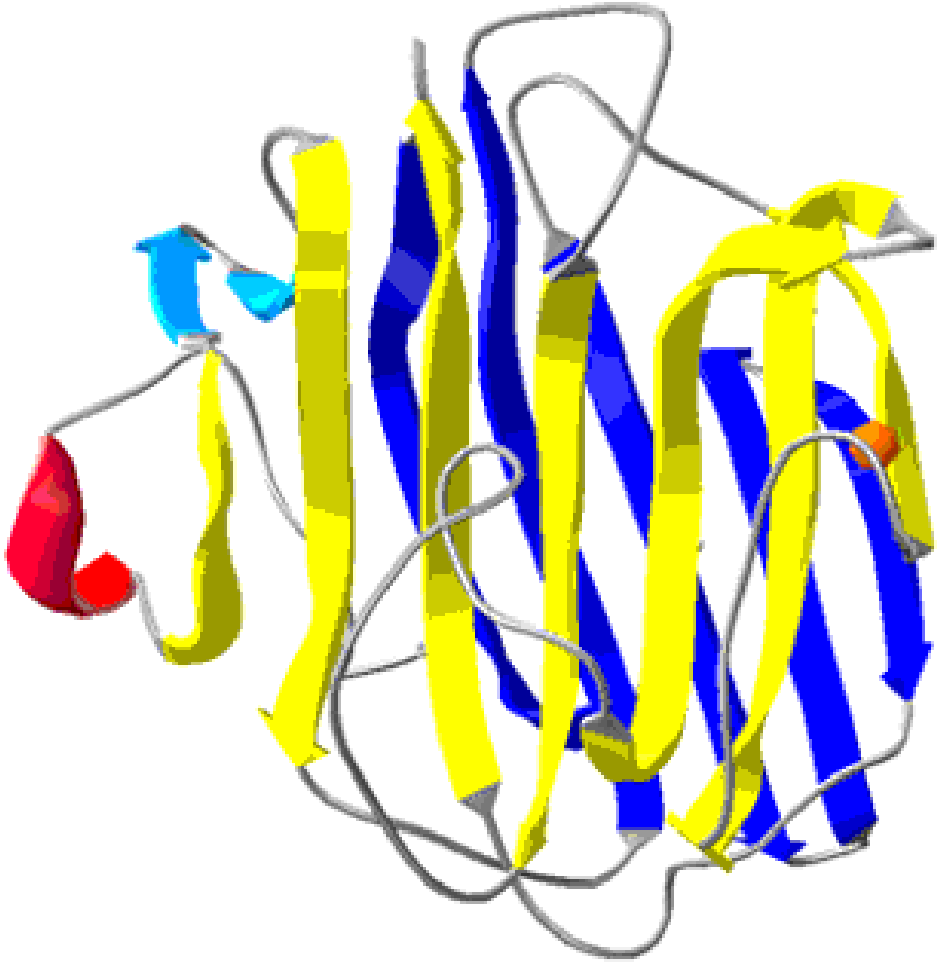
Anti-parallel strands form a β-sheet structure



