بسم الله الرحمن الرحيم

Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Amino Acids & Proteins

Part 2

2nd Medical and Biochemistry (BIQC-101) Lecture

Second Semester

by

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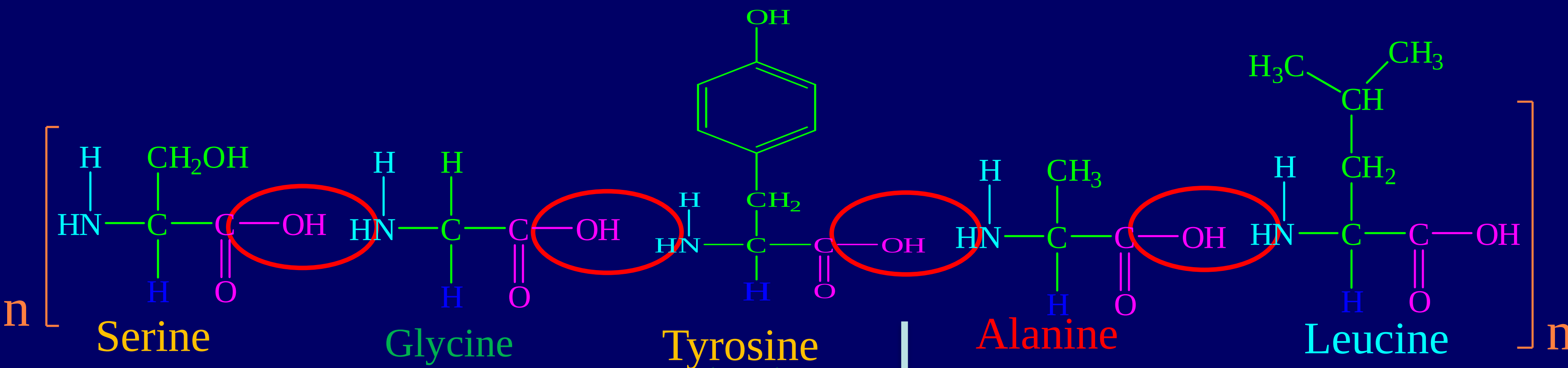
Protein

Learning Objectives

1. Understand that amino acids are linked via peptide bonds to make polypeptides and proteins
2. Understand that each protein molecule can be hundreds of amino acids long and the amino acids must be joined in a precise order.
3. Know that the side-chains (R groups) of the amino acids can interact with one another to fold the protein into a particular shape which is essential for the protein to function correctly.
4. Describe, using examples, the relationship between protein structure and function.
5. Define denaturation and list factors led to protein denturation
6. List some medical application of denaturation

Protein structure

Proteins are polymers – specifically polypeptides – formed from sequences of amino acids. A single amino acid monomer may also be called a residue indicating a repeating unit of a polymer.

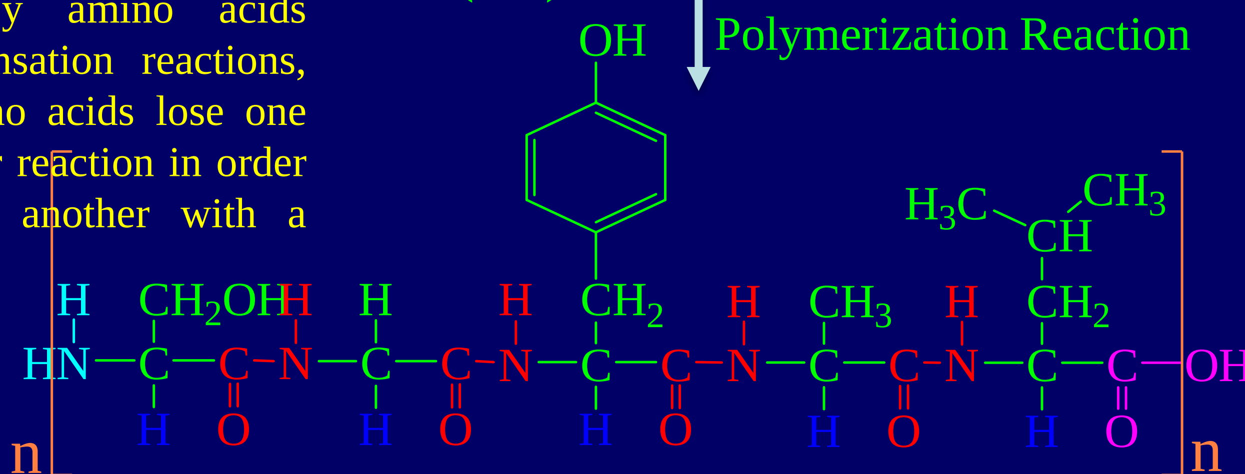


$-(n-1)H_2O$

Condensation Reaction or Polymerization Reaction

$n > 100$

Proteins form by amino acids undergoing condensation reactions, in which the amino acids lose one water molecule per reaction in order to attach to one another with a peptide bond.



Amino terminal end N-terminal

Carboxyl terminal end C-terminal

Protein structures range in size from 100 to several thousand amino acids.

By physical size, proteins are classified as nanoparticles, between 1–100 nm.

