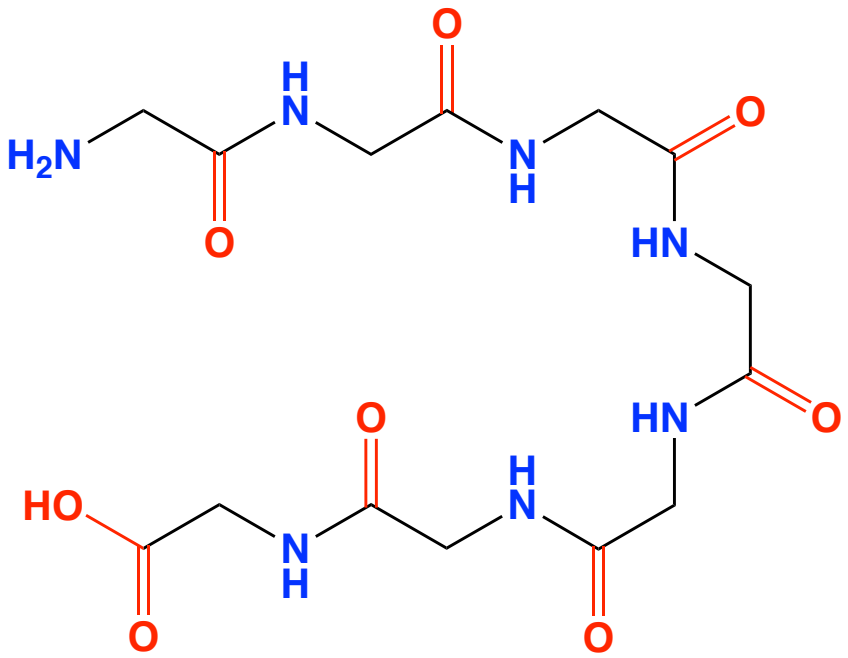
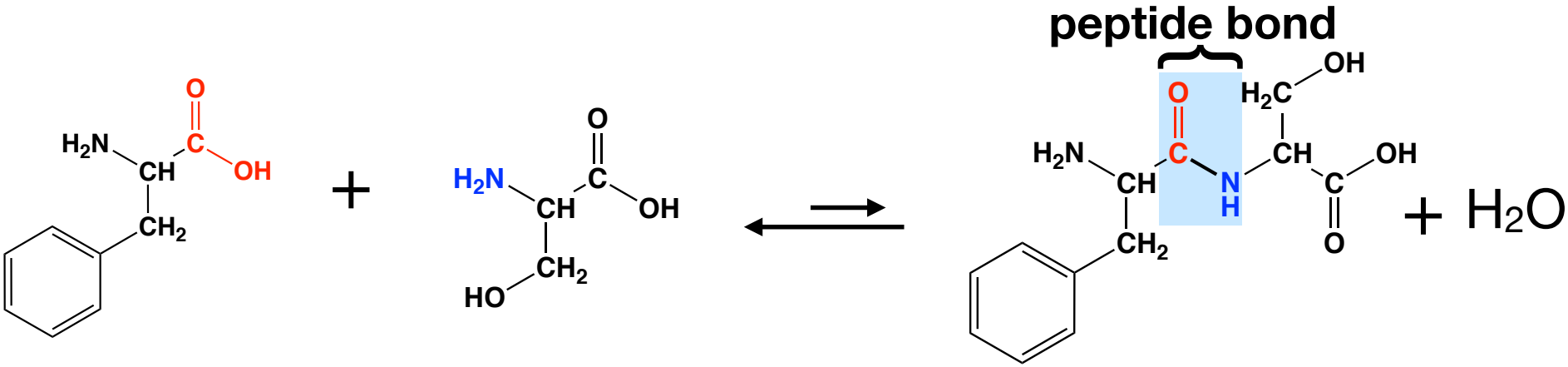
Peptide bond

