PROTEINS

OCCURRENCE

Proteins are present in every cell of humans, animals, plant tissues, tissue fluids and in micro organisms.

They account for about 50% of the dry weight of a cell.

MEDICAL AND BIOLOGICAL IMPORTANCE

Proteins are involved in the transport of substances in the body (Hemoglobin transports oxygen).

Enzymes which catalyze chemical reactions in the body are proteins.

Proteins are involved in defense function. They act against bacterial or viral infection (immunoglobulins).

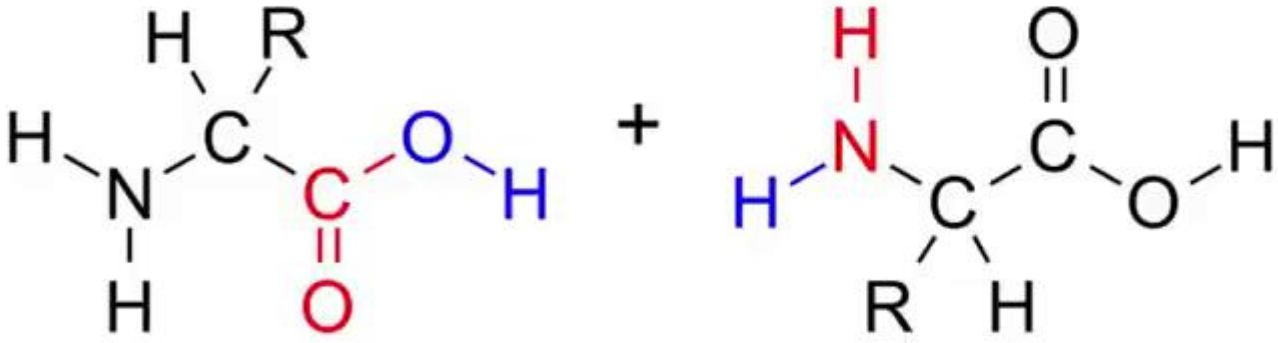
Serve as hormones (control biochemical events).

Some proteins have role in contraction of muscles (myosin, actin).

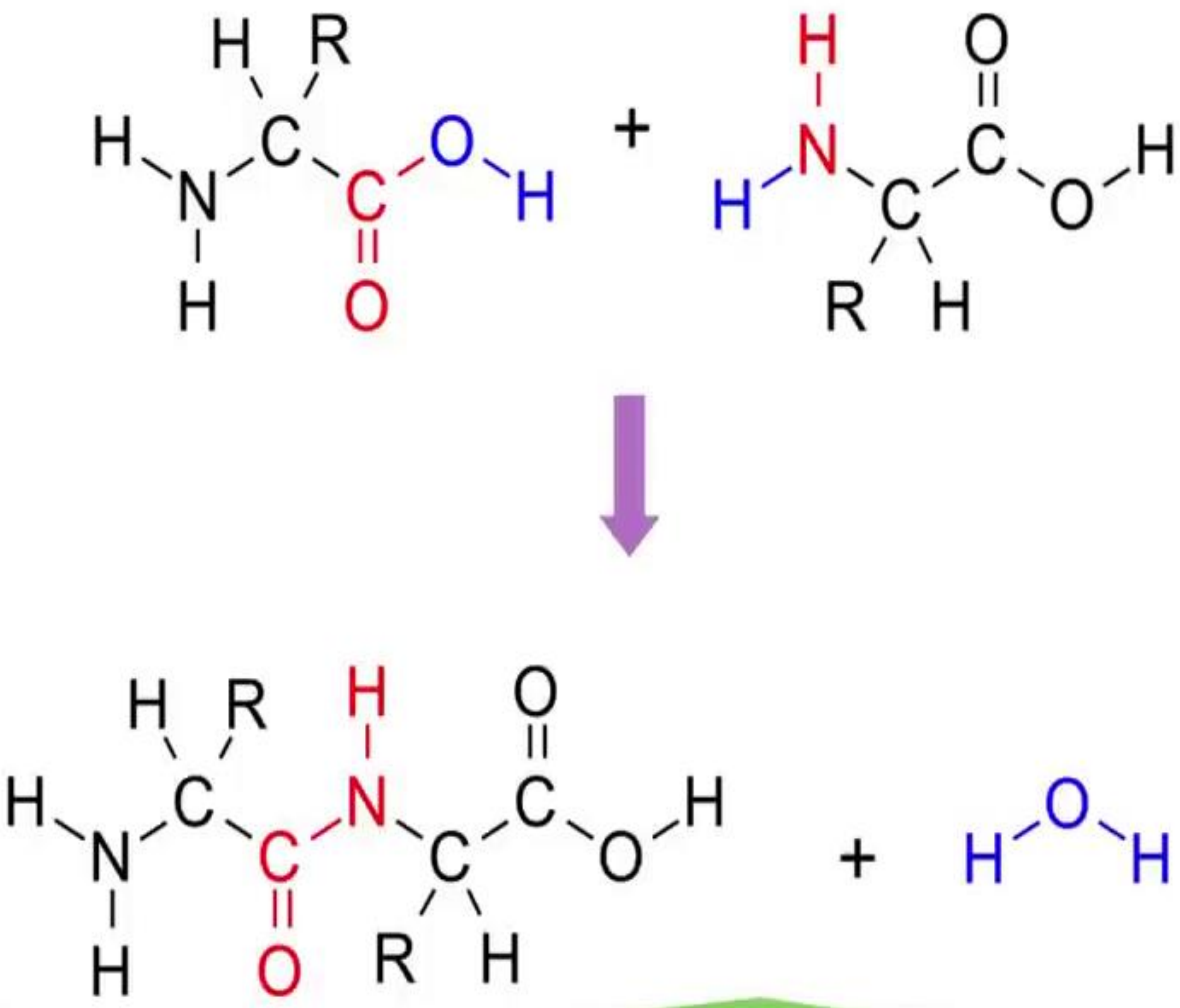
Involved in controlling gene expression (Transcription factors).

Serve as nutrients and storage function (Casein, Ferritin that stores iron).

Some proteins are structural components of tissues (keratin).



peptide bond formation is a dehydration (loss of H_2O)


H R
H C O
N C H
H O
+
H
N C H
H C O
R H
H R H O
H C N C H
N C C O
H O R H
+
H O H

CLASSIFICATION OF PROTEINS

No single universally satisfactory system of protein classification

One system classifies proteins according to their **composition/structure.**

One system classifies them according to **solubility.**

One system classifies them according to their **shape.**

Classification of proteins based on their **function**.

Classification of proteins based on their composition

Three major classes according to their composition/ structure.

Simple proteins: Made up of amino acids only. On hydrolysis, they yield only amino acids. Examples include Human plasma albumin, Trypsin, Chymotrypsin, Pepsin and Insulin.

Conjugated proteins: They are proteins containing non-protein part attached to the protein part either via covalent bond, non-covalent bond or hydrophobic interaction.

The non-protein part is the prosthetic group and on hydrolysis, these proteins yield non-protein compounds and amino acids.

$$\text{Conjugated protein} \longrightarrow \text{Protein} + \text{Prosthetic group}$$

Derived proteins: Are formed from simple and conjugated proteins. There are two classes of derived proteins.

