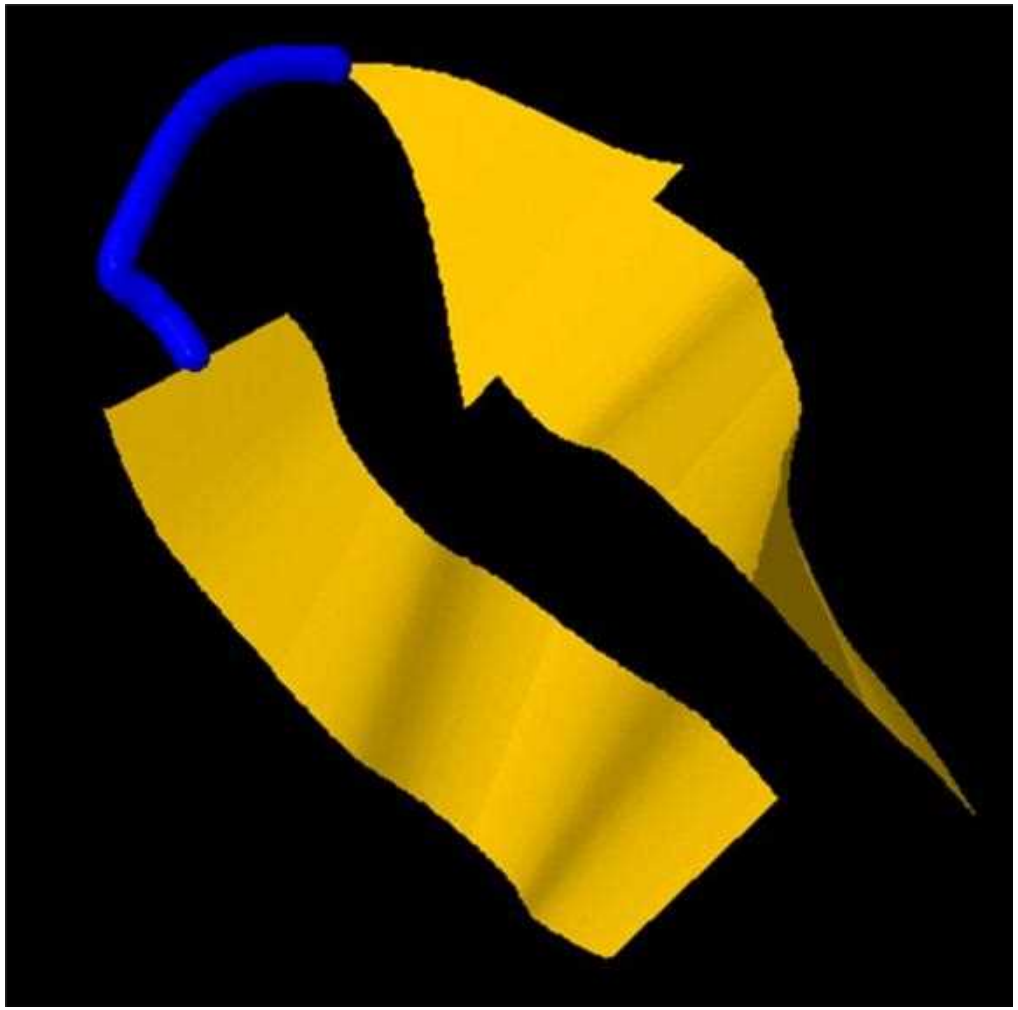
Common structural motifs

Beta-hairpin

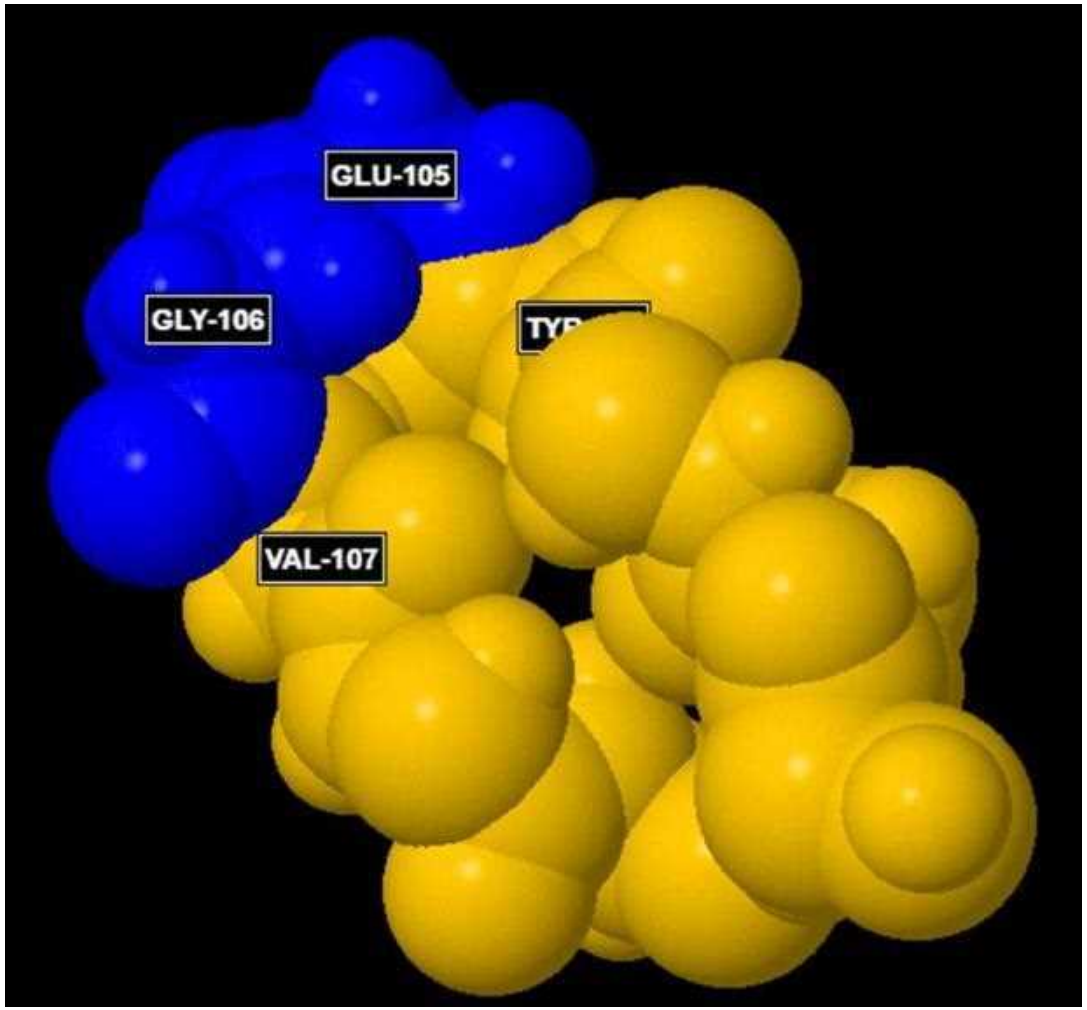
A very simple structural motif involving beta-sheets is the **beta-hairpin**, in which two antiparallel strands are connected by a short loop of two to five residues. One of these residues is often glycine or proline, as both can adopt the dihedral angle conformations required for a tight turn or beta-bulge loop. Individual strands can also be connected in more complex ways by longer loops that may contain alpha-helices.

Beta-hairpin in Intestinal Fatty acid binding protein (I-FABP)

Beta-turn in I-FABP
Nine residues are shown



Space-filling model without side chains. Note the tight packing of the backbone atoms in the turn (residues 104–107).

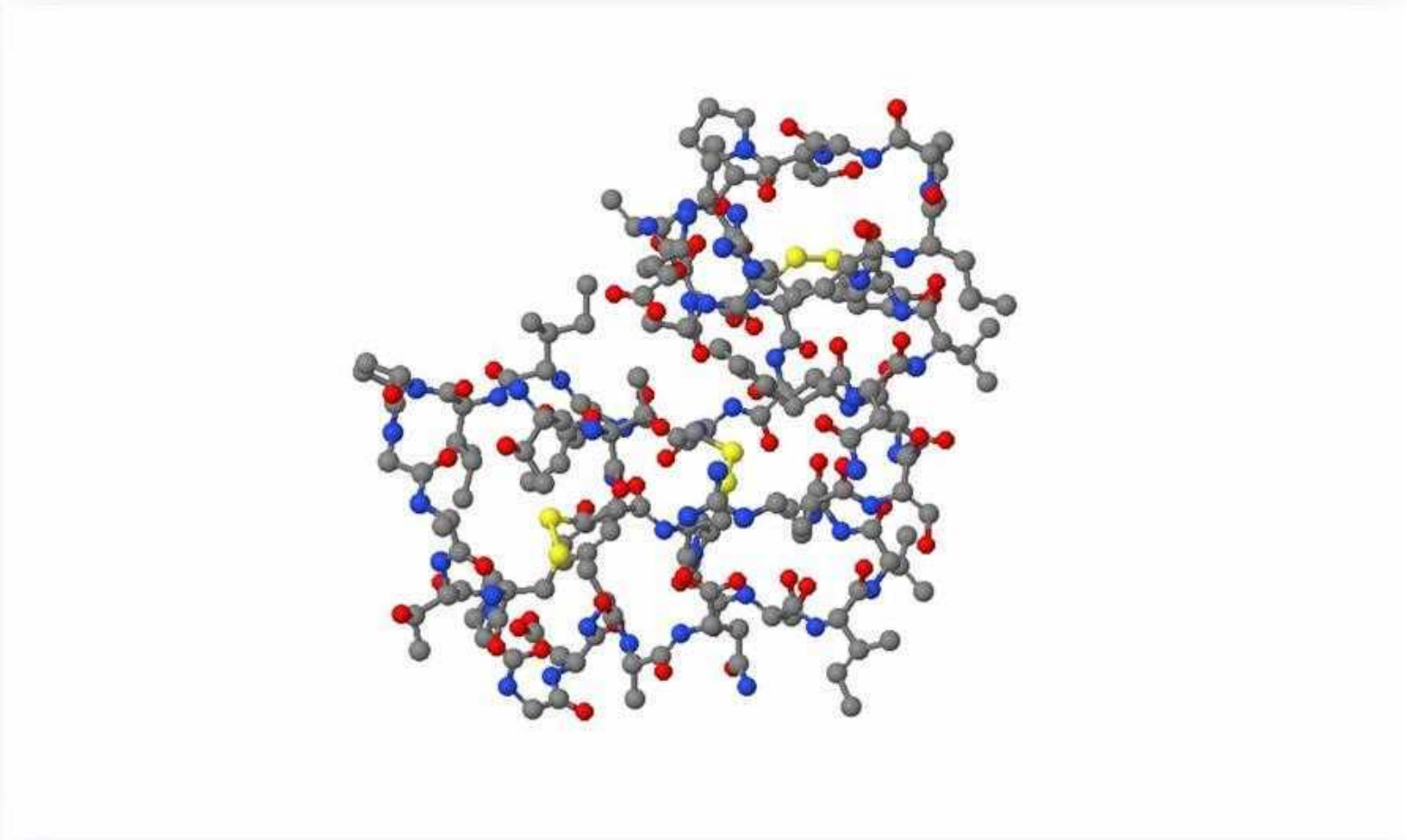


Jsmol (Jmol) - a Java program for visualizing 3D molecular structures

The concept of a β-sheet is elegant, but recognizing them in protein structures would be nearly impossible without Jsmol's ability to display β-sheet as arrows.

Jmol advantages:

- Availability: Free to use and open source.
- Cross-platform: Runs on Windows, macOS, Linux, and web browsers.
- Educational features:
- Support for educational materials and interactive tasks.
- Ability to create scenarios to demonstrate chemical processes



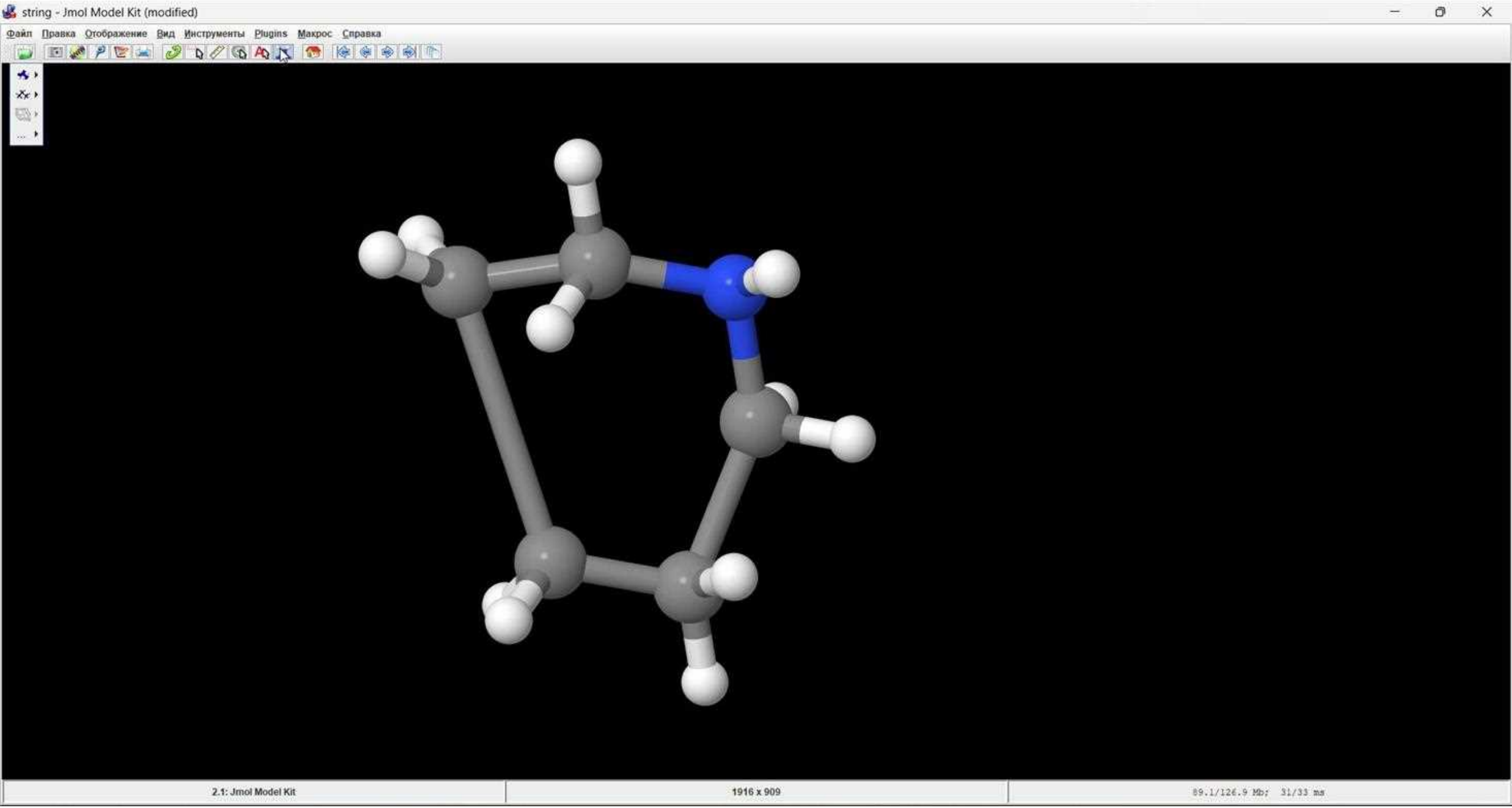
Where can Jmol be used?

In education:- Demonstration of molecular structures.

In research:

- Analysis of protein and DNA structures.
- Visualization of molecular modeling results.

Supports formats: PDB, CIF, XYZ, and others.


string - Jmol Model Kit (modified)
Файл Правка Отображение Вид Инструменты Plugins Макрос Справка
2.1: Jmol Model Kit
1916 x 909
89.1/126.9 Mb; 31/33 ms

2.1: Jmol Model Kit

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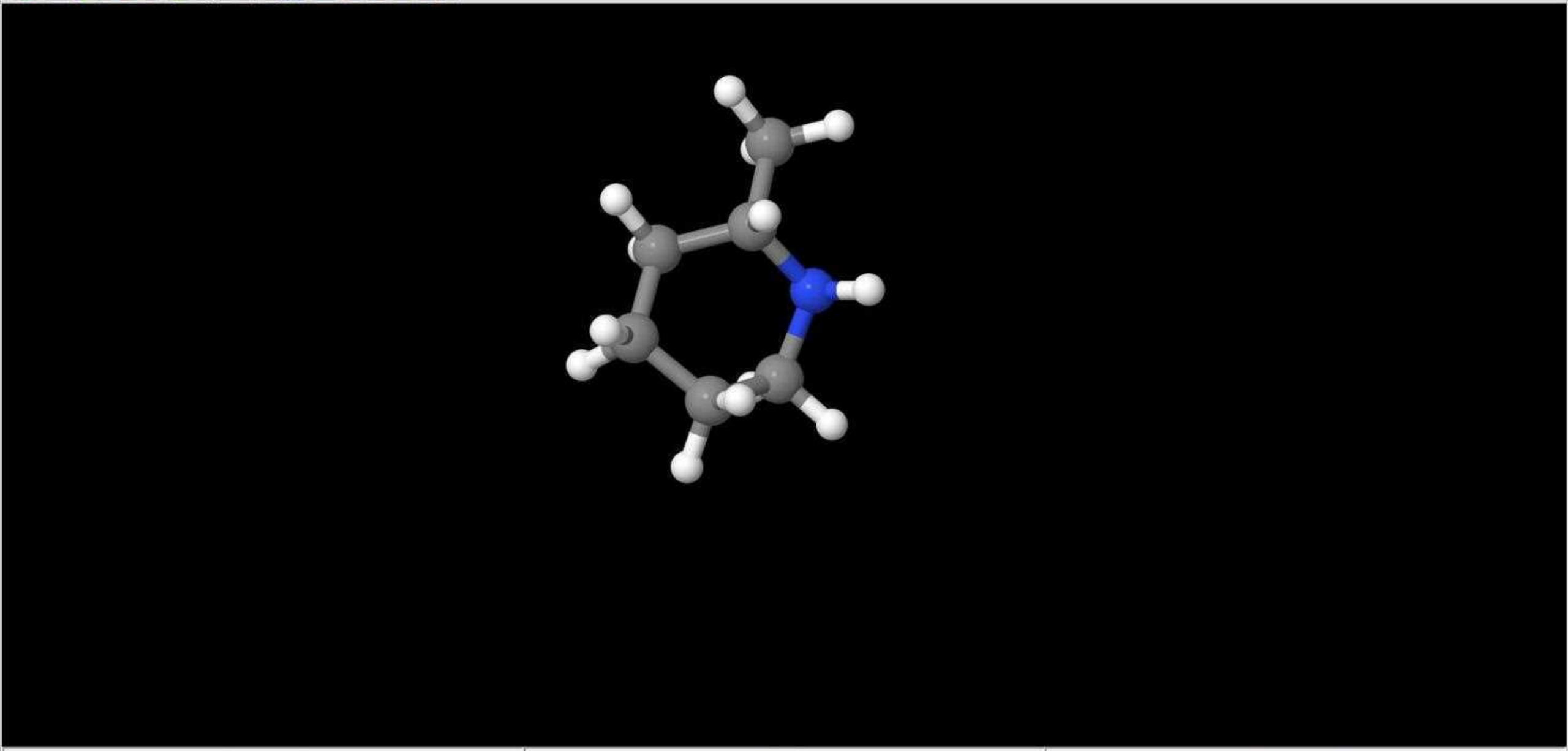