β-pleated sheet



Sugar-binding protein



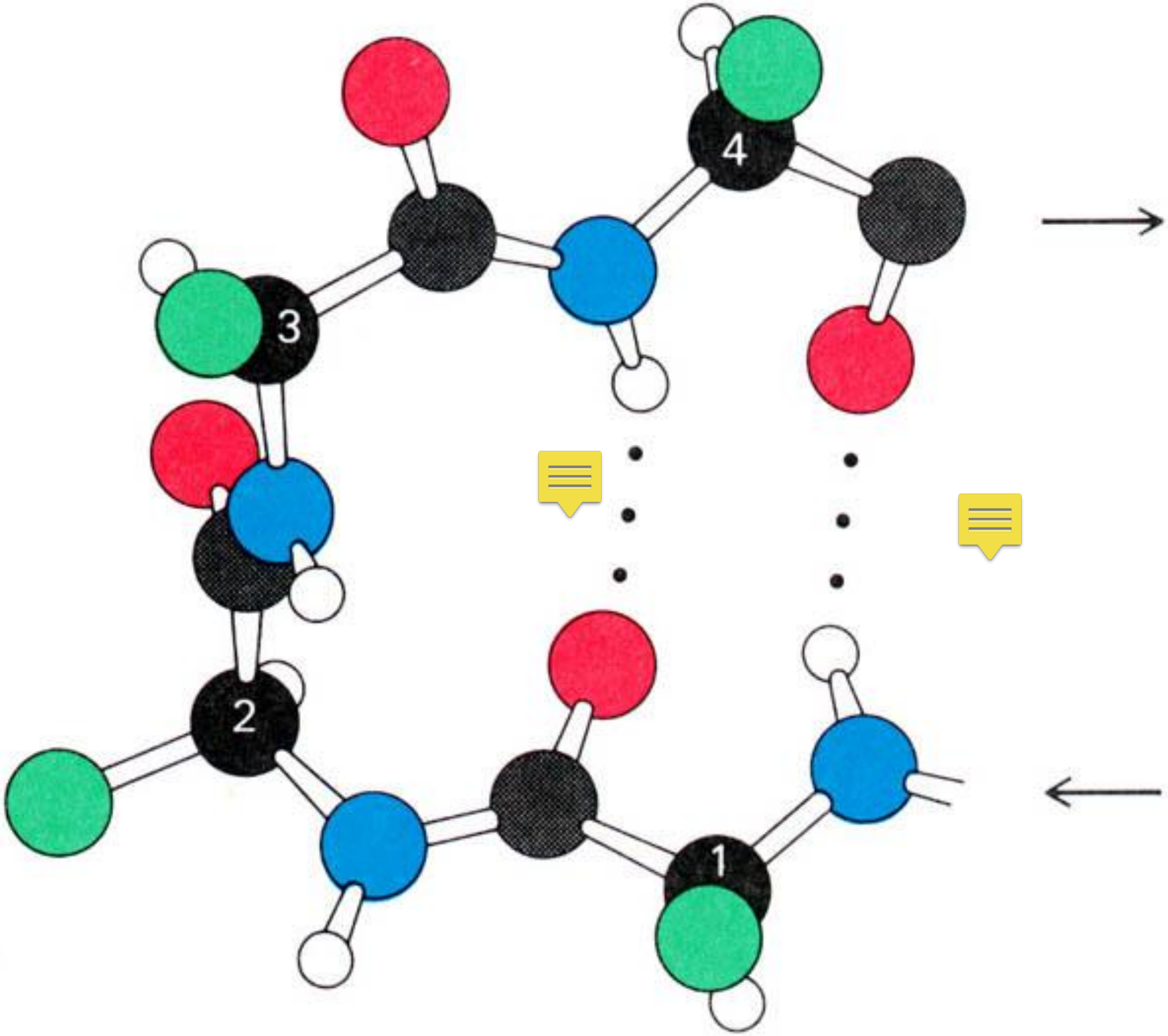
The two workhorses of protein 2º structure

- The α-helix 1.5 Å translation per residue
- The β-sheet 3.0 Å translation per residue
- Hydrogen bonds are key to stabilizing secondary structures

β-turns

- Designates the 4-residue segment through which the protein chain turns 180°
- Sometimes called “reverse turns”
- Can link two β-strands, two helices, strand to helix, etc.
- On the surface of a globular protein

