

Intracellular Protein Biosynthesis: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. Authors Abdulsalam Alhalmi and Amer Abdulrahman proposed the topic of the review, did the literature search and wrote and edited the final draft of the manuscript. Author NA managed the literature searches as well as contributed to figures. All authors read and approved the final manuscript.

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ABSTRACT

Proteins are macromolecules made up of many amino acids that linked together by peptide bond to make a protein molecule. The sequence and the number of amino acids determines each protein unique structure and specific function. Proteins play a vital role in living systems and play important biological functions. Biosynthesis of protein occur in our body cells in order to support the biological function in our body. Intracellular protein synthesis is a complex process that involve the transformation of information and instructions from a genetic material DNA inside the nucleus to form mRNA molecules that transferred to the cytoplasm and linked to the cytoplasmic ribosome. Subsequently, the mRNA and further encode a sequence of amino acid in a specific order and number to form a polypeptide chains that finally undergoes conformational changes and folding to form a particular structure protein. This review will focus on the two consecutive stages of protein biosynthesis; transcription and translation, and their substage processes; initiation, elongation, and termination. Briefly, overview the role of protein in the biological function and the different types of protein structure.

Keywords: *Proteins; amino acids; peptide; transcription; translation.*

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1. INTRODUCTION

Proteins are macromolecules that consist of one or more chains of amino acids that are linked together by peptide boundaries in a specific order. There are 20 different types of amino acids, and the order and number in which the different amino acids are arranged helps to determine the role of this particular protein. Proteins play a crucial role in the normal functioning of cells. They are an essential part of the structure, regulation and function of cells, tissues and body organs. Protein is the cornerstone of our lives and occurs in every cell of the body. Proteins are molecular platform that perform various essential functions in our body. According to the sequence of amino acids, each protein has unique specific functions such as the catalysis of biochemical reactions (enzymes), the synthesis and repair of DNA (DNA polymerase and DNA ligase), the mechanical carrier (actin and myosin), immune protection (immunoglobulins), movement, material transport through the cell (channel and carrier protein), transmission of nerve impulses (blood pressure-dependent potassium channel protein), reception and transmission of chemical signals (neurotransmitters), growth regulation and differentiation (somatotropin) [1,2].

Proteins are supplied mainly from two sources: animal proteins and vegetable proteins. Animal protein sources such as meat, fish, milk and eggs, which are considered high quality protein because they contain all the essential amino acids that are digestible and useful for the body [3], while the vegetable protein sources such as cereals, vegetables and nuts do not contain essential amino acids [4].

Biosynthesis of intracellular proteins is a biochemical process in which proteins are synthesized in several steps from simple amino acids in cells using simple information stored in DNA. Mainly, there are two phases for protein biosynthesis, transcription and translation. Transcription is the transfer of genetic information from DNA to mRNA in the nucleus. This phase includes three stages, Initiation, extension and termination. Once the mRNA is synthesized, it is transported to the cytoplasm to transport instructions to the ribosomes. Translation involves reading the information and instructions from the ribosome mRNA using the tRNA, which places the amino acids in the right order, and the rRNA, which allows binding between amino acids to create ultimately a

polypeptide chain. Finally, another polypeptide chain is processed to form the final protein [5]. This review highlights the concept of protein, the type of protein structure, the function of protein, and the process of protein synthesis in human cells.

2. INTRACELLULAR PROTEIN SYNTHESIS

The genetic material, DNA, stores the information necessary to prompt the cell to perform all of its functions. Cells use the genetic code stored in the genetic material DNA to synthesize proteins that ultimately determine the structure and function of the cell. This genetic code is in the specific set of nucleotides bases that make up each gene along the DNA molecule. In order to read this code, the cells must perform two successive steps [6].

2.1 Transcription

An RNA copy of the DNA sequence of a gene is made during transcription. This step is carried out by enzymes called RNA polymerases, which combine nucleotides into a strand of RNA using a strand of DNA as a template. This copy called the messenger RNA molecule (mRNA), which leaves the nucleus and enters to the cytoplasm, where it controls the synthesis of the protein. Transcription consists of three phases: initiation, extension, and termination [2,7].

2.1.1 Initiation

The RNA polymerase attaches to a DNA sequence called a promoter, a specific sequence of nucleotides, which is located at the beginning of a gene and triggers the start of transcription. Once linked, the RNA polymerase separates the DNA strands, and provides the single-stranded template required for transcription (Fig. 1).