(i) **Primary derived proteins:** They are formed from natural proteins by the action of heat or alcohol. The peptide bonds are not hydrolyzed.

Example: Coagulated proteins like cooked-egg albumin.

(ii) **Secondary derived proteins:** They are formed from partial hydrolysis of proteins.

Examples: gelatin (obtained by boiling skin, bones with water, obtained from cows).

Sub-classification of Derived Protein

Definition : Derived from simple and conjugated proteins.

2 Sub classes

Primary derived protein	Secondary derived
Denatured protein	*Partially hydrolysed protein*
No cleavage of peptide bonds	Cleavage of peptide bonds
No decrease in MW	Decrease in MW
Change in the structure of the protein	Protein becomes smaller

Proteins classification according to their solubility

Albumins: Soluble in water and salt solutions (Albumin of plasma, egg albumin and lactalbumin of milk).

Globulins: Sparingly soluble in water but soluble in salt solutions (Globulins of plasma and ovoglobulins of egg).

Glutelins: Soluble in dilute acids and alkalis (Glutenin of wheat, oryzenin of rice, zein of maize).

Protamins: Soluble in ammonia and water (Salmine from salmon fish).

Classification of proteins based on shape

Proteins are divided into two classes based on their shape.

1. **Globular proteins:** Polypeptide chain(s) of these proteins are folded into compact globular (spherical) shape.

Examples: Hemoglobin, myoglobin, albumin, chymotrypsin.

2. **Fibrous proteins:** Polypeptide chains are extended along one axis.

Examples: keratin, collagen and elastin.

Protein classification based on biological functions

Enzymes

Biochemical catalysts

Speed up the metabolic reactions in cells

DNA polymerase, Hexokinase, Alcohol dehydrogenase.

Hormones

They are regulatory molecules involved in the control of many cellular functions

Insulin and glucagon

Respiratory pigments

Hemoglobin, Myoglobin.

Transport proteins

Transport materials in the cells, form channels in the plasma membrane. Examples include transferrin, fatty acid binding proteins and serum albumin.

Contractile proteins

Utilize ATP to ensure muscle contraction actin and myosin.

Storage proteins

Ferritin that stores iron and casein that act as a reserve of amino acids for the milk.

Protection against harmful agents.

The antibodies/immunoglobulins that recognize antigens expressed on the surface of viruses, bacteria and other infectious agents.

Proteins involved in nerve transmission.

Acetylcholine at synapses.

PRIMARY STRUCTURE

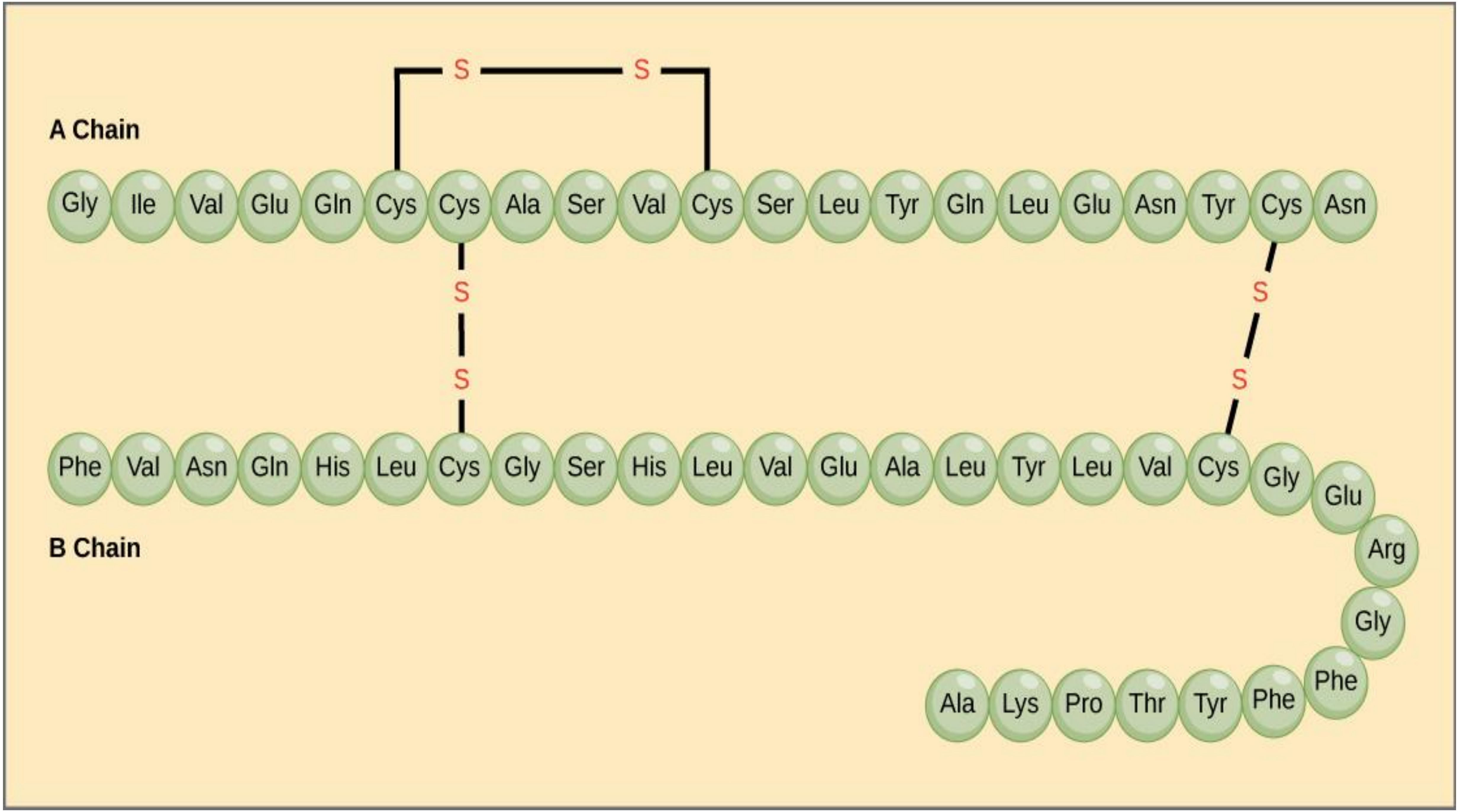
The linear sequence of amino acid residues in a polypeptide chain.

Bonds responsible for the maintenance are peptide and disulfide bonds.