Protein Function

Proteins are the most versatile macromolecules in living systems and serve crucial functions in essentially all biological processes. They function as:

1. Catalysts
2. Transport and store other molecules such as oxygen,
3. Provide mechanical support and immune protection
4. Generate movement.
5. Transmit nerve impulses
6. Control growth and differentiation.

The Three-Dimensional Structure of Proteins

- To be able to perform their biological function, proteins fold into one or more specific spatial conformations driven by a number of non-covalent interactions such as hydrogen bonding, ionic interactions, Van der Waals forces, and hydrophobic packing and disulfide bond.
- Proteins spontaneously fold up into three-dimensional structures that are determined by the sequence of amino acids in the protein polymer. Thus, proteins are the embodiment of the transition from the one-dimensional world of sequences to the three-dimensional world of molecules capable of diverse activities.
- Proteins have four levels of structure:

1. Primary (1°)
2. Secondary (2°)
3. Tertiary (3°)
4. Quaternary (4°)

Primary protein structure

Proteins are made up of a long chain of amino acids. Even with a limited number of amino acid monomers – there are only 20 amino acids commonly seen in the human body – they can be arranged in a vast number of ways to alter the three-dimensional structure and function of the protein. The simple sequencing of the protein is known as its primary structure.

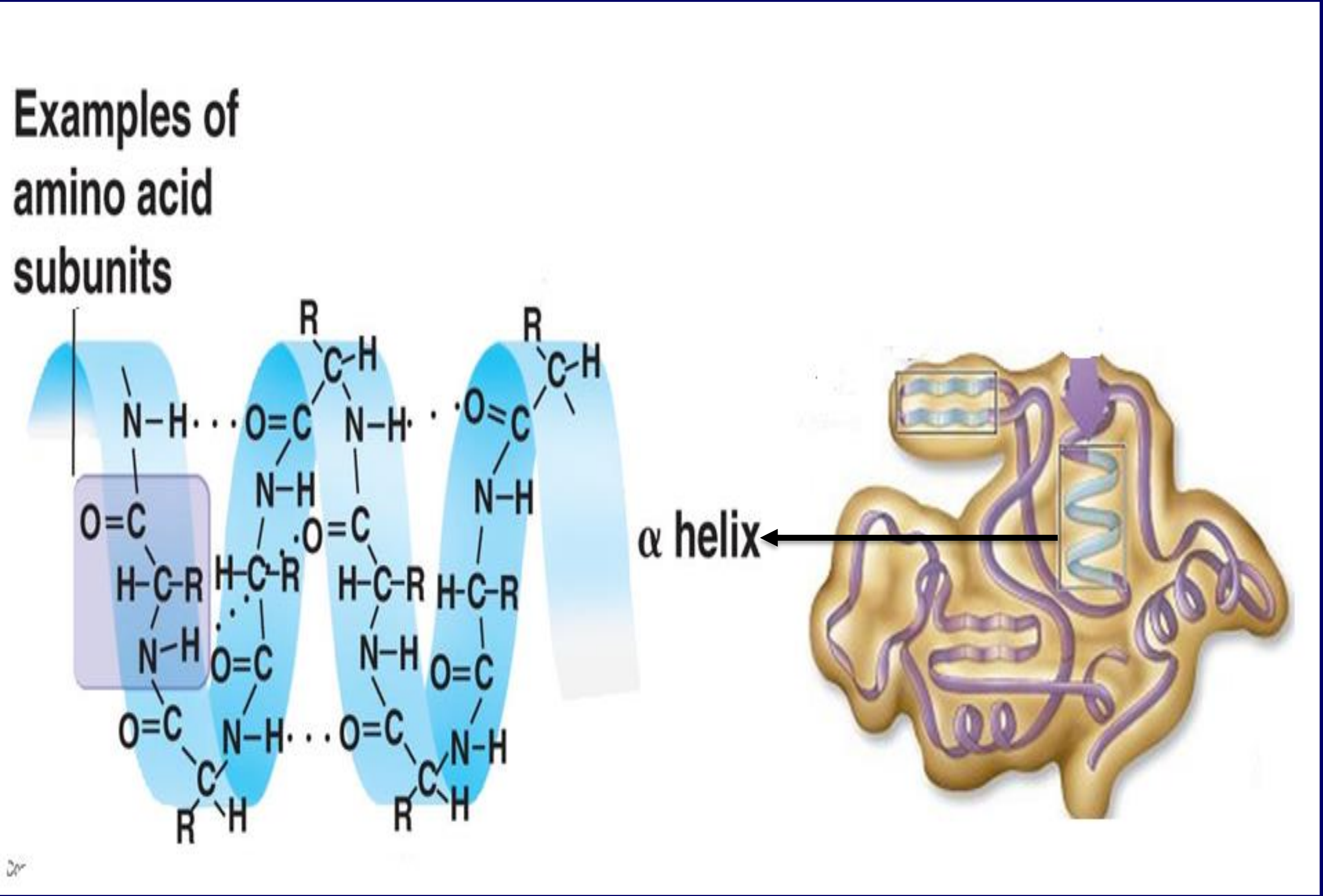
Primary structure is amino acids connected by peptide bond

Secondary Structure

- The secondary protein structure depends on the local interactions between parts of a protein chain, which can affect the folding and three-dimensional shape of the protein. There are two main things that can alter the secondary structure:

1. α-helix:

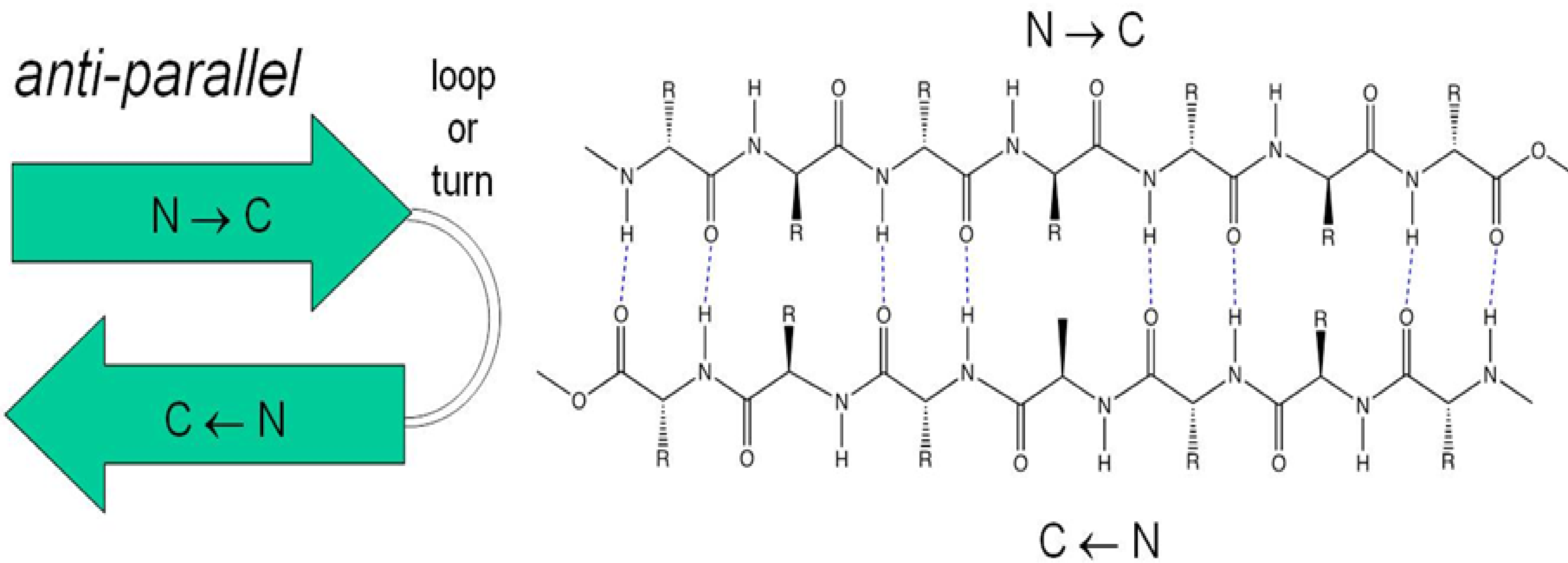
- In an α helix, the carbonyl (C=O) of one amino acid is hydrogen bonded to the amino H (N-H) of an amino acid that is four down the chain. (E.g., the carbonyl of amino acid 1 would form a hydrogen bond to the N-H of amino acid 5.)
- This pattern of bonding pulls the polypeptide chain into a helical structure.
- The R groups of the amino acids stick outward from the α helix, where they are free to interact.