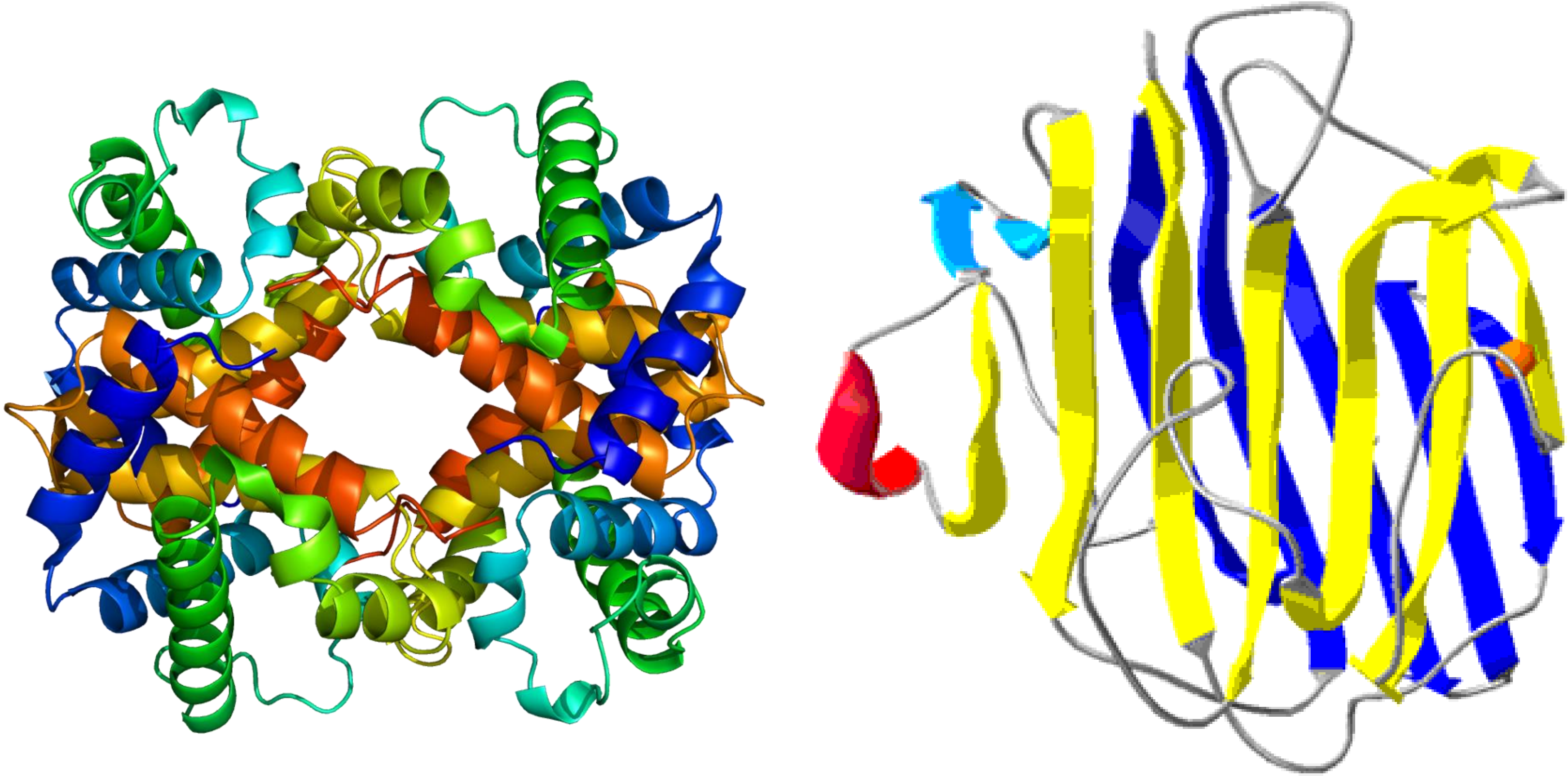
β-turn



Residues found in β-turns

- Frequently found:
  - Gly, Asn, Pro, Ser
  - Pro most common at position 2

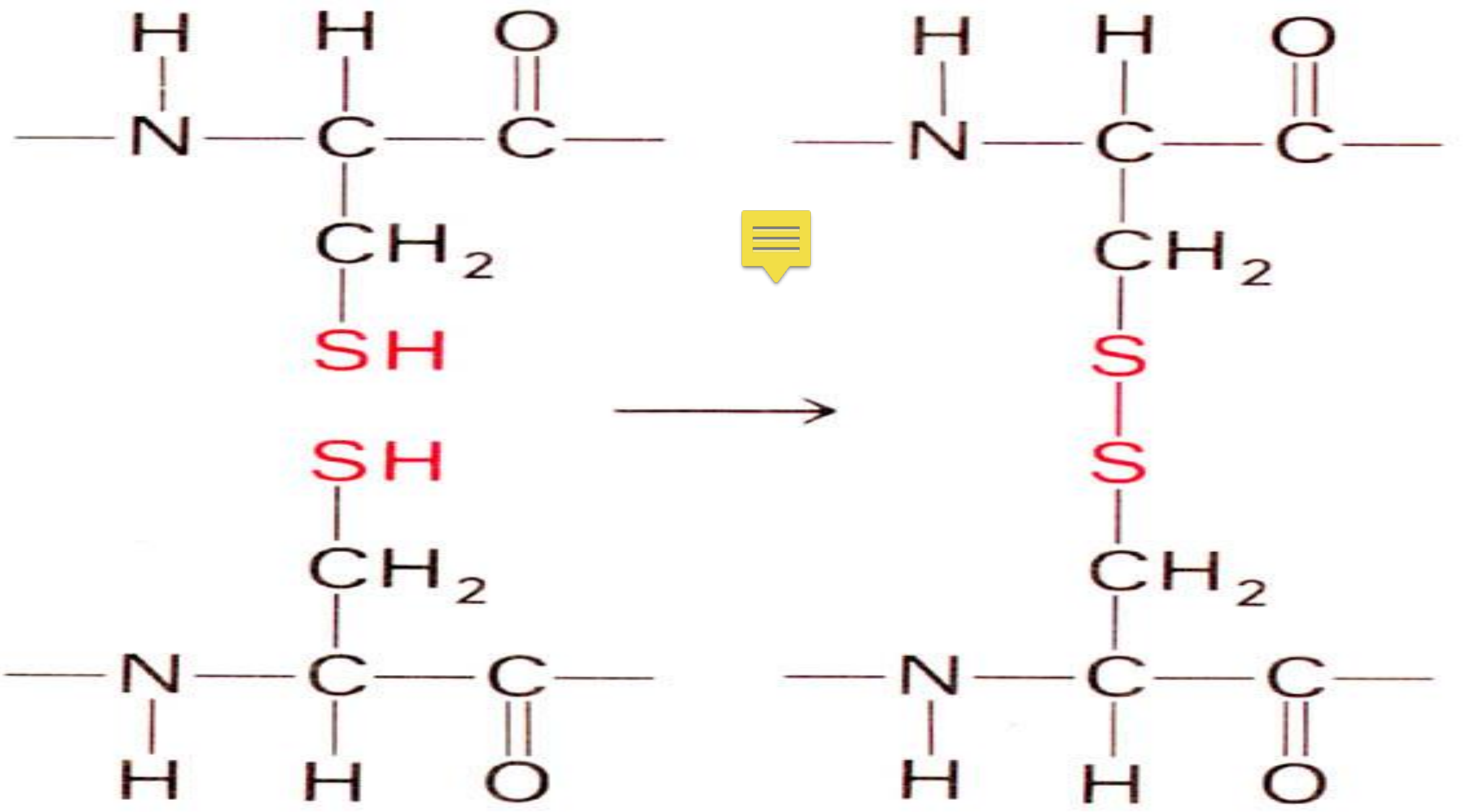
β-turns and loops connect helices & strands



Protein 3^{o} structure

- Defines the final folded structure of the protein
- Represents the assembly of α-helices, β-sheets, β-turns, or disordered regions
- Disulfide (S-S) bonds covalently link different parts of the protein together

The disulfide bond is a feature of protein 3^{o} structure



Protein 3^o structure

- Segments without periodicity are described as disordered
- Structure defined by sequence
- Proteins are dynamic (e.g., enzymes) and exist in different conformational states