2.1.2 Elongation

A single strand of DNA, the template strand, acts as a template for RNA polymerase. As it reads this template one base at a time, the polymerase aligns the corresponding nucleic acid (A, C, G, or U) with its complementary base on the strand that codes for DNA to construct mRNA molecule from complementary nucleotides, that form a chain, which grows from 5' to 3'. The RNA transcript contains the same information as the non-template DNA strand (coding), but contains

the base uracil (U) instead of thymine (T) (Fig.1).

2.1.3 Termination

When the polymerase has reached the end of the gene, sequences of specific triplet codes (UAA, UAG or UGA) called termination signal or stop signal, activate enzymes to complete transcription, and release the mRNA transcript from RNA polymerase (Fig.1).

2.2 Translation

Translation is the process of synthesizing a chain of amino acids called a polypeptide. After the mRNA has released from the nucleus, it leaves towards the cytoplasm to binds to a ribosome. During translation, the nucleotide bases of the mRNA are read by codons which consist of three RNA bases. Each "codon" encodes a particular amino acid. Each tRNA molecule has an anticodon that is complementary to the mRNA codon, and the bound amino acid at the other end. When the mRNA molecule is ready for translation, the two subunits enter and bind to the mRNA. The ribosome provides a substrate for the translation, collection, and alignment of the mRNA molecule with the molecular "translators"

that are supposed to decode the code. Then transfer RNA (tRNA) from the shuttle to the ribosome, using aminoacyl RNA synthetases [6], which are individually encoded by sequential codon triplets on the mRNA, and build the polypeptide chain that fully synthesizes the protein. A transfer tRNA molecule can read its recognized mRNA codon, and bring the amino acid corresponding to the growing chain. When the polypeptide chain is complete, the mRNA detaches from the ribosome and the protein is released. Typically, multiple ribosomes attach to a single mRNA molecule at the same time, allowing multiple proteins to be made from mRNA at the same time [7]. Translation process pass by three main stages: initiation, elongation, and termination.

2.2.1 Initiation

The Initiation stage starts with attachment of a ribosome to an mRNA transcript. For translation to begin, the start codon 5'AUG must be recognized. This is a codon specific to the amino acid methionine, which is nearly always the first amino acid in a polypeptide chain. At the 5' cap of mRNA, the small 40s subunit of the ribosome binds. Subsequently, the larger 60s subunit binds to complete the initiation complex [10].