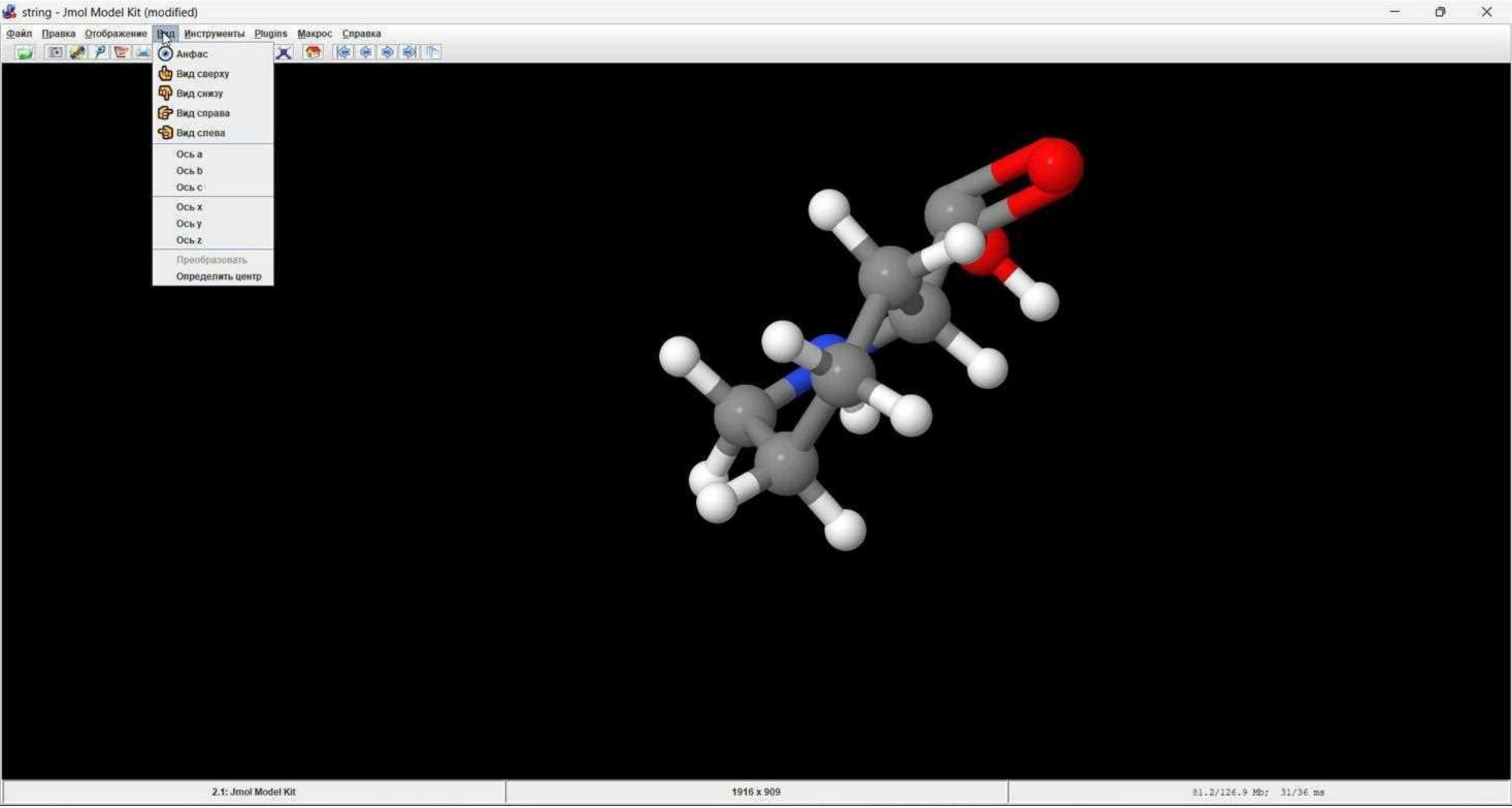
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Анфас
Вид сверху
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Вид слева
Ось a
Ось b
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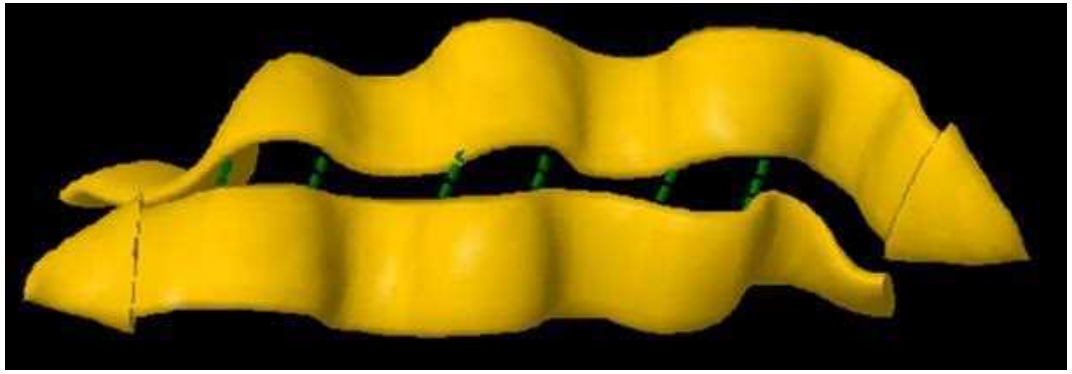
Ось x
Ось y
Ось z
Преобразовать
Определить центр
2.1: Jmol Model Kit
1916 x 909
81.2/126.9 Mb; 31/36 ms

PyMOL - program for visualizing 3D molecular structures

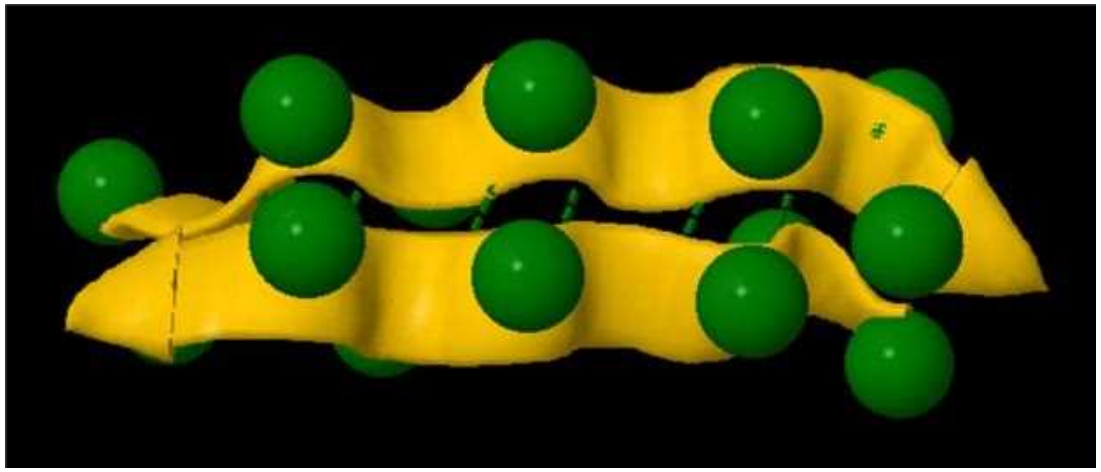
To visualize the structure of peptides and proteins you will use the PyMOL.
The professor B. He will tell you about it later.
 Link: https://ww/pyymol.org/

β-sheet

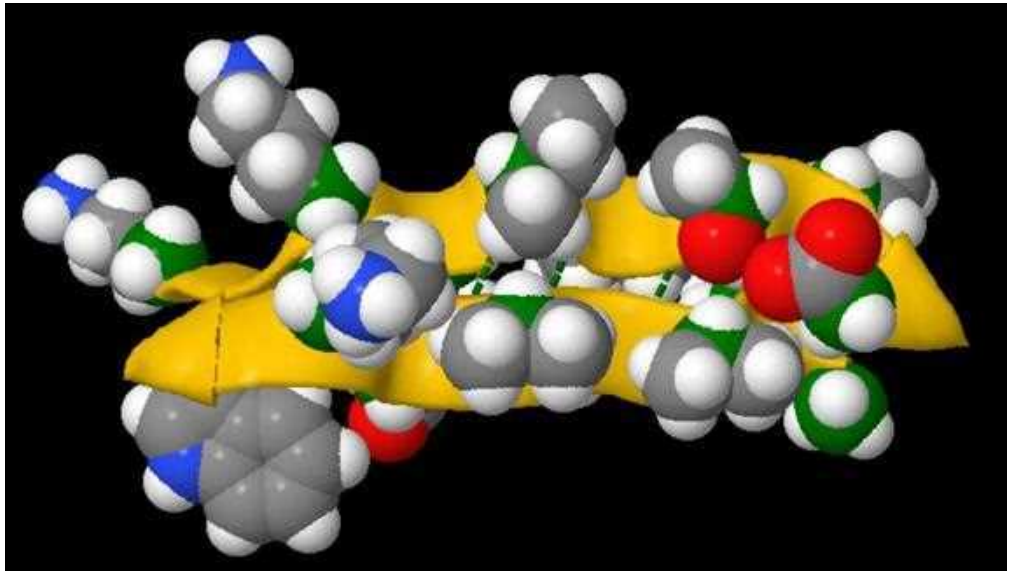
The arrowhead always indicates the C-terminus of the strand



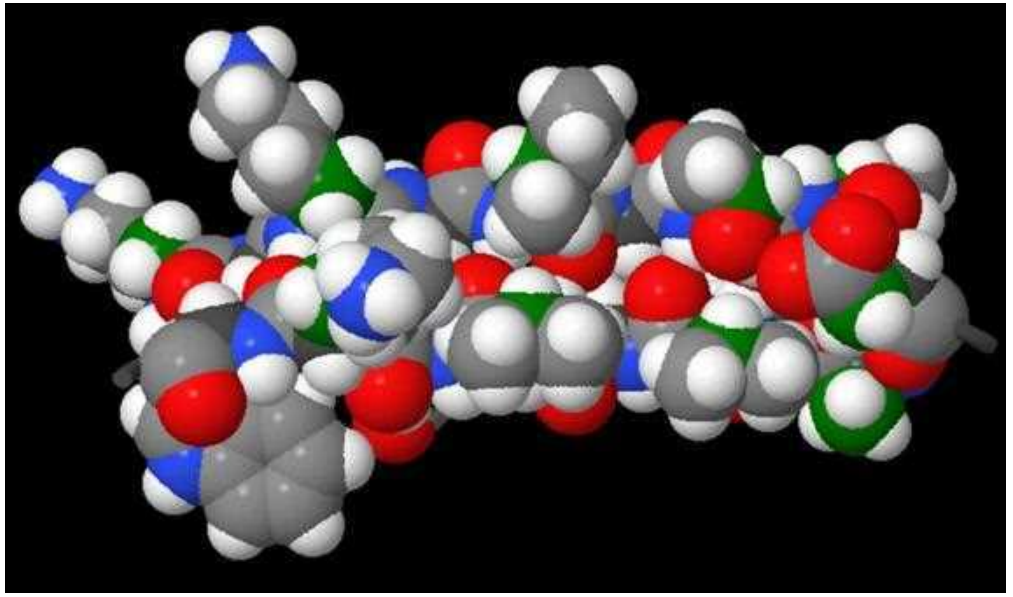
The β-carbons of the two chains are shown. Note the very regular pattern of β-carbons alternating above and below the main band



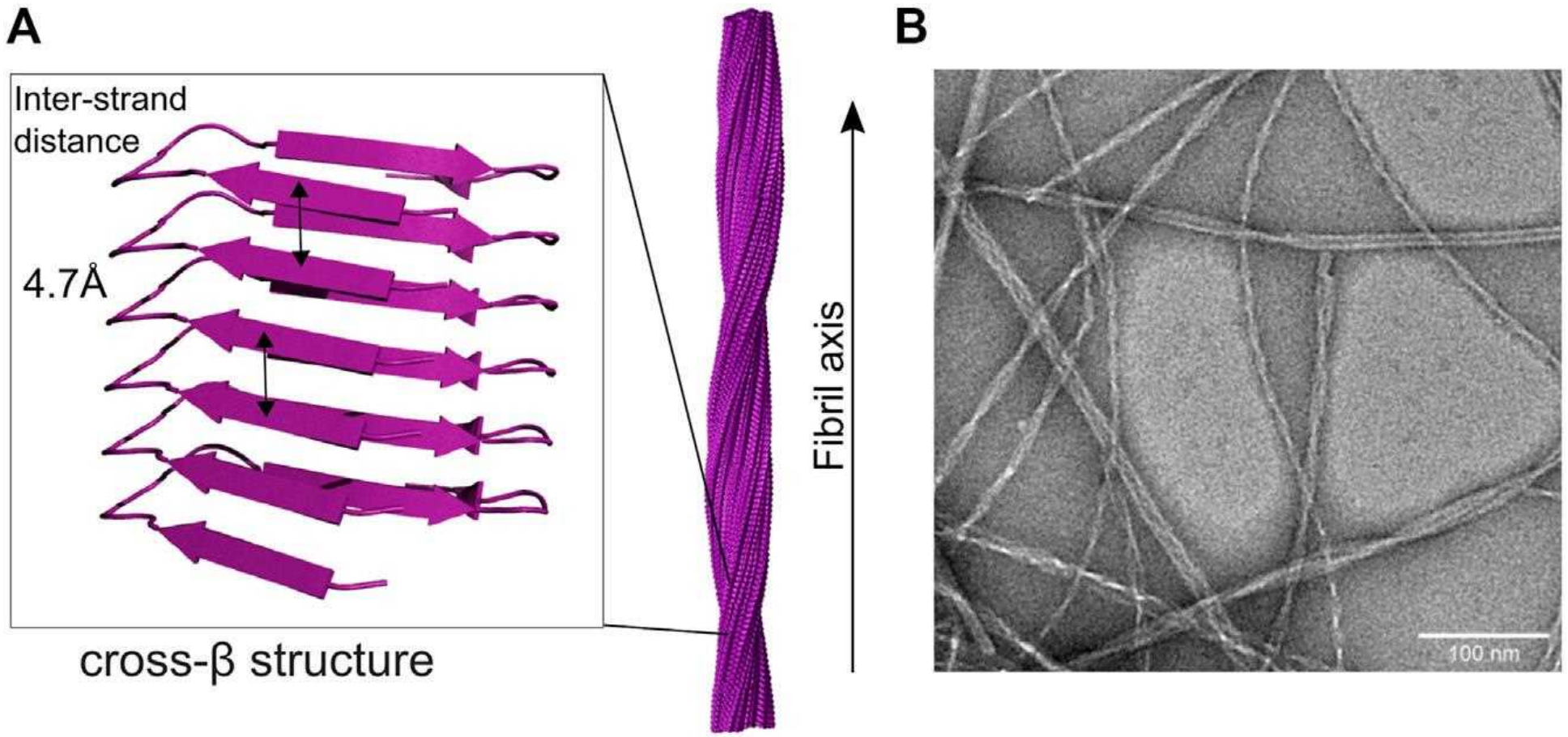
The side chains in the β-sheet are shown. β-carbons are shown in green



Both strands. The α-carbons are colored dark gray



B-sheet is involved in the formation of fibrils



Cross-beta and fibril structure of amyloid fibrils (**A**) in the fibril, monomers form beta-sheet structures along the long axis of the fibril, with beta strands arranged perpendicular to the fibril axis. The characteristic spacing of the sheets gives rise to typical diffraction peaks, hence cross-beta structure. Multiple protofilaments twist around each other, thereby forming the elongated fibril structure [here seen for IAPP (Röder et al., 2020)] (**B**) The twisted, elongated fibril structure can be seen under the electron microscope, here for IAPP fibrils. Note the polymorphism of the observed fibrils.

10.3389/fmolb.2022.1045616

Situational tasks

1. What types of bounds are formed between:

a) arginine radicals and glutamic acid;

b) water molecule and tyrosine radical;

c) isoleucine radicals and leucine.

Support your answer with relevant/corresponding drawings.

2. Identify which of the following peptides is more polar:

A). Lys-Asp or Asp-Tyr; B) Phe-Glu or Tyr-Thr

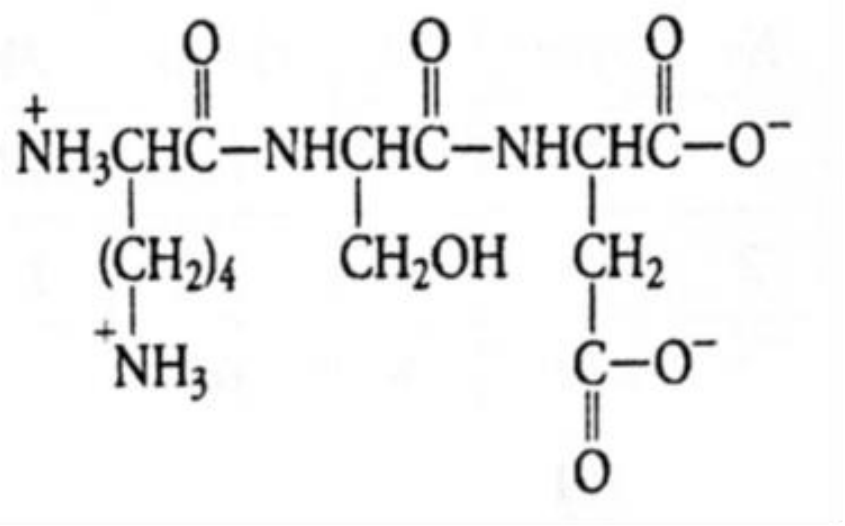
Explain your answer.

3. From each pair choose an amino acid, radical of which more likely will participate in the formation of hydrophilic protein shell:

A) Lys or Leu; B) Ser or Ala; C) Phe or Tyr; D) Val or Thr

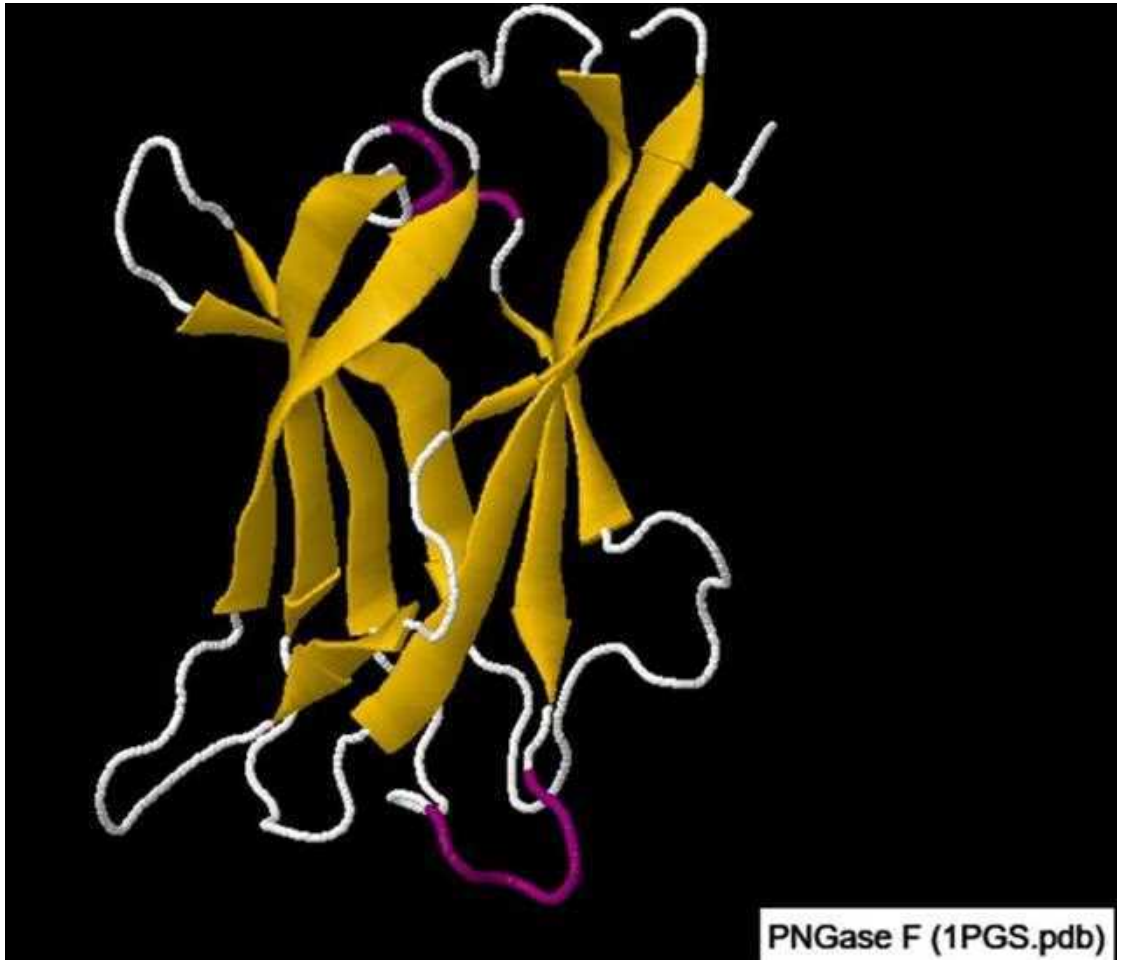
Situational tasks

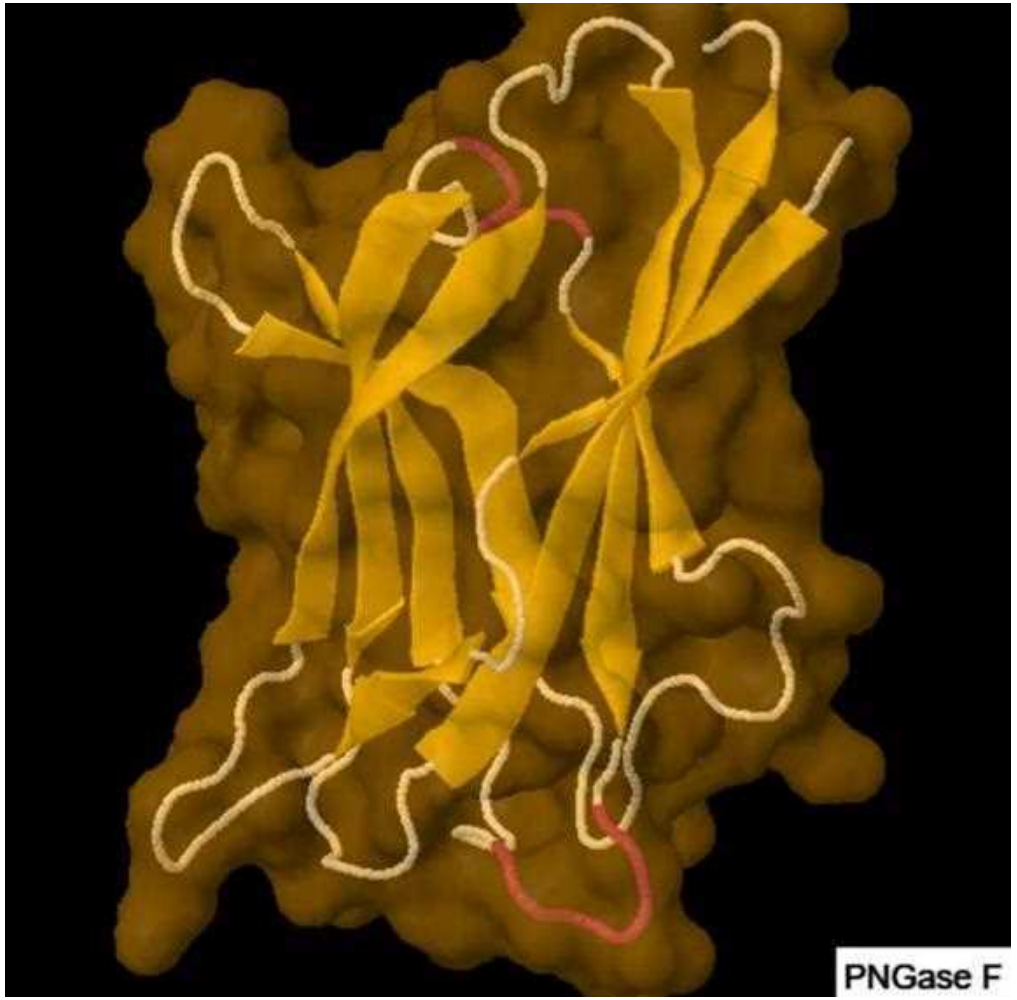
4. Write the structure of each peptide at pH=10. Identify peptide bounds, N-terminus and C-terminus. There are: A). Alanine-phenylalanine; B). Glutamyl-lysine; C). Glutamyl-tyrosine.
5. Write the structure of each peptide at pH=12. Identify peptide bounds, N-terminus and C-terminus. There are: C). Phenylalanine-leucine.
6. There is a tripeptide:
A). Name the tripeptide;
B). Determine at which pH, tripeptide is in this state