Protein 4^{o} structure

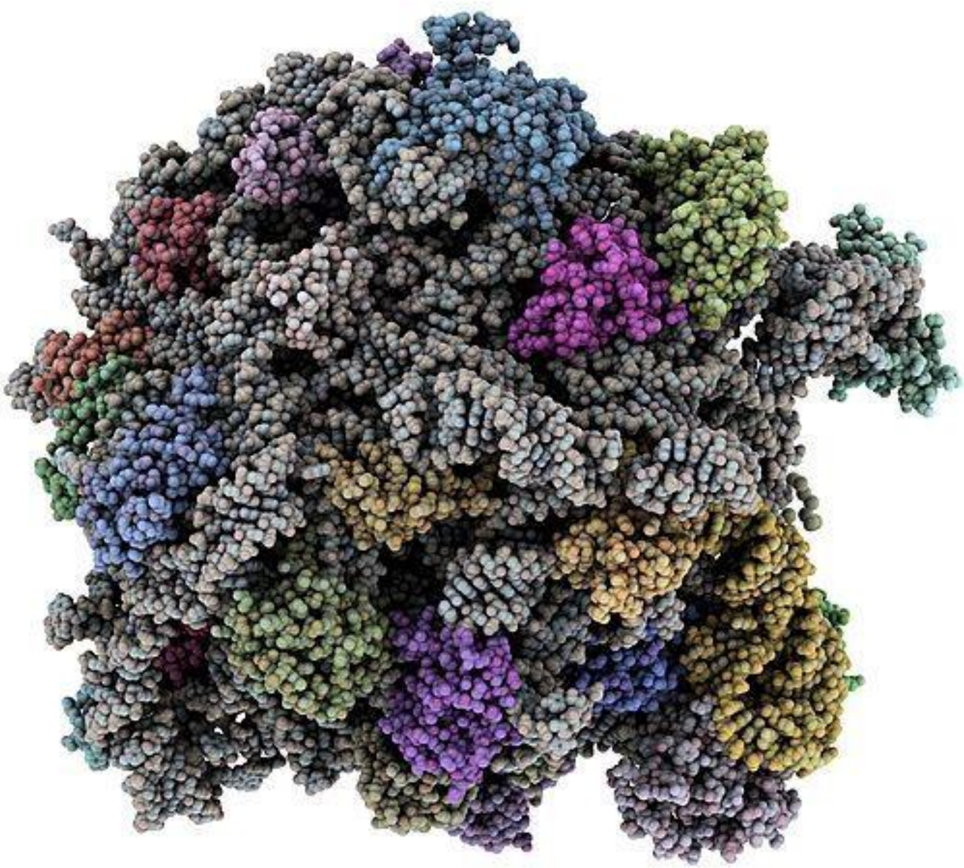
- Describes proteins where function depends upon the assembly of two or more subunits
- Subunits interact through the same forces as occur within individual subunits
- Subunits can be identical, or may all be different

Protein 4^{o} structure

- **Monomer**
- **Dimer**
- **Trimer**
- **Tetramer**
- **Pentamer**
- **Hexamer**
- **Heptamer**
- **Octamer etc.**

- **Can be of identical subunits or of different subunits**
- **Hemoglobin**
  - **2 alpha (α) chains**
  - **2 beta (β) chains**

