Proteins. Functions, Structure, classification

Agenda

1. **Functions of Proteins**
2. **Overview of Protein Structure - levels of organization of protein molecules**
   - ❑ **Primary Structure**
   - ❑ **Secondary Structure**
   - ❑ **Tertiary and Quaternary Structures**

3. **Classification of proteins**

1. Functions of Proteins

Proteins perform the following functions:

1. Structural:

- in connective tissue - collagen, elastin, keratin.
- membrane construction and cytoskeletal formation (on the cell membrane, there are integral, semi-integral and surface proteins) - for example, ***spectrin, glycophorin***).
- the construction of organelles - for example, ribosomes.

2. Enzymatic:

Almost **all enzymes are proteins**.

(Although the existence of ribozymes, i.e., RNAs with catalytic activity is discovered recently).

3. Signaling (Hormonal) function (Peptide **hormones** or **protein hormones**):

- Regulation and coordination of metabolism in different cells of the body, since some hormones are proteins by nature - insulin, growth hormone, etc.

4. Receptors:

- Receptor proteins of target cells selectively bind hormones, mediators.

5. Transport:

- Transfer of substances in the blood (lipoproteins, hemoglobin, transferrin) or through membranes (Na^+,K^+- ATPase, Ca^{2+}- ATPase).

6. Nutritive and reserve - egg albumin, milk casein.

7. Protective - immunoglobulins (antibodies), blood coagulation proteins (protection from blood loss).

8. Regulatory Proteins - regulate genes expression;

9. Proteins-toxins: pseudomonas exotoxin (PE), diphtheria toxin (DT), etc.

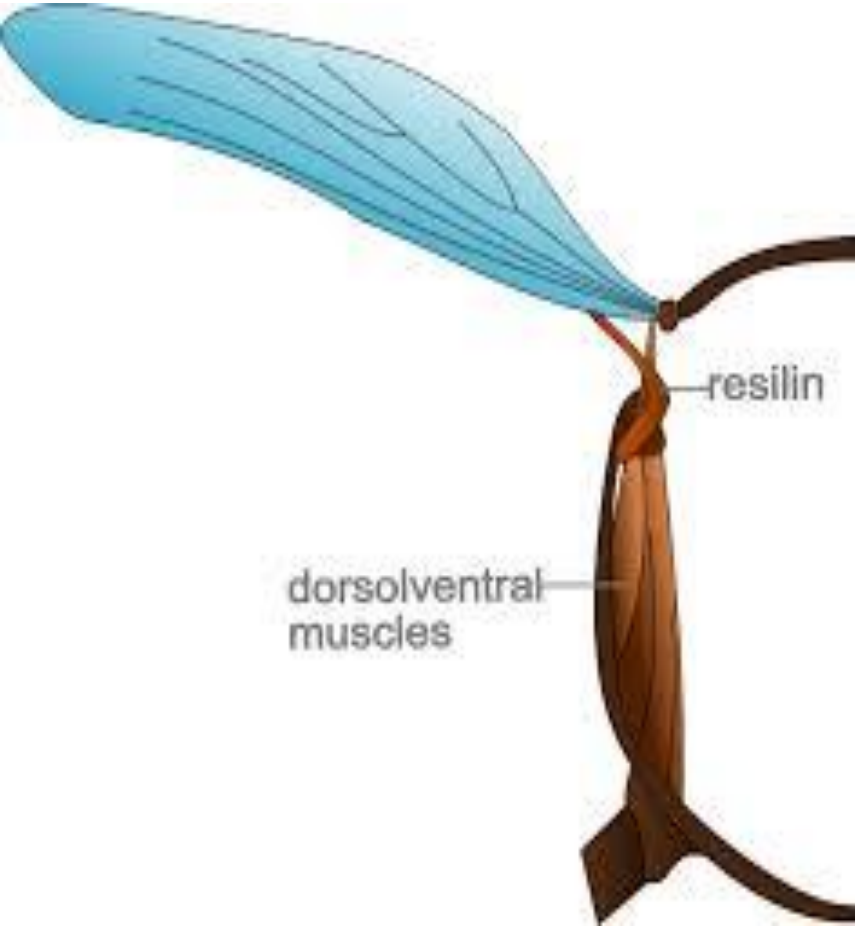
10. Proteins - Inhibitors of enzymes;

11. Viral envelope proteins,

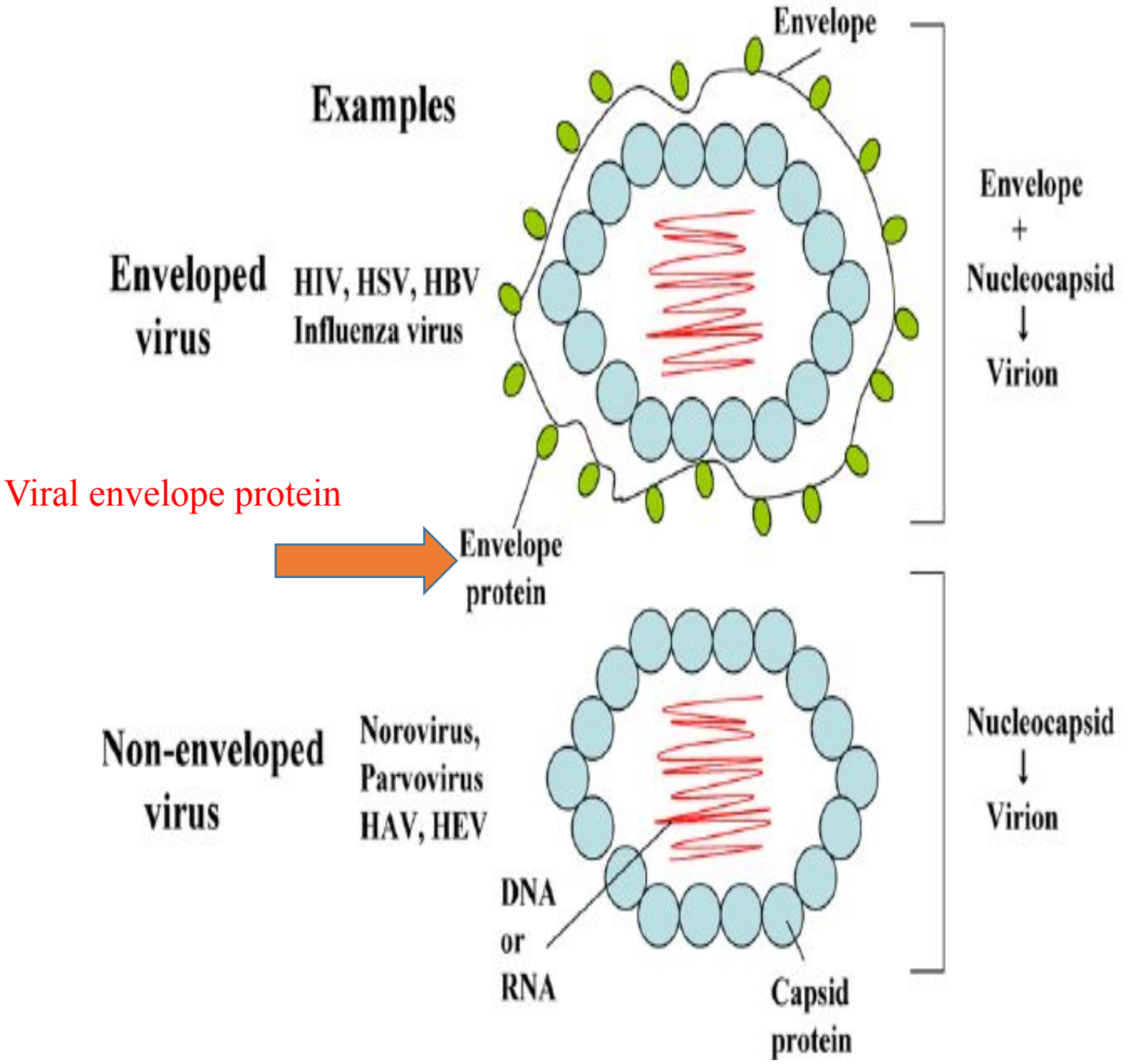
12. Proteins with other functions.