Coupling of two amino acids



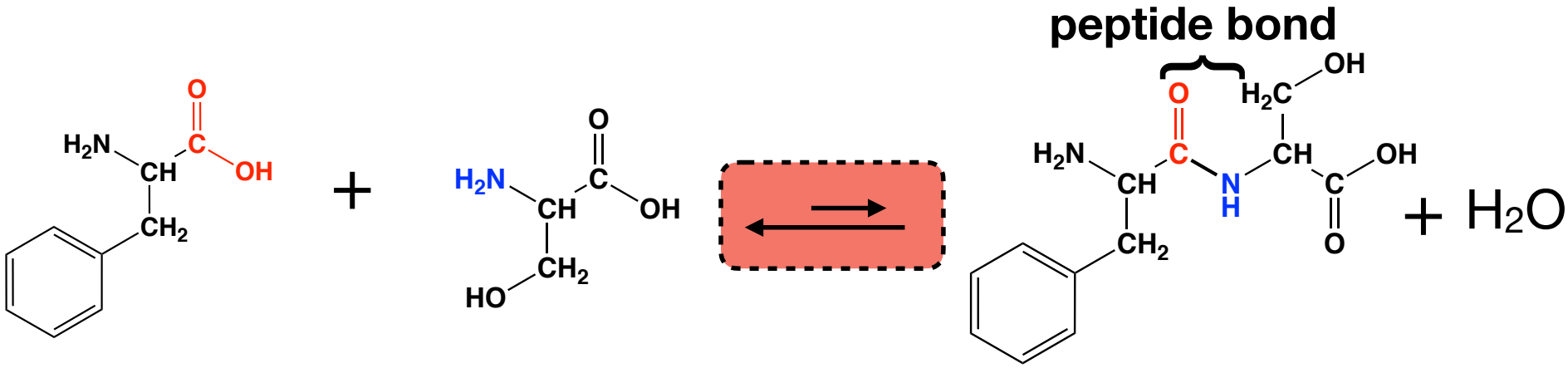
Peptide bond formation

- Proteins are *linear polymers* formed by linking the α-carboxyl group of one amino acid to the α-amino group of another amino acid. This type of linkage is called a peptide bond (or an *amide* bond).



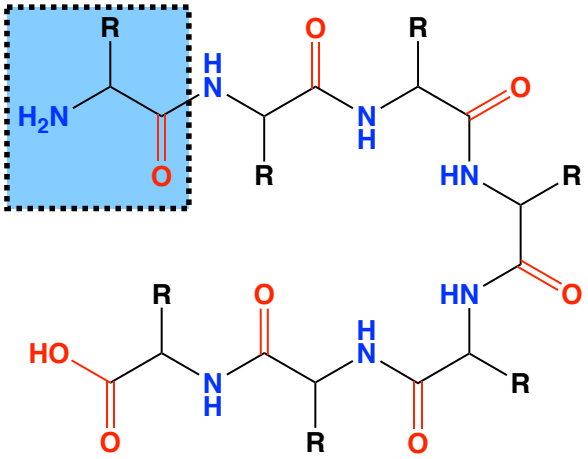
- The formation of a dipeptide from two amino acids is accompanied by the loss of a water molecule.

Peptide bond formation requires energy



- The equilibrium of the peptide bond formation reaction lies on the side of hydrolysis rather than synthesis. So, the biosynthesis of peptide bonds requires an input of free energy.
- Peptide bonds are quite *stable kinetically* because the rate of hydrolysis is extremely slow; the lifetime of a peptide bond in aqueous solution in the absence of a catalyst ~ 1000 years.

What is a “polypeptide”?



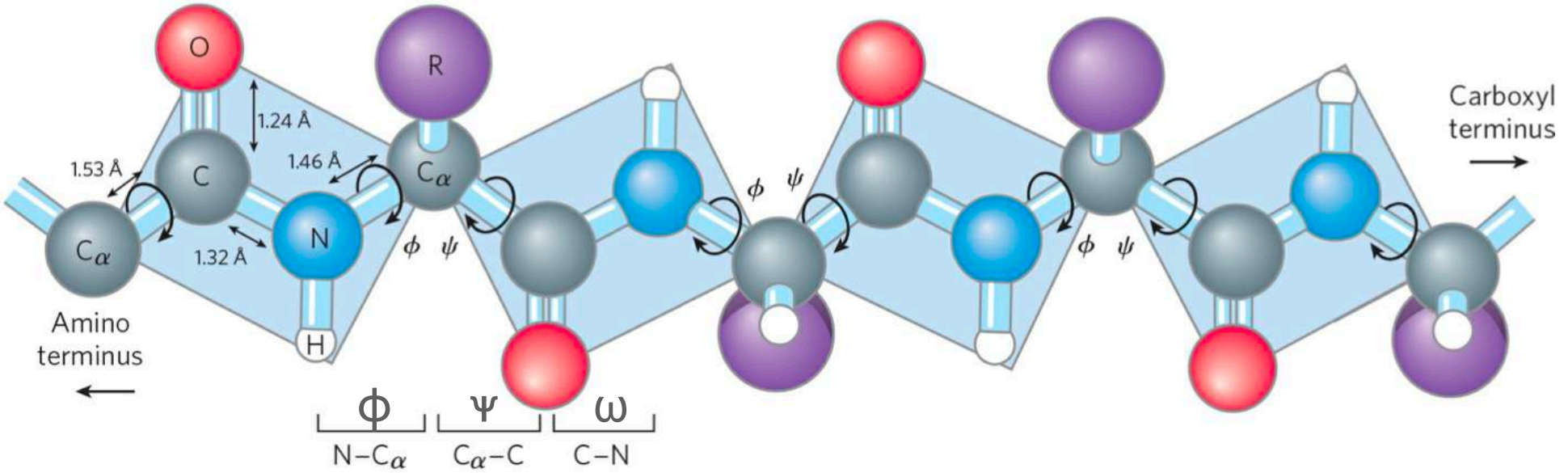
- When a series of amino acids are joined by peptide bonds they form a polypeptide chain
- Each amino acid unit within this polypeptide chain is referred to as a “**residue**”