Beta-Sandwiches

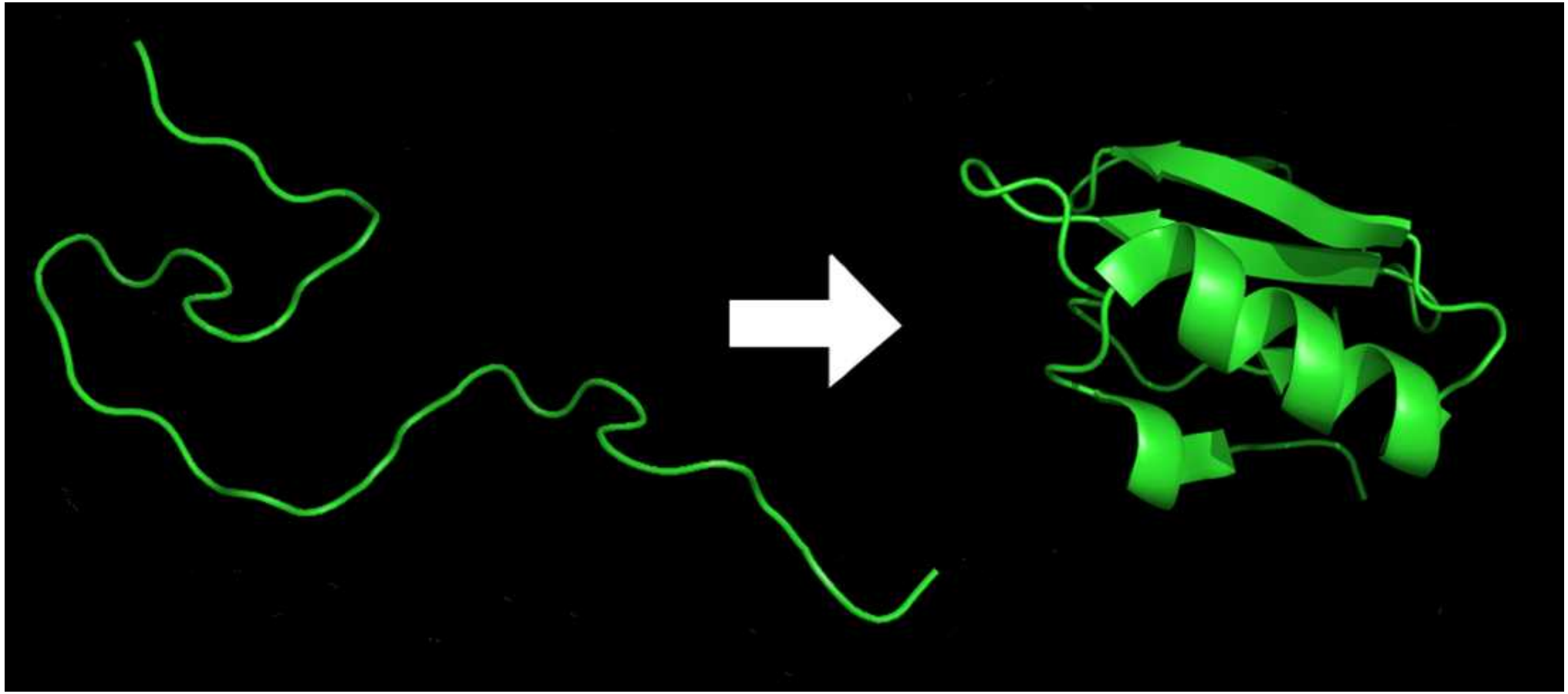
The simplest all-beta fold is the beta-sandwich, in which two essentially independent sheets pack face-to-face, forming a sandwich-like structure. The two beta-sheets are typically twisted. The sheets packing at an angle to each other allows for efficient interdigitation of the inward-pointing side chains. The beta-sandwich is the most common of all known protein folds in the Structural Classification of Proteins (SCOP) database, largely due to its simple yet versatile design





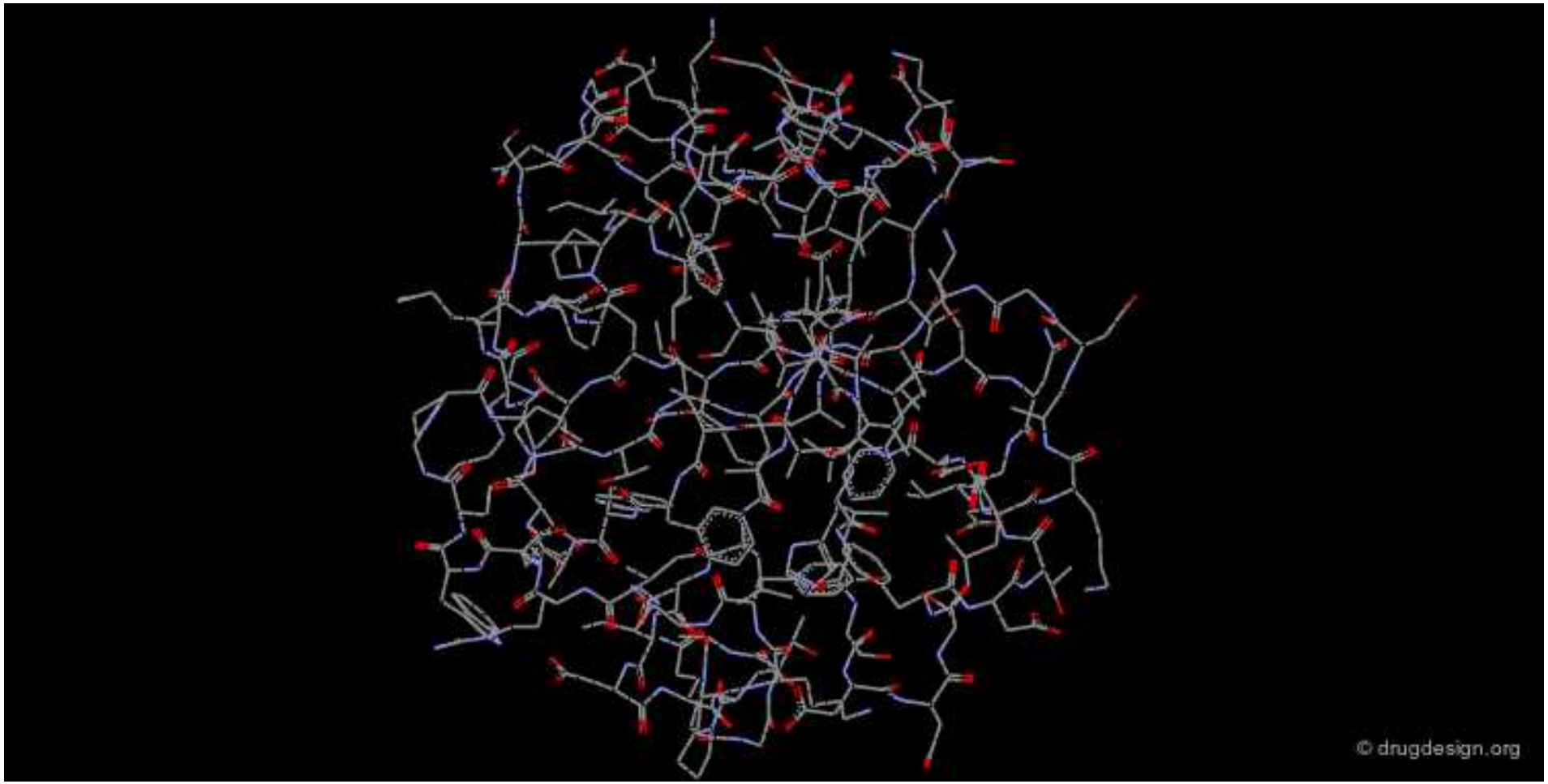
Tertiary structure of protein -packing of the polypeptide chain in space

- *The tertiary structure of a protein is formed by additional folding of the peptide chain due to intramolecular interactions of side radicals.*



Tertiary structure of protein -packing of the polypeptide chain in space

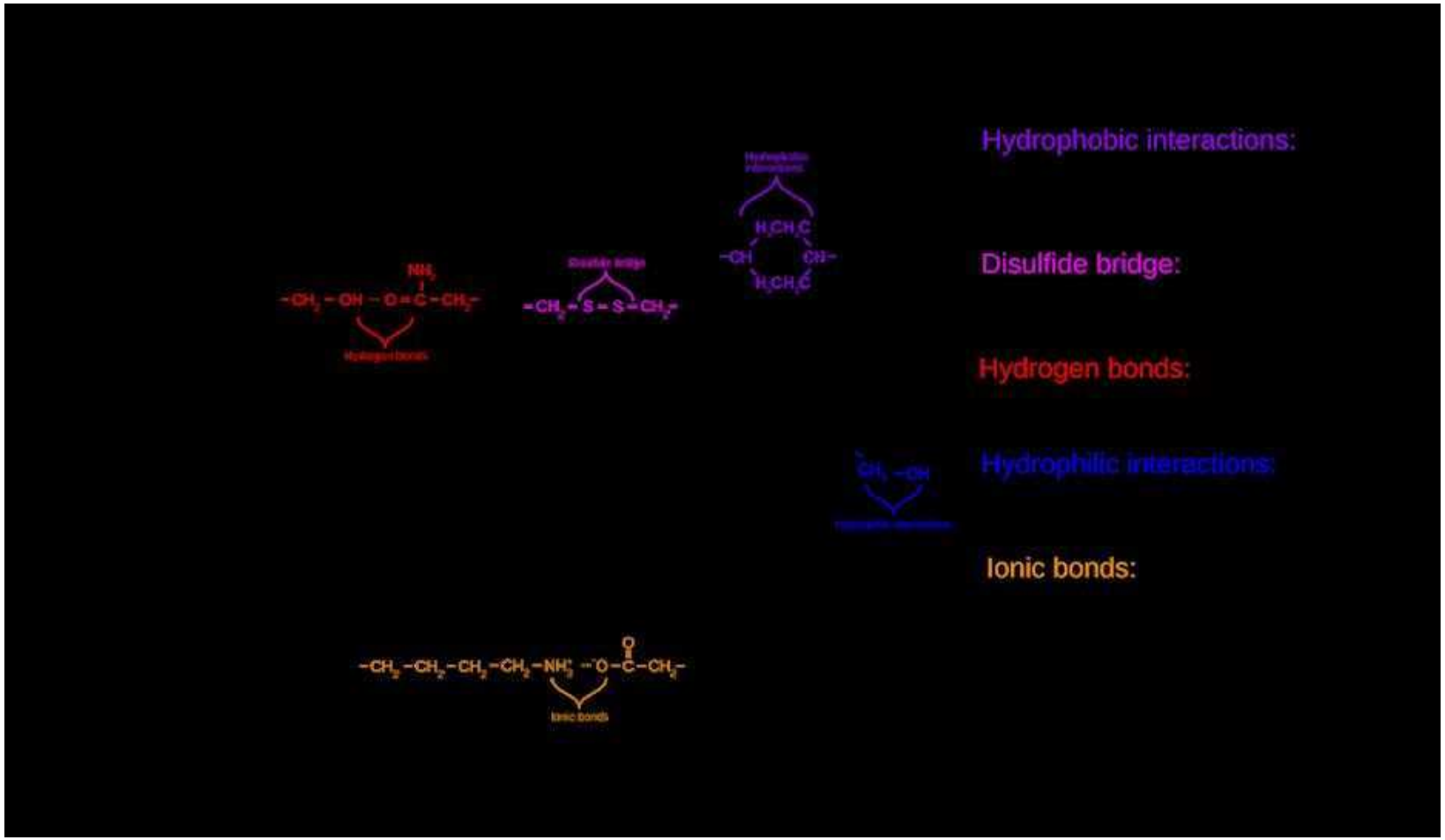
- *The main driving force behind the formation of three-dimensional structure is the interaction of AA radicals with water molecules.*
- *Non-polar hydrophobic amino acid radicals group within the protein molecule and form "dry" hydrophobic zones. Polar radicals are oriented toward water*

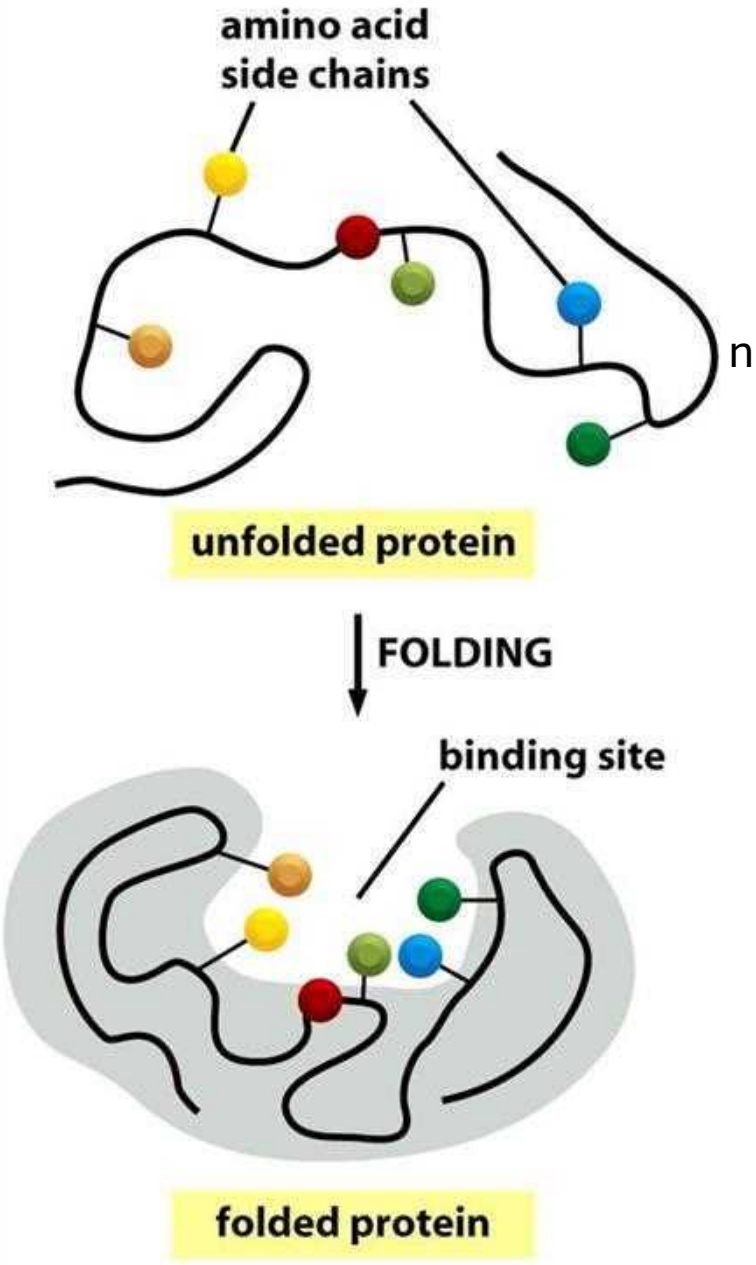


Tertiary structure of protein

The tertiary structure is formed by:

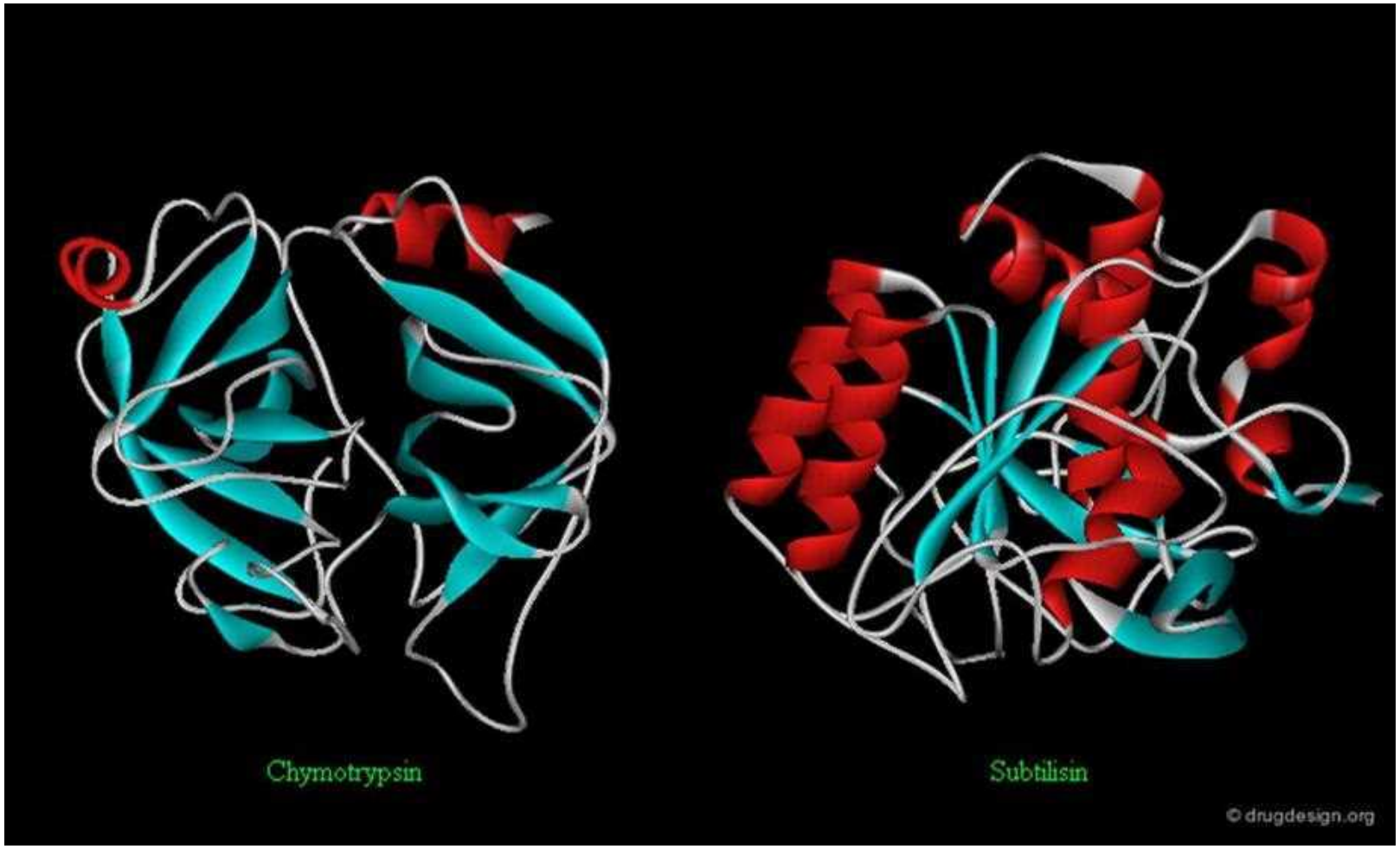
- the formation of a covalent disulfide bond (between cysteine radicals)
- the emergence of non-covalent interactions between side radicals: ionic, hydrogen, and hydrophobic