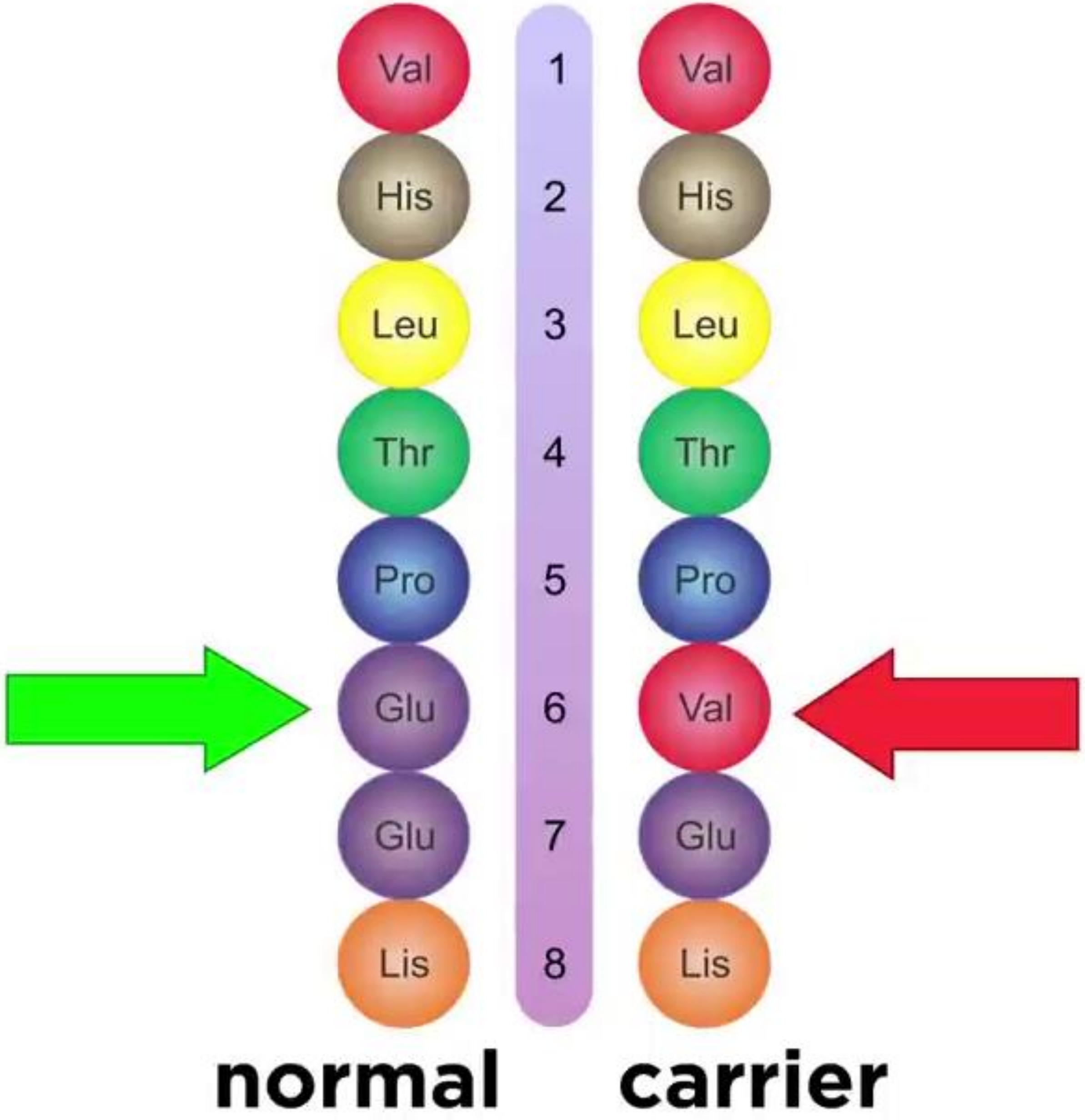
Primary Structure of Insulin

Two polypeptide chains (A and B) covalently linked by disulfide bonds.

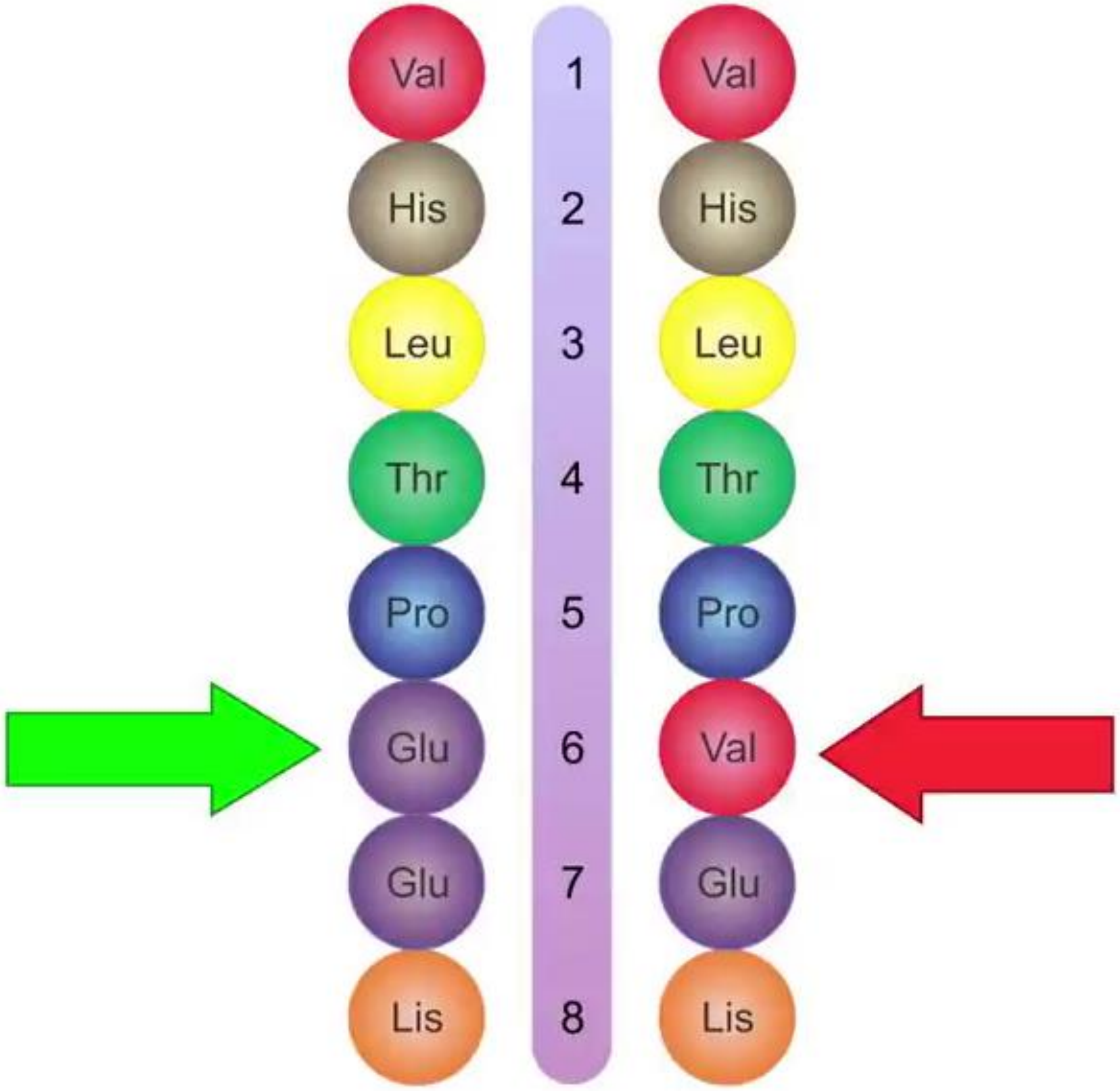
The A chain has N-terminal glycine and C-terminal asparagine. The B chain has phenylalanine and alanine as N-and C-terminal residues respectively.


