CONCEPT: PROTEIN FOLDING

Primary Structure

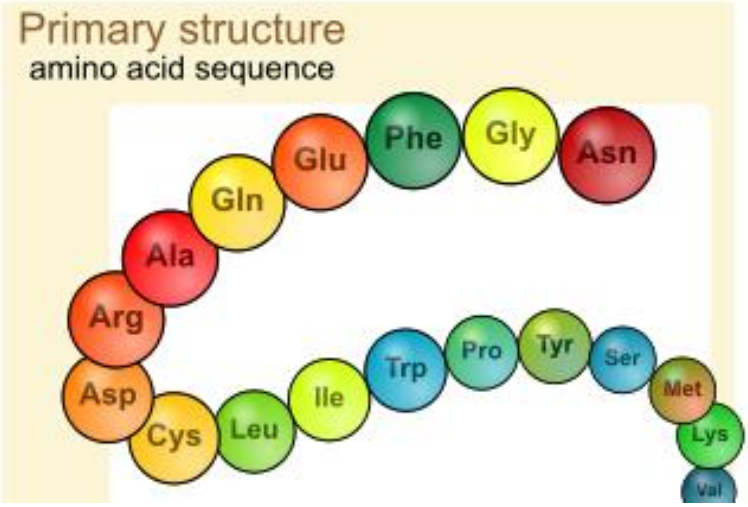
● **Primary structure** is the first of four protein folding levels

□ Primary structure is the _____ sequence of amino acids in a polypeptide chain

□ The sequence of amino acids, and their attached R groups provides information for folding the 3D conformation

□ *Covalent peptide bonds* between amino acids hold together the primary structure

EXAMPLE: Primary structure of a protein



Secondary Structure

● The **secondary structure** refers to _____ structures formed by the polypeptide backbone.

□ The **alpha helix** is one secondary folding pattern

- Hydrogen bonds made between every fourth amino acid (carboxyl group bound to amino group)

- Forms a rigid cylinder that can be right handed or left handed

- Is abundant in skin protein

□ A **beta sheet** is another main secondary folding pattern

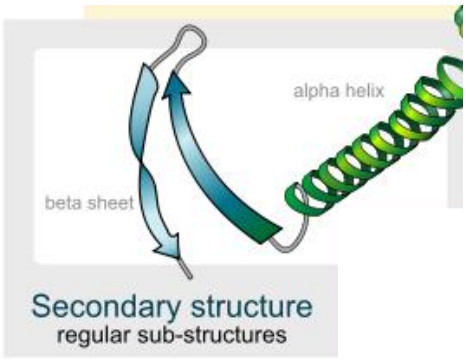
- Hydrogen bonds made between segments of the polypeptide chain that are arranged side by side

- Can be **parallel** (two chains in the same direction) or **antiparallel** (two chains in opposite directions)

- Is abundant in silk proteins

□ **Disulfide bonds** between the side chains of cysteine can link proteins together and increase stability

EXAMPLE: Secondary structure of a protein



Tertiary Structure

● The **tertiary structure** refers to ____ conformations formed by a single polypeptide chain. Can be functional or structural

□ **Structural motifs** are combinations of two or more secondary structures that form a 3D structure

- A **coiled coil** is 2-3 helices that wrap around each other to form a very stable structure

- The *helix-turn-helix* and *helix-loop-helix* are two common structural motifs named by their helical structure

- Each structural motif usually has a specific function

□ Protein **domains** are segments of the polypeptide chain (40-350 aa) that fold into independent stable structures

- Each domain usually has a specific _____

- Certain domains are found in multiple proteins (SH2 domains is found in 120 polypeptide chains)

  - **Domain shuffling** is an evolutionary process that linked domains in new combinations

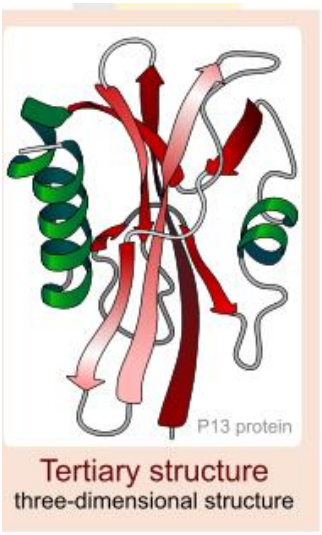
- Two-thirds of proteins contain 2+ domains