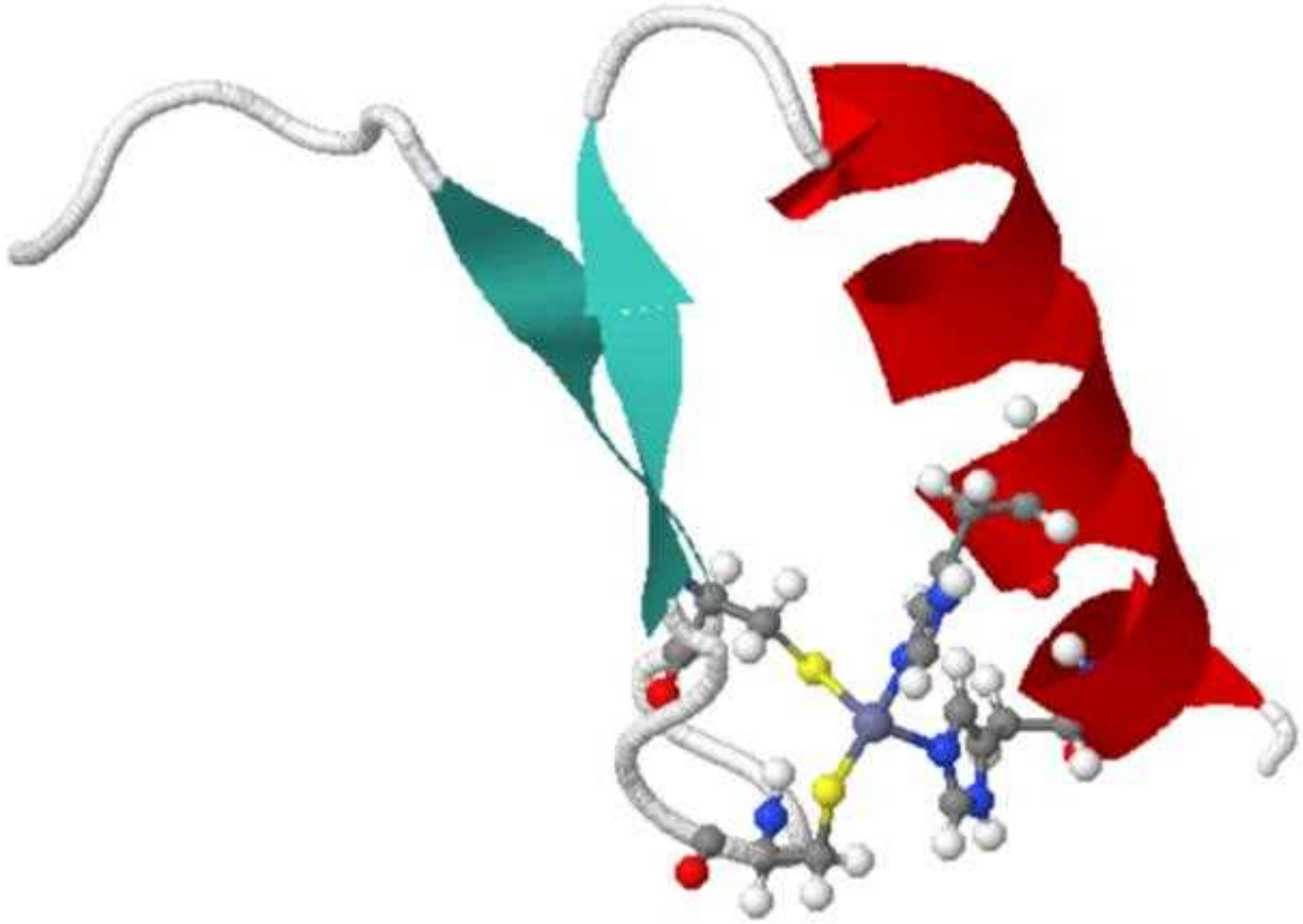
Protein Folding and Functions

It's important to note that the presence of a common fold is not necessarily associated with any functional classification. In general, a particular type of function is not limited to a particular fold, and a particular fold is not limited to a particular type of function. For example, the following two enzymes (chymotrypsin and subtilisin) are serine proteases: they have the same catalytic mechanism, but they fold very differently



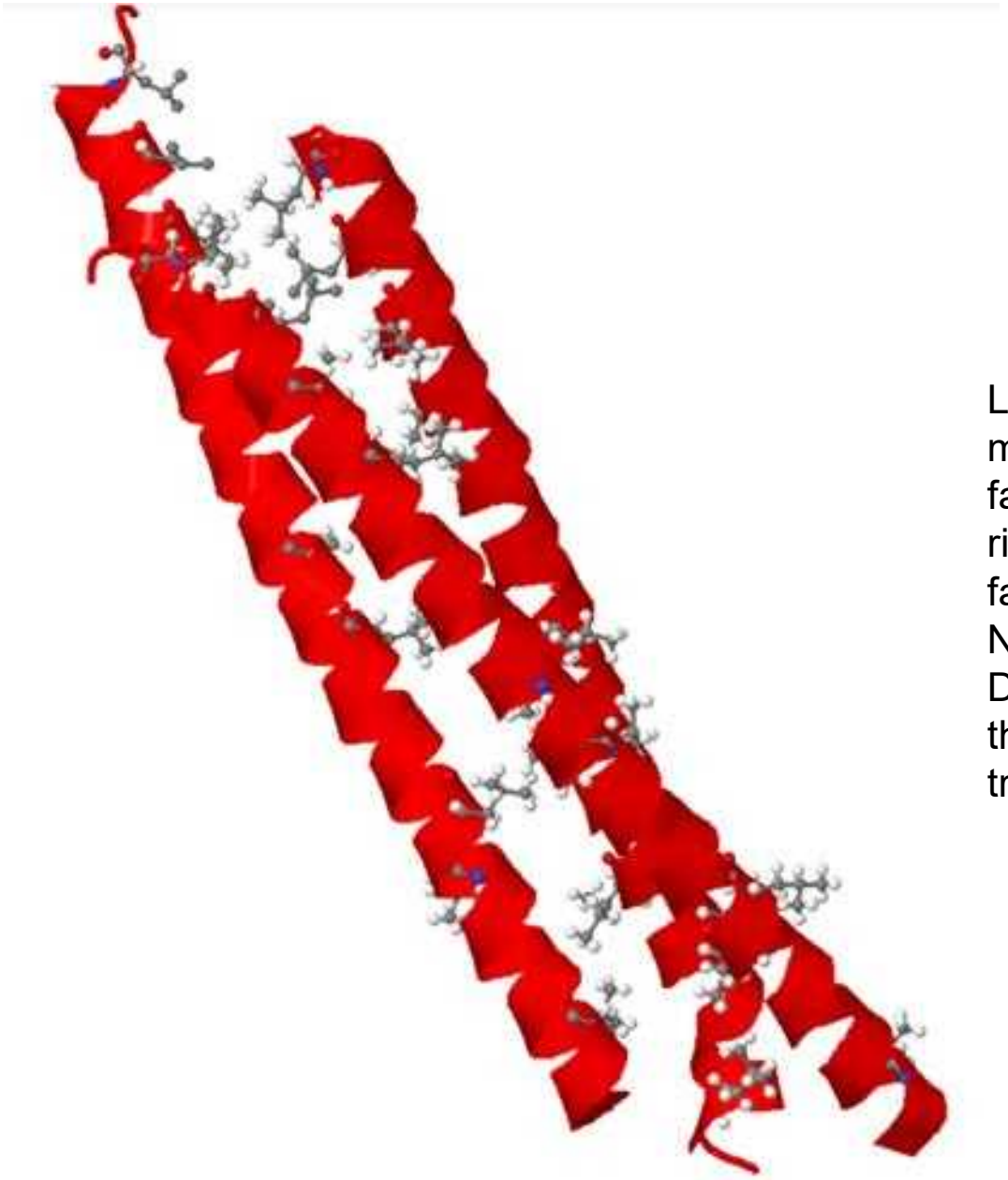
Domain’s

A domain is a compactly folded part of a polypeptide chain, consisting of approximately 150-200 amino acids and performing specific functions



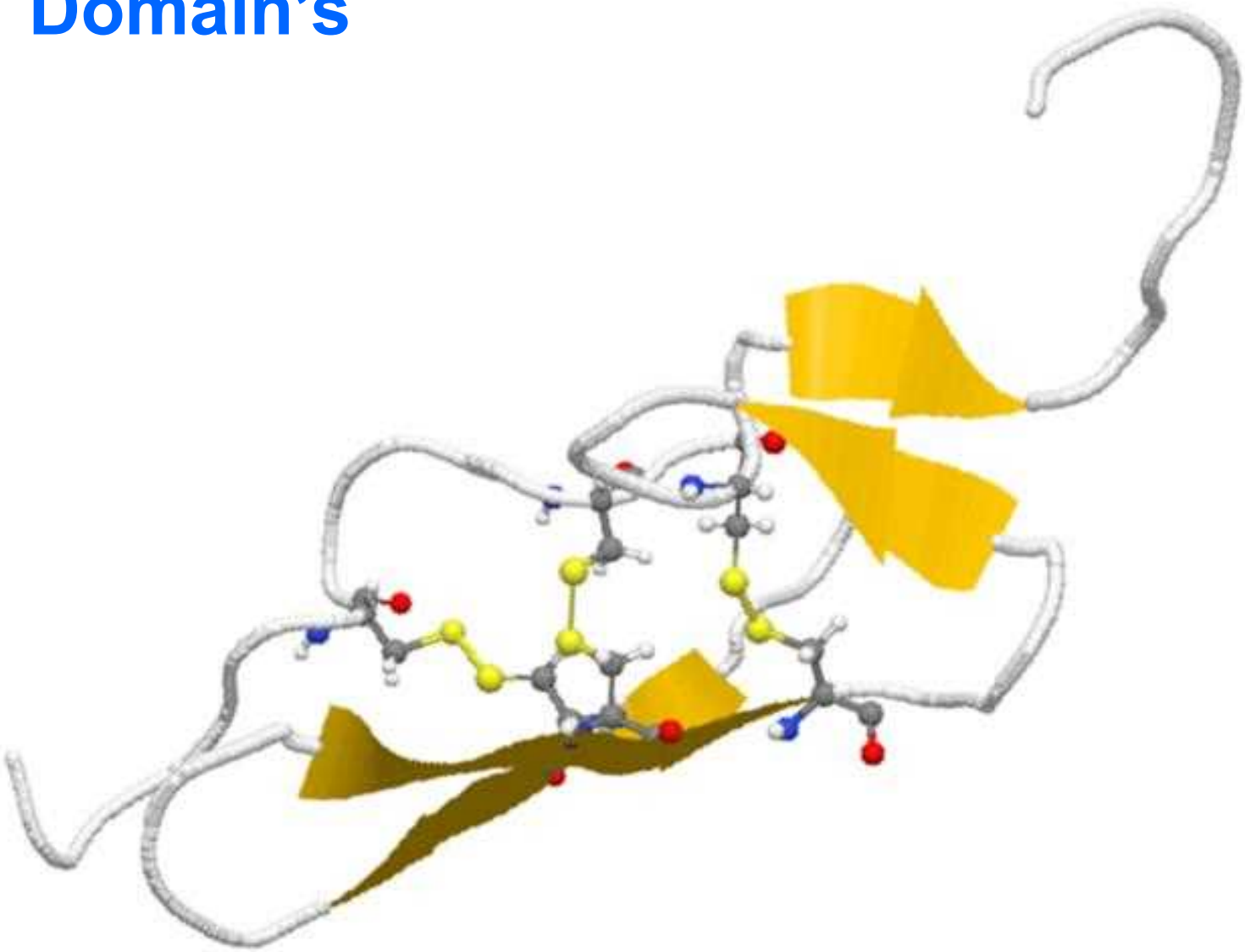
Zinc finger is defined as a versatile DNA-recognition element characterized by a short stretch of 30 amino acids that binds zinc ions (Zn2+) which stabilizes the fold

Domain’s



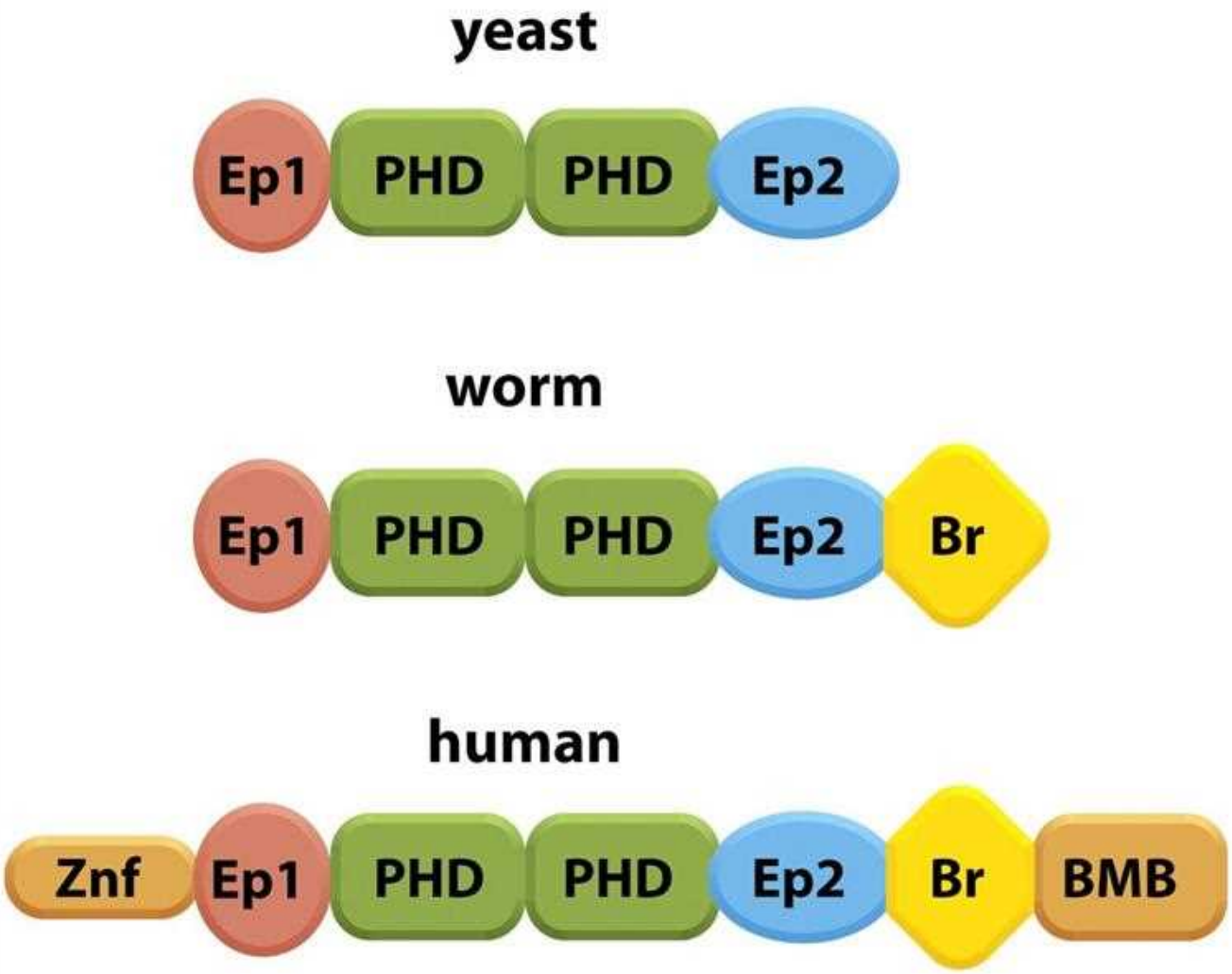
Leucine zipper refers to a structural motif found in certain transcription factors, characterized by a leucine-rich region at the C-terminus that facilitates dimerization and a basic N-terminal domain that enables DNA binding. This motif is pivotal in the function of basic leucine zipper transcription factors

Domain’s



An EGF-like domain is a protein domain with a structure similar to the epidermal growth factor (EGF), typically 30–45 amino acids long, and characterized by six conserved cysteine residues. These domains form disulfide bonds and are found in many proteins, often involved in cell signaling, protein-protein interactions, and calcium binding

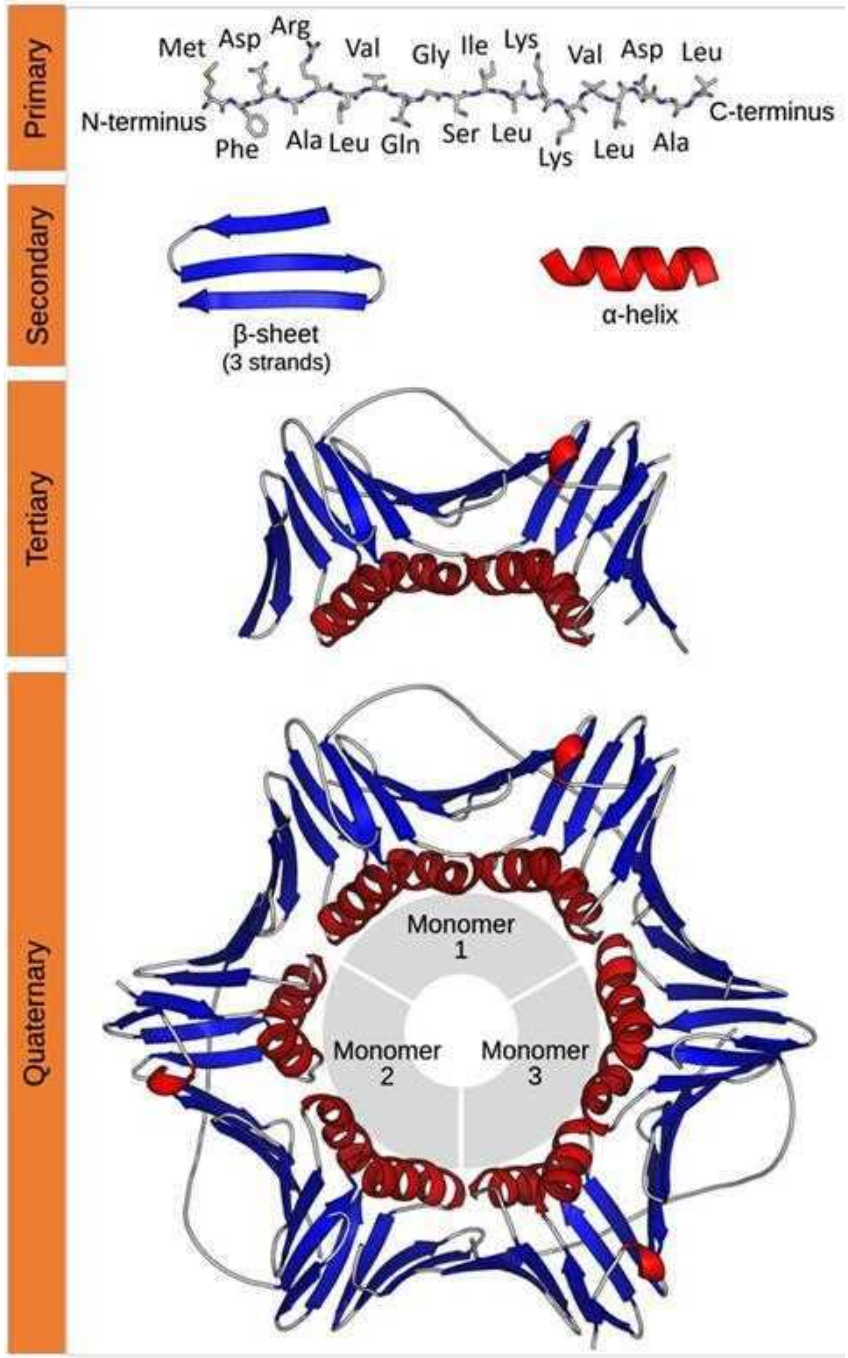
Domain’s



Domain structure of a group of evolutionarily related proteins that are thought to have a similar function. In general, there is a tendency for the proteins in more complex organisms, such as humans to contain additional domains - as is the case for the DNA-binding protein compared here

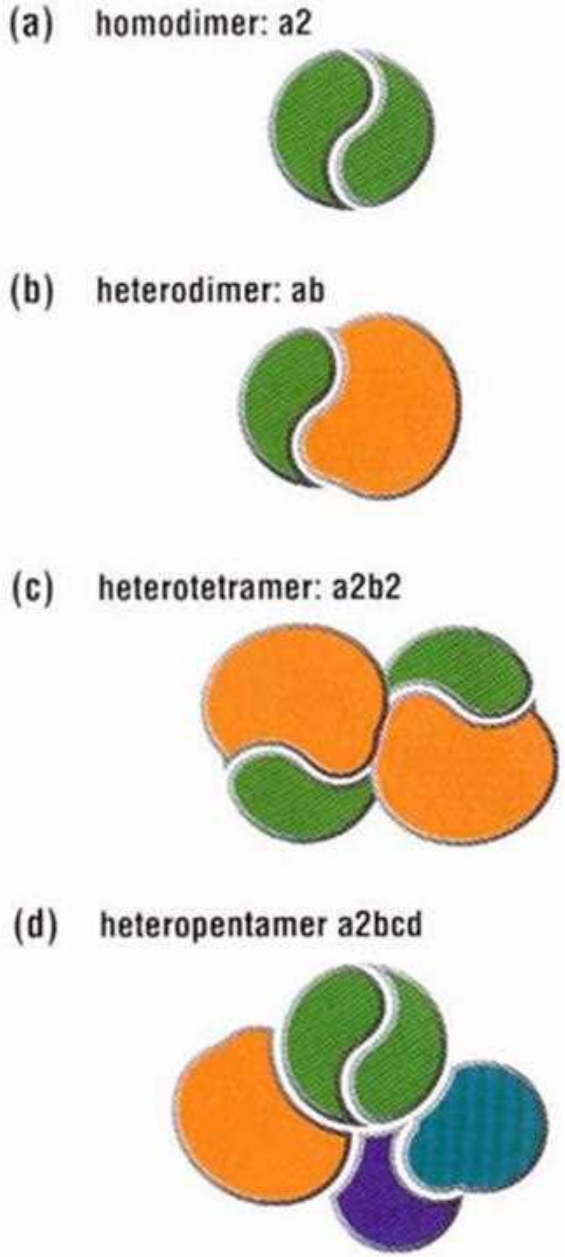
Quaternary Structure of Proteins

- Proteins with multiple polypeptide chains have a quaternary structure, which is formed by the association of several polypeptide subunits.
- Quaternary structure is the spatial arrangement and interactions between polypeptide units. These subunits work together to form a complex oligomeric protein.
- The molecular interactions of quaternary structure are the same as those of tertiary structure: hydrogen and ionic bonds, hydrophobic interactions, and disulfide bonds.
- While tertiary interactions exist between amino acids of a single polypeptide chain, quaternary interactions exist between different polypeptide chains.