A polypeptide chain has polarity because its ends are different: an α-amino group is present at one end and an α-carboxyl group at the other.

amino-terminal (N-terminal) Tyr-Gly-Gly-Phe-Leu **carboxy-terminal (C-terminal)**

By convention, the amino end is taken to be the beginning

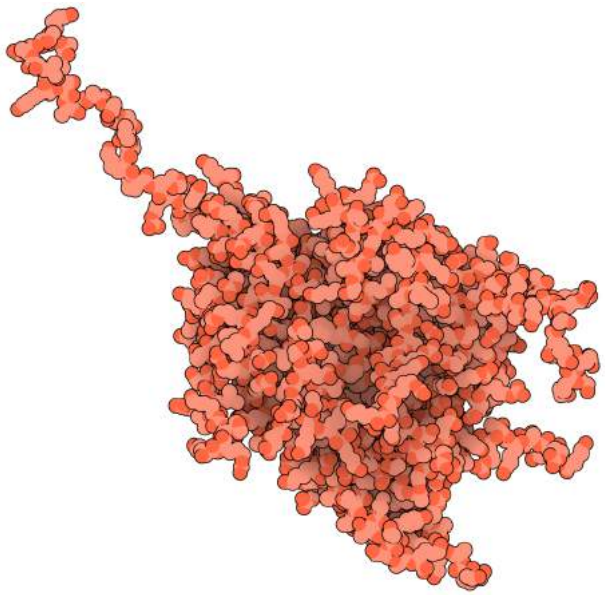
Planar nature of the peptide bond



- The peptide bond (the C=O and N-H) all reside in a single plane. Thus, **there is no rotation around the**  **bond.**
- Peptide conformation is defined by the **dihedral angles (torsion angles) called ϕ (phi) and ψ(psi)** that reflect rotation about the N-Cα and Cα-C bonds in the peptide backbone.

