7.3 PROTEIN STRUCTURE

Protein Structure

A protein's shape is critical to its function. For example, an enzyme can bind to a specific substrate at an active site. If this active site is altered because of local changes or changes in overall protein structure, the enzyme may be unable to bind to the substrate. To understand how the protein gets its final shape or conformation, we need to understand the four levels of protein structure: primary, secondary, tertiary, and quaternary.

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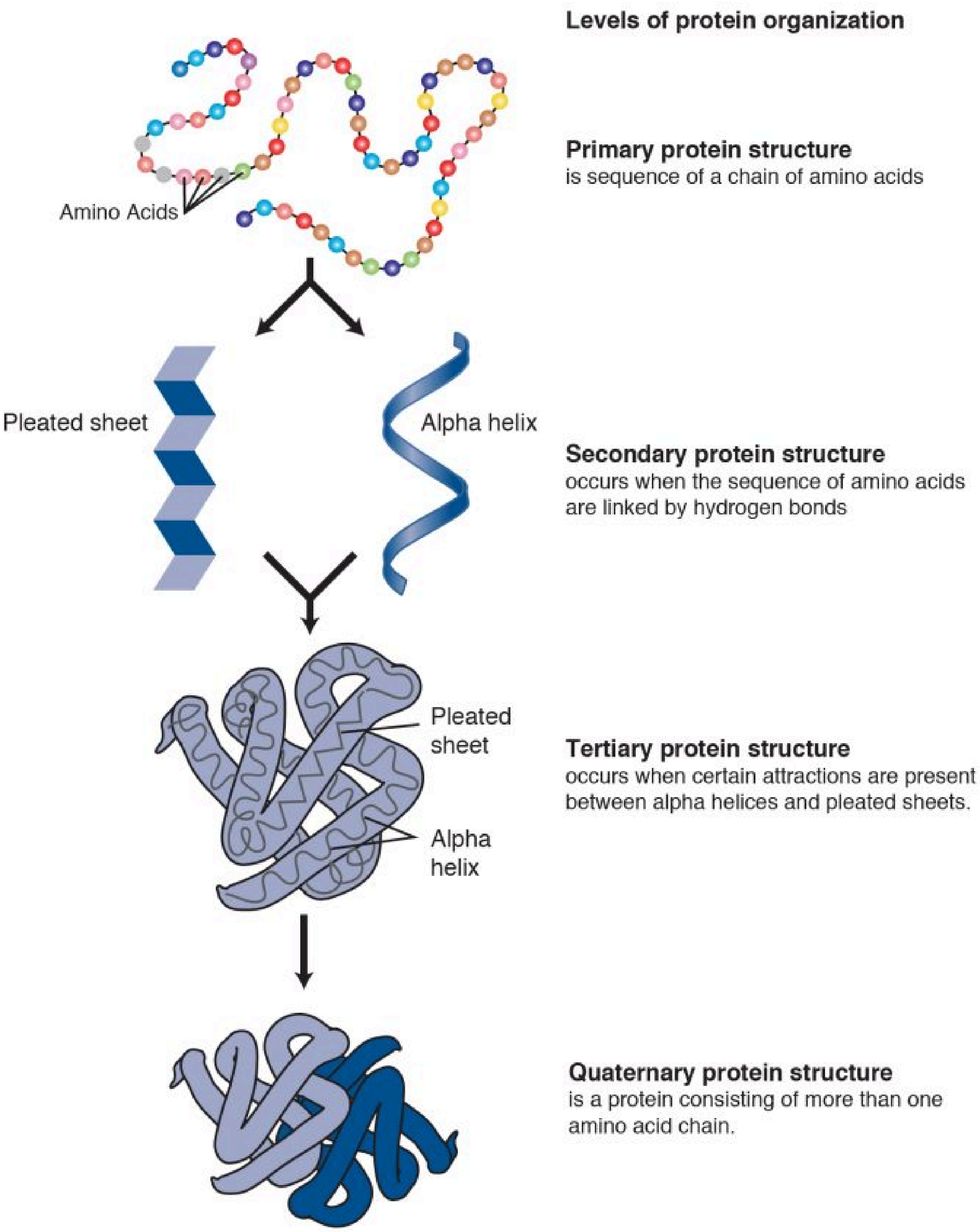

Primary protein structure
is sequence of a chain of amino acids

Secondary protein structure
occurs when the sequence of amino acids are linked by hydrogen bonds

Tertiary protein structure
occurs when certain attractions are present between alpha helices and pleated sheets.