Quaternary Structure of Proteins

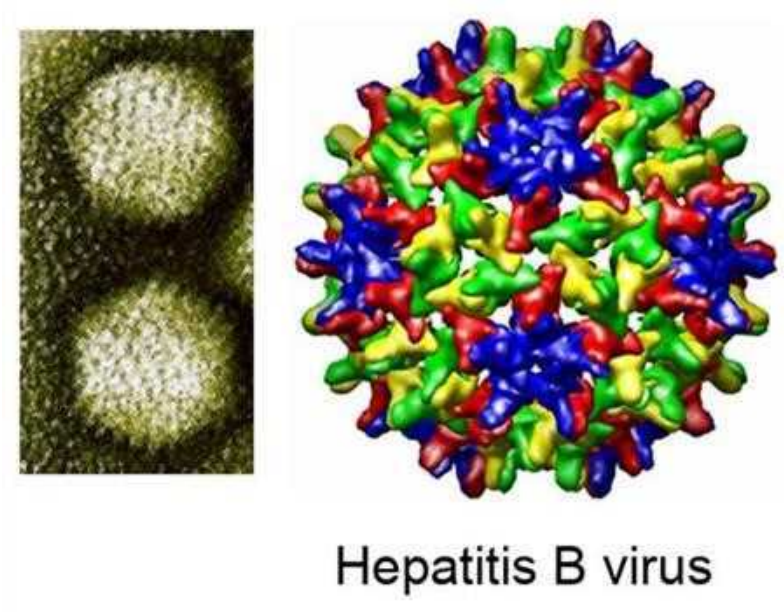
- The assembly of several polypeptide chains into a single coherent structure.
- The arrangement of the subunits results in the formation of a stable structure.
- The subunits may be identical or different.
- A common abbreviation for describing such proteins is the use of Greek letters for each subunit type and a subscript to indicate the number of units.
- A protein designated α2βγ consists of two α units and one β and γ unit each.



Quaternary Structure of Proteins

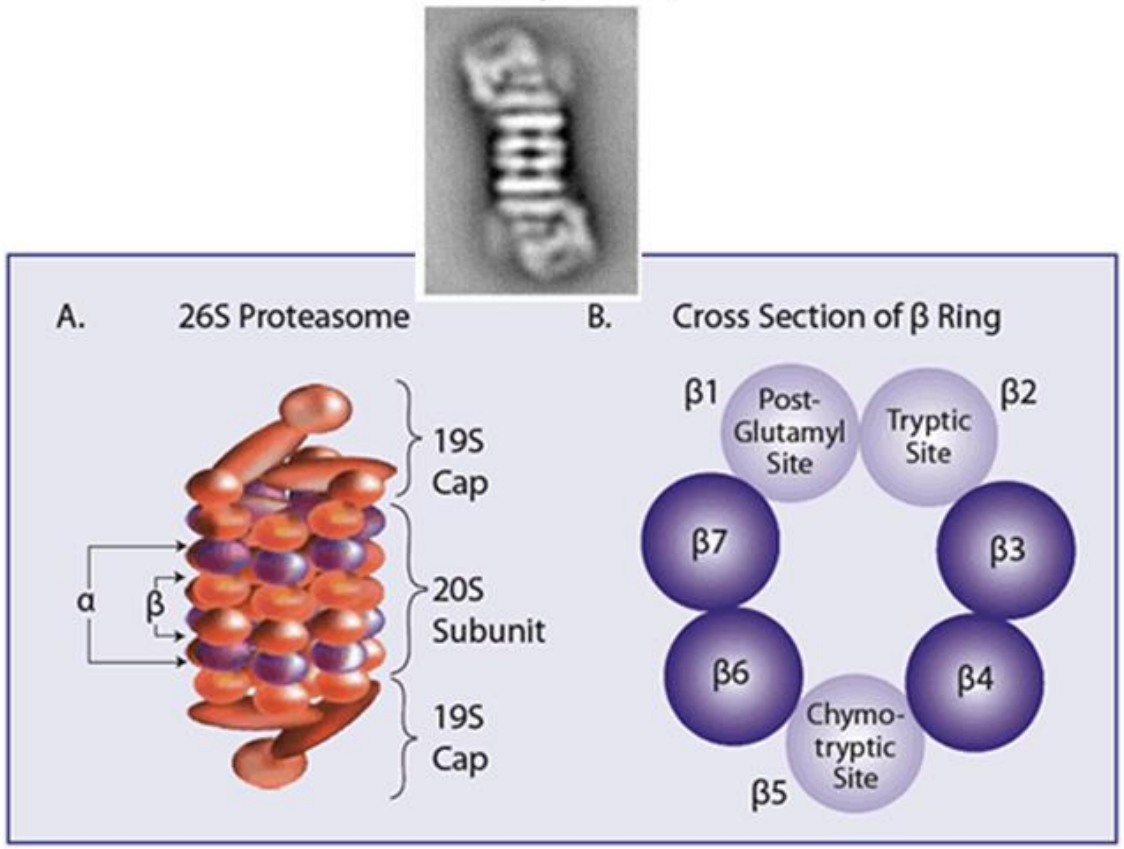
The quaternary structure adds stability by:

- Reducing the surface-to-volume ratio of the smaller subunit
- Simplifying the construction of large complexes



Hepatitis B virus

Viral capsids often consist of multiples of 60 proteins

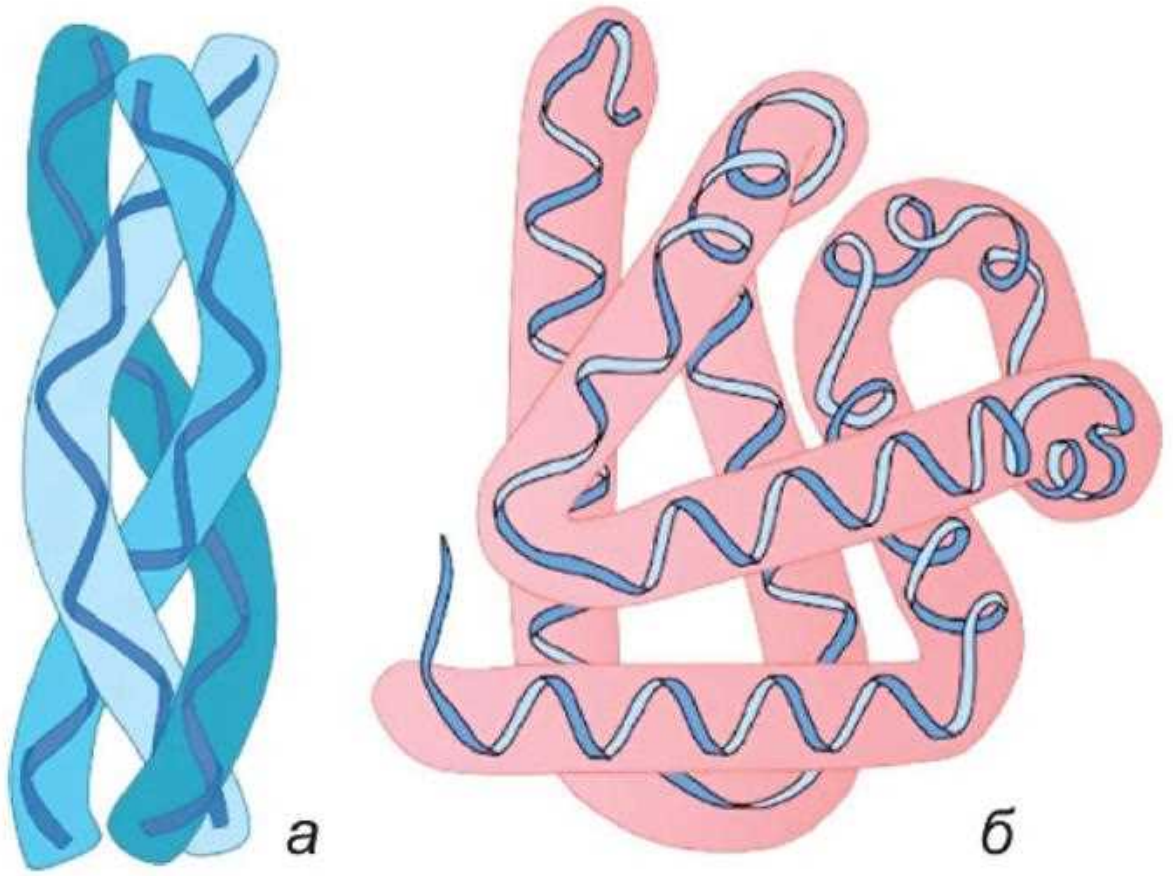


The 20s subunit of the proteasome contains four heptameric rings (4 x 7 = 28 subunits)

There are two forms of **tertiary and quaternary structure**

- Fibrillary (from the *lat.* filament) is an elongated (thread-like) molecule formed by an a-helix (collagen) or b-sheet structure. This structure is characteristic of proteins that form the fibrous structures of tissues. Examples: *collagen, fibroin, and keratin.*

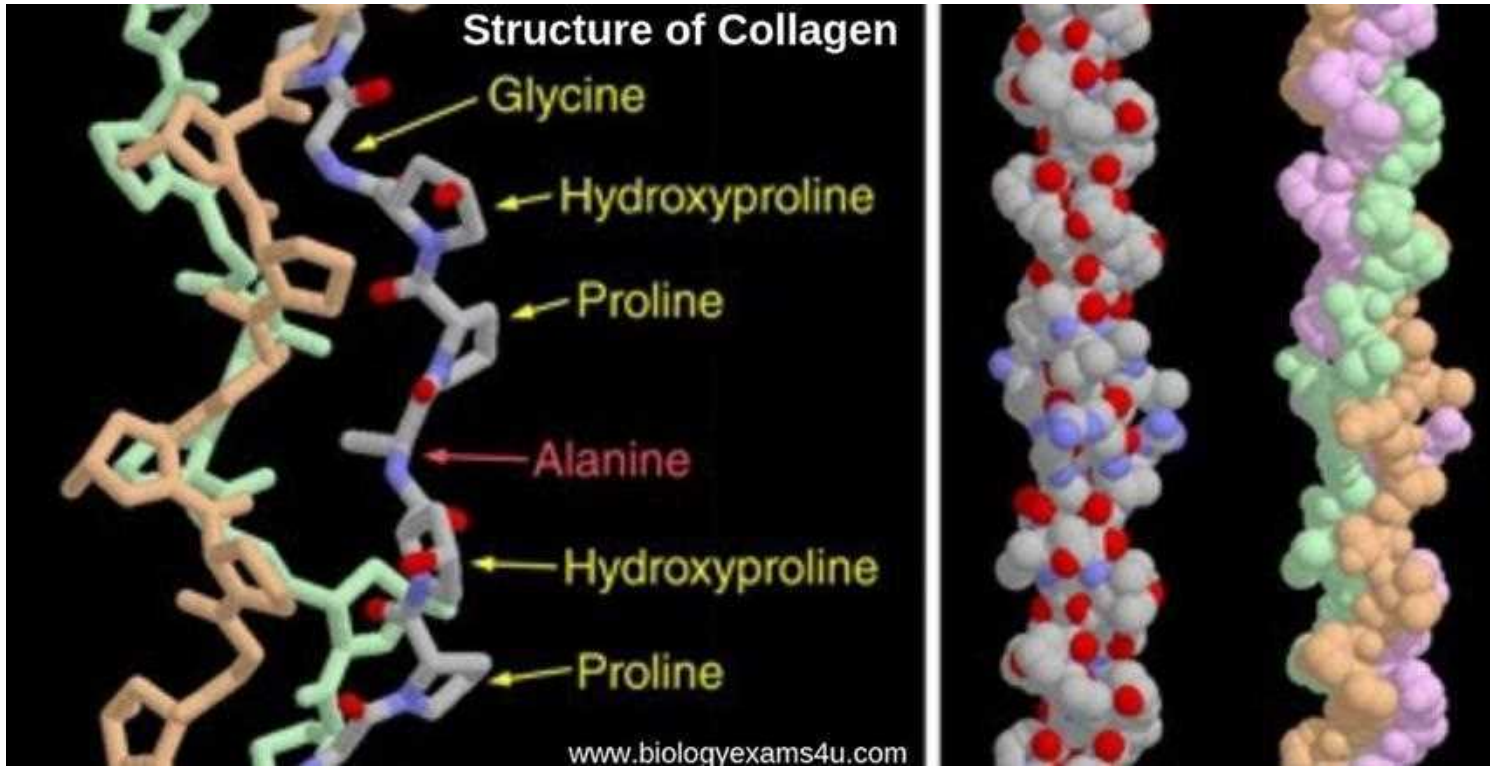
- Globular (from the lat. globula - sphere) is a spherical or elliptical shape. It is more soluble. Example: *albumins and globulins*

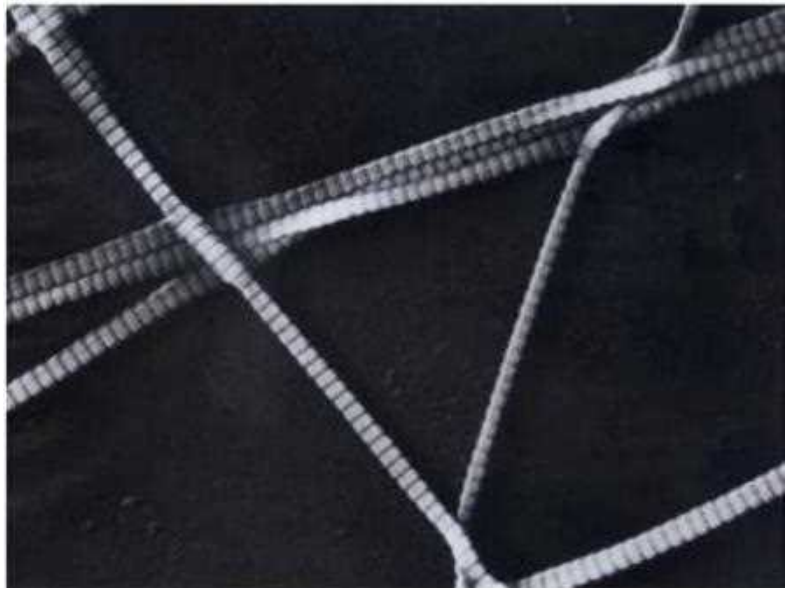


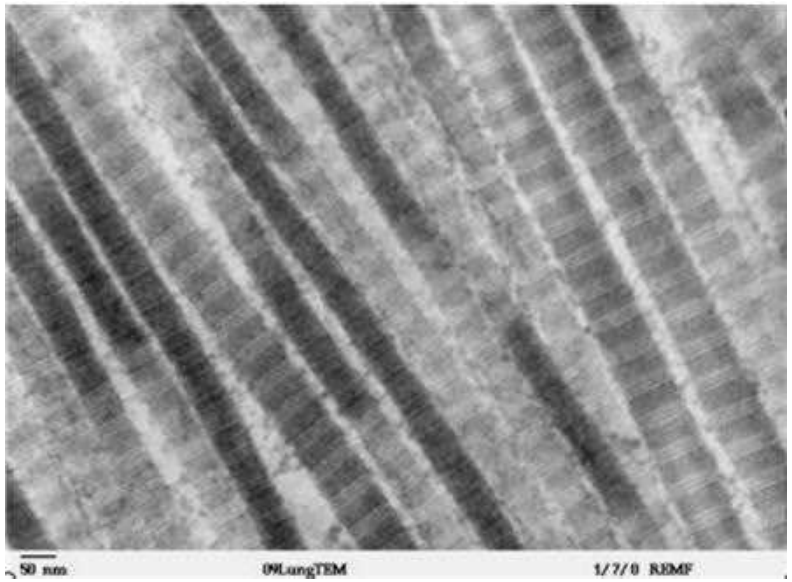
Structure of fibril (a) and globular (b) protein molecules