A Chain
Gly Ile Val Glu Gln Cys Cys Ala Ser Val Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn
S S
S S
S S
Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Ala
B Chain

sickle cell disease

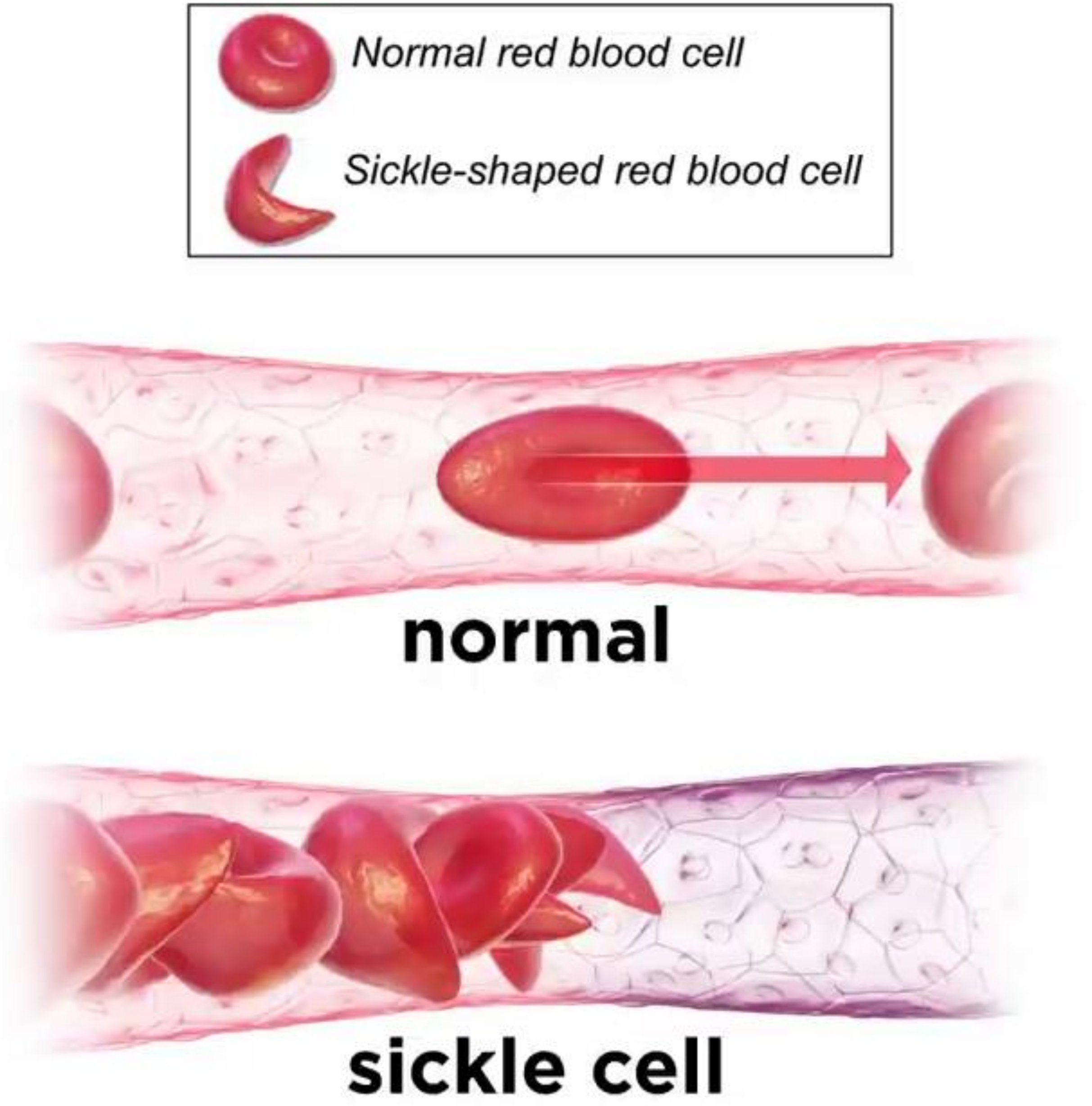


sickle cell disease



folding pattern of hemoglobin changes

sickle cell disease



SECONDARY STRUCTURE

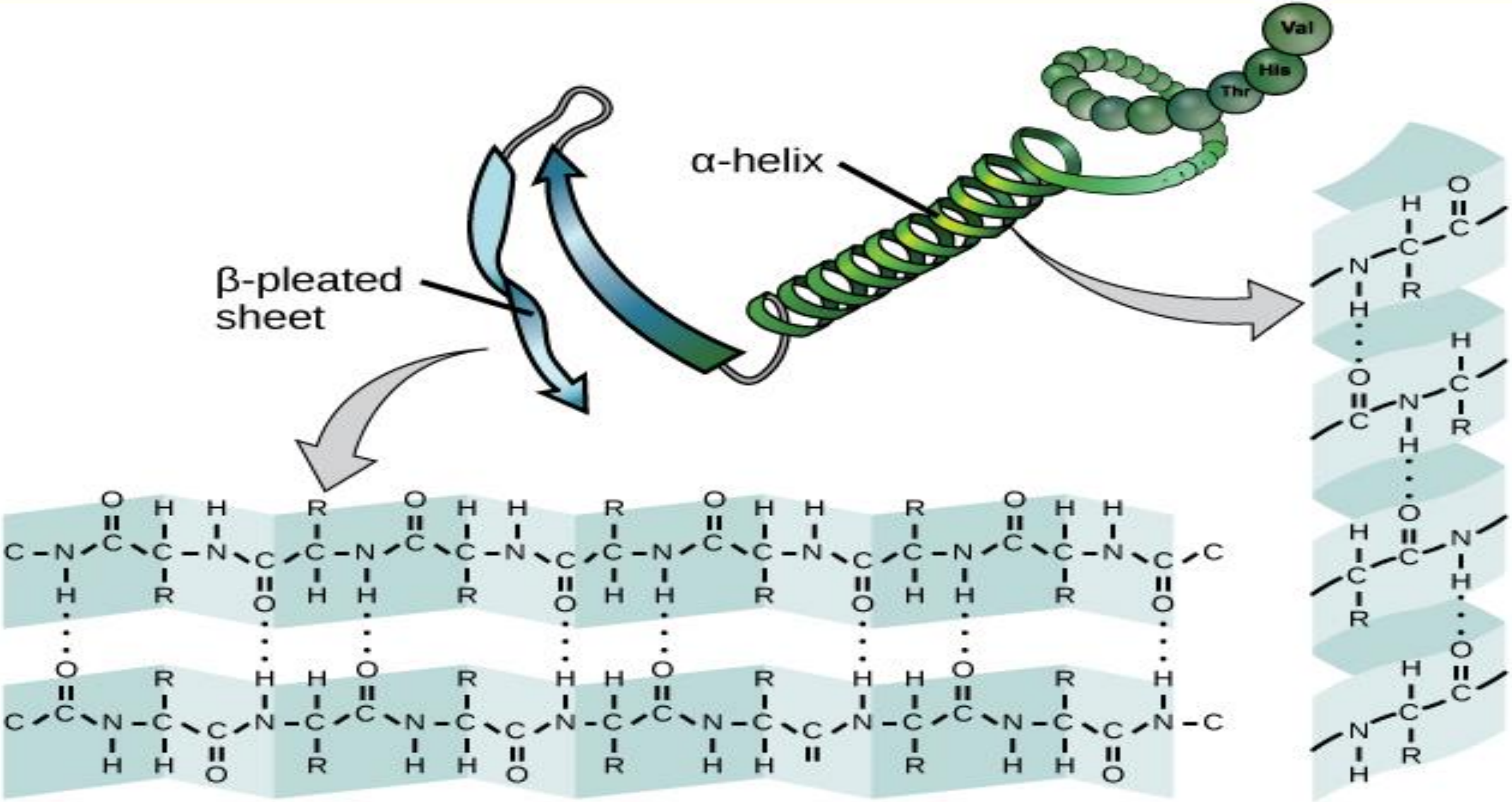
The local folding of the polypeptide in some regions gives rise to the secondary structure of the protein.