Peptides and Proteins

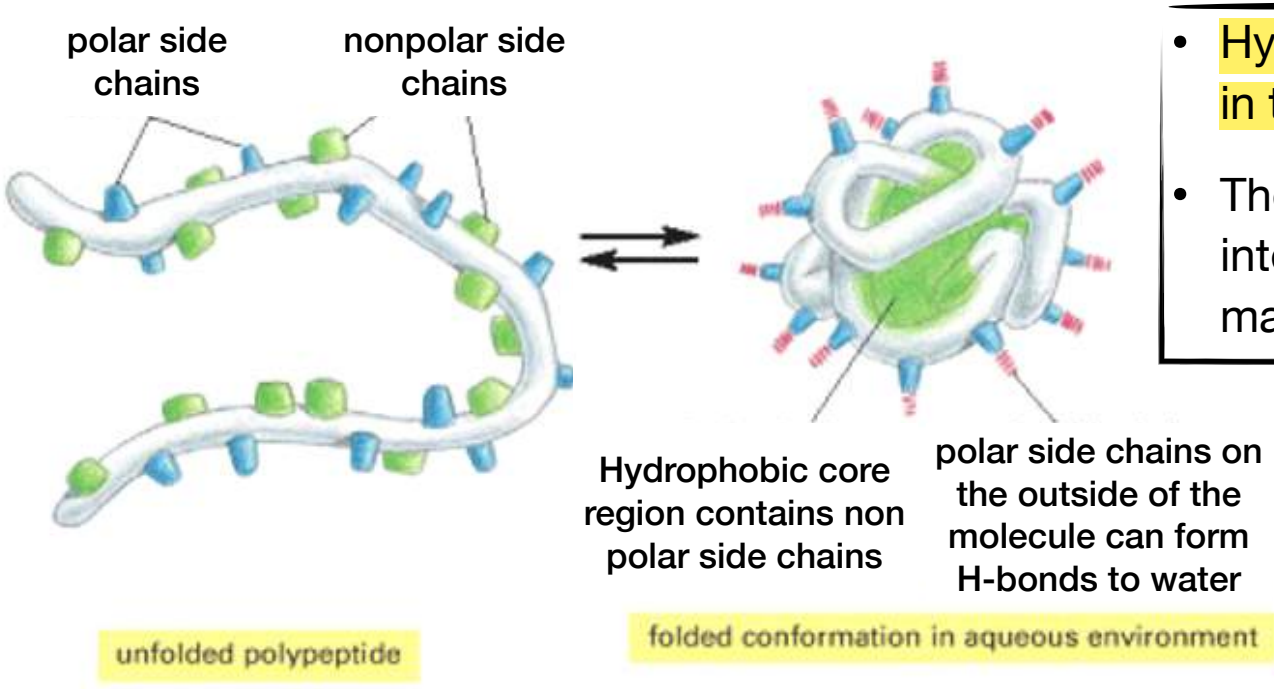
Polymers of amino acids



Protein conformation

3D structure of polypeptide chain

- A polypeptide chain folds into a unique shape that is stabilized by non-covalent interactions between regions in the linear sequence of amino acids to form a protein.



- Hydrophobic residues are largely buried in the protein interior, away from water
- The no. of H-bonds and ionic interactions within the protein is maximized

Importance of protein conformation and structure

- The spatial organization of a protein i.e. its shape in three dimensions, is a key to understanding its function.
- Only when a protein is in its correct three-dimensional structure, or conformation, is it able to function efficiently.
- So, protein function is derived from its three-dimensional structure

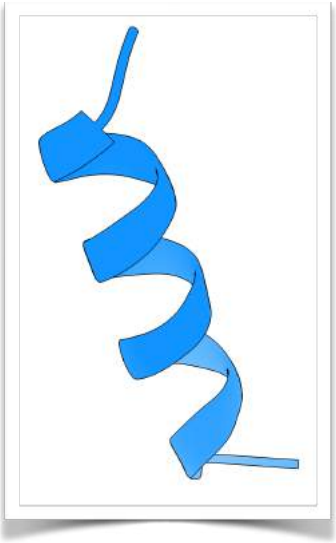
Hierarchical structure of proteins

There are four levels of protein structural organization:

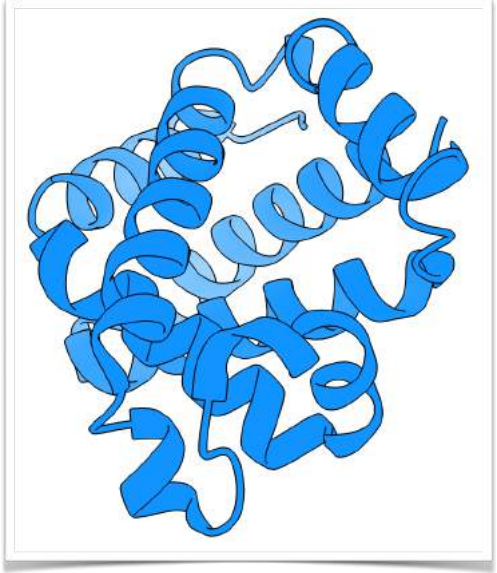
Primary structure

Lys-Glu-Lys-Ile-Glu-Tyr-Tyr-Val-Glu-Trp-Ala-Leu-Asp-Ala

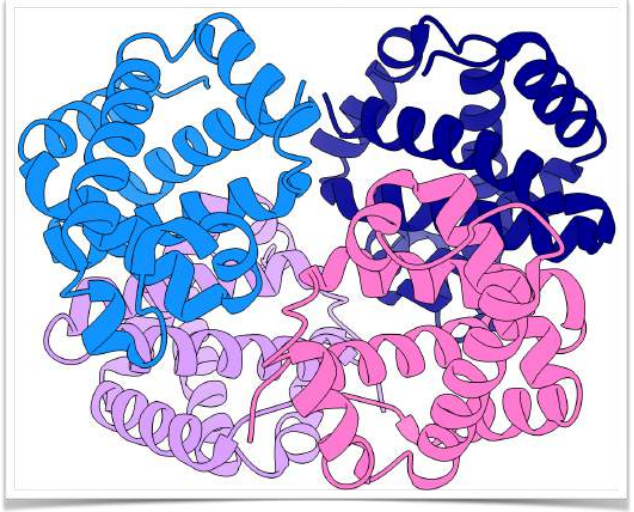
Secondary structure



Tertiary structure



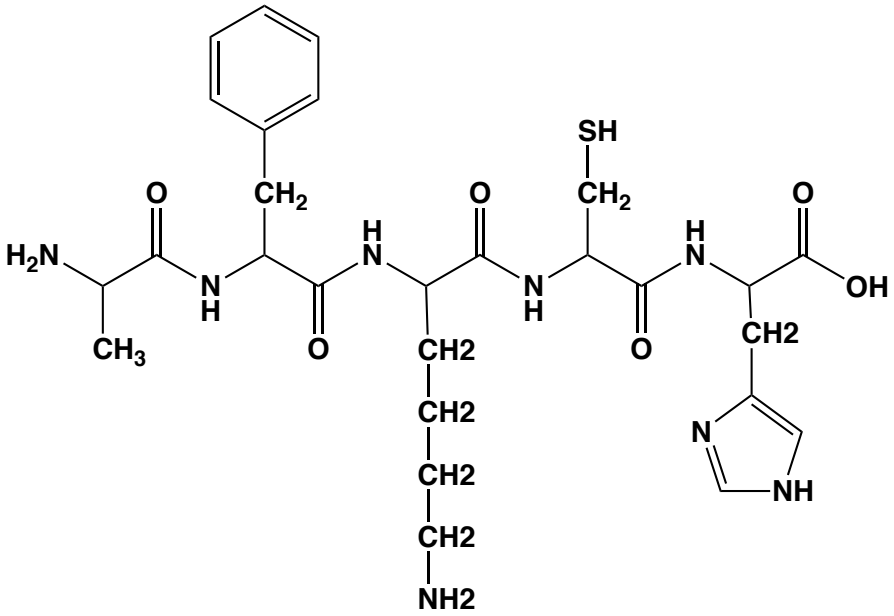
Quarternary structure



Primary structure

Level 1

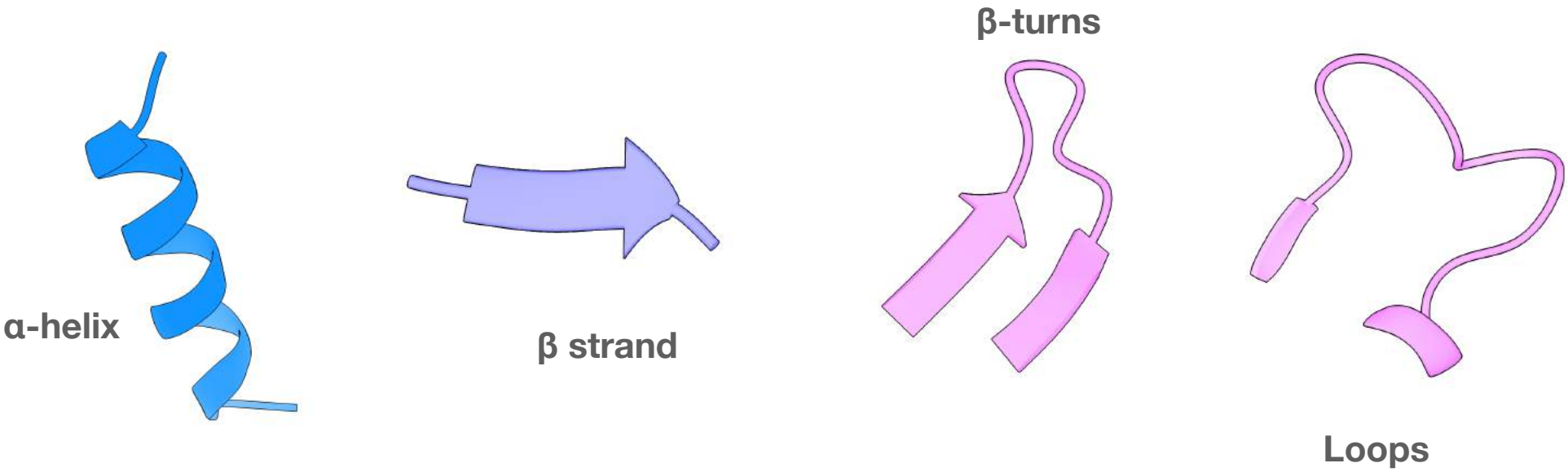
Ala-Phe-Lys-Cys-His-Tyr-Tyr-Val-Glu-Trp-Ala-Leu-Asp