Structure of collagen

Collagen helix model - triple superhelix







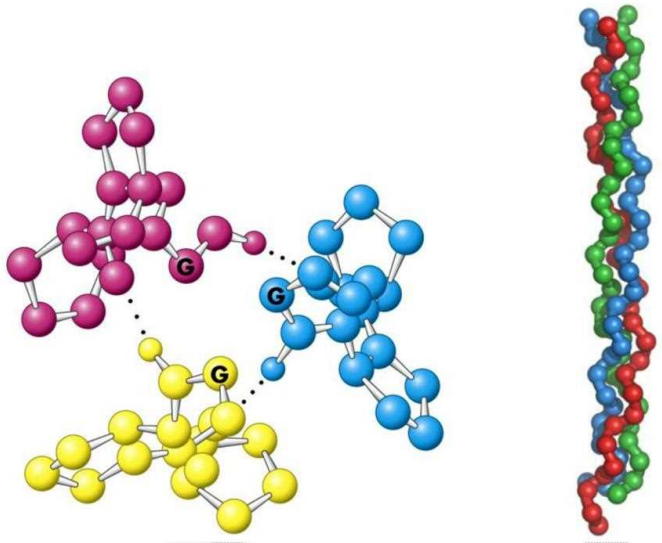
Electron photographs of collagen fibers

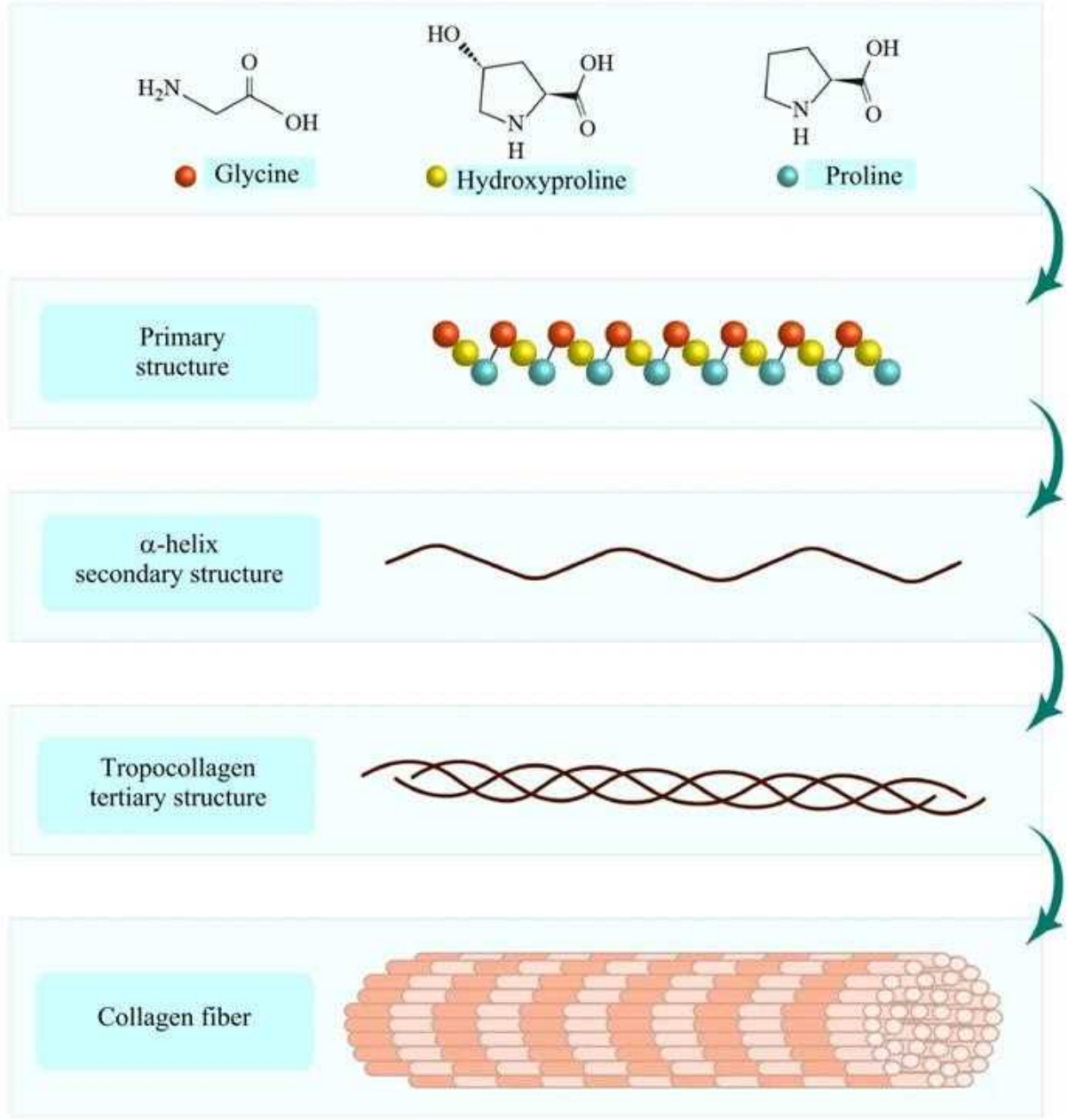
Structure of collagen

Left-handed single helix

96% of the amino acid sequence

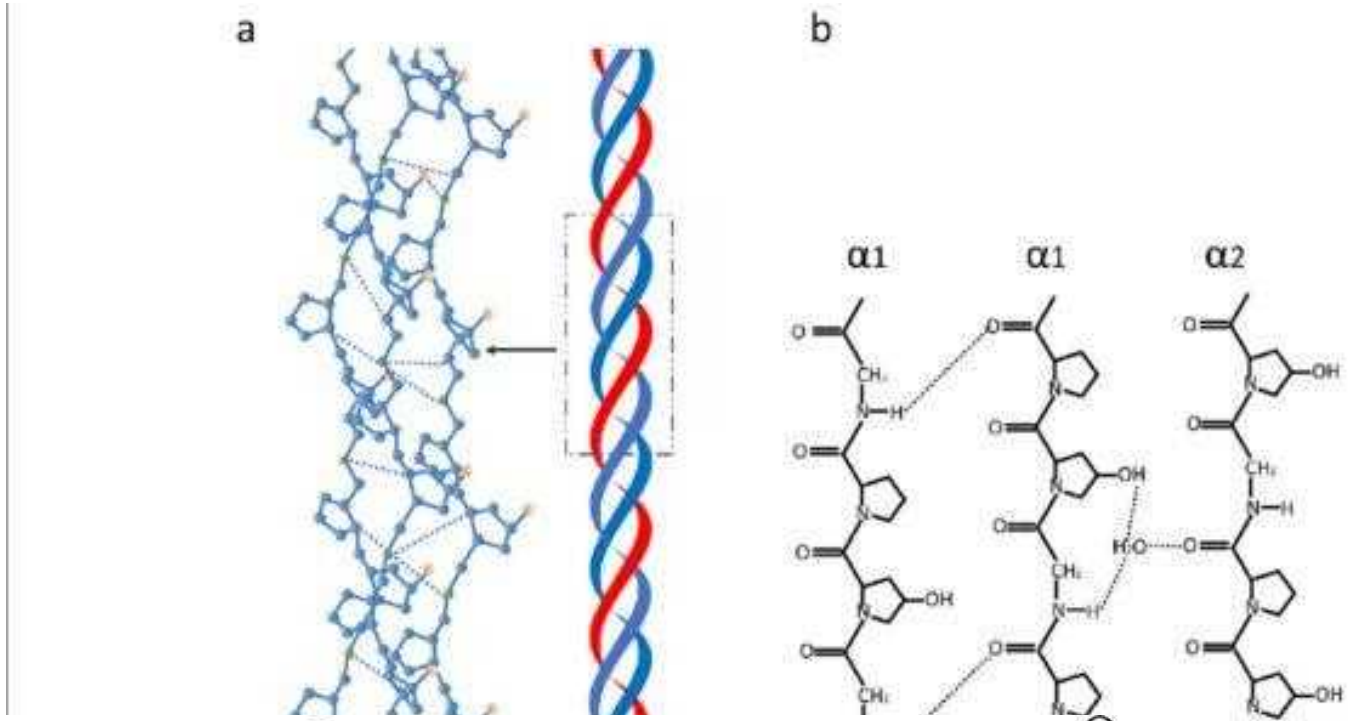
Triple superhelix of collagen

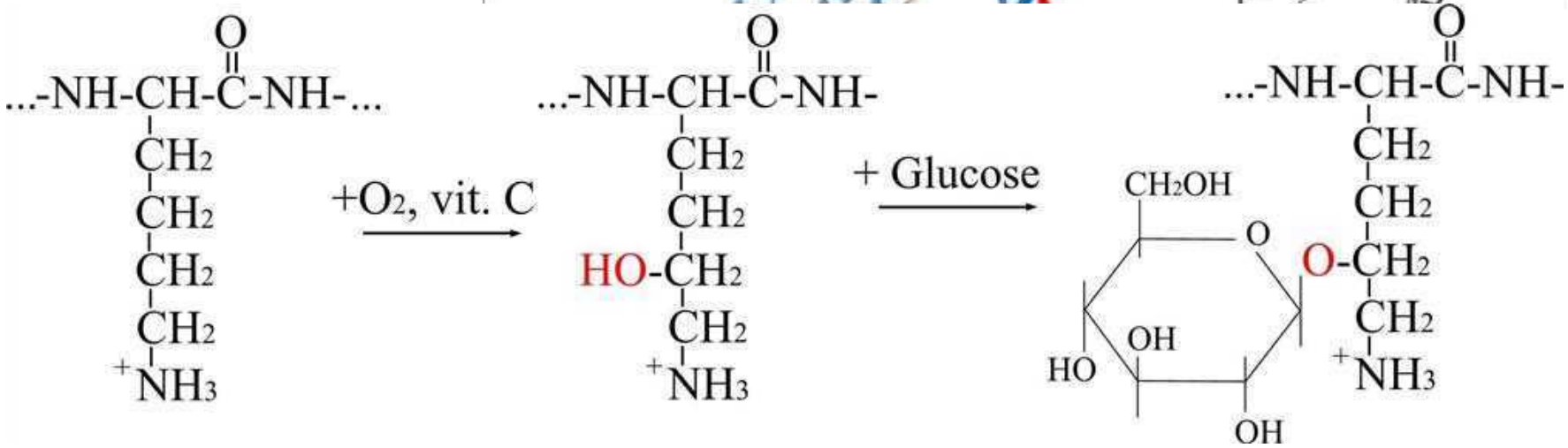




Structure of collagen

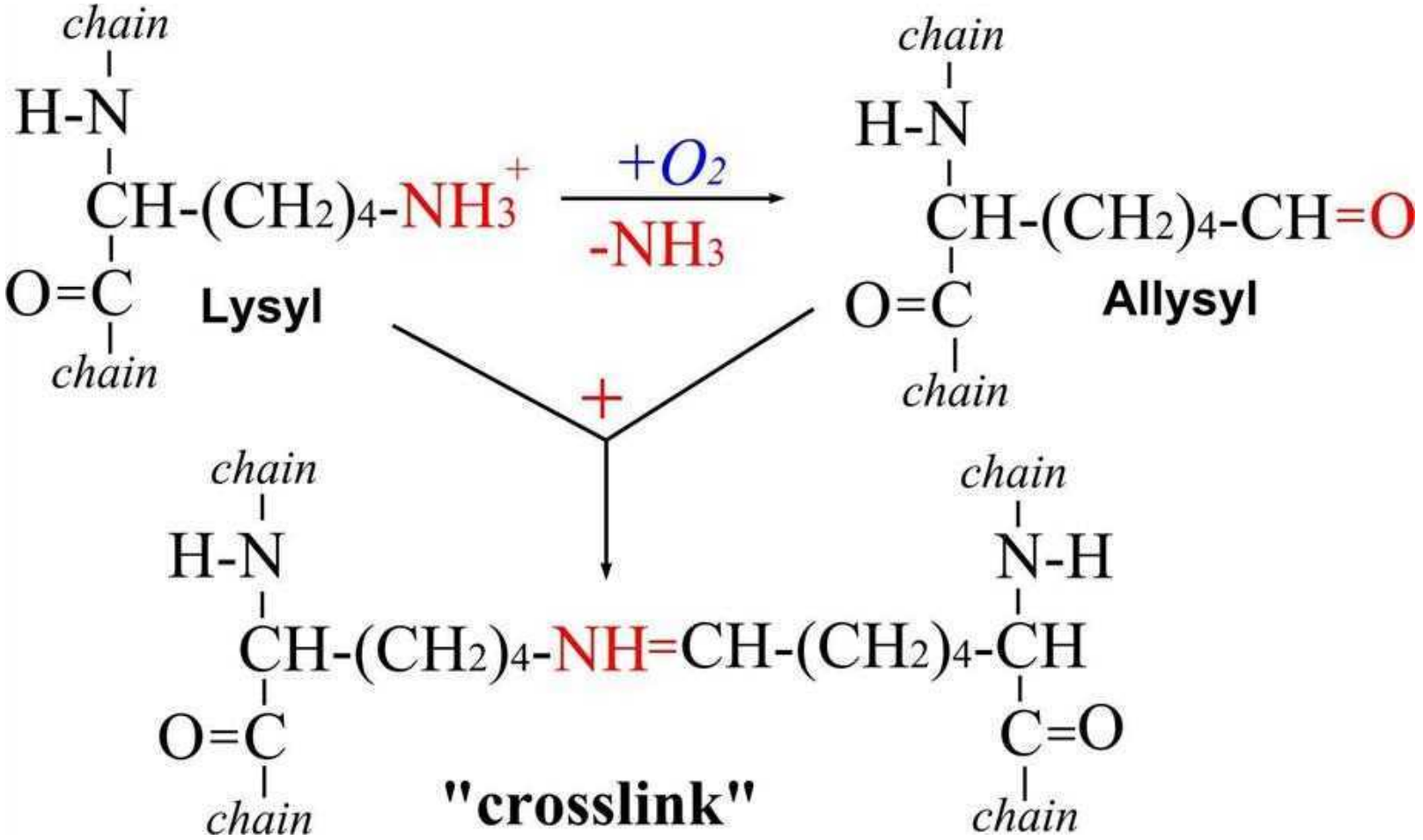
Three chains of tropocollagen are held together by hydrogen bonds between hydroxyproline and hydroxylysine residues





Hydroxyproline and hydroxylysine are formed from proline and lysine through their oxidation with the participation of vitamin C. Glucose or glucosyl galactose residues are then transferred to some of the hydroxylysine residues

Structure of collagen

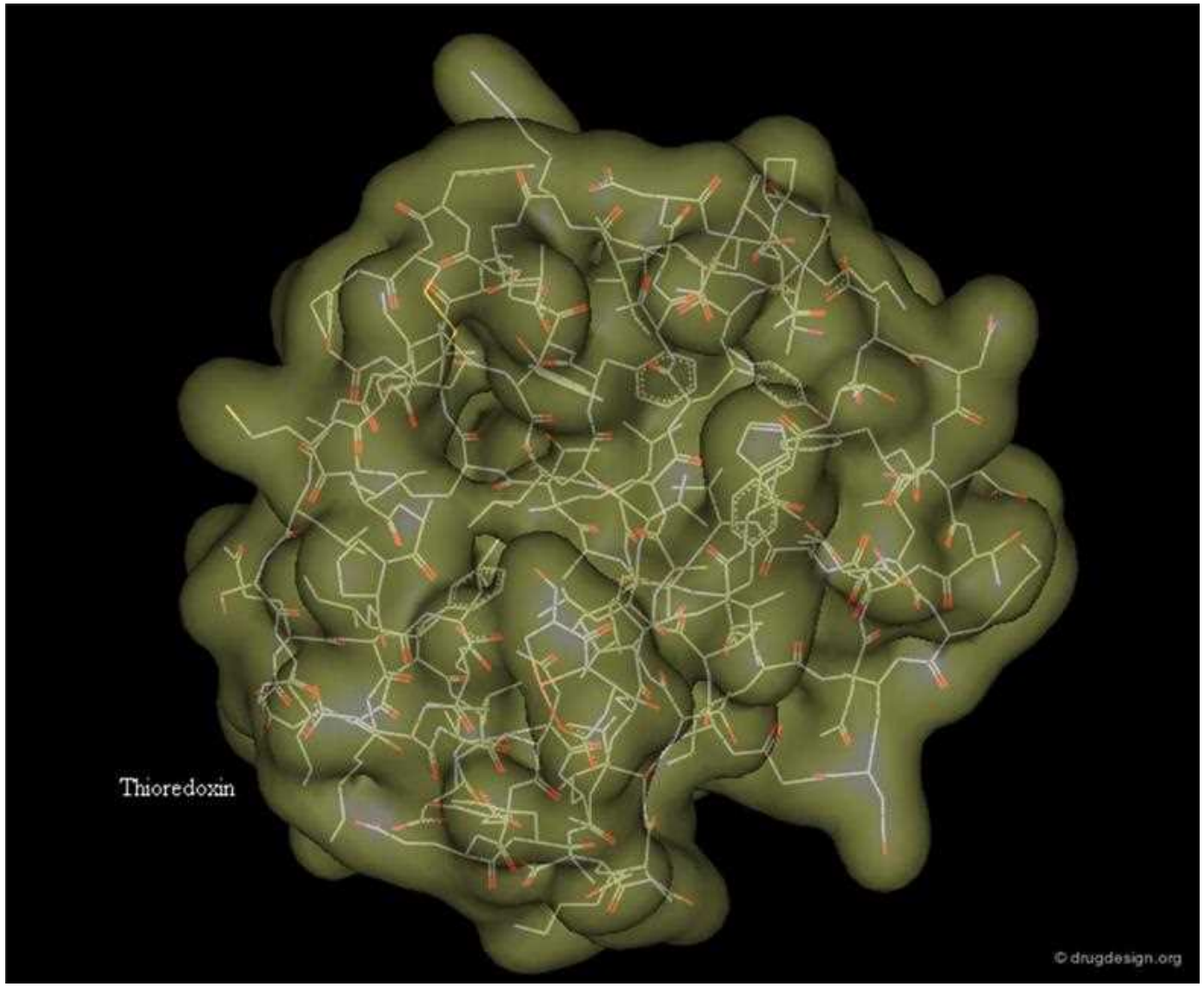


The number of disulfide bonds in collagen is insignificant because it contains little cysteine. Collagen's strength is derived from both intra- and intermolecular covalent bonds—"crosslinks"—formed by lysine and allyl lysine residues. These are products of the oxidative deamination of lysine.

This process continues throughout life.

That's why bones and tendons break more easily in older people, and skin loses elasticity.

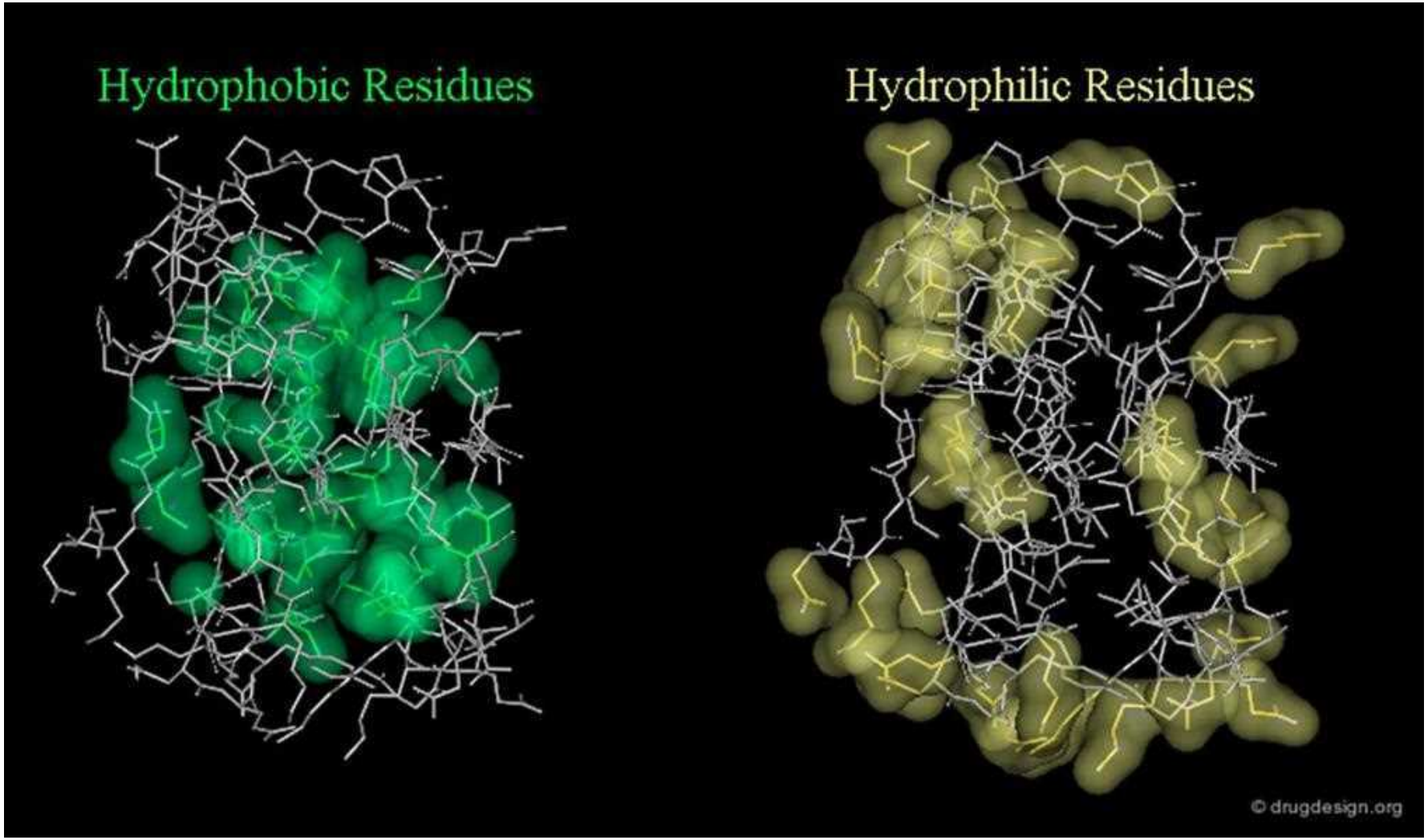
Globular Proteins



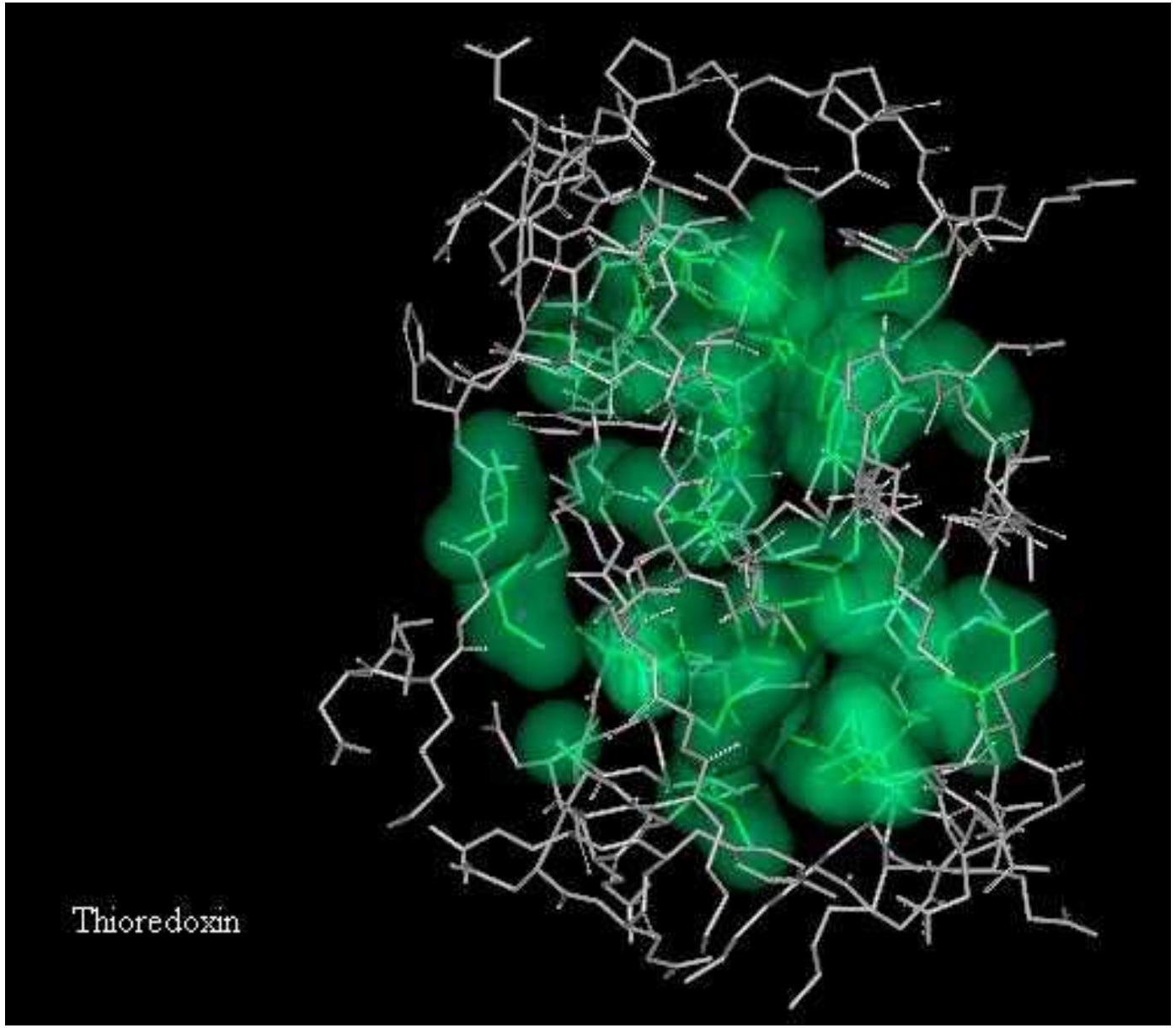
Most proteins found in aqueous, intracellular, or plasma environments are globular. They are either somewhat spherical in shape or composed of several compact domains

Globular Proteins

The globular nature of proteins can be explained by their interaction with the surrounding aqueous solvent. Proteins fold such that most residues with non-polar side chains are buried in the center, creating a hydrophobic core (green side chains), while most residues with polar side chains remain exposed on the protein surface (yellow side chains)

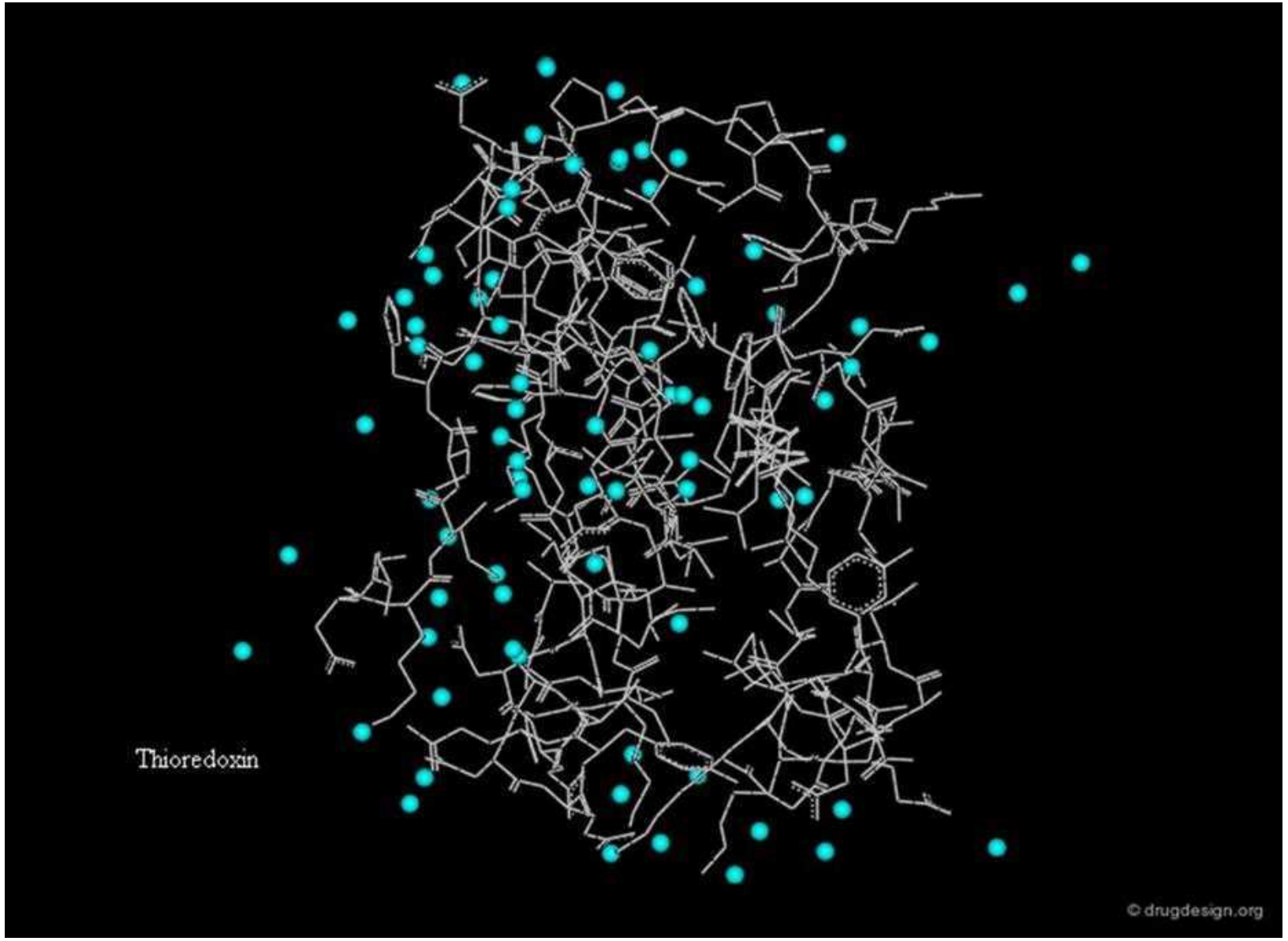


Globular Proteins



The entombment of non-polar residues within the protein core by reducing unfavorable interactions with the surrounding water is known as the "hydrophobic effect." The hydrophobic effect is considered one of the most important forces contributing to the tertiary and quaternary structure of globular proteins.