The most common are the α-helix and β-pleated sheet structures.

The α-helix structure is held in shape by hydrogen bonds.

They 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.

Secondary Protein Structure



TERTIARY STRUCTURE

Three-dimensional folding of polypeptide chain.

It consists of regions of α-helices and β-pleated sheets.

Primarily, the interactions among R groups creates the complex three-dimensional tertiary structure of the protein.

The nature of the R groups found in the amino acids counteract the formation of the hydrogen bonds in secondary structures.

For example, R groups with like charges are repelled by each other and those with unlike charges are attracted to each other (ionic bonds).

When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein, whereas the hydrophilic R groups lay on the outside.

This results in formation of hydrophobic interactions.

Interaction between cysteine side chains forms disulfide linkages in the presence of oxygen, the only covalent bond forming during protein folding.

NON COVALENT BONDS IN TERTIARY STRUCTURES

A. Hydrophobic interactions

They play significant role in maintaining tertiary structure.

B. Ionic bonds

These bonds are formed between oppositely charged groups of amino acid side chains.

These interact electrostatically to stabilize tertiary structure of protein.

They are also called as salt bridges.

C. Hydrogen bonds

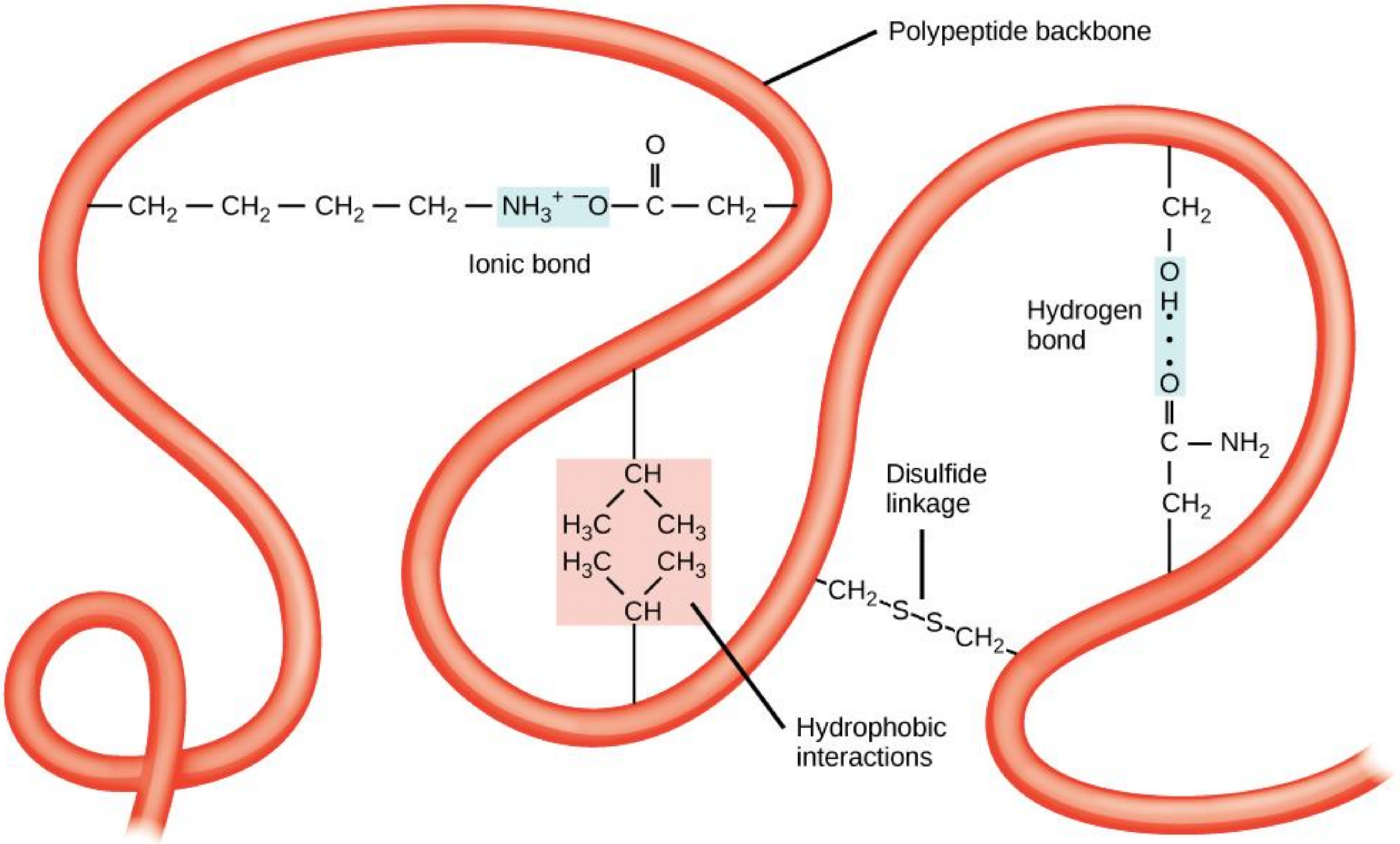
Amino acid side chains are involved in the hydrogen bond formation.

OH group of amino acids and the carbonyl oxygen participate in internal hydrogen bond formation.

D. Disulphide bonds

These are the weak interactions between uncharged groups of protein molecule.

They also contribute to the stability of proteins.