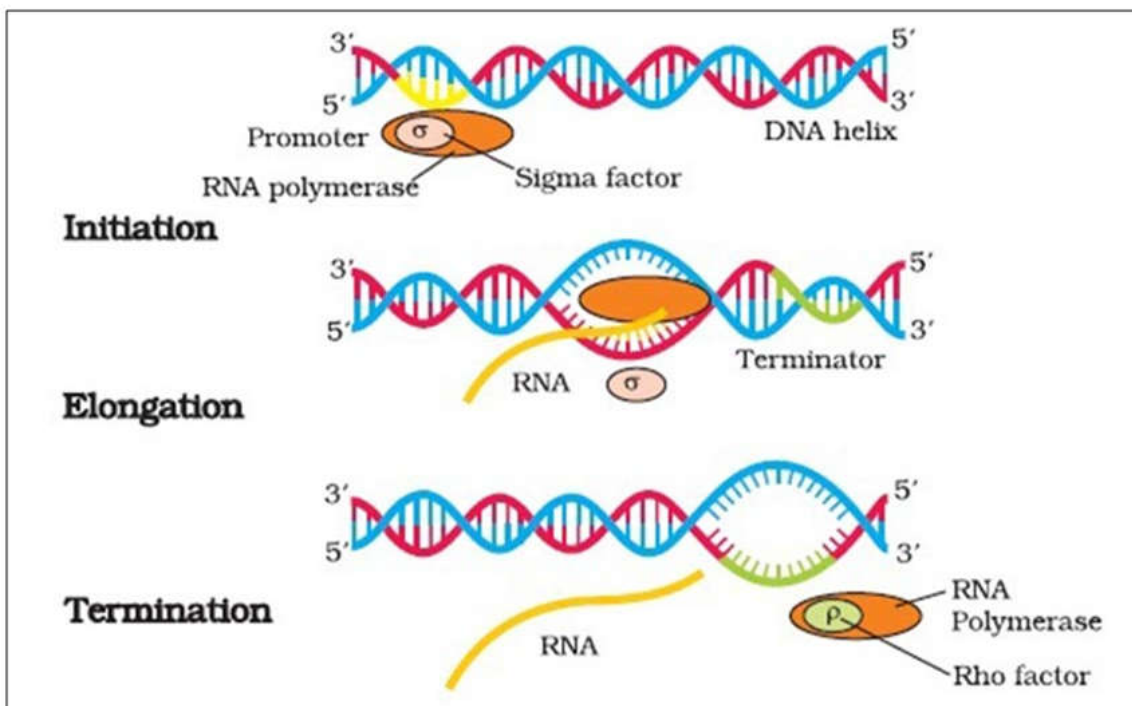


Fig. 1. Illustrative diagram for the process transcription [8]

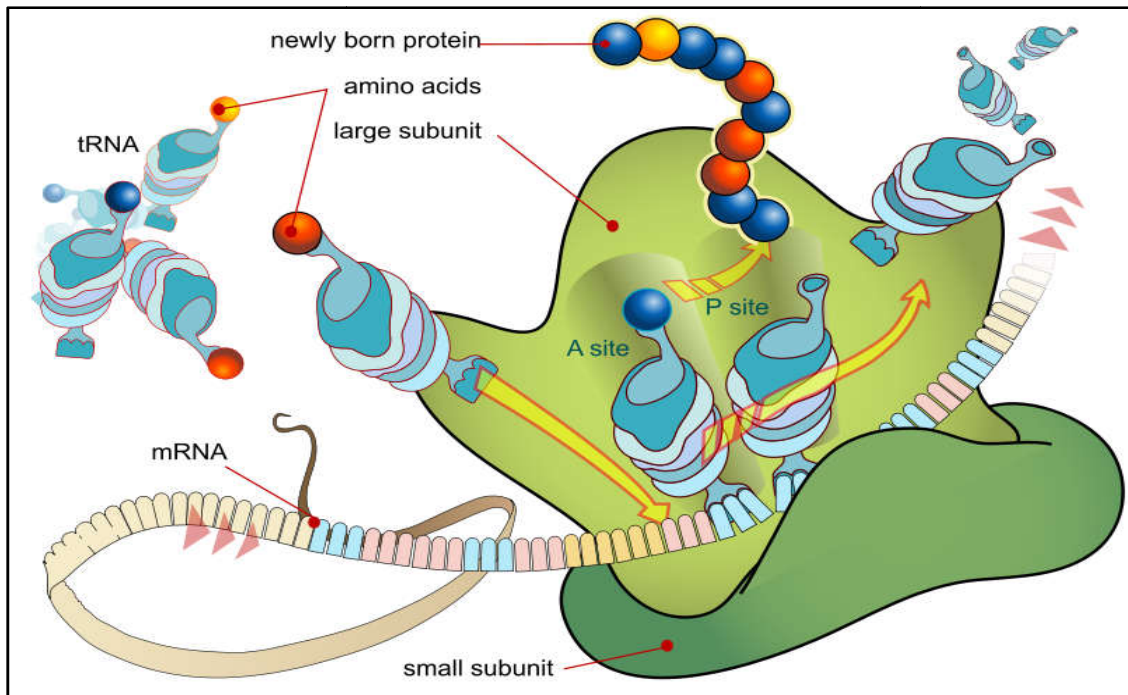


Fig. 2. A simplified view of process of translation of mRNA and the synthesis of proteins by a ribosome [9]