The linear sequence of amino acids within a protein is considered the primary structure of the protein.

Secondary structure

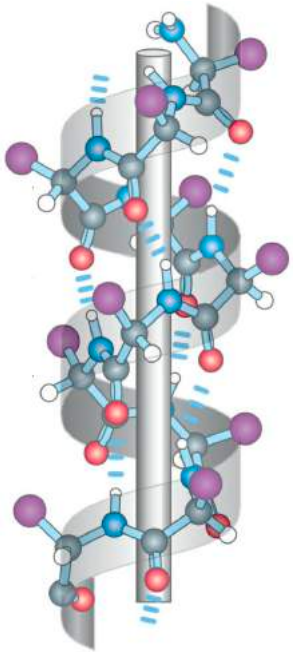
Level 2

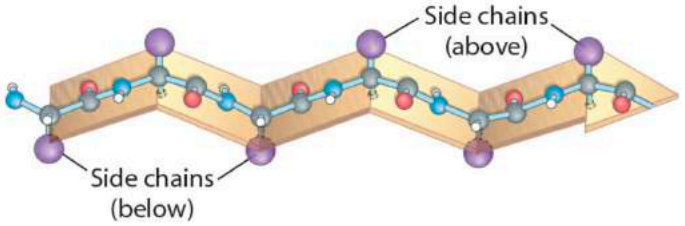


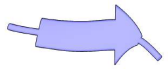
- Folding of the polypeptide chain into local (i) alpha-helices, (ii) beta-sheets, (iii) beta turns and (iv) loops results in secondary structure

Secondary structure (contd.)