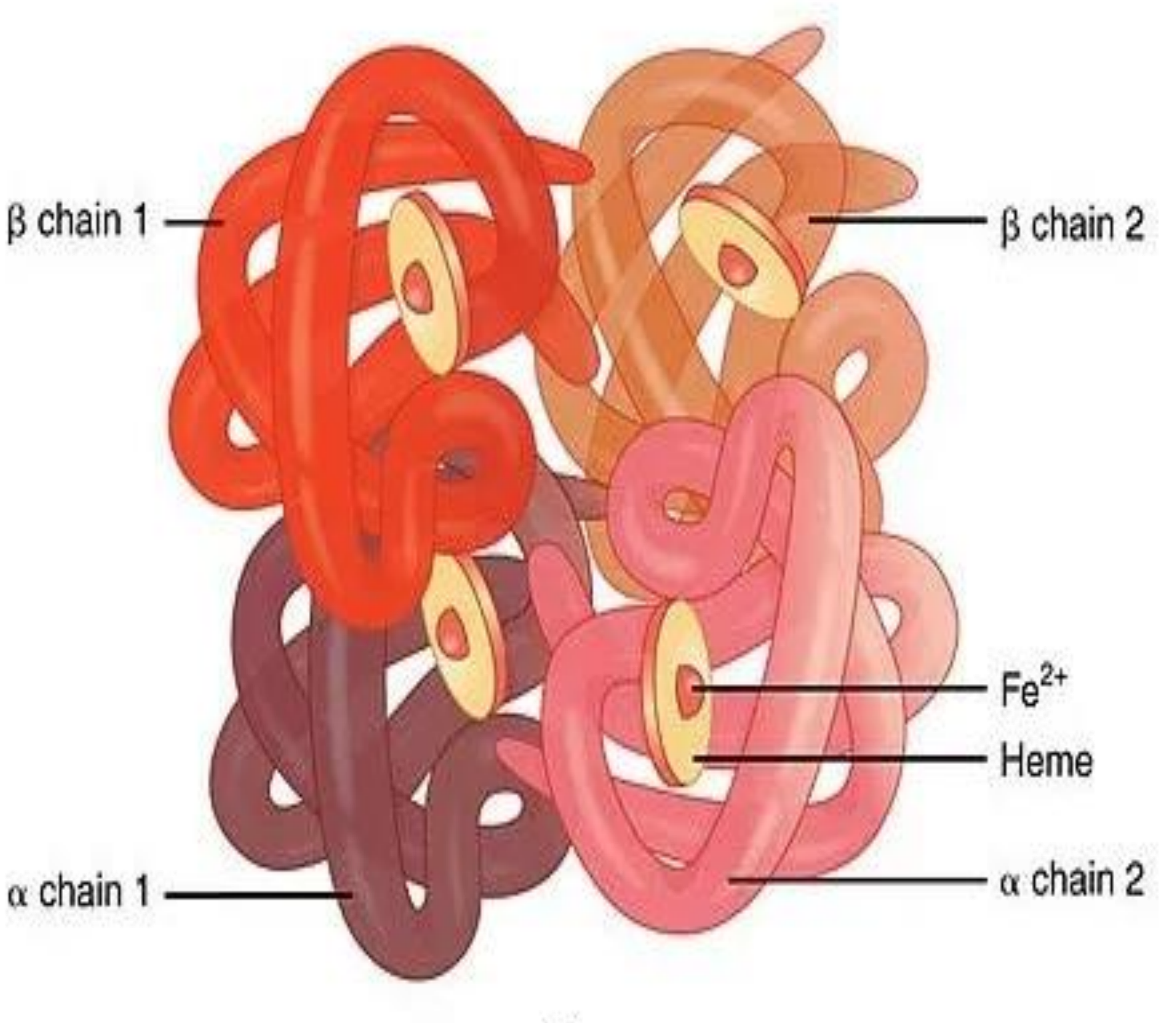
Polypeptide backbone
CH2 — CH2 — CH2 — CH2 — NH3+ −O — C — CH2
O
Ionic bond
CH2
O
H
O
C — NH2
CH2
Hydrogen bond
CH
H3C CH3
H3C CH3
CH
Disulfide linkage
CH2 - S - S - CH2
Hydrophobic interactions

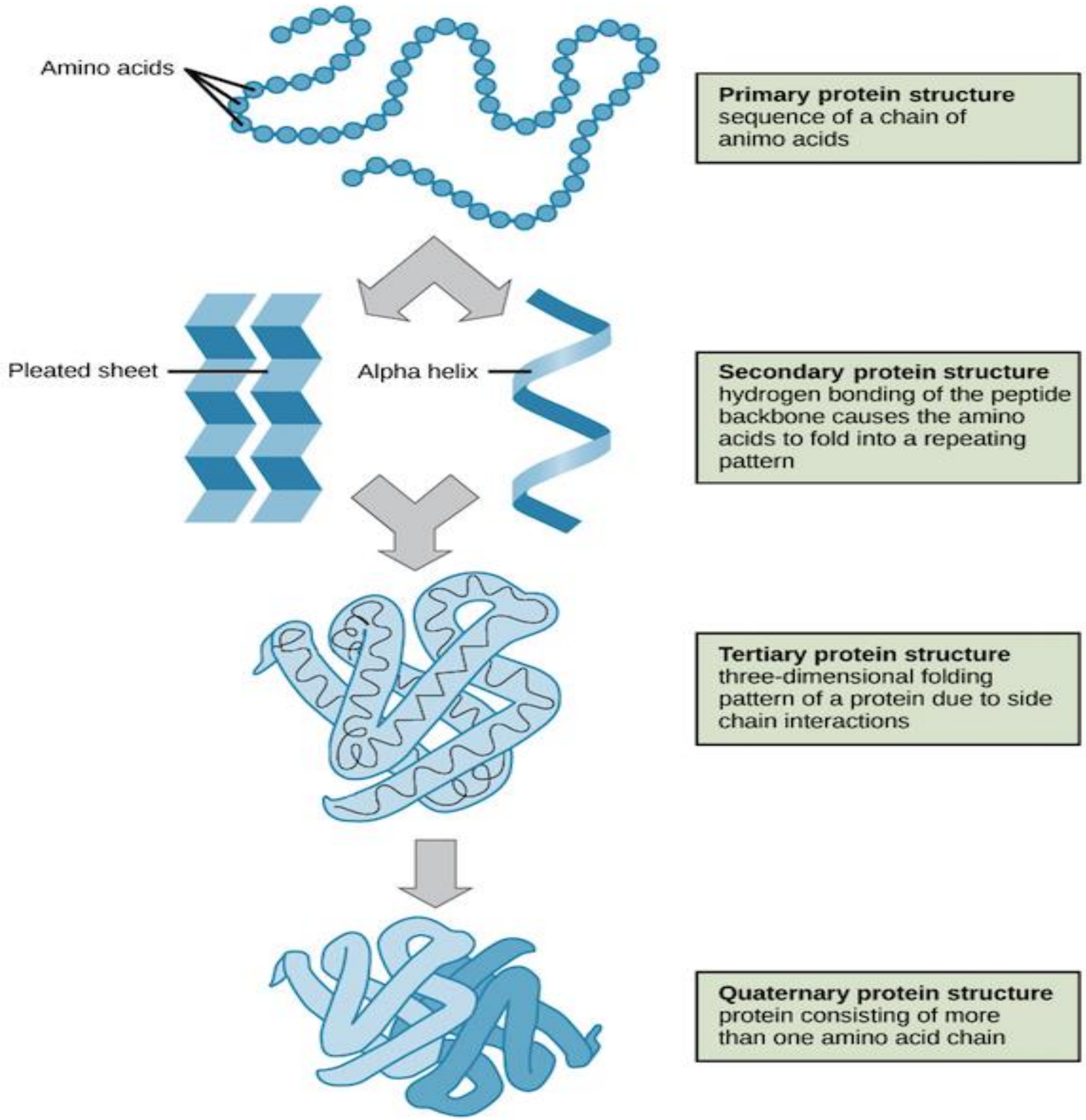
QUATERNARY STRUCTURE

Formed from the interaction of several polypeptides (subunits)

Weak interactions between the subunits help to stabilize the overall structure.