Globular Proteins



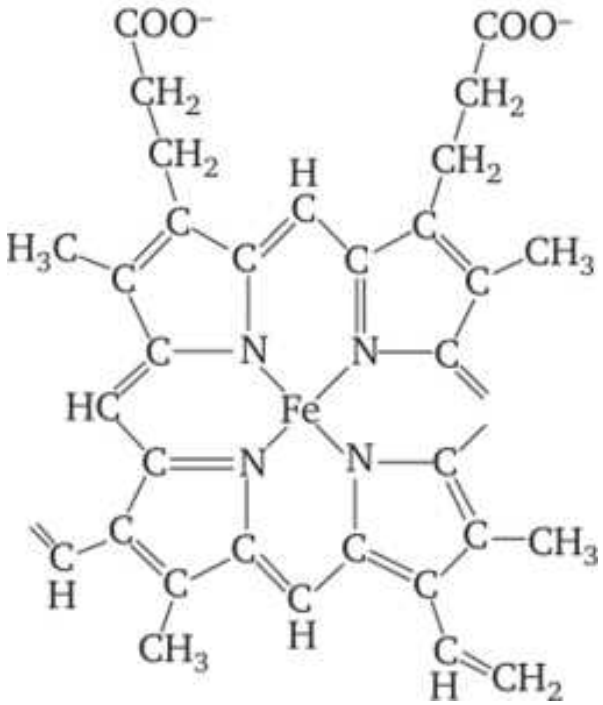
Globular proteins in aqueous solutions are surrounded by a hydration layer. Fixed water molecules (blue spheres) are found primarily in positions where they can form hydrogen bonds with the protein's polar groups.

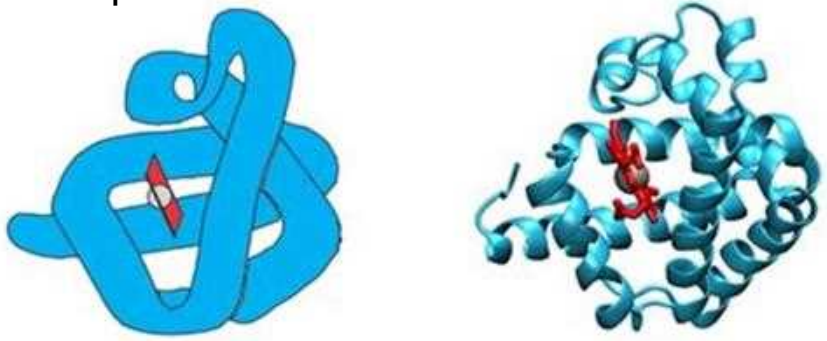
Globular proteins: Hemoglobin and myoglobin

Hemoglobin: a heterodimer of a dimer (α2β2). Oxygen binding in hemoglobin is highly cooperative, achieved through domain rotation compared to myoglobin, which is a monomeric protein

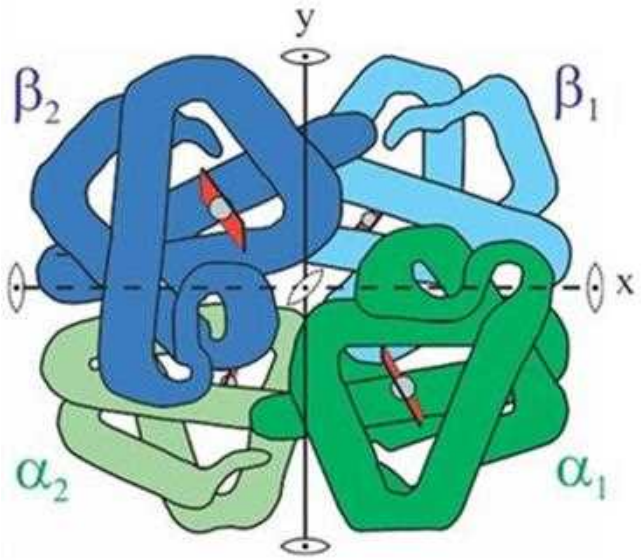
Both proteins contain a hemeporphyrin system with a ferric ion +2 (Fe^{2+}) at the center

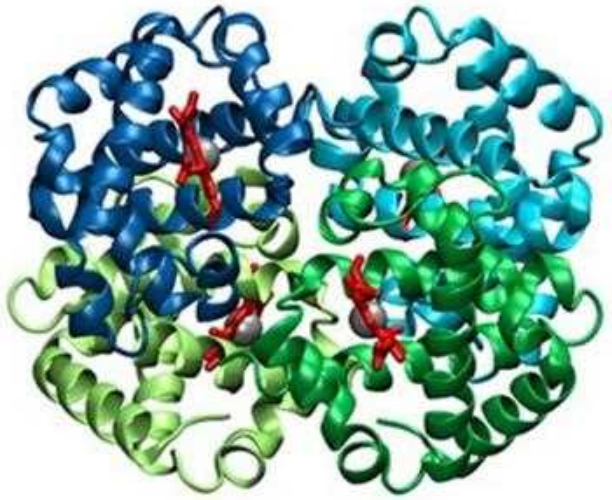
Each of the four hemoglobin subunits has a conformation similar to that of myoglobin.
Accordingly, myoglobin has 1 heme, hemoglobin has 4





myoglobin



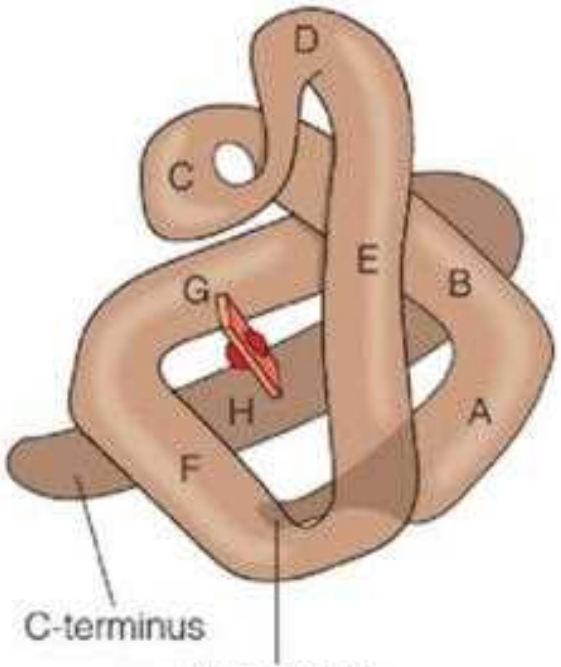


hemoglobin

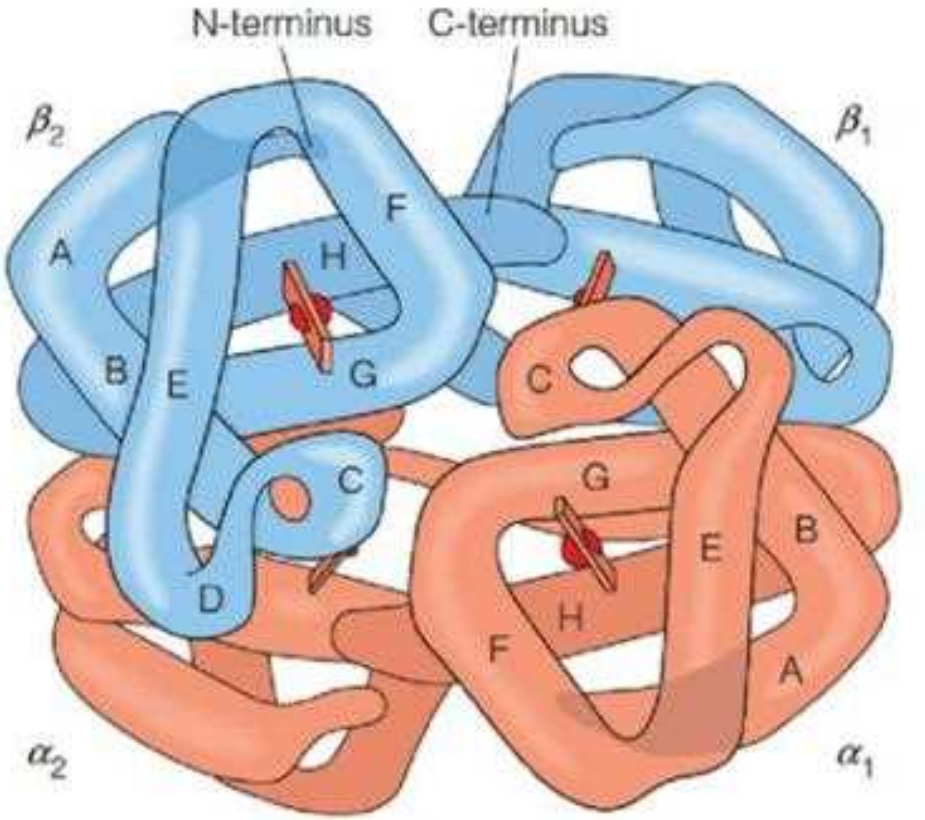
Globular proteins: Hemoglobin and myoglobin

Myoglobin binds to oxygen more strongly than hemoglobin.

Myoglobin's main function is to store oxygen delivered by hemoglobin in muscles.



Myoglobin

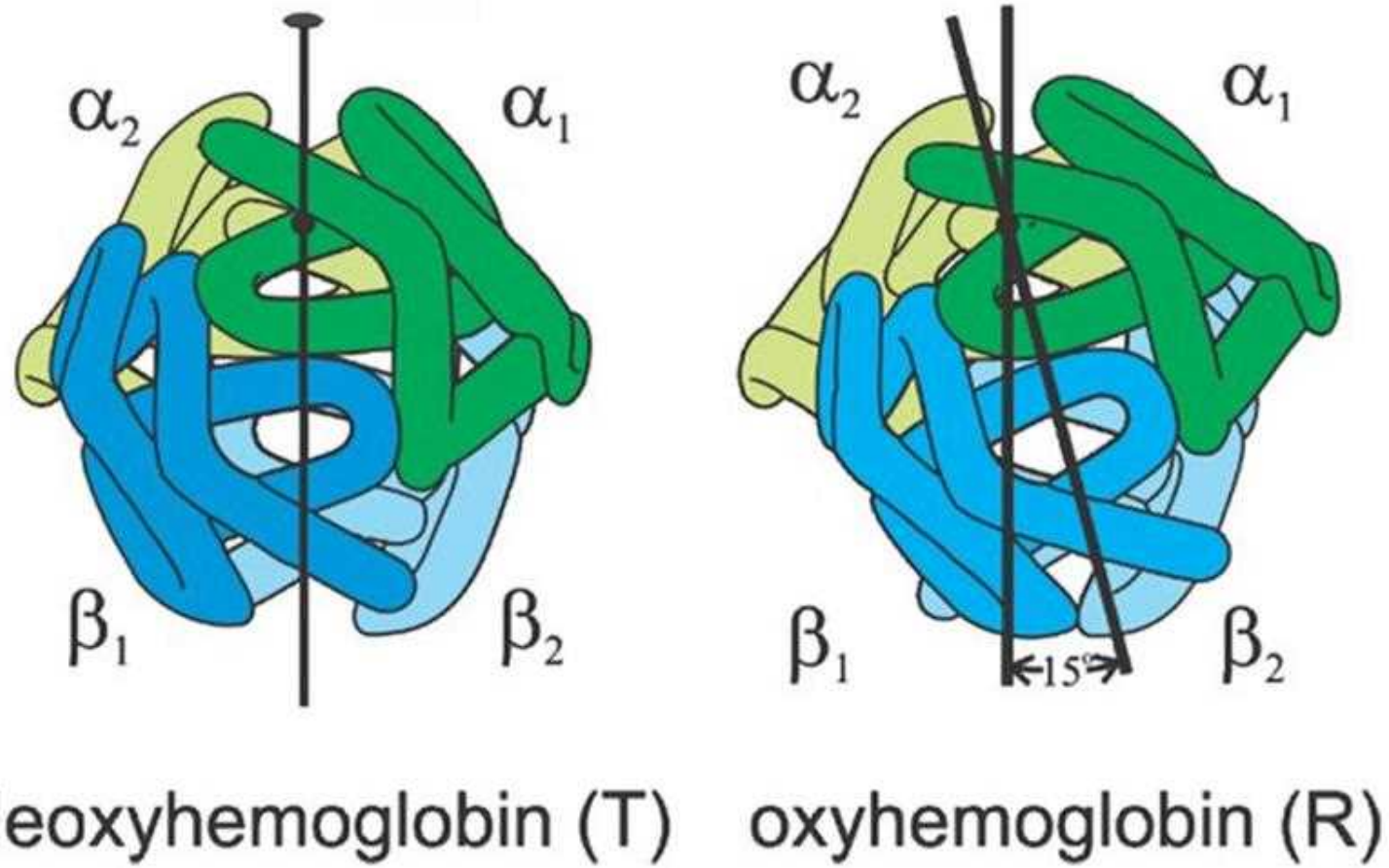


Hemoglobin

The main function of hemoglobin is the transport of oxygen and carbon dioxide

Globular proteins: Hemoglobin and myoglobin

- Each hemoglobin chain is charged (a - positively, b - negatively), so the oppositely charged (ab) chains are bound more strongly than the singly charged (aa) chains.
- The binding forces between dimers are significantly weaker, so they can move relative to each other, assuming two stable states (R and T).
- When the hemoglobin tetramer in the lungs is fully saturated with oxygen, it is in the R-state—oxyhemoglobin (HbO_2). After transferring oxygen to the tissues, hemoglobin transitions to the T-state



Due to the tetrameric nature of hemoglobin, the addition of the first oxygen increases the rate of addition of subsequent oxygen molecules. This is called the «cooperative effect».

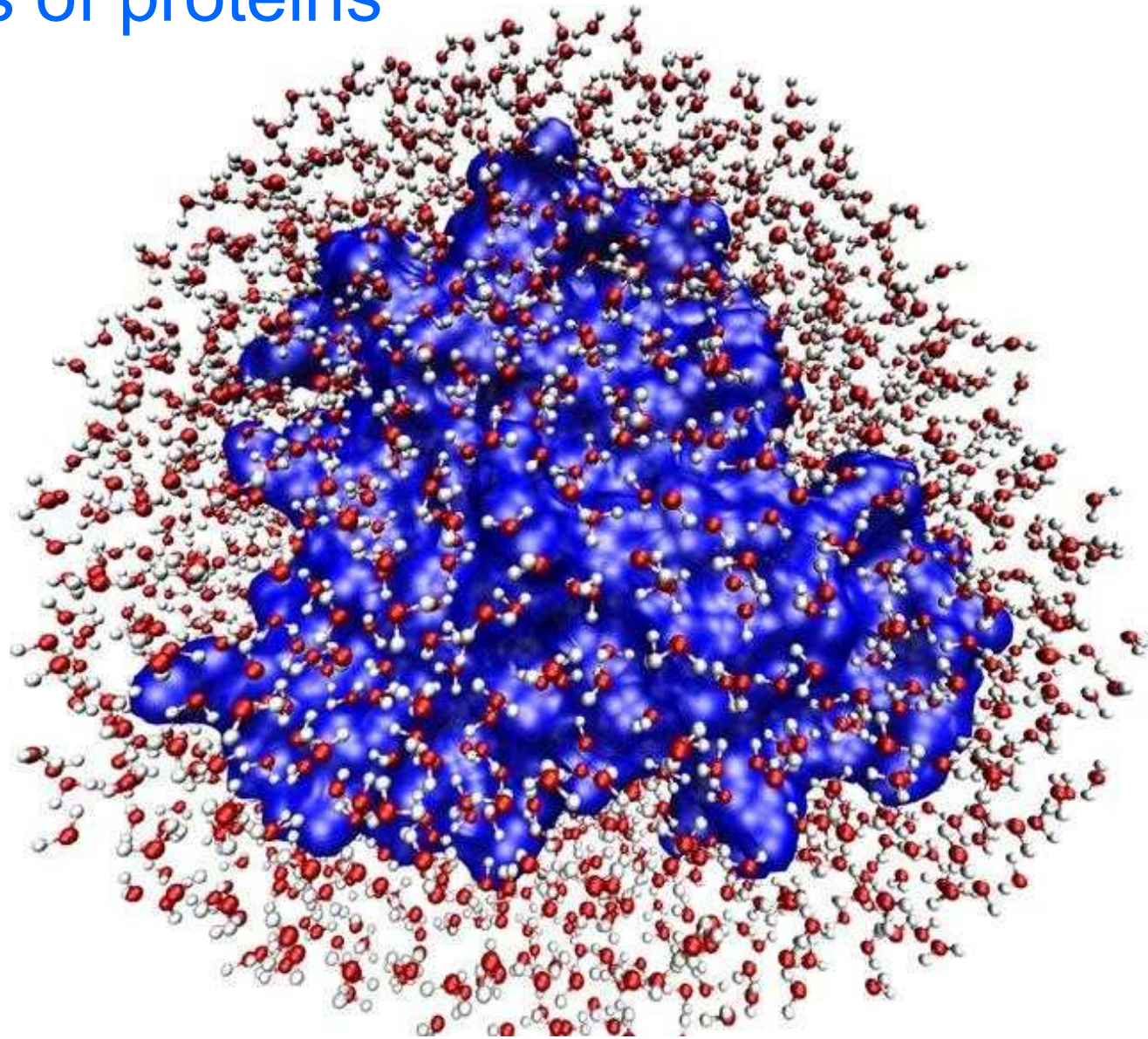
Physico-chemical properties of proteins

Hydration and solubility of proteins

Hydration is the formation of a hydration shell on the surface of a protein due to the binding of its free polar groups (-COO, -NH_3, -OH, -SH) with water dipoles.

The hydration shell prevents the aggregation of protein molecules.
Based on solubility, proteins are divided into:

- albumins - highly soluble in water and saline solutions;
- globulins - highly soluble in saline solutions, but poorly soluble in water;
- prolamins - soluble in 70% alcohol, but insoluble in water and absolute alcohol;
- histones - soluble in saline solutions;
- scleroproteins - insoluble in water and saline solutions.