Quaternary protein structure
is a protein consisting of more than one amino acid chain.

The four levels of protein structure. (Protein structure by the National Human Genome Research Institute is in the public domain).

Primary Structure

The unique sequence of amino acids in a polypeptide chain is its primary structure. For example, the pri-

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MGDVEKGKKI FIMKCSQCHT VEKGGKHKTG PNLHGLFGRK TGQAPGYSYT AANKNKGIIW GEDTLMEYLE NPKKYIPGTK MIFVGIKKKE ERADLIAYLK KATNE

Primary sequence of human cytochrome c protein. Each letter corresponds to an amino acid. The sequence of cytochrome c is in the public domain.

The gene encoding the protein ultimately determines the unique sequence for every protein. A change in nucleotide sequence of the gene's coding region may lead to adding a different amino acid to the growing polypeptide chain, causing a change in protein structure and function.

For example, in sickle cell anemia, the hemoglobin β-chain has a single amino acid substitution, causing a change in protein structure and function. Specifically, glutamic acid in the β-chain is replaced by valine. What is most remarkable to consider is that a hemoglobin molecule is comprised of two alpha and two beta chains that each consist of about 150 amino acids. The molecule, therefore, has about 600 amino acids. The structural difference between a normal hemoglobin molecule and a sickle cell molecule—which dramatically decreases life expectancy—is a single amino acid out of the 600.

Because of this change of one amino acid in the chain, hemoglobin molecules form long fibers that distort the biconcave, or disc-shaped, red blood cells and causes them to assume a crescent or "sickle" shape, which clogs blood vessels. This can lead to myriad serious health problems such as breathlessness, dizziness, headaches, and abdominal pain for those affected by this disease.

Secondary Structure

The local folding of the polypeptide in some regions gives rise to the secondary structure of the protein. The most common are the α-helix and β-pleated sheet (or simply β-sheet) structures. Both structures are held in shape by hydrogen bonds. The hydrogen bonds form between the oxygen atom in the carbonyl group in one amino acid and another amino acid that is four amino acids farther along the chain.