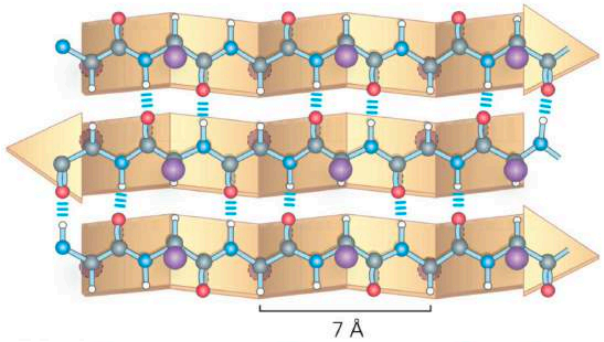
α-helix



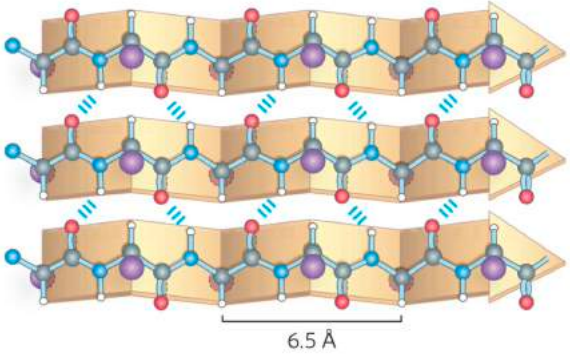




β strand

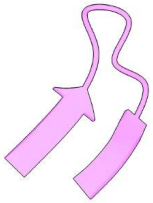


Anti-parallel

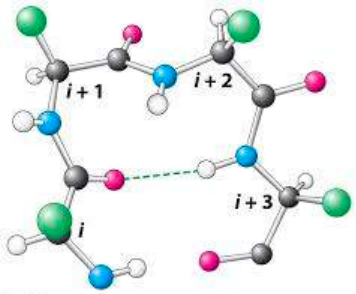


Parallel

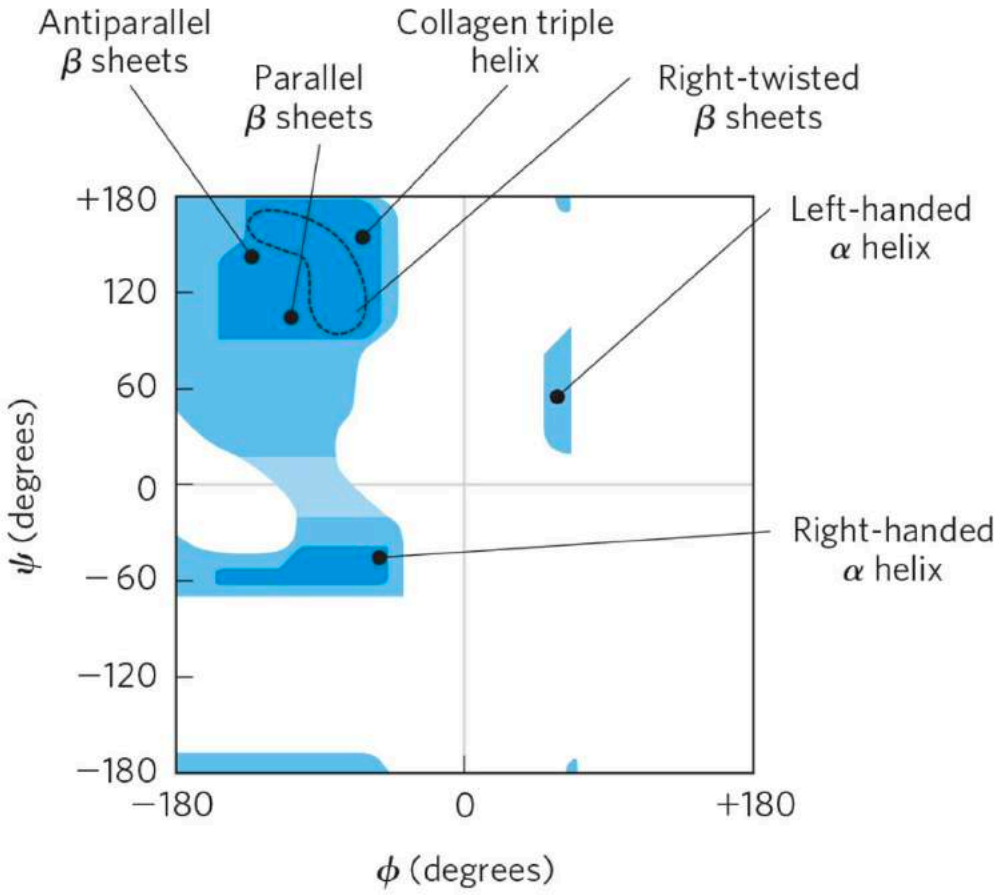
β sheet



β-turn

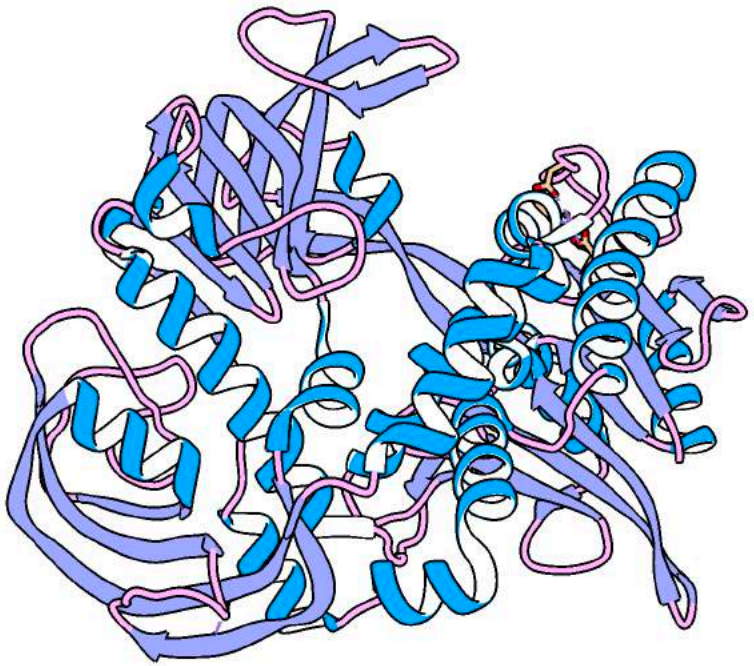


Ramachandran plot



Tertiary structure

Level 3

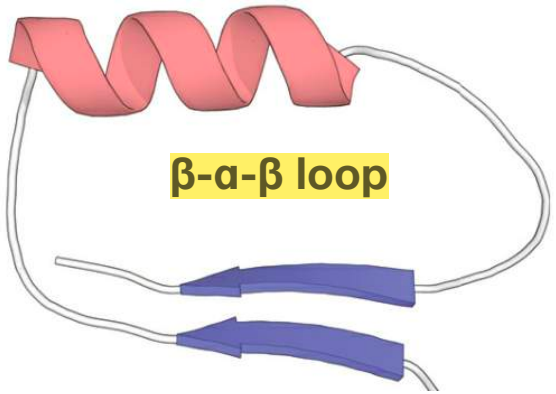


- It is the complete three-dimensional structure of a polypeptide chain
- Secondary structural elements are brought together with various loops and turns in a single polypeptide chain and pack into a larger independently stable structure

Domains are regions or parts of a polypeptide chain that can fold stably and independently or could undergo movements as a single entity with respect to the entire protein.