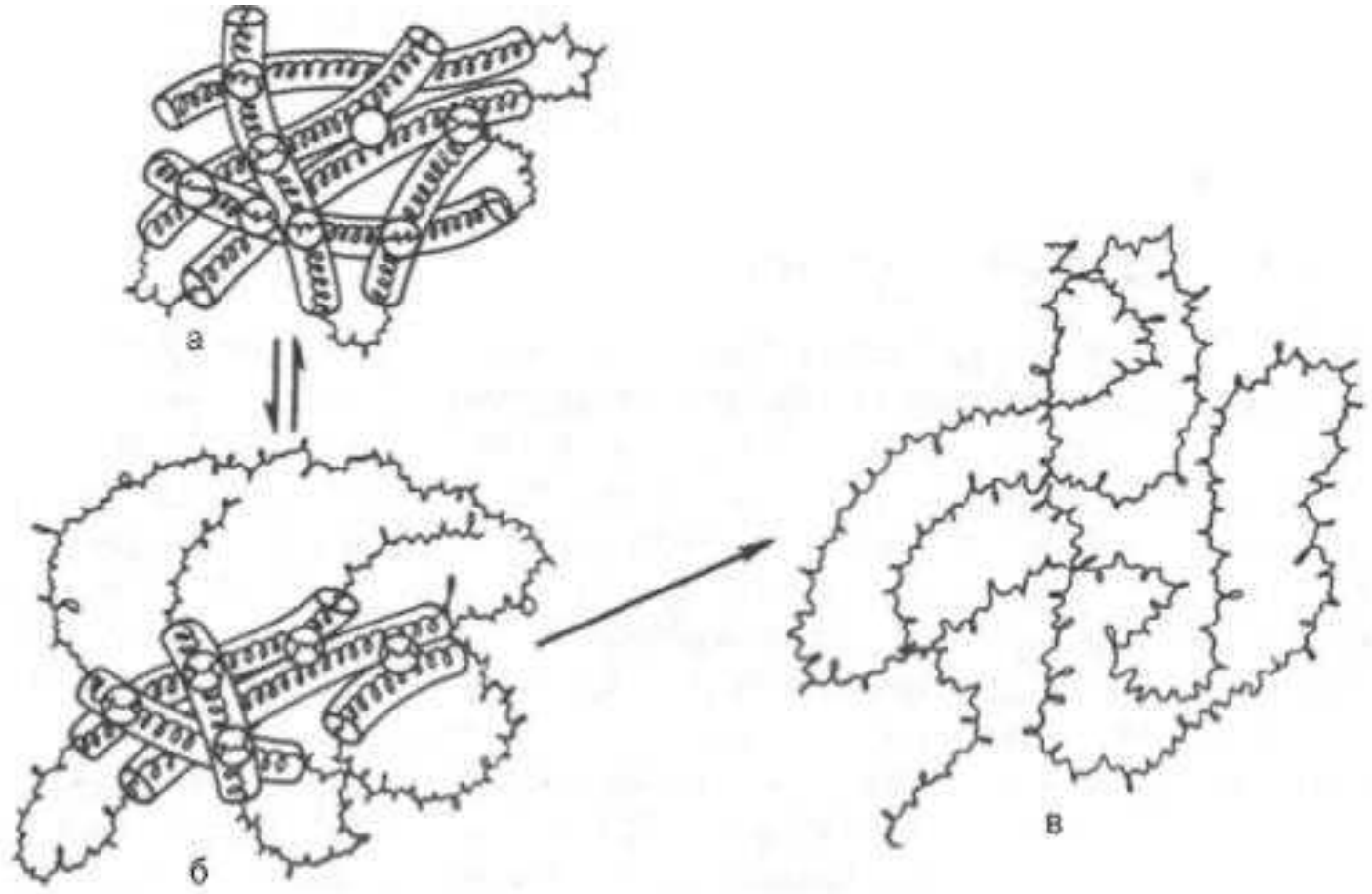


The hydration shell of myoglobin

Protein denaturation

Denaturation is the loss of a protein's natural (native) conformation, which leads to the loss of its physiological function

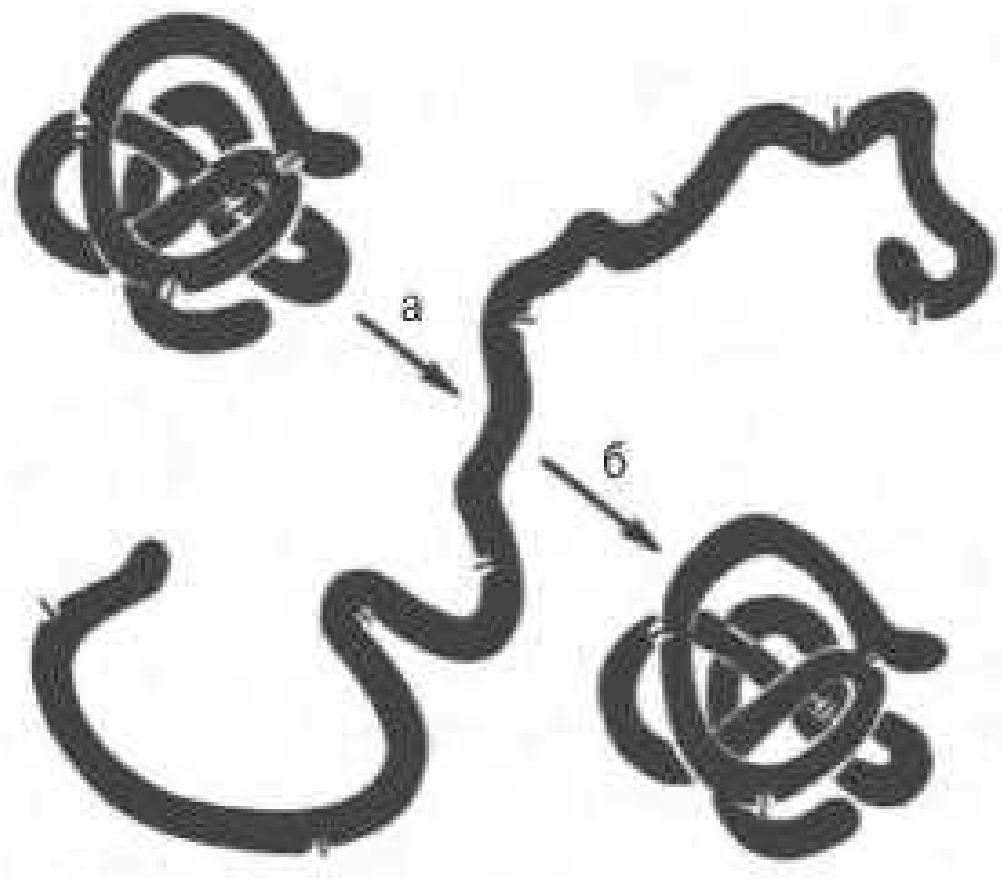
The protein loses all types of structures (quaternary, tertiary and secondary) except the primary one due to the destruction of non-covalent bonds that form these structures



Protein denaturation

Denaturing agents

- Elevated *temperature*
- *Ultraviolet and ionizing radiation*
- Mechanical energy
- *pH changes*
- *Organic compounds* that denature proteins (alcohol, urea)
- *Heavy metal* salts that break disulfide bonds
- *Oxidizing and reducing agents*

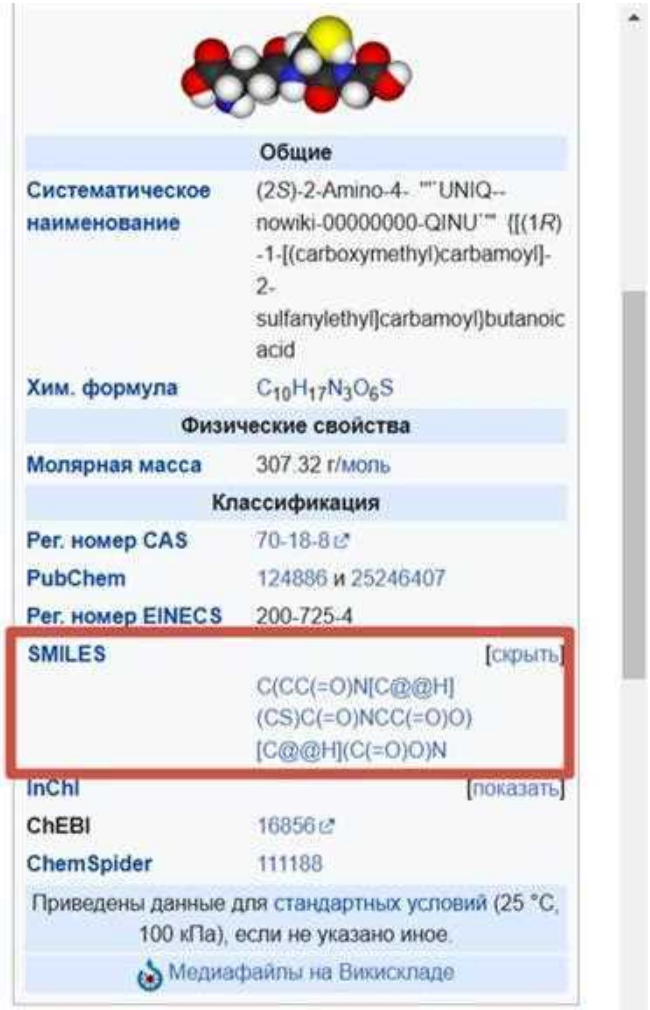


Depending on the degree of destruction and the nature of the protein, denaturation can be reversible or irreversible.With reversible denaturation, restoration of the protein's native structure is possible—renaturation

Situational tasks

Using the Jmol (Jsmol) program, build models (van der Waals, ball-and-stick, stick) of glutathione

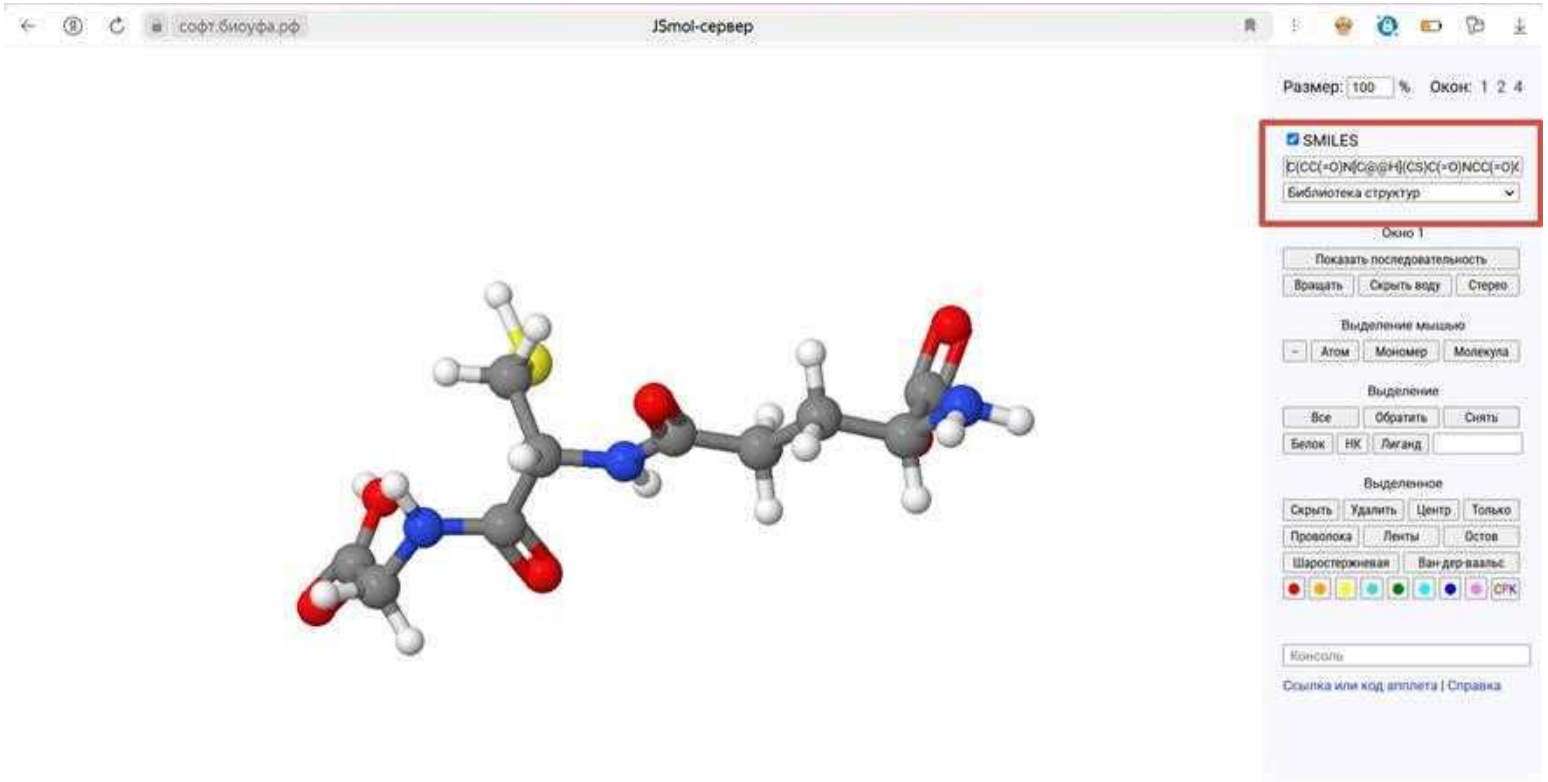
Measure the distance between any two atoms



Общие	
Систематическое наименование	(2*S*)-2-Amino-4- ""UNIQ--nowiki-00000000-QINU'"" {[(1*R*)-1-[(carboxymethyl)carbamoyl]-2-sulfanylethyl]carbamoyl}butanoic acid
Хим. формула	$C_{10}H_{17}N_3O_6S$
Физические свойства	
Молярная масса	307.32 г/моль
Классификация	
Рег. номер CAS	70-18-8
PubChem	124886 и 25246407
Рег. номер EINECS	200-725-4
SMILES	[скрыть] C(CC(=O)N[C@@H](CS)C(=O)NCC(=O)O)[C@@H](C(=O)O)N
InChI	[показать]
ChEBI	16856
ChemSpider	111188

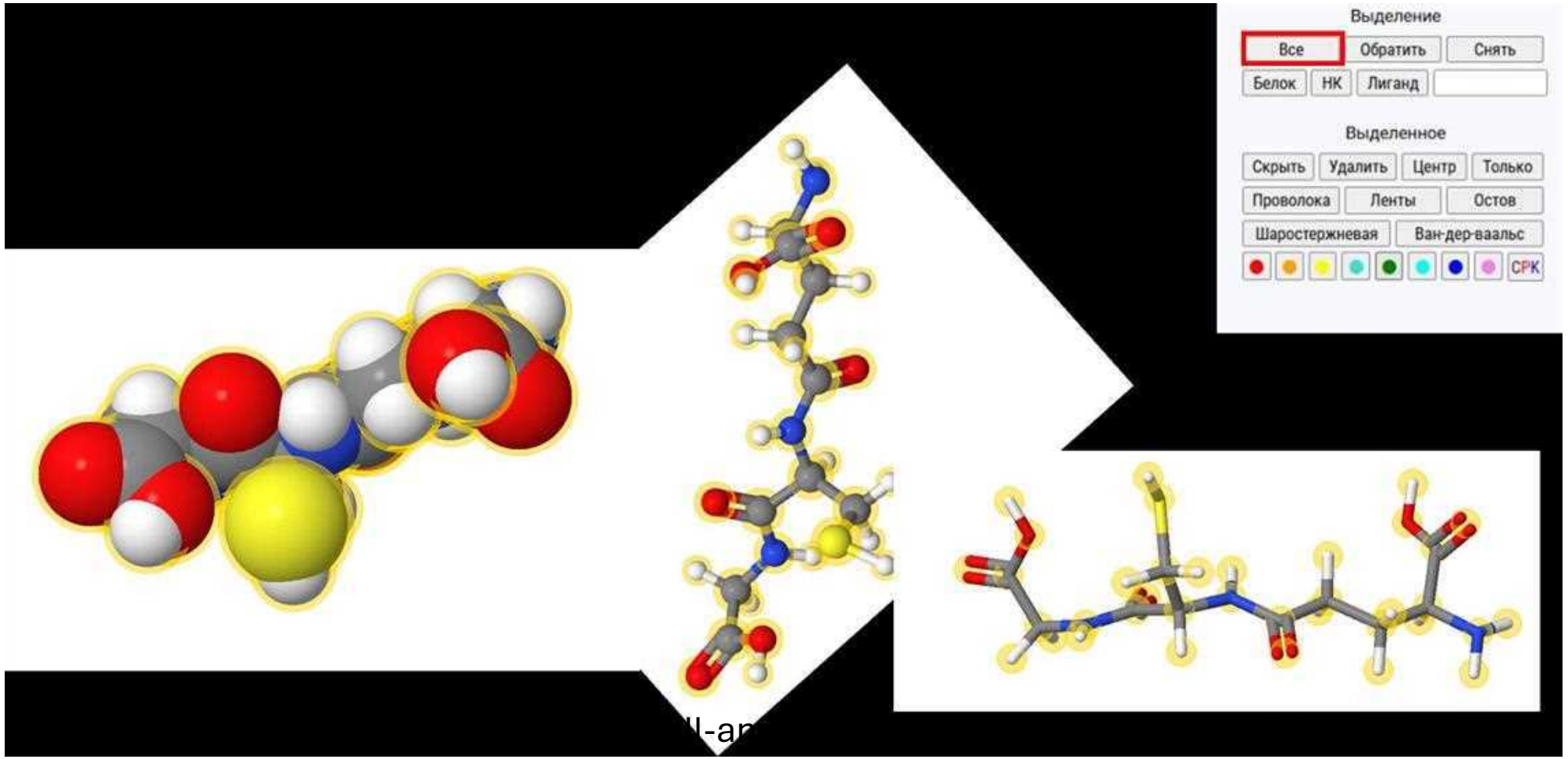
Приведены данные для стандартных условий (25 °C, 100 кПа), если не указано иное.

Медиафайлы на Викискладе



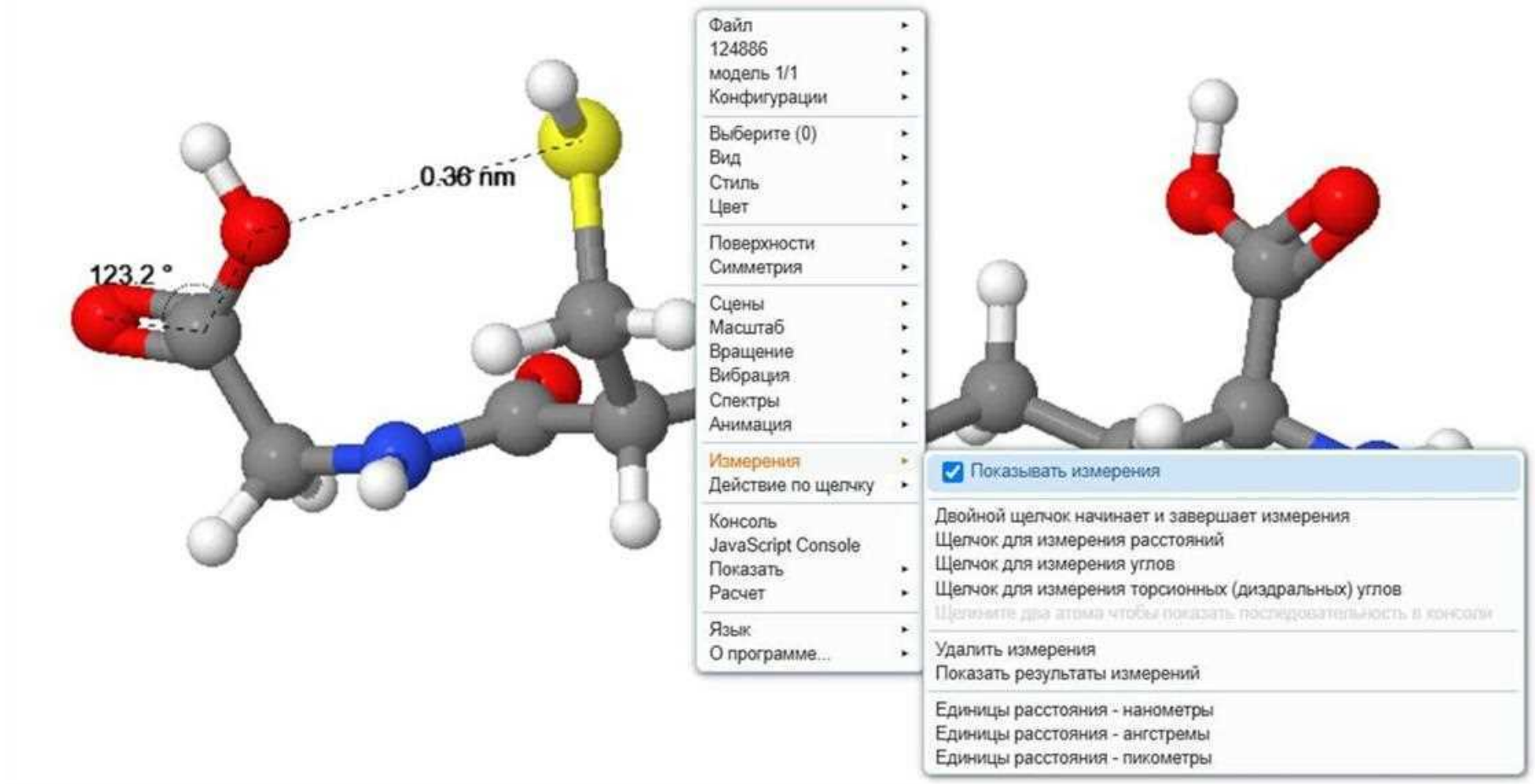
Situational tasks

Using the Jmol (Jsmol) program, build models (van der Waals, ball-and-stick, stick) of glutathione



Situational tasks

Measure the distance between any two atoms



Thank you for your attention!