The subunits are linked by disulfide bonds.





Amino acids
Primary protein structure
sequence of a chain of
animo acids
Pleated sheet
Alpha helix
Secondary protein structure
hydrogen bonding of the peptide
backbone causes the amino
acids to fold into a repeating
pattern
Tertiary protein structure
three-dimensional folding
pattern of a protein due to side
chain interactions
Quaternary protein structure
protein consisting of more
than one amino acid chain

DENATURATION OF PROTEINS

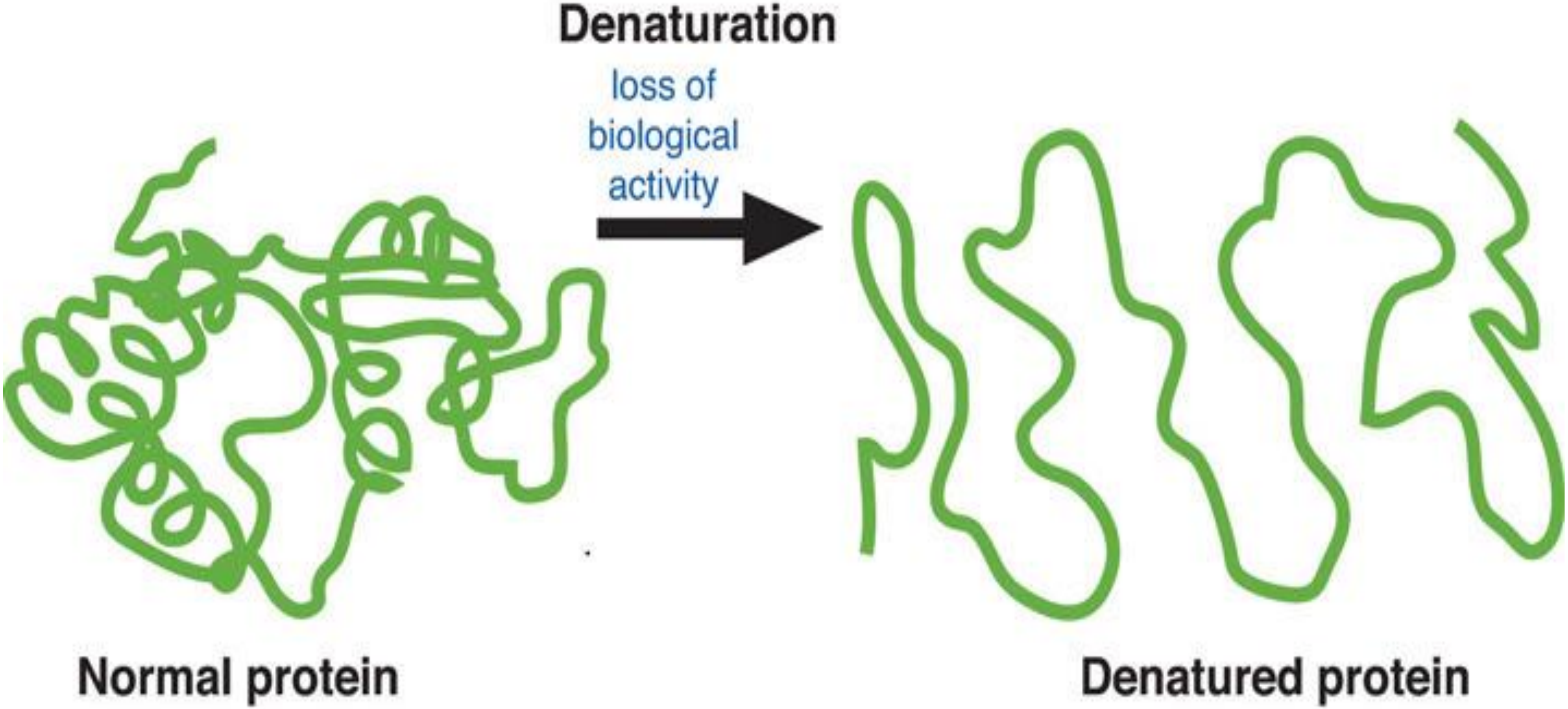
Loss of native conformation of proteins (no loss in primary sequence)

On denaturation, physical chemical and biological properties of a protein are altered.

Some of the changes in properties are:

1. Decreased solubility
2. Unfolding of polypeptide chain
3. Loss of quaternary, tertiary and secondary structure
4. Decreased or loss of biological activity
5. More susceptible to action of enzymes

agents: pH, temp, ionic strength, solubility



CAUSES OF DENATURATION

High temperatures

Extreme alkaline or acidic pH

UV radiation

Treatment with organic solvents like ethanol, acetone etc.

Vigorous shaking

Exposure to heavy metals like Pb, As and Cd

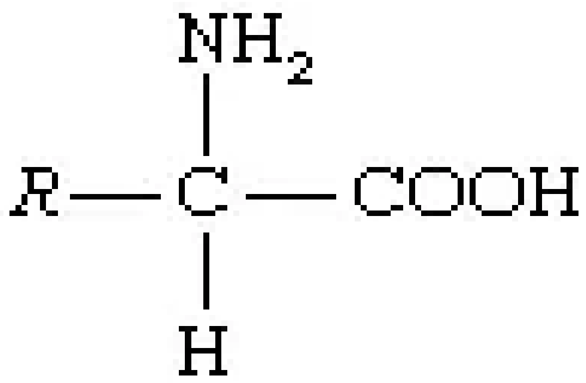
Detergents like sodium dodecyl sulfate

AMINO ACIDS

Organic molecules

Consist of a central carbon atom attached to a basic amino group (—NH_2), an acidic carboxyl group (—COOH), a hydrogen atom and an organic *R* group (side chain).

The side chain is unique to each amino acid.



Amino acid classification

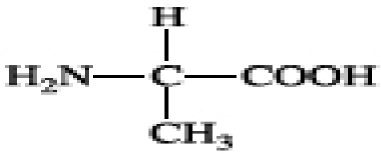
Based on the polarity (distribution of electric charge) of the R group.

Nonpolar amino acids

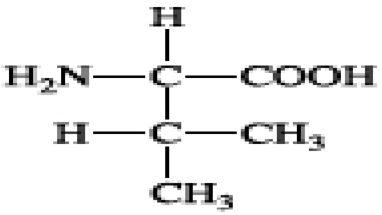
Glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, tryptophan and methionine.