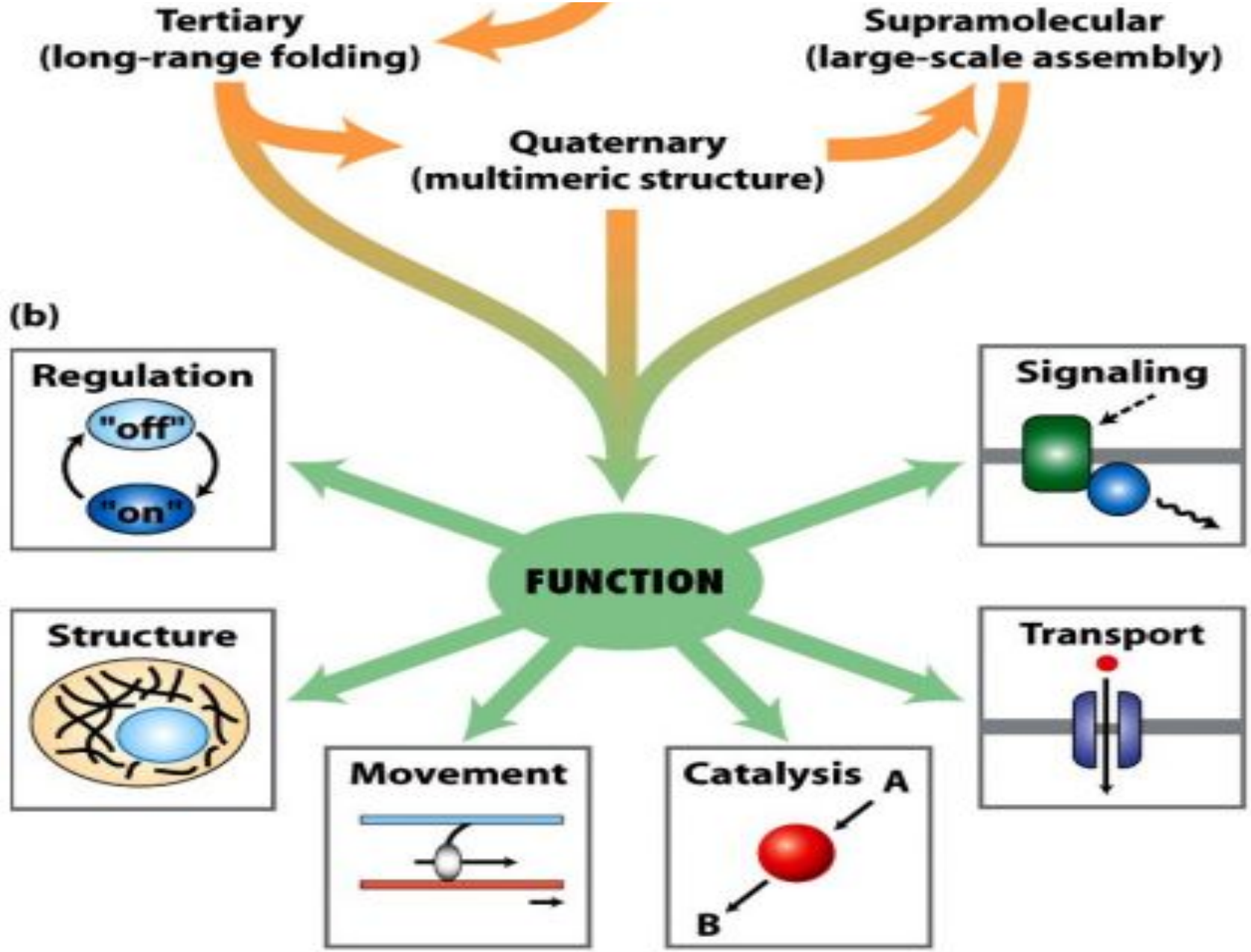
There are proteins that are the subject of special study (proteins with other functions):

- **Monellin -** isolated from an African plant, **has a very sweet taste**, non-toxic and does not contribute to human obesity.
- **Resilin** – polymeric **rubber-like** protein with outstanding **elasticity**, makes "hinges" in the attachment places of **insect wings**, serves to connect wings and body. **Resilin** is critical in the flight and jumping systems of insects.
- Proteins with **antifreeze properties** – found in polar (Antarctic) fish, protect blood from freezing.



Resilin provides soft rubber-elasticity to mechanically active organs and tissue.
It helps insects to flap the



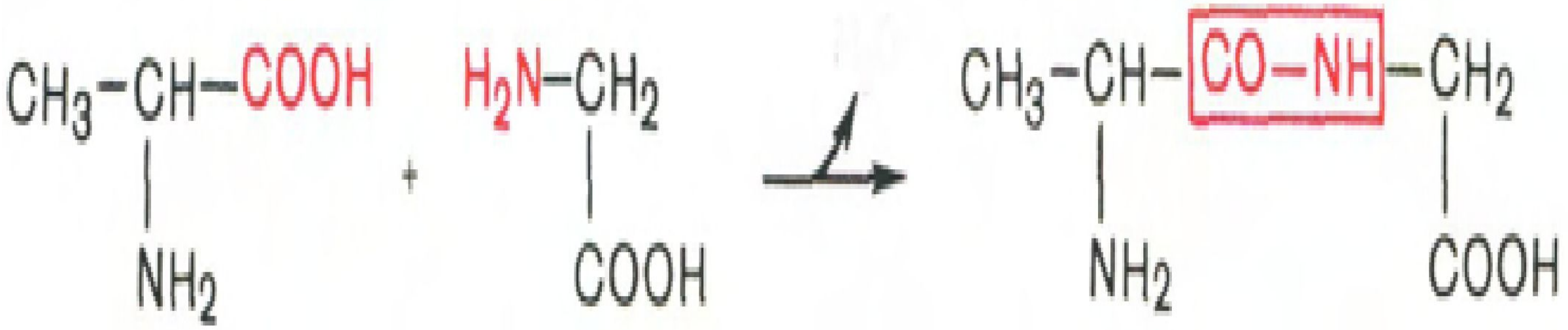

Tertiary
(long-range folding)
Supramolecular
(large-scale assembly)
Quaternary
(multimeric structure)
(b)
Regulation
"off"
"on"
Signaling
FUNCTION
Structure
Transport
Movement
Catalysis
A
B

2. STRUCTURE – LEVELS OF PROTEIN Molecule ORGANIZATION

- **PRIMARY STRUCTURE OF PROTEINS** - This is the amino acids sequence in a polypeptide chain.

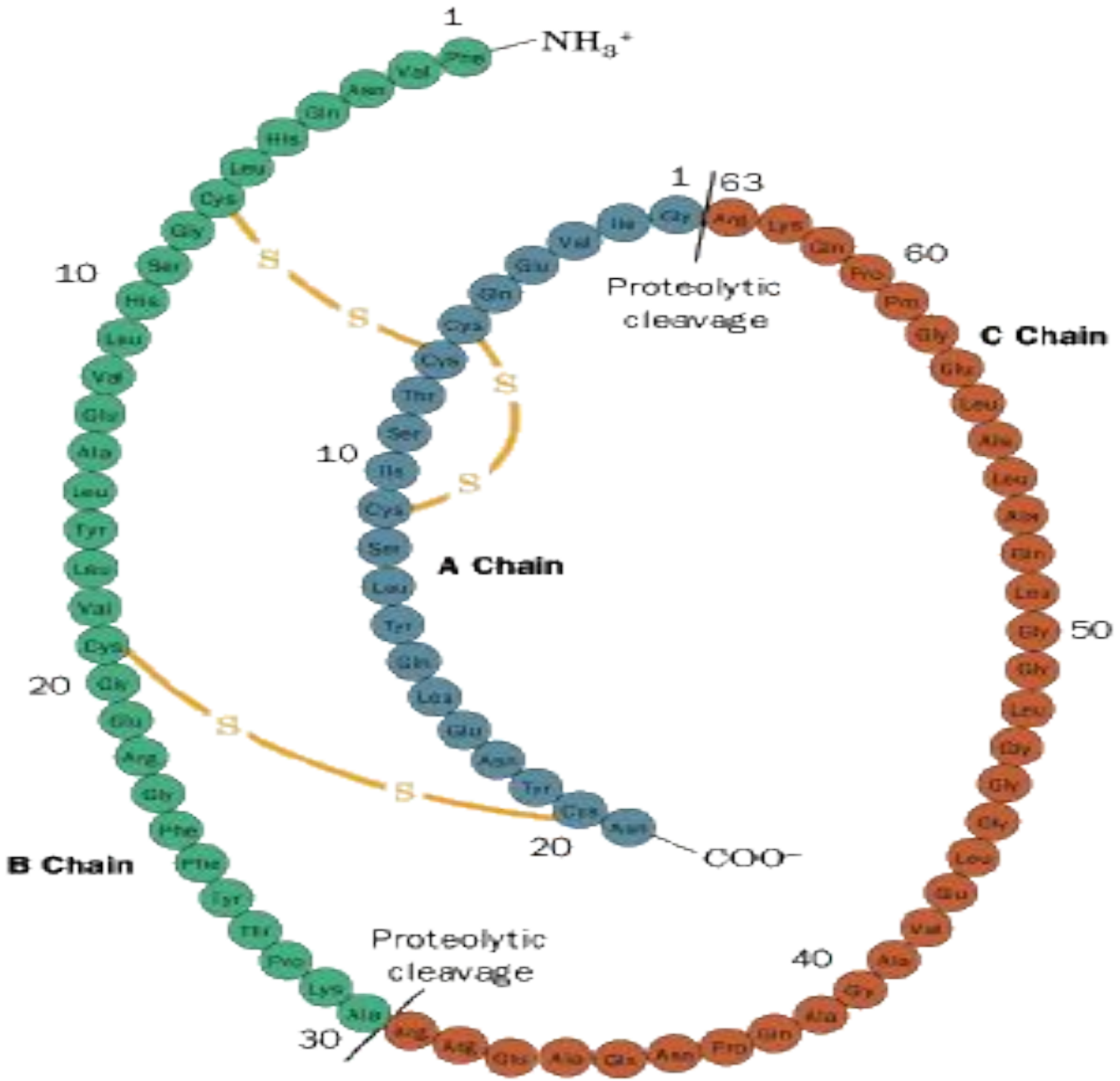
  - Emil Fischer (1902) formulated the ***polypeptide theory*** of protein structure. He was able to establish the type of bond that would connect amino acids together in chains, namely, **the peptide bond**, and he obtained the dipeptides and later the tripeptides and polypeptides.