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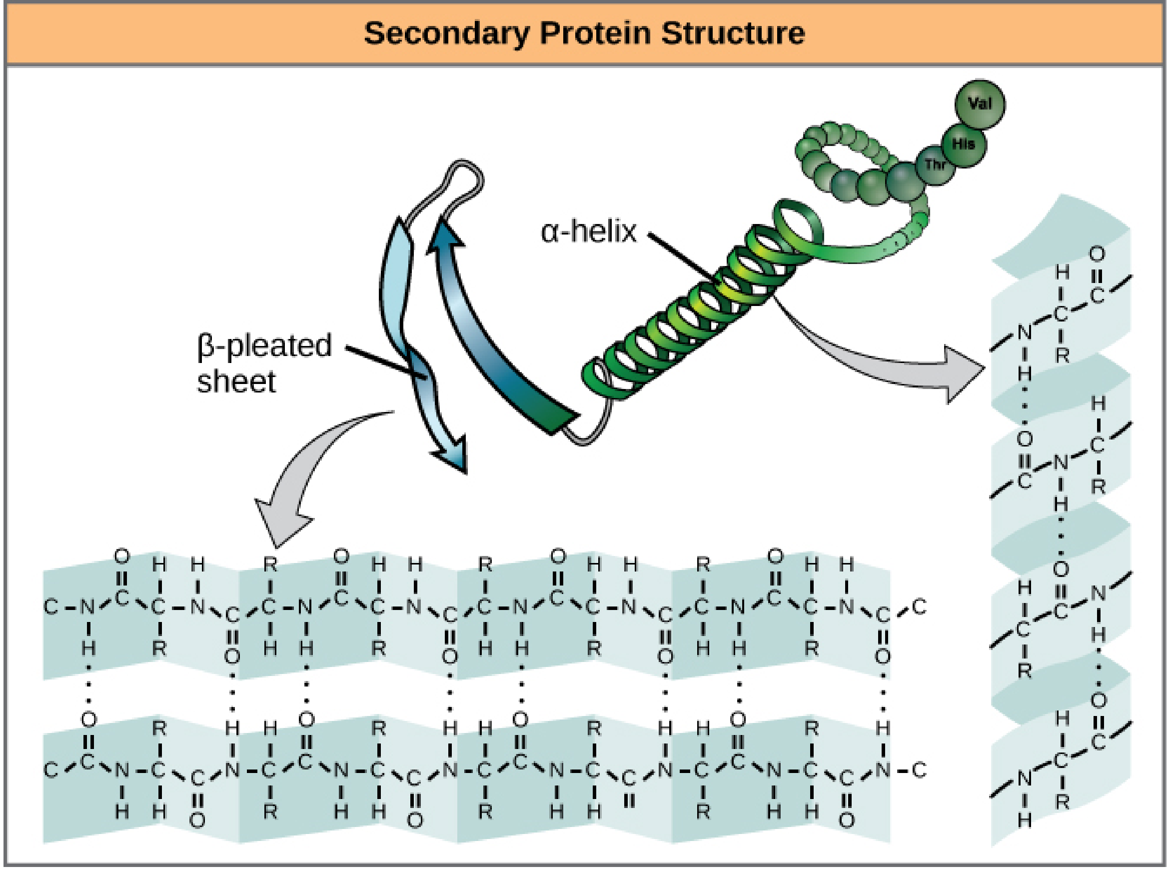
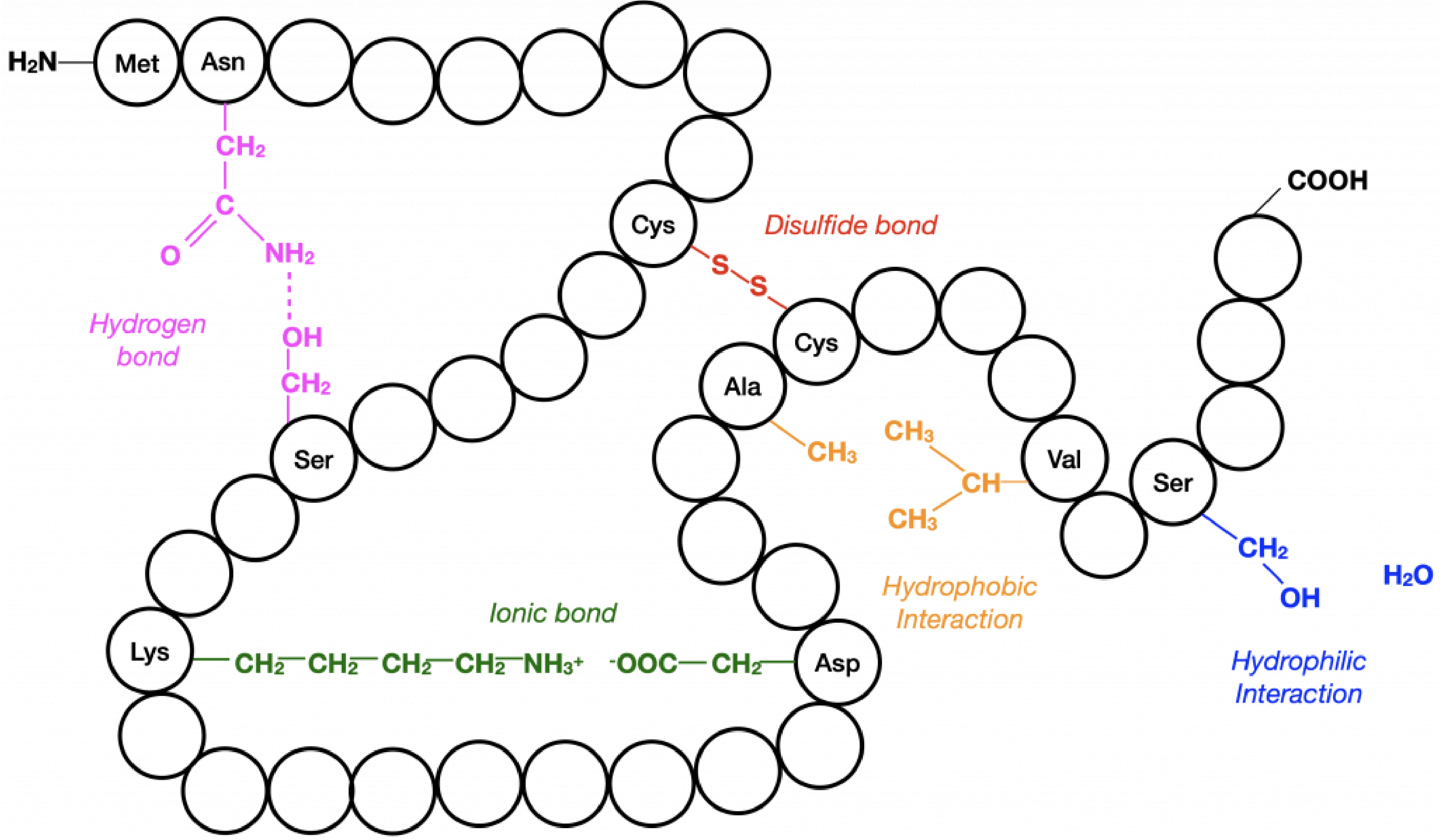