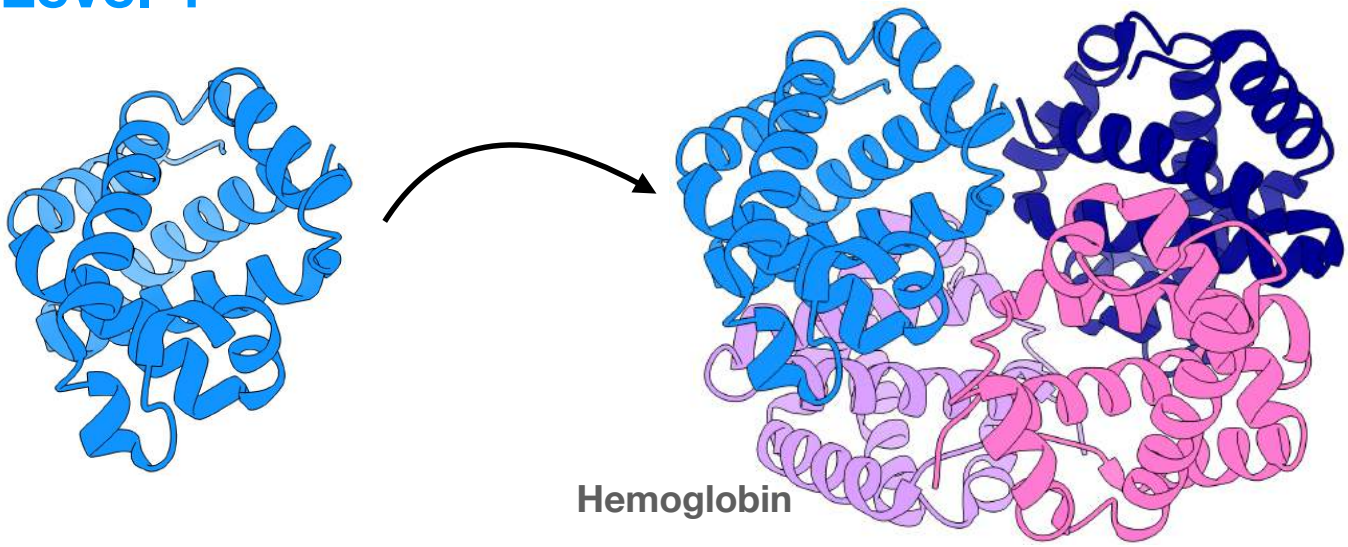
Secondary structural motifs

- The complex structures of globular proteins can be analyzed by examining folding patterns called **motifs** (also called **folds** or **supersecondary structures**).
- The many thousands of known protein structures are generally assembled from a repertoire of only a few hundred motifs.



Quarternary structure

Level 4



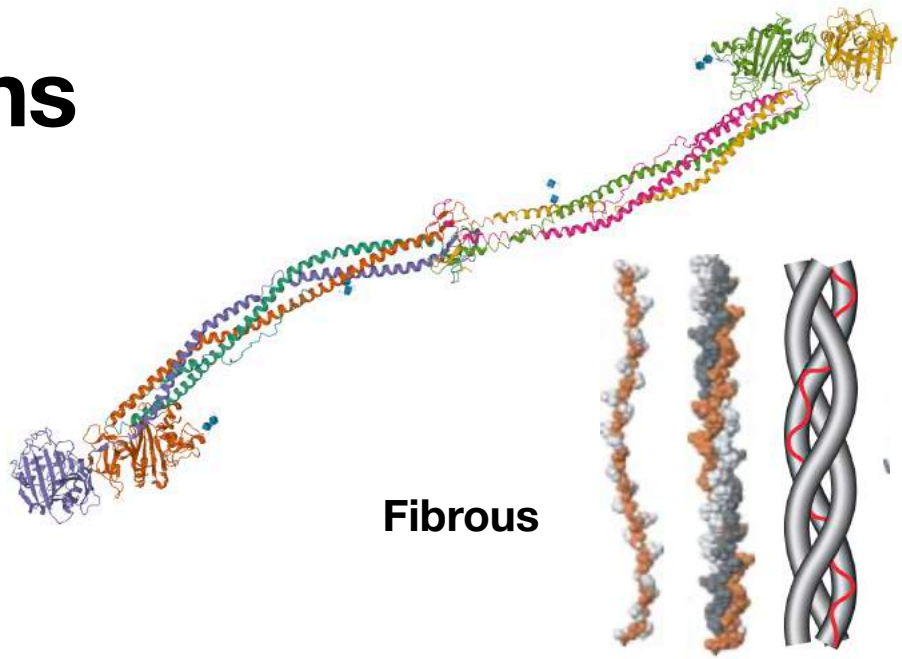
Hemoglobin

Subunits are separate polypeptide chains that can form a stable folded structure by itself

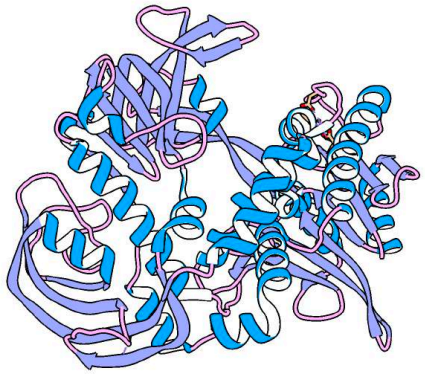
- Quaternary structure results from interactions between the **subunits** of multisubunit (multimeric) proteins or large protein assemblies.
- Some multimeric proteins have a repeated unit consisting of a single subunit or a group of subunits.

Globular vs Fibrous proteins

- Two general classes of proteins based on structure: **fibrous** and **globular**
  - **Fibrous proteins**
    - Mainly structural roles
    - Have simple repeating elements of secondary structure
    - Collagen, keratin, fibrinogen
  - **Globular proteins**
    - More complicated tertiary structures
    - Often containing several types of secondary structure in the same polypeptide chain.
    - Elastase, ribonuclease A



Fibrous



Globular