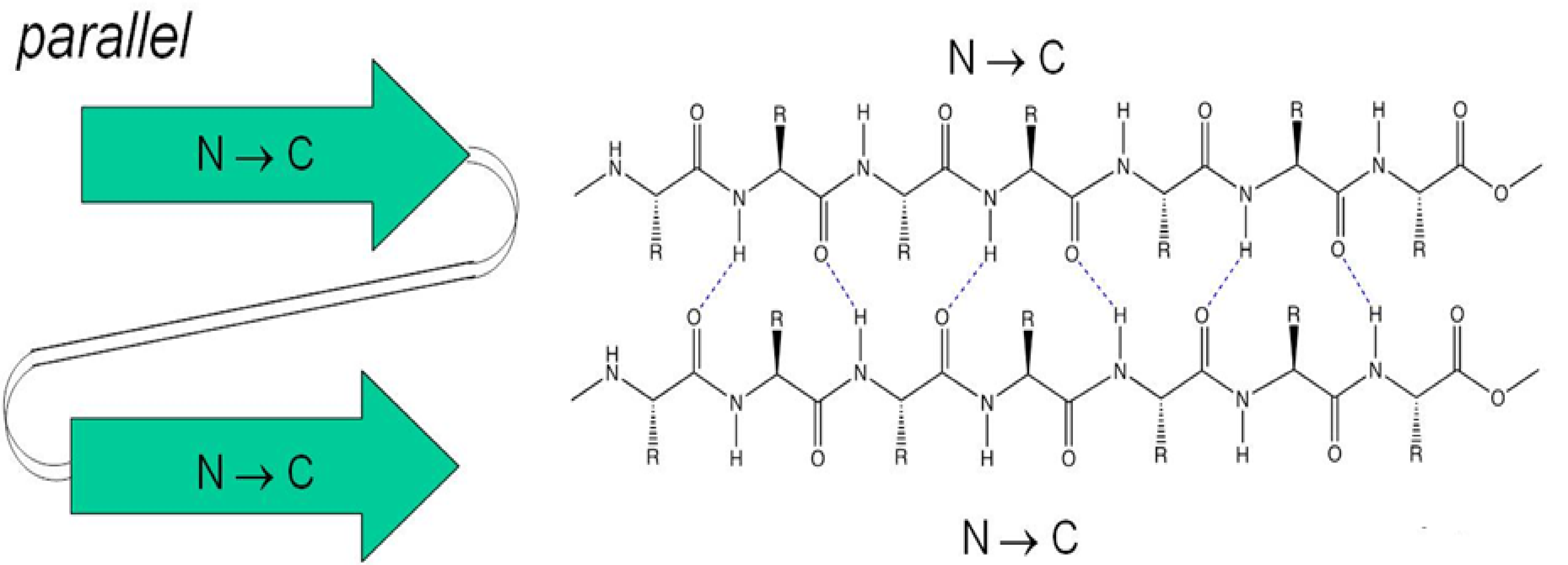


Examples of amino acid subunits
α helix

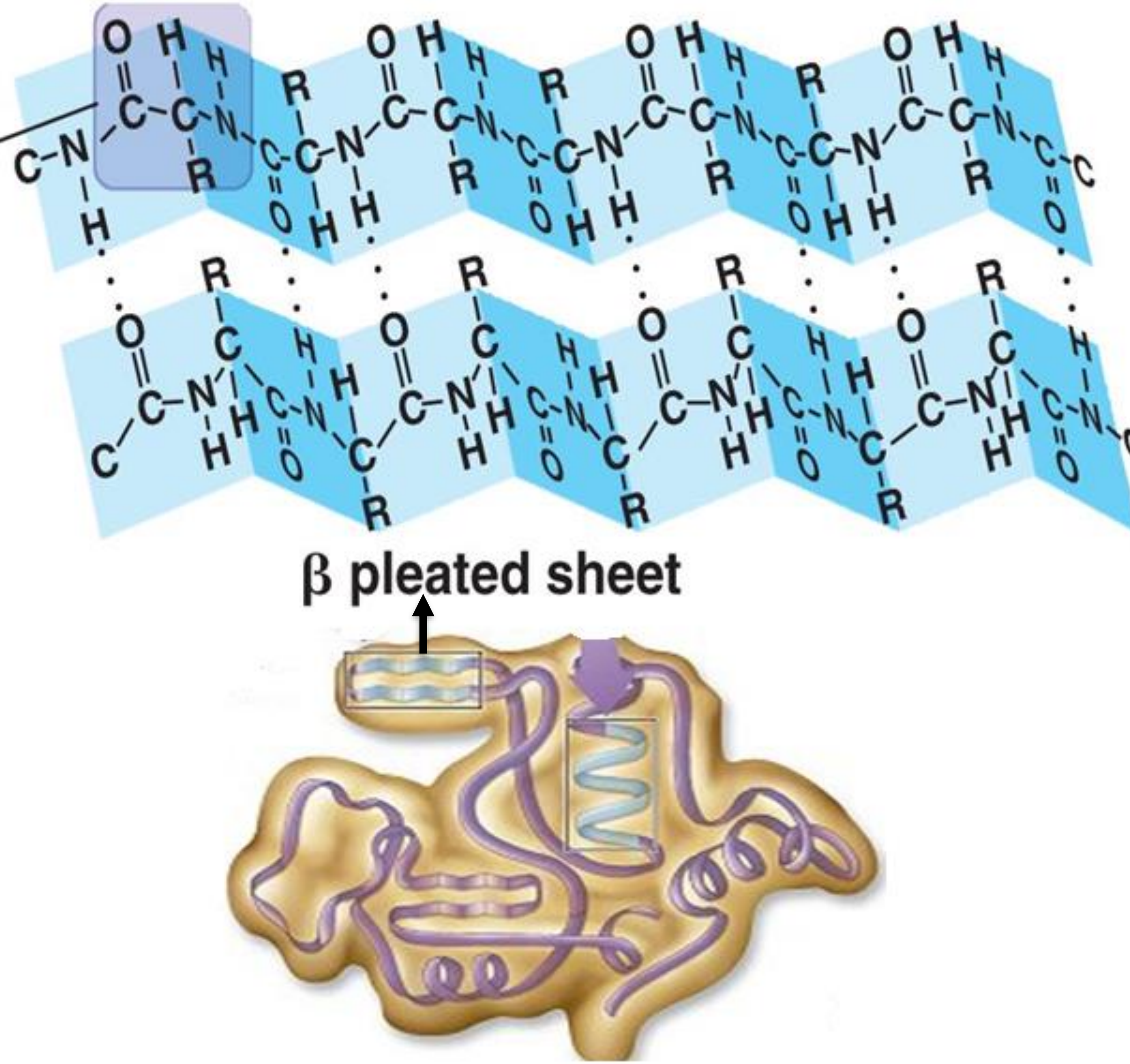
2. β-pleated sheet:

- ❖ In a β pleated sheet, two or more segments of a polypeptide chain line up next to each other, forming a sheet-like structure held together by hydrogen bonds.
- ❖ The hydrogen bonds form between carbonyl and amino groups of backbone, while the R groups extend above and below the plane of the sheet.
- ❖ The strands of a β pleated sheet may be parallel, pointing in the same direction (meaning that their N- and C-termini match up), or antiparallel, pointing in opposite directions (meaning that the N-terminus of one strand is positioned next to the C-terminus of the other).


anti-parallel
loop
or
turn
N → C
C ← N
N → C
C ← N


parallel
N → C
N → C
N → C
N → C

Examples of amino acid subunits

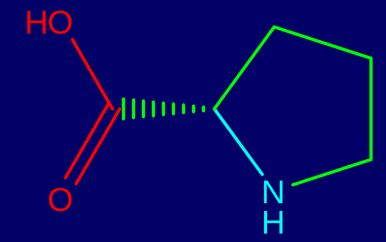


Certain amino acids are more or less likely to be found in α-helices or β pleated sheets.

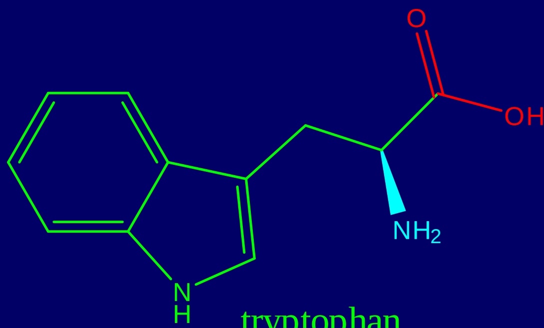
For instance, the amino acid proline is sometimes called a "helix breaker" because its unusual R group (which bonds to the amino group to form a ring) creates a bend in the chain and is not compatible with helix formation.

Proline is typically found in bends, unstructured regions between secondary structures.

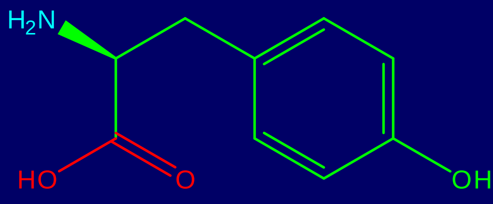
Similarly, amino acids such as tryptophan, tyrosine, and phenylalanine, which have large ring structures in their R groups, are often found in β pleated sheets, perhaps because the β pleated sheet structure provides plenty of space for the side chains