  - On the example of the interaction of **alanine and glycine**, the formation of a peptide bond and a **dipeptide** (with the release of a water molecule) can be represented by the following equation:



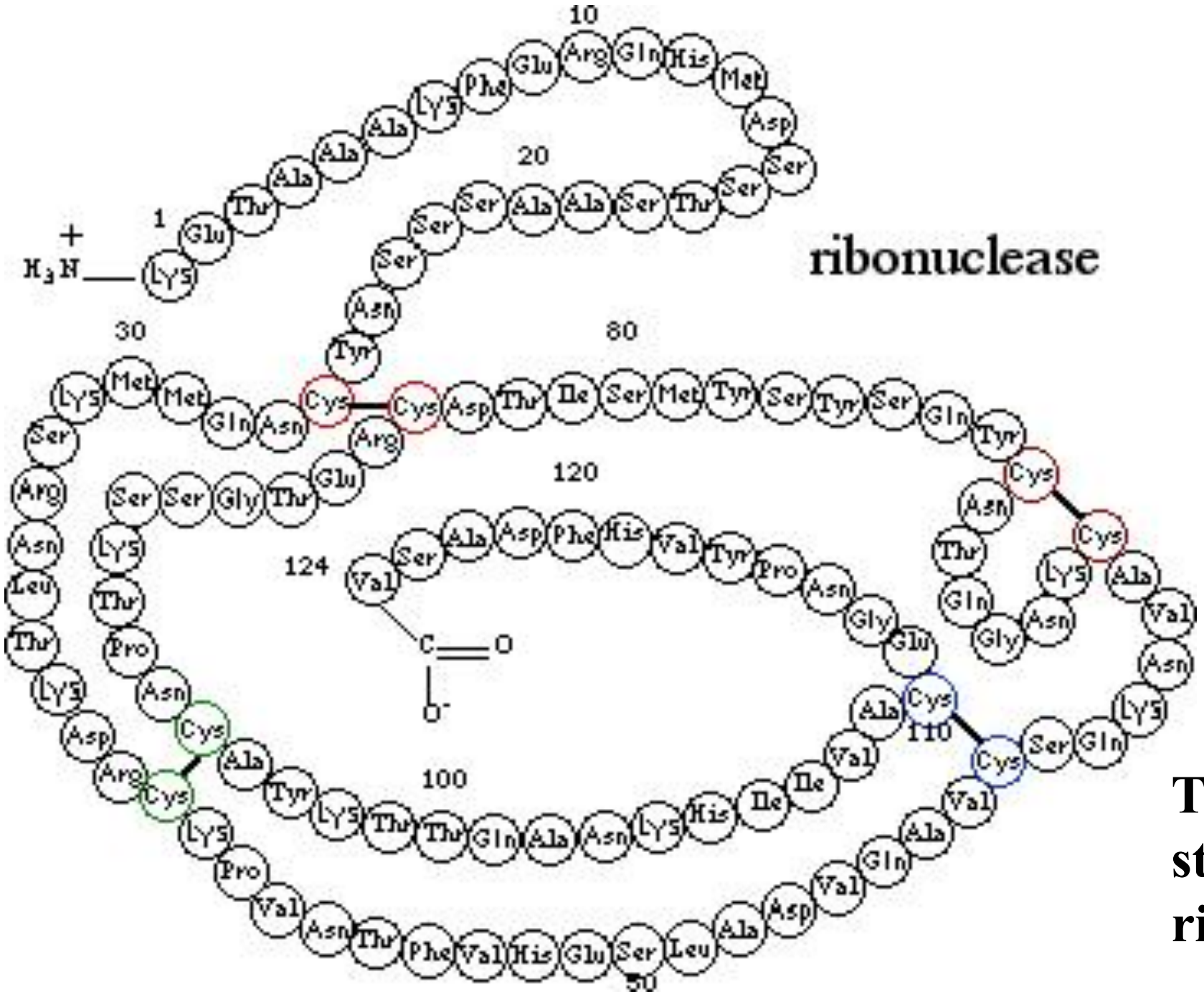
Alanine **Glycine** ***Alanilglycine***

The sequence and ratio of amino acids in the primary structure determines the formation of the secondary, tertiary and quaternary structures.



C-chain needed to direct proper disulfide bond formation

Primary structure of porcine proinsulin



The primary structure of RNase – ribonuclease

- **SECONDARY STRUCTURE**: Polypeptide chains can Fold into Regular structures.

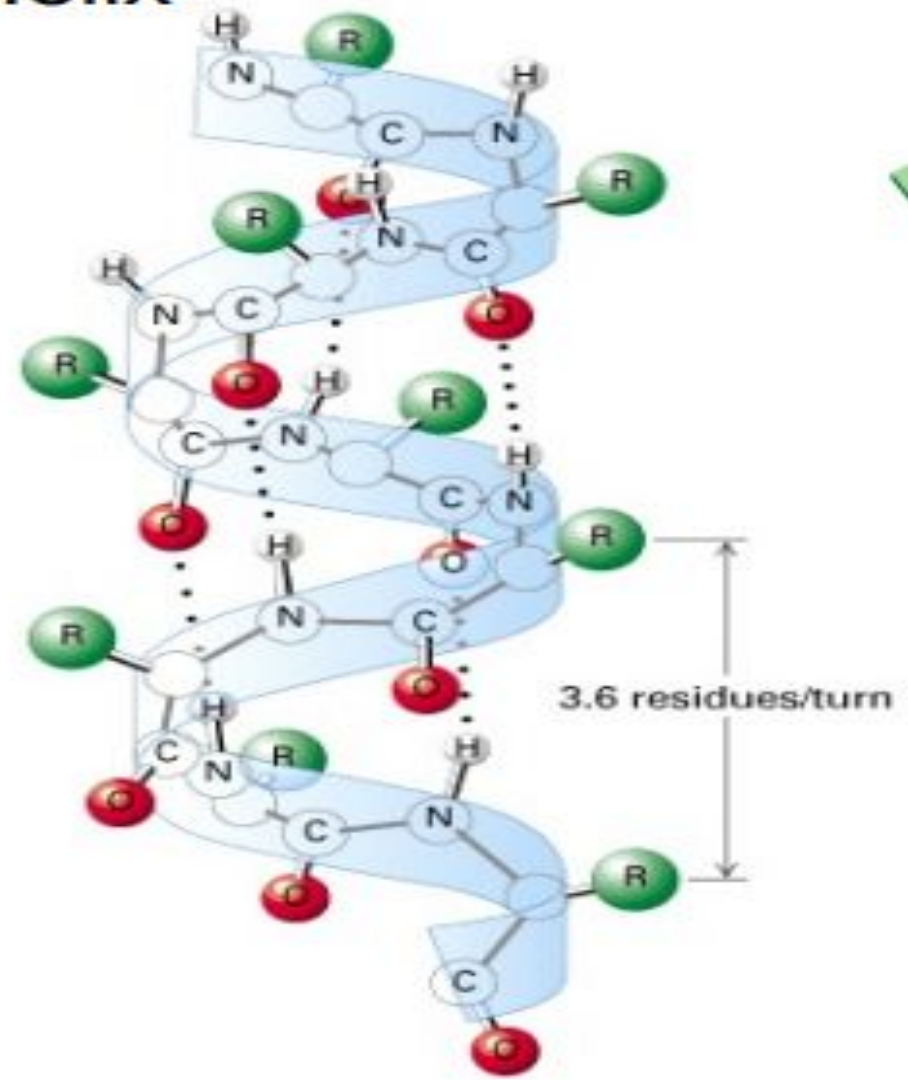
- By this structure of a protein a method of folding, twisting (folding, packing) a polypeptide chain into a helical or some other conformation is meant.
- This is a method of folding a polypeptide chain into an ordered structure in which amino acids that are **closely located** along the chain interact (**local folding**).
- The formation of the secondary structure is caused by the desire of the peptide to accept the conformation with the greatest number of hydrogen bonds between groups.

Three variants of the secondary structure can be distinguished:

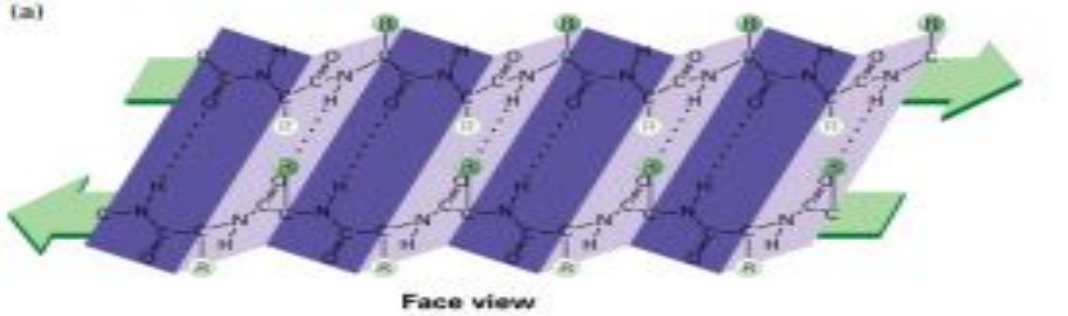
- **α-helix**,
- **β-*pleated sheet*** (beta pleated sheet),
- ***Turns* and *loops***.