The α-helix and β-pleated sheet are secondary structures of proteins that form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone. (Secondary structure by OpenStax is used under a Creative Commons Attribution License).

Every helical turn in an *α*–helix has 3.6 amino acid residues. The polypeptide's R groups protrude out from the *α*-helix chain. In the *β*-pleated sheet, hydrogen bonding between atoms on the polypeptide chain's backbone form the "pleats". The R groups are attached to the carbons and extend above and below the pleat's folds. The pleated segments align parallel or antiparallel to each other, and hydrogen bonds form between the partially positive hydrogen atom in the amino group and the partially negative oxygen atom in the peptide backbone's carbonyl group.

Tertiary Structure

The polypeptide's unique three-dimensional structure is its tertiary structure. This structure is in part due to chemical interactions. The interactions among R groups are most important for creating the protein's complex three-dimensional tertiary structure. For example, R groups with like charges repel each other and those with unlike charges are attracted to each other (ionic bonds). When protein folding takes place, the nonpolar amino acids' hydrophobic R groups tend to be in the protein's interior; whereas, the hydrophilic R groups tend to be on the outside. Interaction between cysteine side chains forms disulfide bonds in the



Interactions that determine a protein's tertiary structure include hydrophobic interactions, ionic bonds, disulfide bonds, hydrogen bonds, and hydrophilic interactions with water molecules. (Tertiary structure by Melissa Hardy is used under a Creative Commons Attribution-NonCommercial License).

All of these interactions, weak and strong, determine the protein's final three-dimensional shape. When a protein loses its three-dimensional shape, it may no longer be functional.

Quaternary Structure

In nature, some proteins form from several polypeptides, or subunits, and the interaction of these subunits forms the quaternary structure. Weak interactions between the subunits help to stabilize the overall structure. For example, insulin (a globular protein) has a combination of hydrogen and disulfide bonds that cause it to mostly clump into a ball shape. Insulin starts out as a single polypeptide and loses some internal sequences in the presence of post-translational modification after forming the disulfide linkages that hold the remaining chains together. Silk (a fibrous protein), however, has a β-pleated sheet structure that is the result of hydrogen bonding between different chains.

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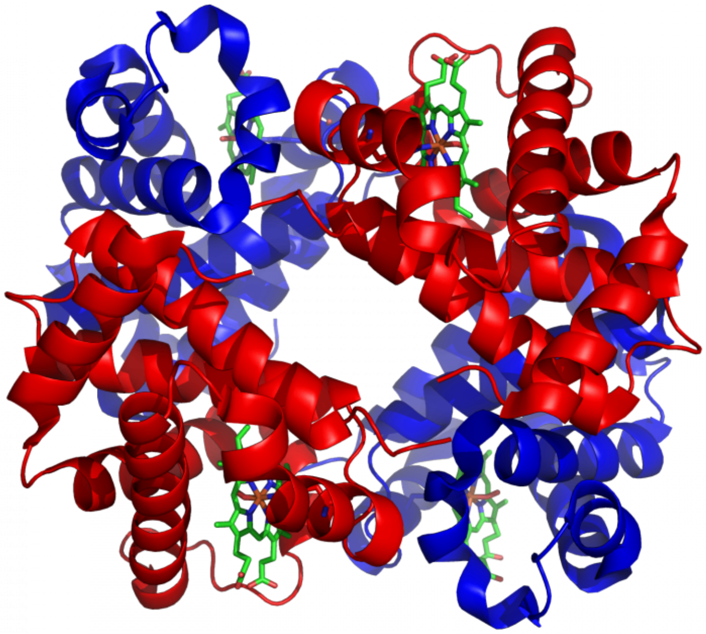

Hemoglobin is composed of four polypeptides, two alpha subunits (shown in red) and two beta subunits (shown in blue). (Hemoglobin by Zephyris is used under a Creative Commons Attribution-ShareAlike license).

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