proline



tryptophan



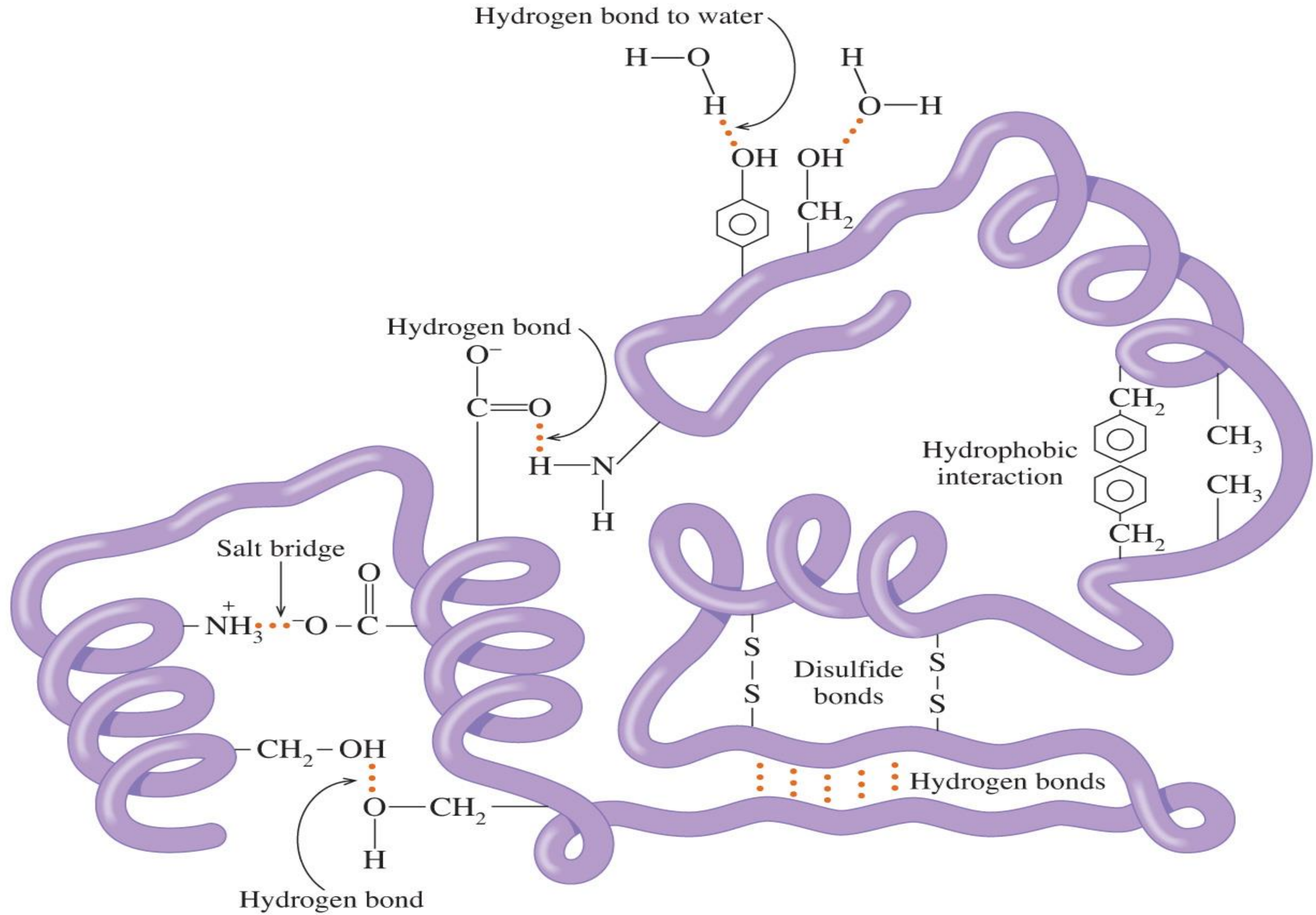
tyrosine

Tertiary structure

- Tertiary structure refers to the three-dimensional arrangement of all atoms in a protein.
- Tertiary structure is formed by the folding in three dimensions of the secondary structure elements of a protein.
- Tertiary structure is held together by interactions between the function groups of the R-groups of residues brought together by folding. This interaction including

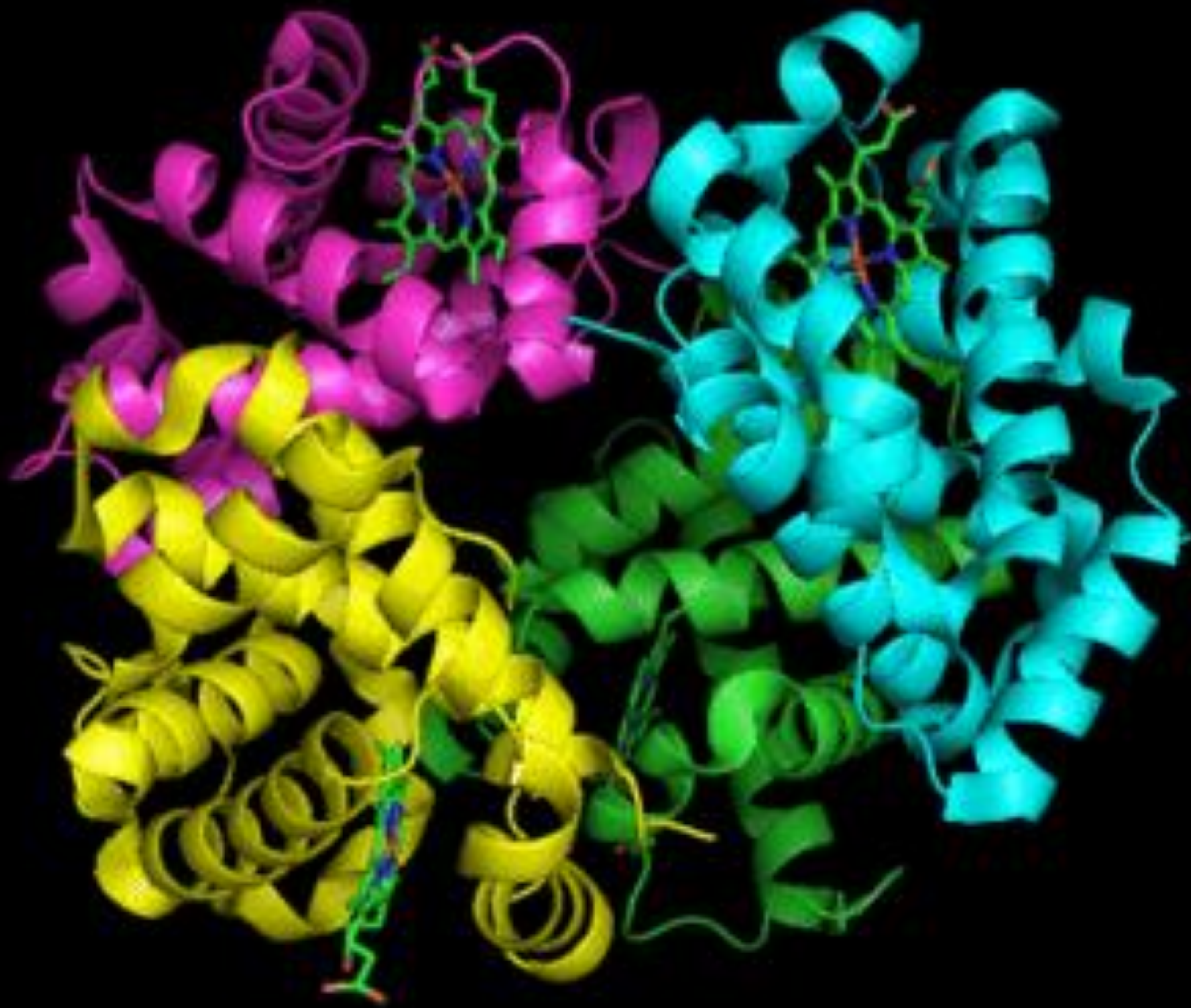
1. Nonpolar or hydrophobic interactions.
2. Polar or hydrophilic interactions.
3. Salt bridges (ionic interactions).
4. Disulfide bonds, which are covalent bonds formed between –SH groups of two cysteine molecules.