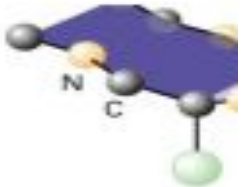
Secondary structure

α Helix

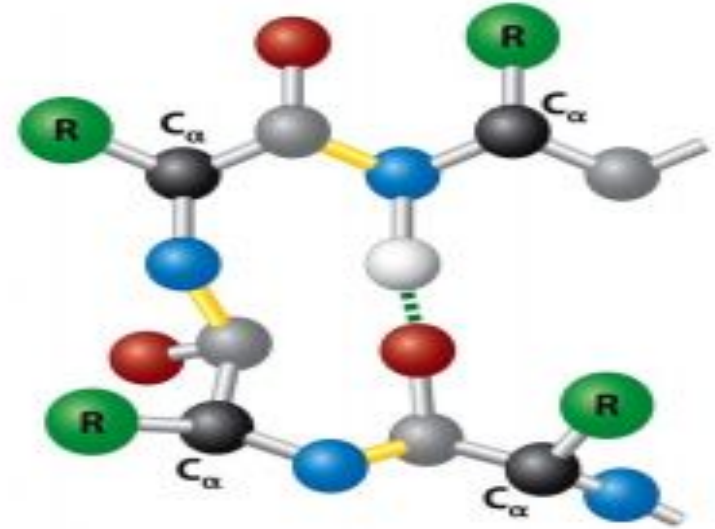


β Sheet



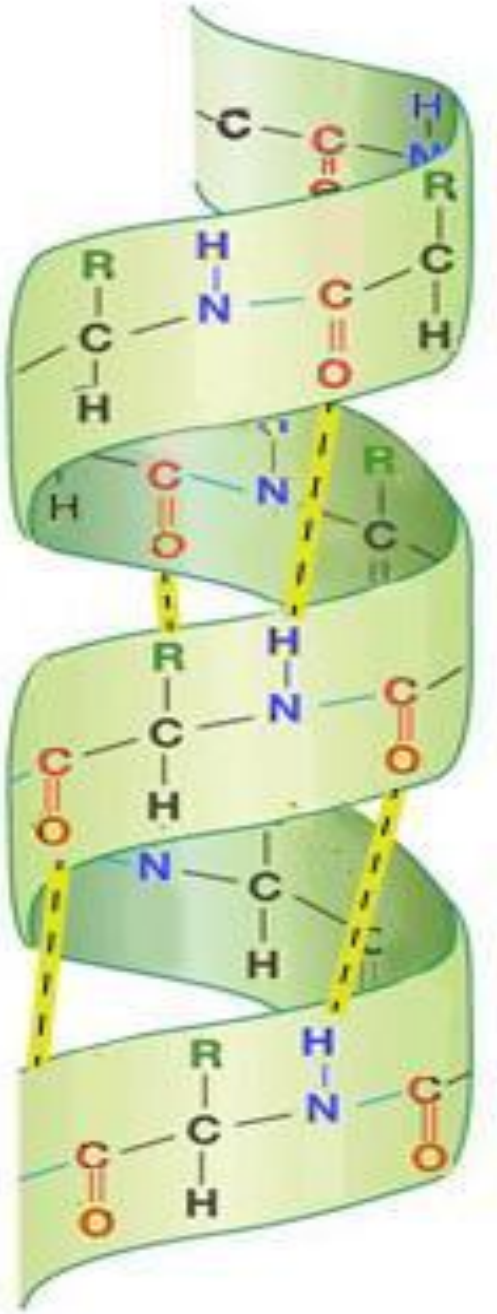


β (U)-turn

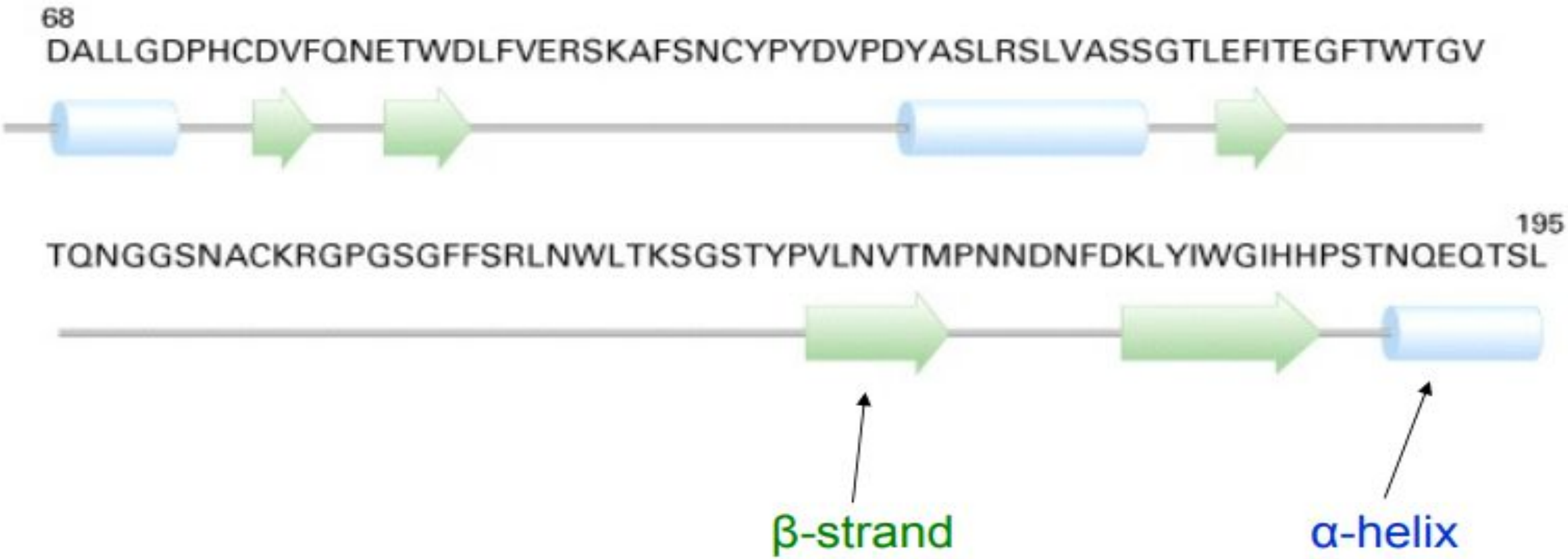


α-helix.

- This is a right-handed helices, formed by hydrogen bonds between the peptide groups of each 1st and 4th amino acid residues. The side chains of the amino acids composing the structure extend outward in a helical array.
- The height of the turn is 0.54 nm and corresponds to 3.6 amino acid residues (An idealized α helix has 3.6 residues per turn)
- 5 turns correspond to 18 amino acids and occupy 2.7 nm.



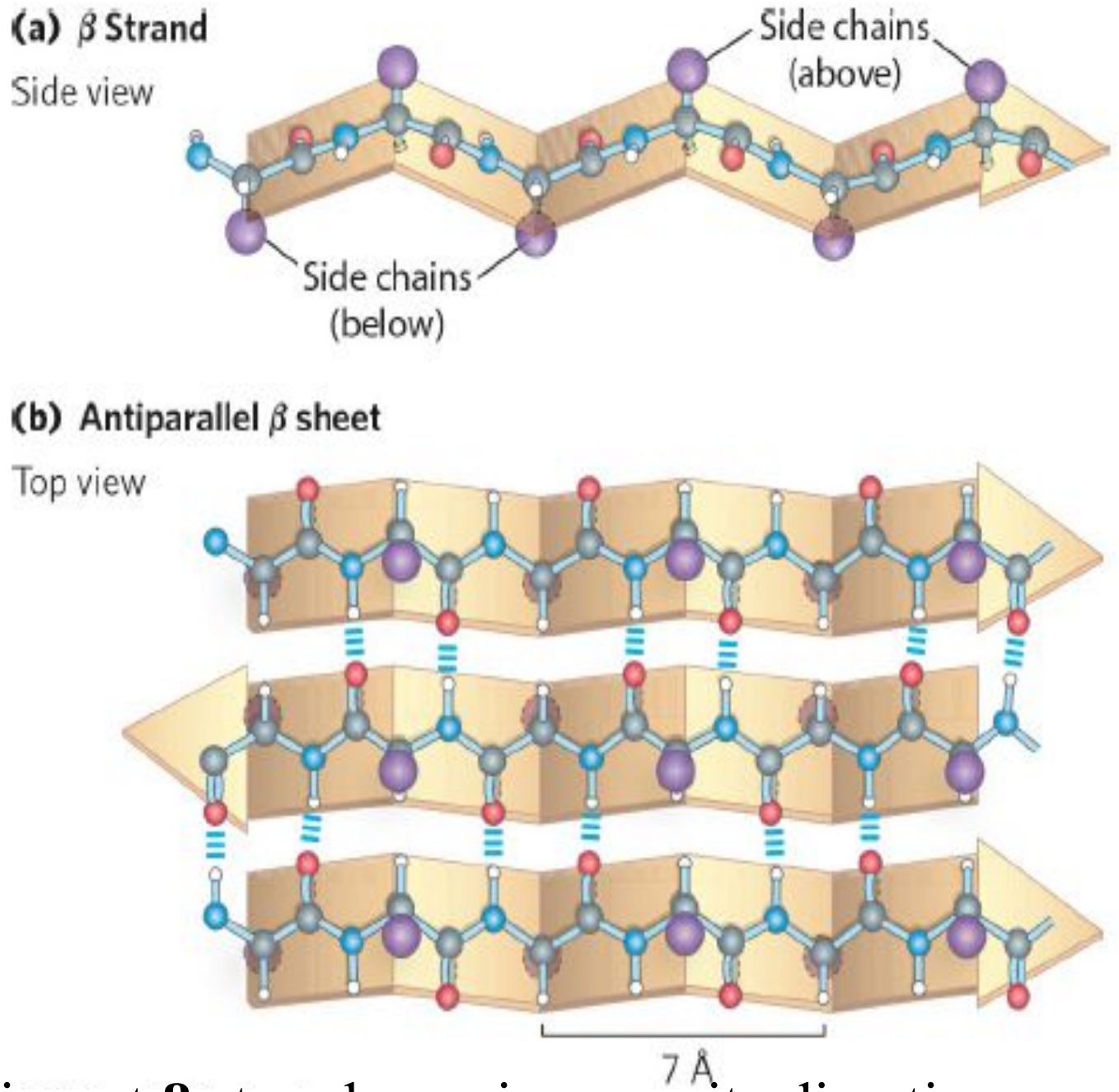
Primary and secondary structure (example: hemagglutinin)