Yeast ribosome has 64 different proteins



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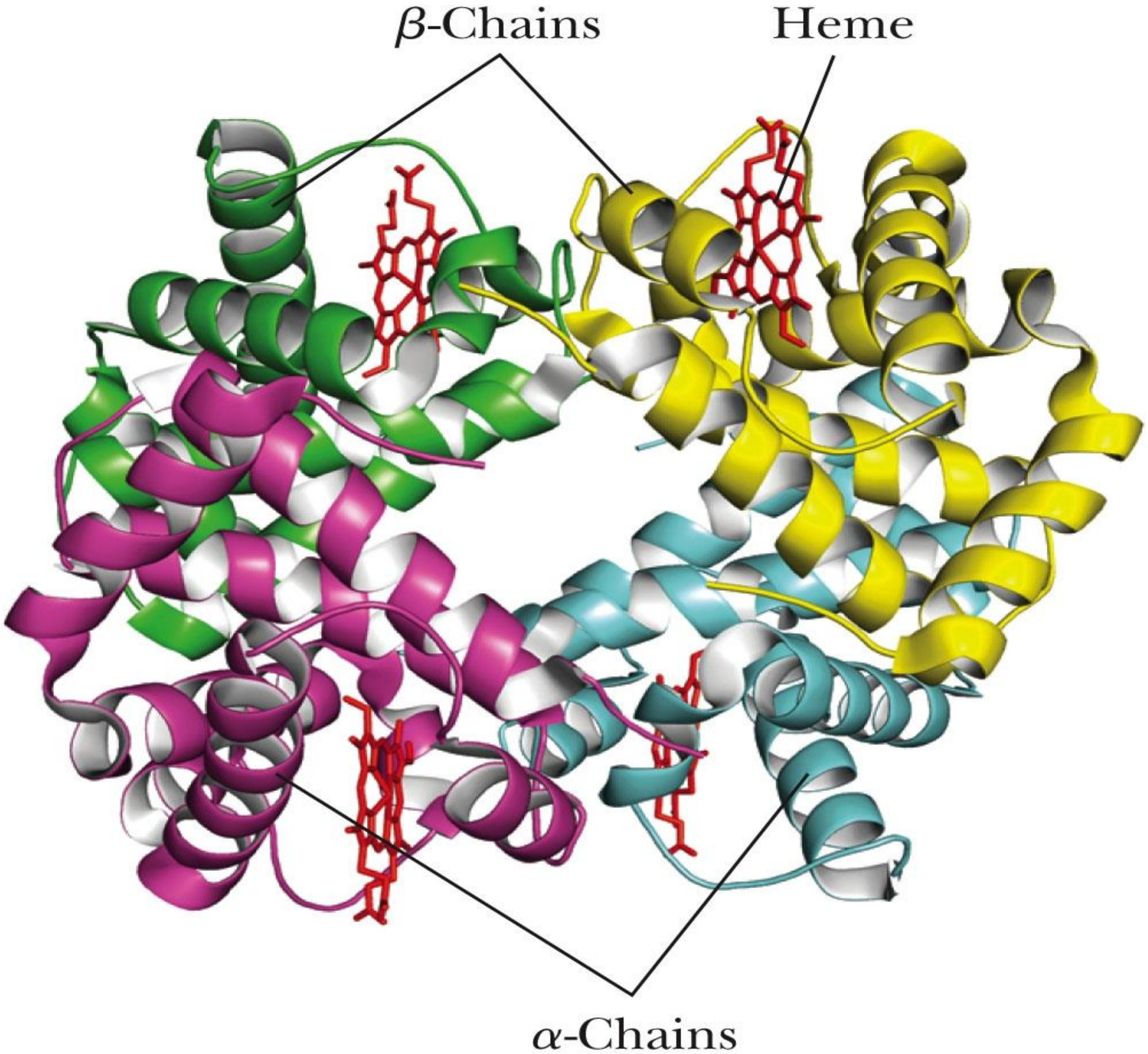
Hemoglobin is a tetramer



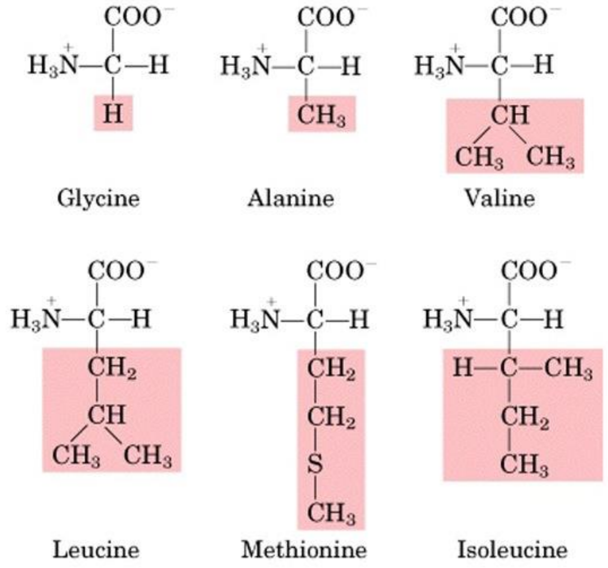
Hemoglobin is dynamic

- **Conformational changes between oxygenated (R) and deoxygenated (T) state**
- **https://www.youtube.com/watch?v=H3DHvJ_MEtk**

Summary

- Key role of peptide bonds in 1° structure
- Key role played by hydrogen bonds in 2° structure
- Key role played by van der Waals packing and hydrophobic effect in 3° and 4° structure
- What is the role of water in protein folding?