- Proteins that are compact are known as globular proteins. Proteins that are extended are known as fibrous proteins.


Hydrogen bond to water
H—O
H
H
O—H
OH
OH
CH2
Hydrogen bond
O⁻
C═O
H—N
H
CH2
CH3
Hydrophobic interaction
CH3
CH2
Salt bridge
O
NH3
O—C
S
S
Disulfide bonds
S
S
CH2—OH
Hydrogen bonds
O—CH2
H
Hydrogen bond

Quaternary Structure

- Quaternary structure refers to the arrangement of subunits and their contacts within a protein that containing 2 or more subunits. Each subunit is a separate polypeptide chain.
- Multi subunit proteins are referred to as oligomers. Each subunit within an oligomer is usually assigned a Greek letter to identify it.
- The chains within a multi subunit protein can be the same or different.
- Individual chains typically are held together by noncovalent interactions.
- Hemoglobin, an oxygen transport protein, is an example of a protein with a quaternary structure. It consists of four polypeptide chains or subunits. It has two identical alpha subunits and two identical beta subunits. All four subunits must be present for the protein to function as an oxygen carrier.
- Not all proteins have a quaternary structure.



SUMMARY OF LEVELS OF STRUCTURE AND STABILIZING FORCES IN PROTEINS

Level of Structure	Forces Stabilizing Structure
Primary (1°)	Peptide bonds
Secondary (2°)	Hydrogen bonding along the protein backbone between amino acids close together in sequence
Tertiary (3°)	London forces, hydrogen bonding, dipole–dipole and ion–dipole interactions, salt bridges, and disulfide bonds between amino acids far away from each other in sequence.
Quaternary (4°)	Same as tertiary structure but between subunits

Denaturation of Proteins

Denaturation is a process in which proteins or nucleic acids lose the quaternary structure, tertiary structure, and secondary structure which is present in their native state.

Denaturation occur by applying some external stress or chemicals such as a strong acid or base, a concentrated inorganic salt, an organic solvent (e.g., alcohol or chloroform), radiation or heat.

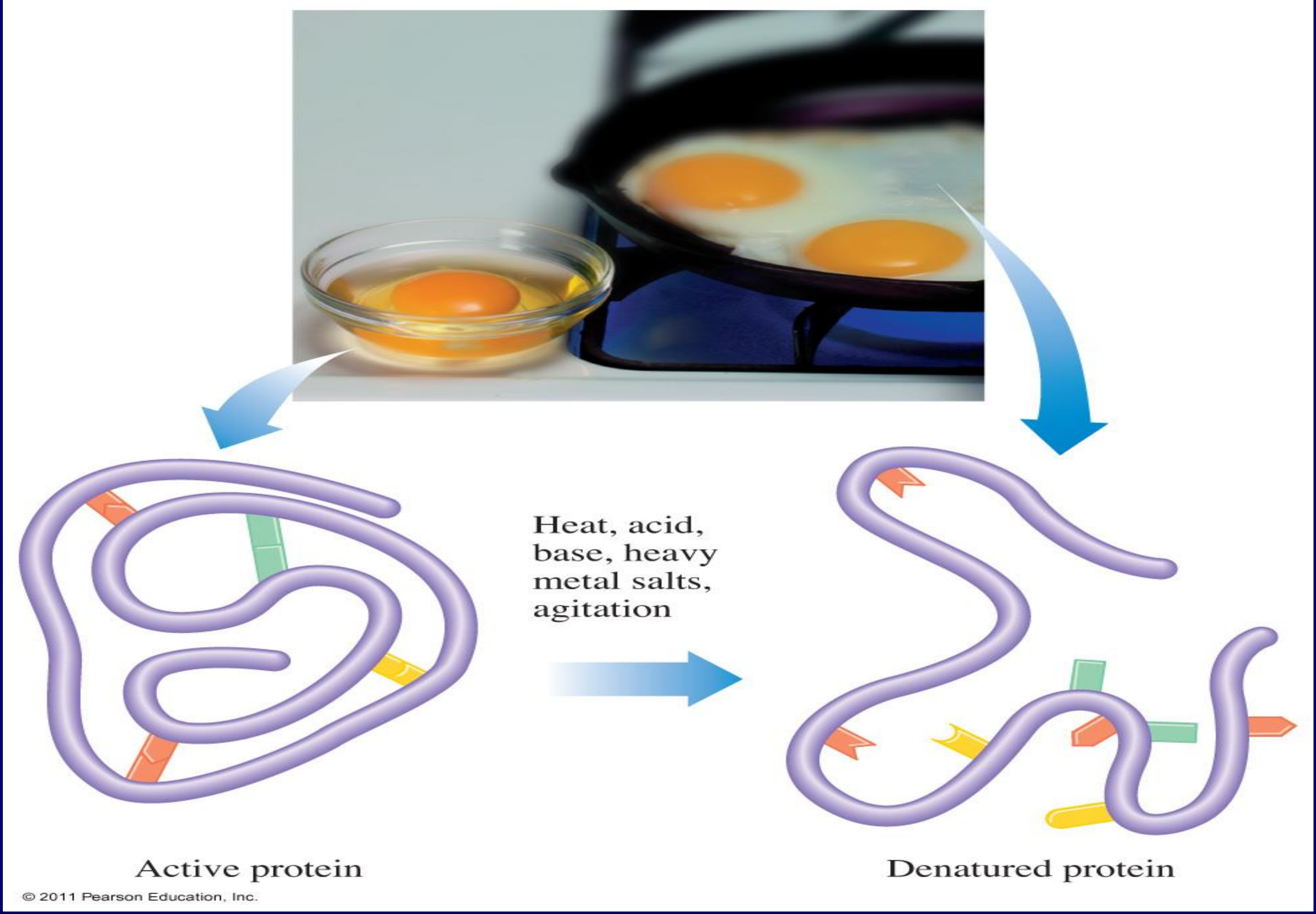
If proteins in a living cell are denatured, this results in disruption of cell activity and possibly cell death.