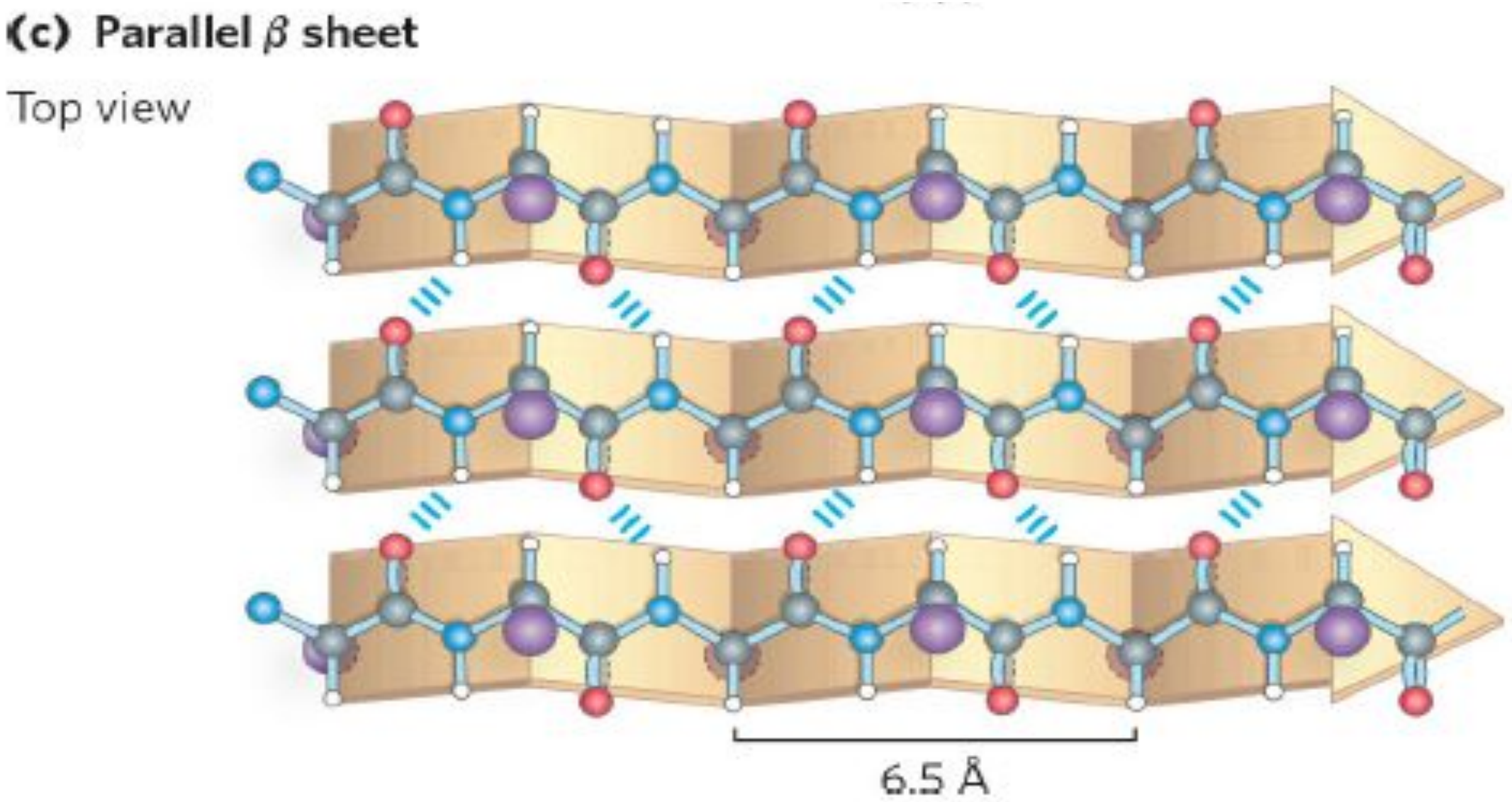
Beta Sheets

are stabilized by Hydrogen Bonding between Polypeptide Strands.

- the **β sheet** is composed of two or more polypeptide chains called b *strands*.
- In the **β** conformation, the backbone of the polypeptide chain is extended into a zigzag rather than helical structure.
- Hydrogen bonds form between adjacent segments of polypeptide chain within the sheet.

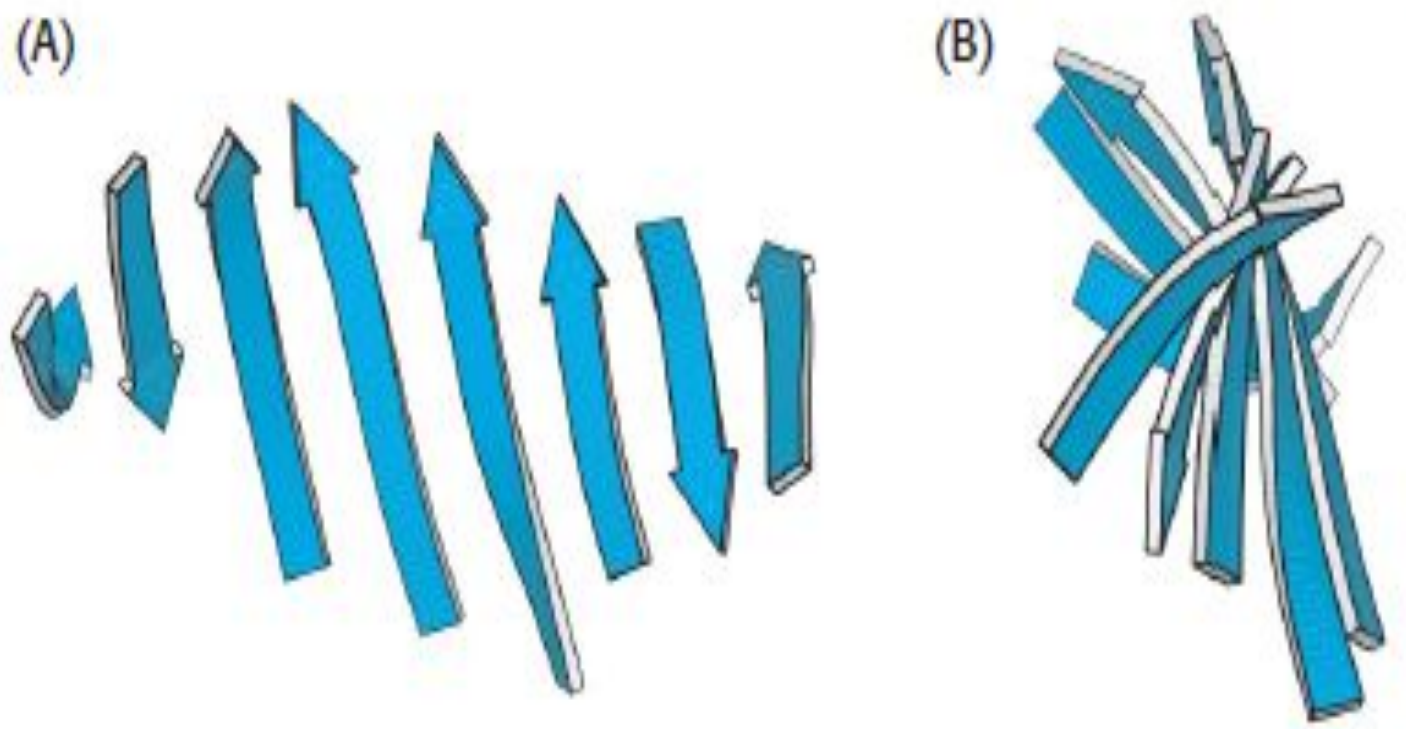


Adjacent **β** strands run in opposite directions.



Adjacent b strands run in the same direction. Hydrogen bonds connect each amino acid on one strand with two different amino acids on the adjacent strand.

- In schematic representations, b strands are usually depicted by broad arrows pointing in the direction of the carboxyl-terminal end to indicate the type of β sheet formed – parallel or antiparallel.
- Beta sheets can be almost flat, but most adopt a somewhat twisted shape.