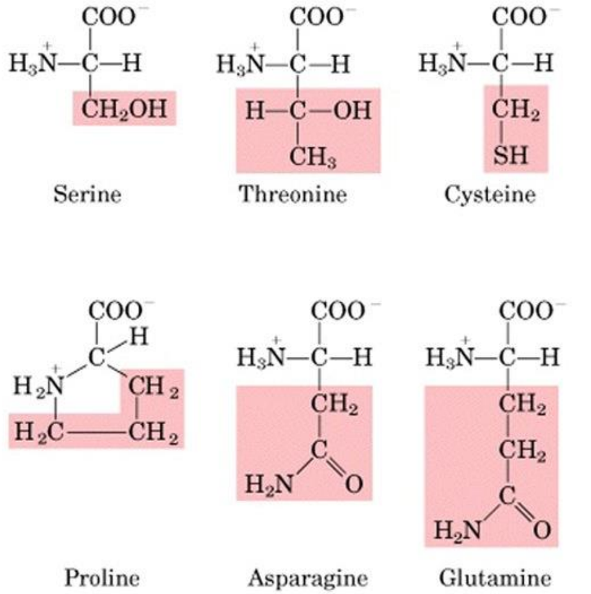
Nonpolar, aliphatic R groups



Glycine Alanine Valine

Leucine Methionine Isoleucine

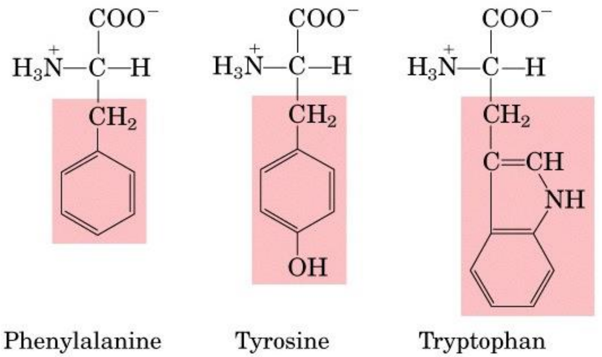
Polar, uncharged R groups



Serine Threonine Cysteine

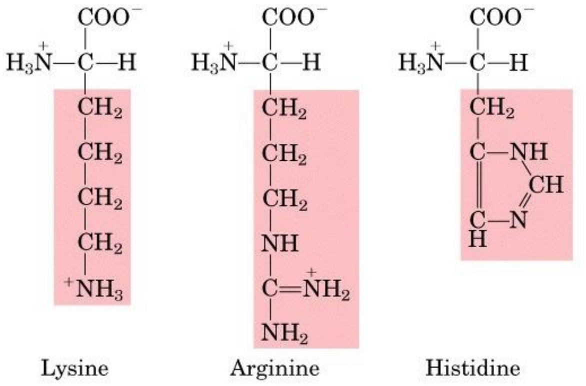
Proline Asparagine Glutamine

Aromatic R groups



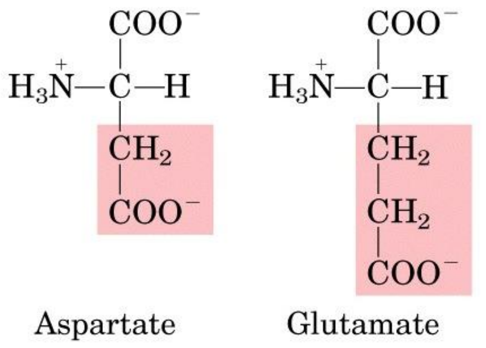
Phenylalanine Tyrosine Tryptophan

Positively charged R groups



Lysine Arginine Histidine

Negatively charged R groups



Aspartate Glutamate