R groups have aliphatic/aromatic groups that make them hydrophobic.

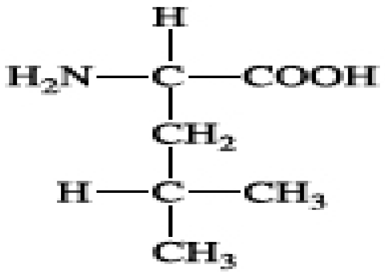
Globular proteins fold into a 3 D shape, burying the hydrophobic side chains in the protein interior.



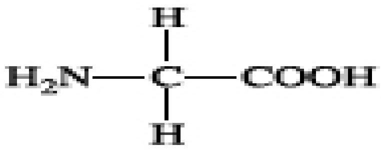
alanine
(Ala, A)



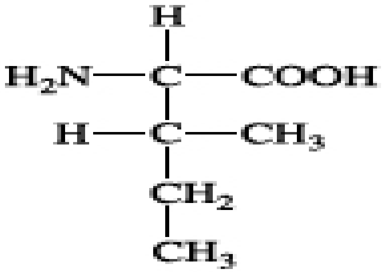
valine
(Val, V)



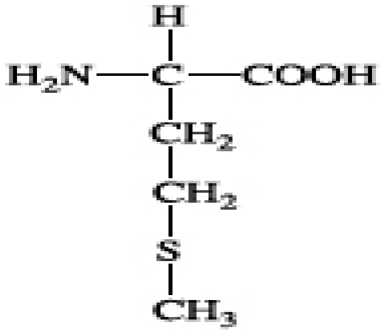
leucine
(Leu, L)



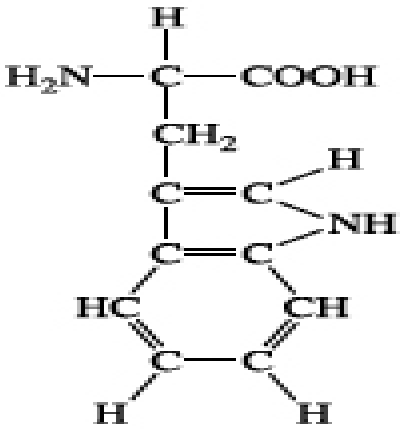
glycine
(Gly, G)



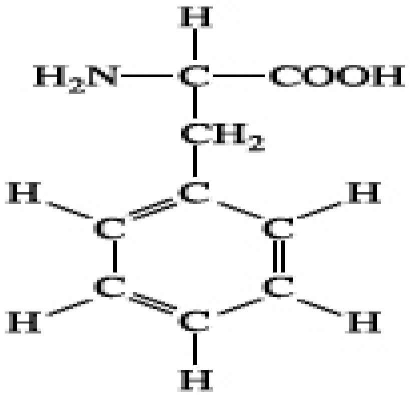
isoleucine
(Ile, I)



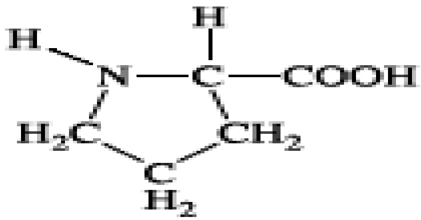
methionine
(Met, M)



tryptophan
(Try or Trp, W)



phenylalanine
(Phe, F)



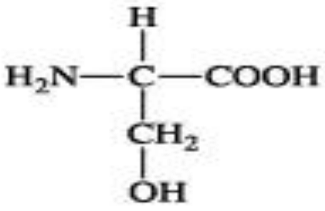
proline
(Pro, P)
an imino acid

Polar, uncharged amino acids

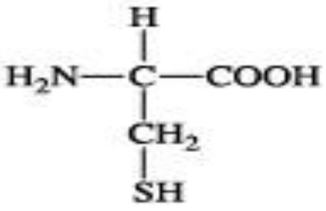
Are serine, cysteine, threonine, tyrosine, asparagine and glutamine.

The side chains in this group possess a spectrum of functional groups.

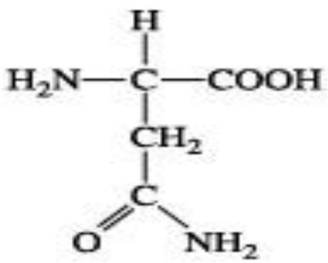
Most have at least one atom (nitrogen, oxygen, sulfur) with electron pairs available for hydrogen bonding to water and other molecules.



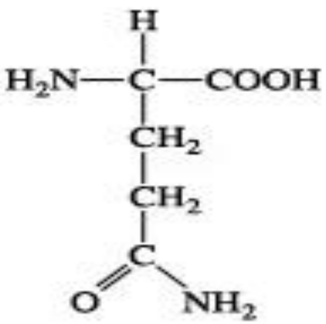
serine
(Ser, S)



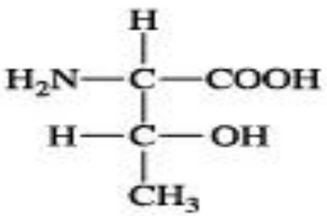
cysteine
(CysH, C)



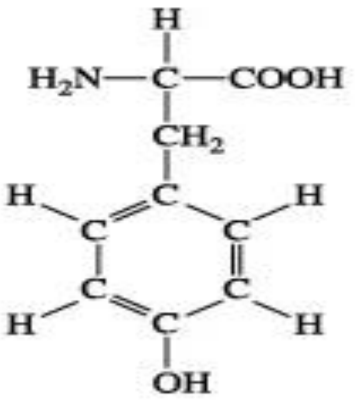
asparagine
(AspNH$_2$ or Asn, N; Asx or B)



glutamine
(GluNH$_2$, GluN,
or Gln, Q; Glx or Z)



threonine
(Thr, T)



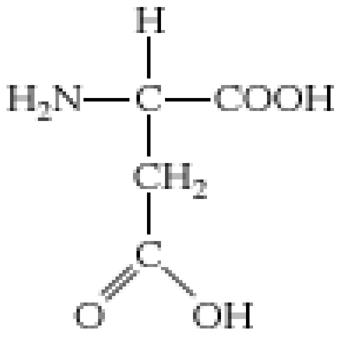
tyrosine
(Tyr, Y)

Acidic amino acids

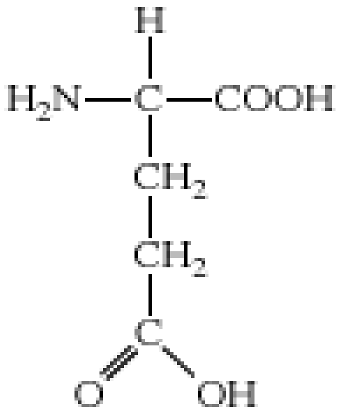
They include aspartic acid and glutamic acid.

Each has a carboxylic acid side chain thus giving it acidic properties.

In ionic forms, the amino acids are called aspartate and glutamate.



aspartic acid
(Asp, D; Asx or B)



glutamic acid
(Glu, E; Glx or Z)

Basic amino acids

Include arginine, histidine and lysine.

Have a basic side chain.