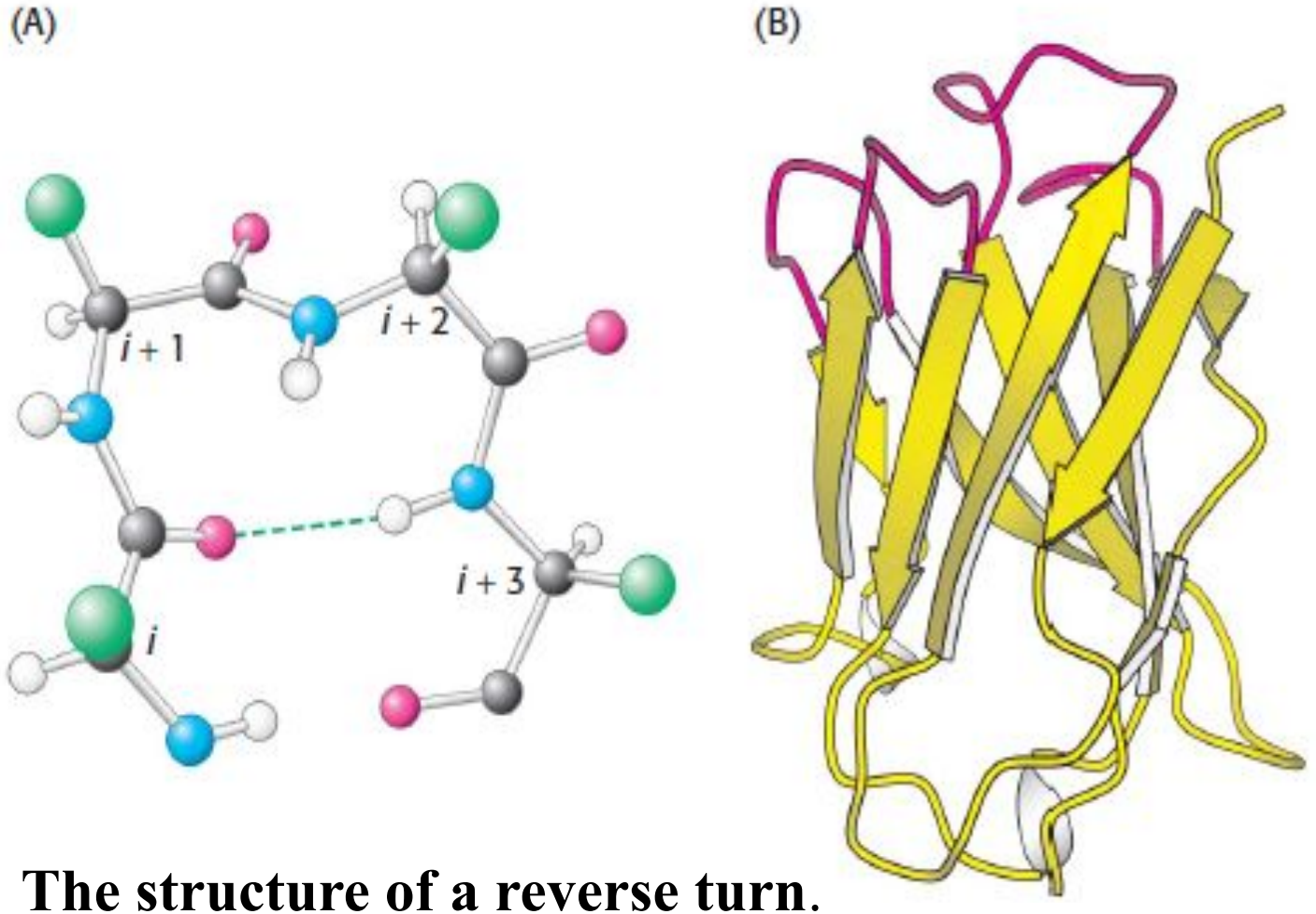
A twisted b sheet.

(A) A schematic model.

(B) The schematic view rotated by 90 degrees to illustrate the twist more clearly.

Turns and Loops

- Most proteins have compact globular shapes, **requiring reversals in the direction** of their polypeptide chains. Many of these reversals are accomplished by common structural elements called *reverse turns* and *loops*.
- Turns and loops invariably lie on the surfaces of proteins and thus often participate in interactions between other proteins and the environment.



The structure of a reverse turn.
(A) The CO group of residue *i* of the polypeptide chain is hydrogen bonded to the NH group of residue *i* + 3 to stabilize the turn.
(B) A part of an antibody molecule has surface loops (shown in red)

Tertiary Structure: water-soluble Proteins fold into Compact structures

- *The tertiary structure,* refers to the spatial arrangement of amino acid residues that are far apart in the sequence and to the pattern of disulfide bonds.
- This level of structure is the result of interactions between the R groups of the peptide chain.
- Thus, the overall three-dimensional arrangement of all atoms in a protein is referred to as the protein's **tertiary structure**.
- The tertiary structure includes *longer-range* aspects of amino acid sequence.

- Some polypeptide chains fold into two or more compact regions that may be connected by a flexible segment of polypeptide chain.
- These compact globular units, called *domains*.

Protein domains.
The cell-surface protein CD4 consists of four similar domains

Bonds involved in the formation of the tertiary structure

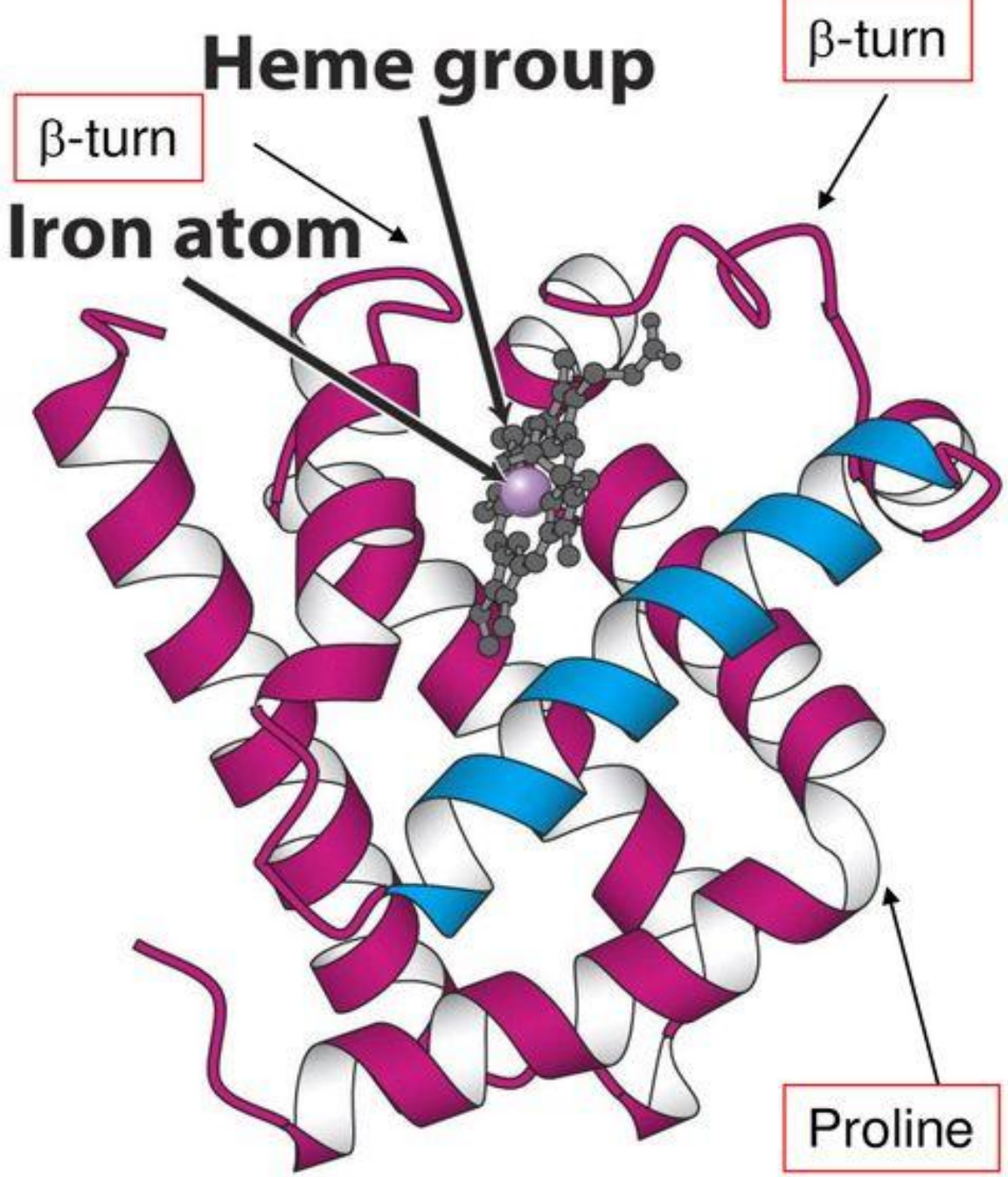
Various bonds are involved in the formation of the tertiary structure:

1. Mainly:

- hydrogen
- Van der Waals communications.