□ Tertiary structure forms two main protein types: *Fibrous proteins* and *Globular proteins*

- **Fibrous proteins** are proteins with an elongated shape

- **Globular proteins** are proteins with a compact shape

EXAMPLE: Tertiary structure of a protein



Quaternary Structure

● The **quaternary structure** refers to a protein complex with _____ one polypeptide chain

□ Only found in **multimeric proteins** which are composed of 2+ polypeptide chains

□ A **subunit** is a single polypeptide chain which is a part of a larger protein complex

- Each subunit can be identical or non-identical to other subunits

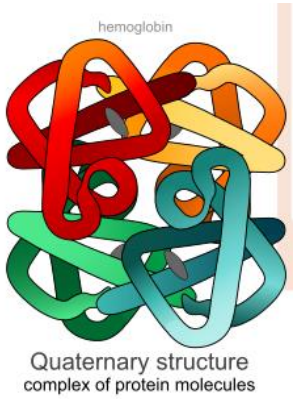
- A **homomeric proteins:** composed of identical subunits

- A **heteromeric proteins:** composed of non-identical subunits

□ Quaternary structure is stabilized by the same non-covalent interactions and *disulfide bonds* as tertiary structure

- *Hydrogen bonds, van der Waals forces, hydrophobic interactions, ionic bonds*

EXAMPLE: Quaternary structure of a protein



Unstructured Regions of a Protein

● **Unstructured regions** (disordered regions) exist between _____ protein structures or domains

□ Provide flexibility to protein structure and folding

- Wrap around target proteins with high specificity but low affinity

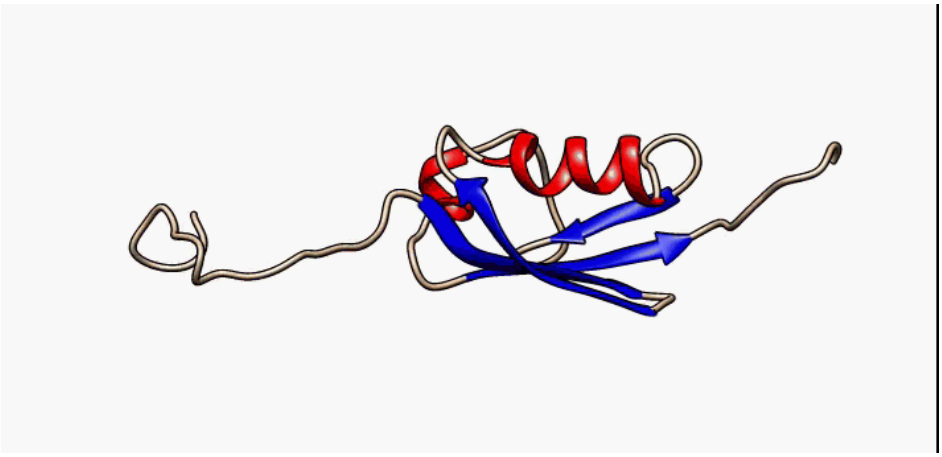
- Can help scaffold proteins together

□ Nearly one-third of eukaryotic proteins have unstructured regions in at least one polypeptide chain

- Some can be found as the _____ polypeptide chain – usually form aggregates in cytosol

□ **Disulfide bonds** between the side chains of cysteine can link proteins together and increase stability

EXAMPLE: Unstructured regions of a protein (grey) surround structured regions (red/blue)



PRACTICE

1. Match the following protein structures with their appropriate definitions
   i. Primary Structure _____
   ii. Secondary Structure _____

iii. Tertiary Structure _____
iv. Quaternary Structure _____

A. 3D conformation of a single polypeptide chain
B. Linear sequence of amino acids
C. Folding of multiple polypeptide chains together
D. Local structures of a single polypeptide chain