Denatured proteins can exhibit a wide range of characteristics, from conformational change and loss of solubility to aggregation due to the exposure of hydrophobic groups.

Denatured proteins lose their 3D structure and therefore cannot function or loss the biological function.

Denaturing agents including:-

Denaturing Agent	Disrupted Forces	Examples
Heat above 50 °C	Hydrogen bonds and hydrophobic interactions	Cooking food
Acids and bases	Salt bridges and hydrogen bonds	Lactic acid from bacteria, which denatures milk proteins in the preparation of yogurt and cheese
Organic compounds	Disulfide bonds	Thiols, which are used in hairstyling for hair straightening or permanent waves
Heavy metal ions Ag^{+}, Pb^{2+}, Hg^{2+}	Disulfide bonds and salt bridges	Mercury and lead poisoning
Mechanical agitation	Hydrogen bonds and London forces	Whipped cream and meringue made from egg whites


Heat, acid,
base, heavy
metal salts,
agitation
Active protein
Denatured protein
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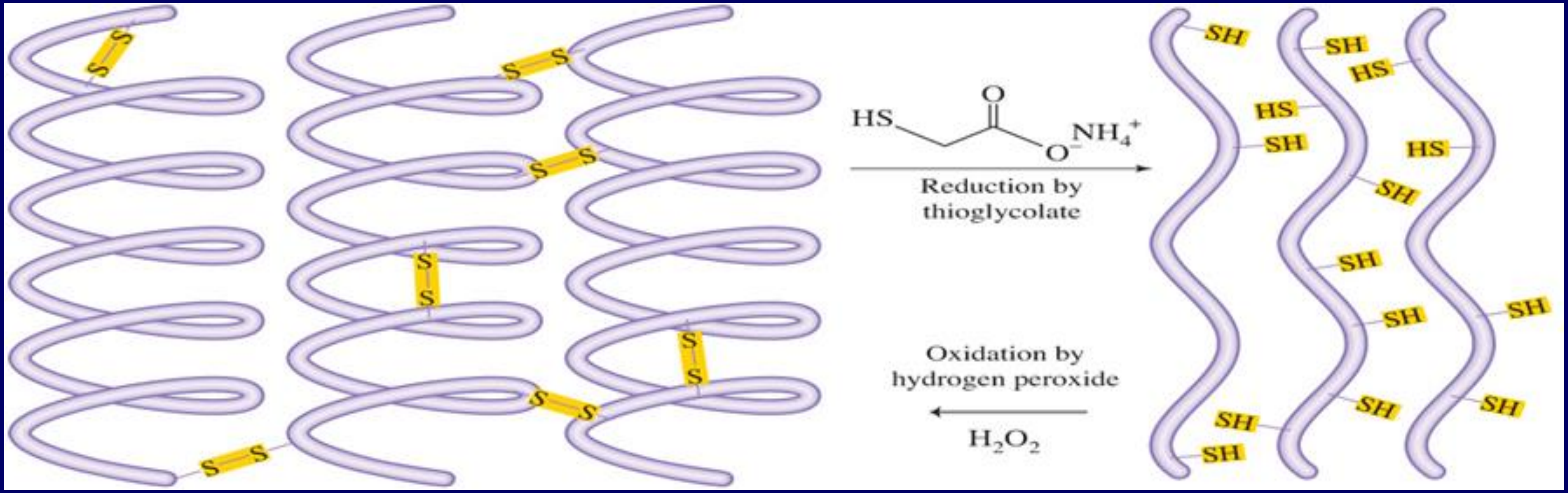
Curling straight hair or straightening curly hair requires protein denaturation. Both processes require disruption of disulfide bonds found in the hair protein keratin.

The disruption of disulfide bonds reshapes the hair and forces the reformation of disulfide bonds in new places.



Ammonium thioglycolate, which reduces (breaks) disulfide bonds, and hydrogen peroxide (reforms disulfide bonds) are two chemical agents used in hairstyling.

The process of denaturation is used as an antidote for lead or mercury poisoning.

- ❖ Egg whites can be given to an individual who has ingested a heavy metal such as Lead (plumbism) .
- ❖ Egg whites are denaturized by the heavy metals and a precipitate is formed.
- ❖ Vomiting is induced to eliminate the metal-protein precipitate.


Thank you for your attention