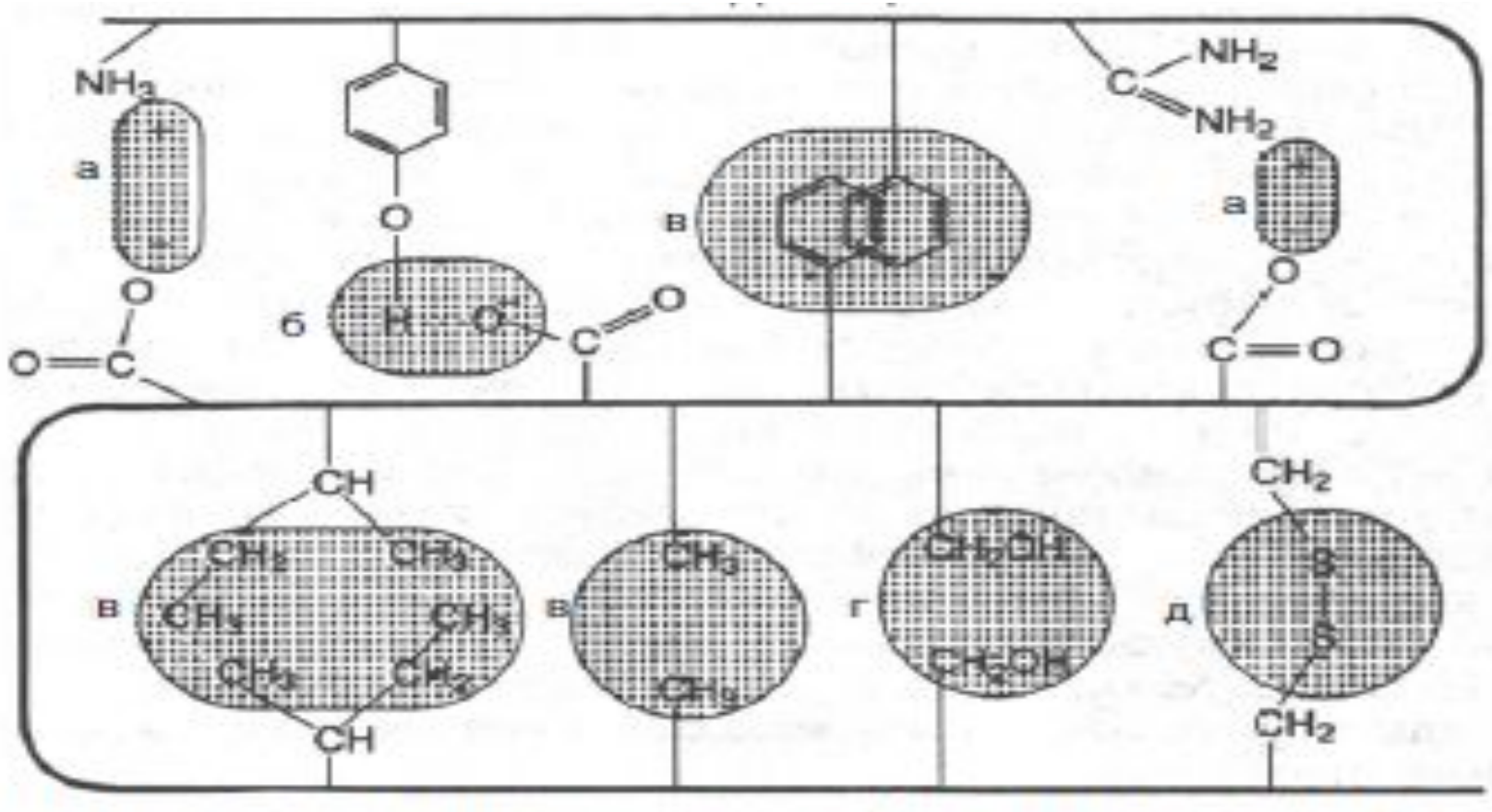
2. **Additional,** but ve hano less significant:

- disulfide
- pseudopeptide
- Ionic bonds.



- The main driving force in the emergence of a three-dimensional structure is the **interaction of amino acid radicals with water molecules**.
- In this case, the non-polar **hydrophobic radicals** of amino acids seem to sink **into the protein molecule**, forming dry zones there, while the **polar radicals are oriented towards the wa**ter (out).

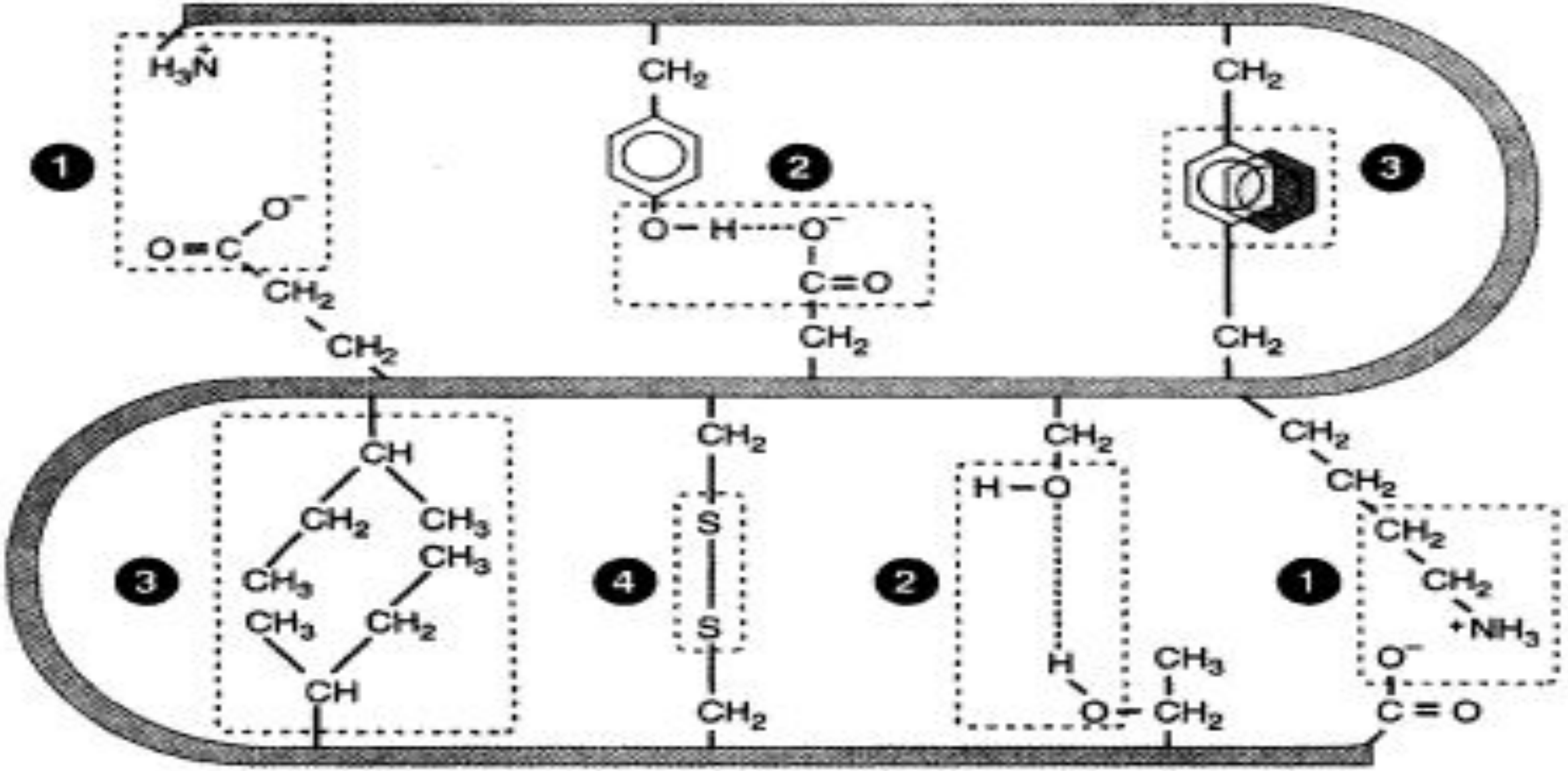
Polypeptide chain



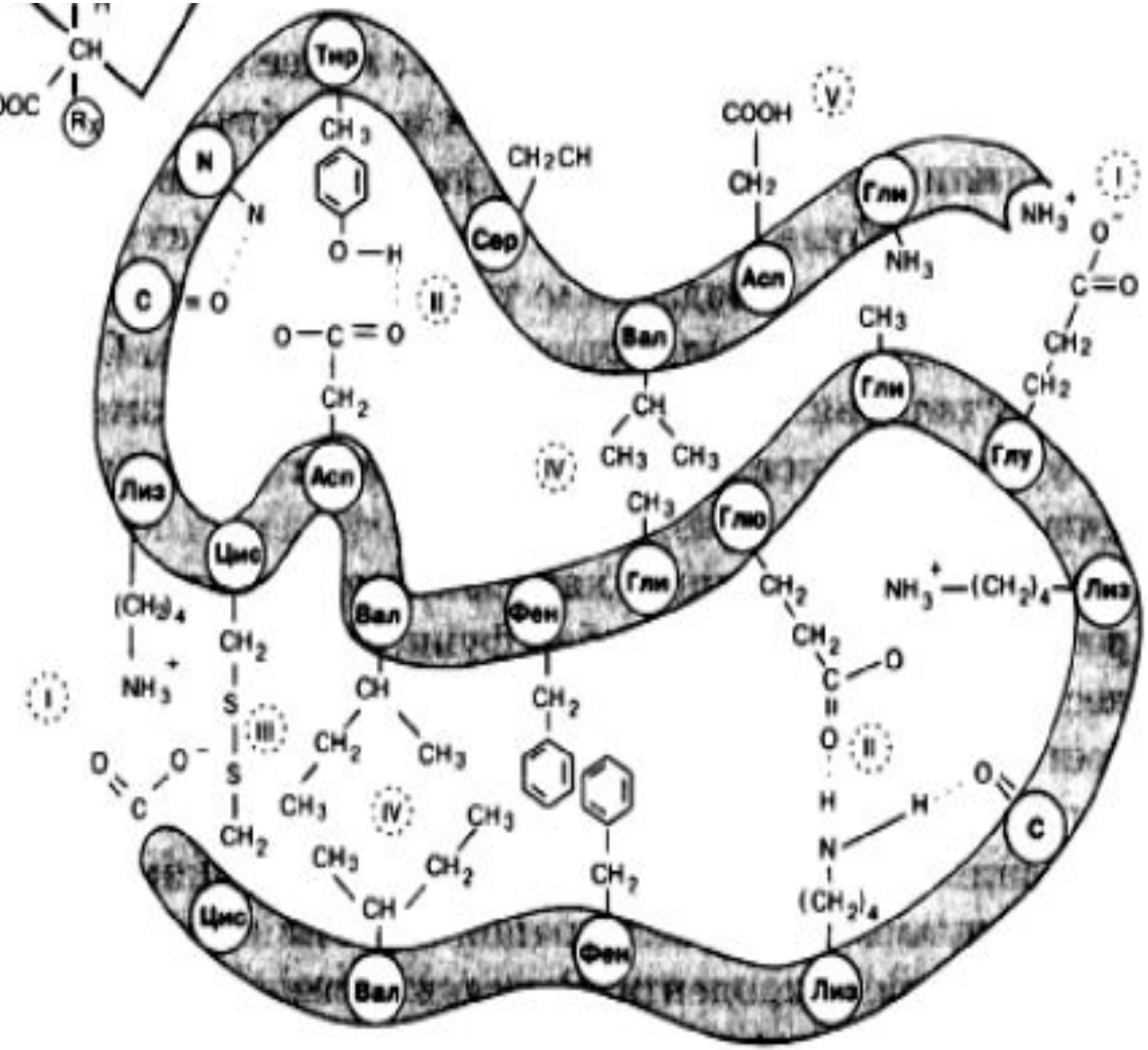
Types of non-covalent bonds stabilizing the tertiary structure:

a – electrostatic interaction; **b** – hydrogen bond;

c (в) – hydrophobic interactions of nonpolar groups; **g** (г) – dipole-dipole interactions; **d** – disulfide (covalent) bond.



1 – Ionic (electrostatic attraction); **2** – hydrogen bond;
3 – hydrophobic interactions of nonpolar groups; **4** – disulfide (covalent) bond.

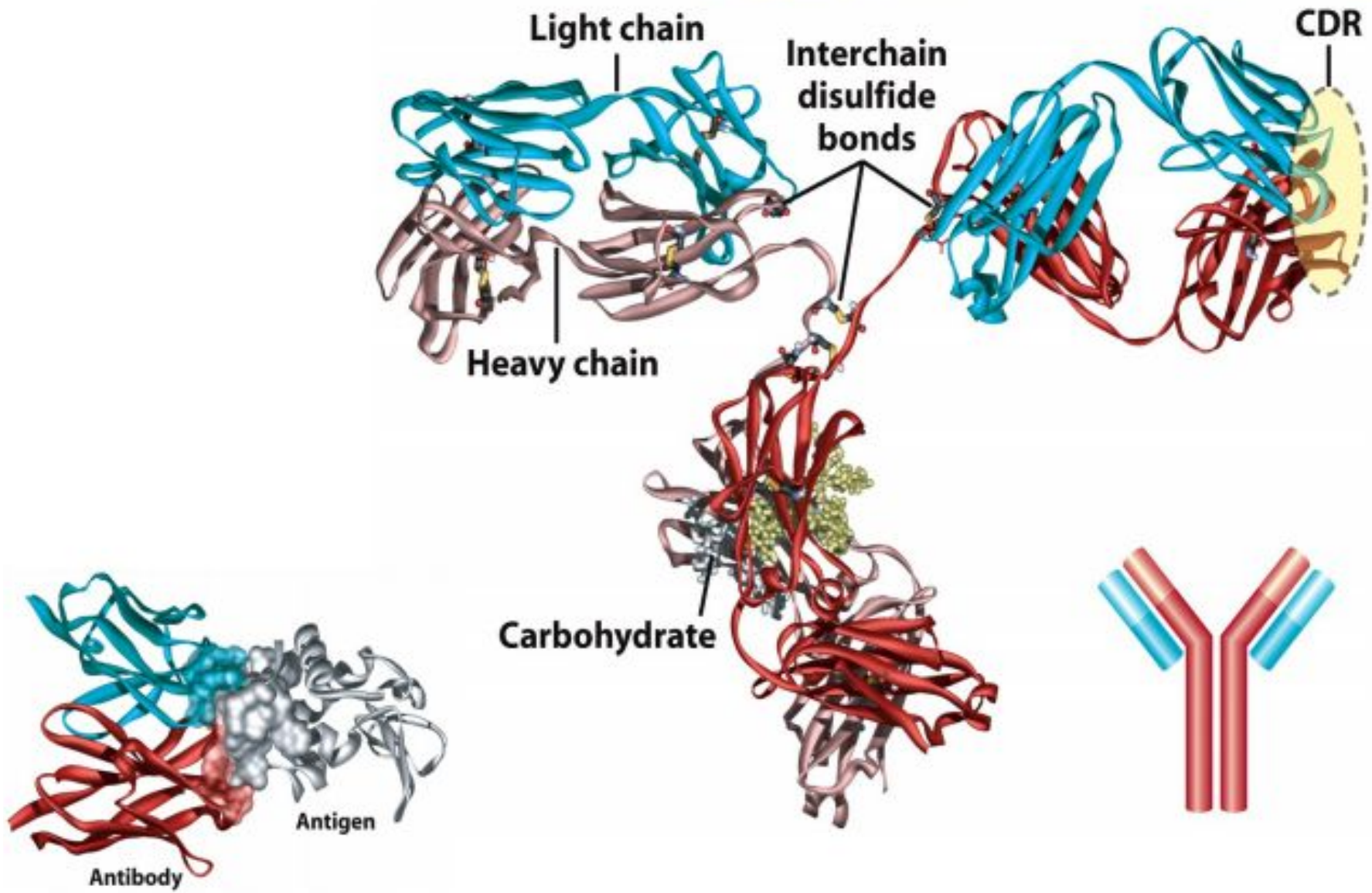


1 – Ionic (electrostatic attraction);
2 – hydrogen bond;
3 – disulfide bond
4 – hydrophobic interactions,
5 – hydrated groups.

Quaternary Structure: Multiple Polypeptide Chains Can Assemble into a Single Protein

- Proteins consisting of more than one polypeptide chain display quaternary structure; each individual polypeptide chain is called a subunit.
- Quaternary structure can be as simple as two identical subunits or as complex as dozens of different subunits. In most cases, the subunits are held together by noncovalent bonds.

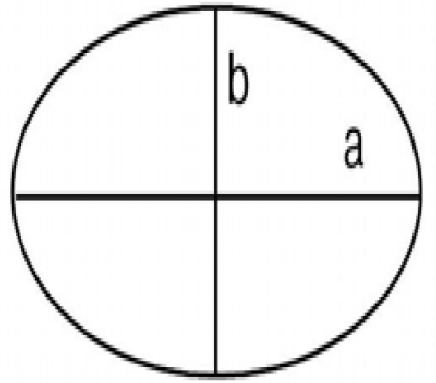
Quaternary structure



SUMMARY on Protein Tertiary and Quaternary Structures

- Tertiary structure is the complete three-dimensional structure of a polypeptide chain. Many proteins fall into one of two general classes of proteins based on tertiary structure: fibrous and globular.
- Fibrous proteins, which serve mainly structural roles, have simple repeating elements of secondary structure.
- Globular proteins have more complicated tertiary structures, often containing several types of secondary structure in the same polypeptide chain. The first globular protein structure to be determined, by x-ray diffraction methods, was the structure of *myoglobin*.
- The complex structures of globular proteins can be analyzed by examining folding patterns called *motifs* (also called folds or supersecondary structures). Domains are regions of a polypeptide chain that can fold stably and independently.
- 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, each unit called a protomer.

3. Protein classification



a / b < 10

Proteins are classified:

A) **By function** (see above - “protein functions”).

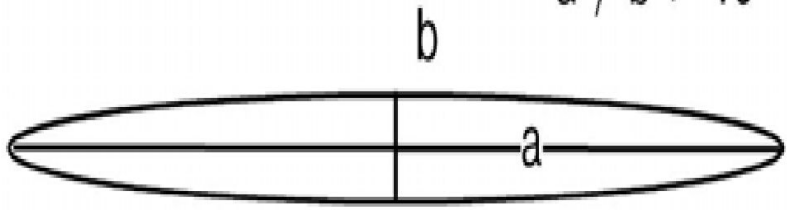
B) **By structure**:

1. by **The shape of the molecule**:

- **Globular** proteins – the ratio of the longitudinal and transverse axes is <10 and in most cases does not exceed 3-4. They are characterized by compact folding of polypeptide chains.

For example: *insulin, albumin, plasma globulins*.

a / b > 10



- **Fibrillar (fibrous) proteins** – axis ratio is >10. They consist of bundles of polypeptide chains helically wound on each other and connected by transverse covalent and hydrogen bonds.

2. By the number of protein chains in one molecule:

- ✔ **monomeric protein** - have one subunit (protomer),
- ✔ **polymer protein**– have several subunits.

For example: hemoglobin (4 subunits), lactate dehydrogenase (4 subunits), creatine phosphokinase (2 subunits), E. coli RNA polymerase (5 chains),

3. By the chemical composition:

- ✔ **Simple proteins** – contain only amino acids (*albumins, histones, protamines, collagen, elastin*).
- ✔ **Complex proteins** – in addition to amino acids, have non-protein components. A non-protein group is called **a ligand** (in ***phosphoproteins, lipoproteins, chromoproteins, glycoproteins, nucleoproteins***).

As a ligand can be :

- molecules that perform a structural function in a protein:
  - lipids, carbohydrates, nucleic acids, mineral elements,

- any other organic and inorganic compounds: *heme* in hemoglobin:
  - **copper** (Cu) in *ceruloplasmin*;
  - molecules transferred by proteins**:** ***iron*** in *transferrin*, hemoglobin residue in *haptoglobin*, ***heme*** in *hemopexin*.