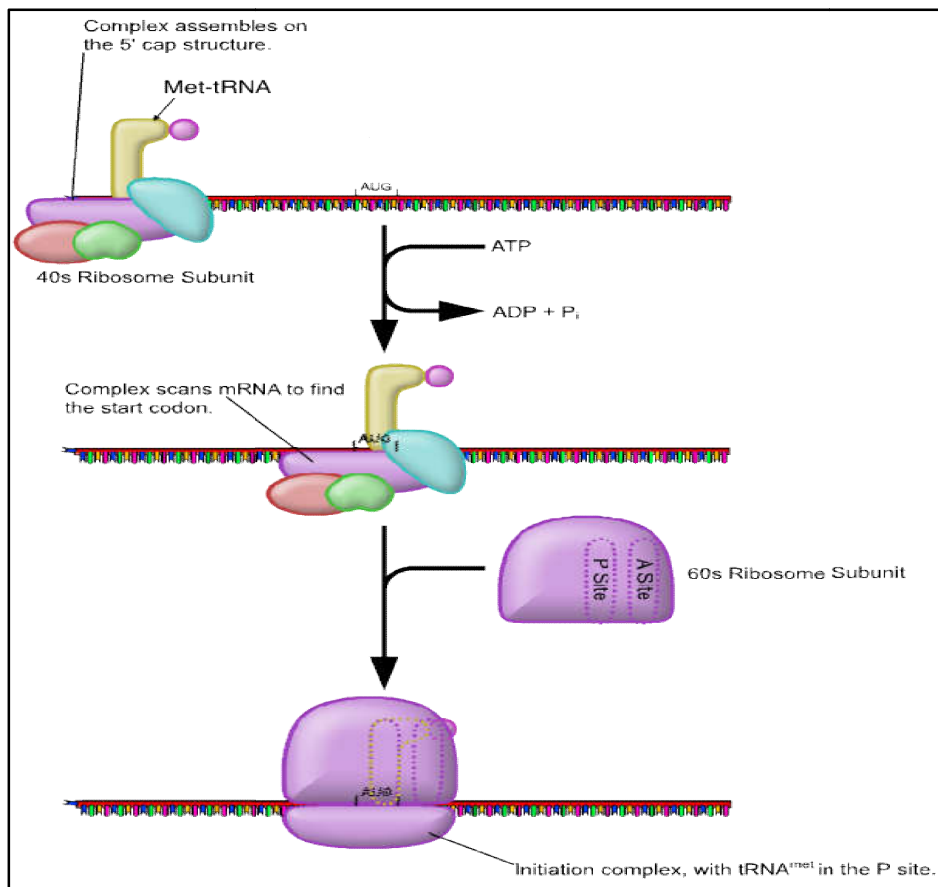


Fig. 3. Initiation of DNA translation [11]

2.2.2 Elongation

The process of binding of amino acids together to make long chains of polypeptides, that happens with the help of ribosome, which has two tRNA binding sites; the P site which holds the peptide chain, and the A site which accepts the tRNA. While Methionine-tRNA occupies the P site, the aminoacyl-tRNA that is complementary to the next codon binds to the A site using energy yielded from the hydrolysis of GTP. Methionine moves from the P site to the A site to bind with a new amino acid there, where

the growth of the peptide has begun. The tRNA molecule in the P site has no longer attached amino acid, thus it leaves the ribosome. The ribosome then translocate along the mRNA molecule to the next codon, again using energy yielded from the hydrolysis of GTP. Now, the growing peptide lies at the P site, and the A site is open for the binding of the next aminoacyl-tRNA, and the cycle continues. The polypeptide chain is built up in the direction from the N terminal (methionine) to the C terminal (the final amino acid) (Fig. 4) [12].

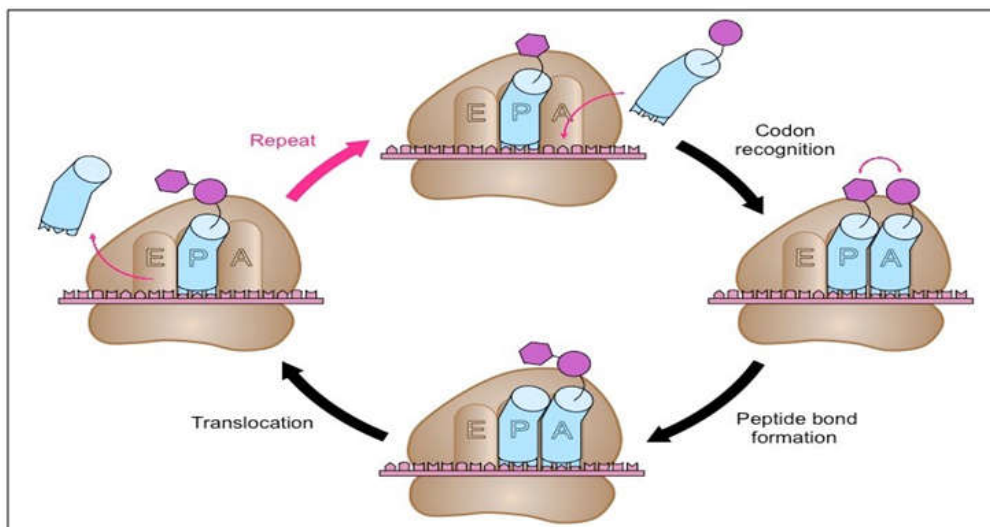


Fig. 4. Elongation of polypeptides chain [11]

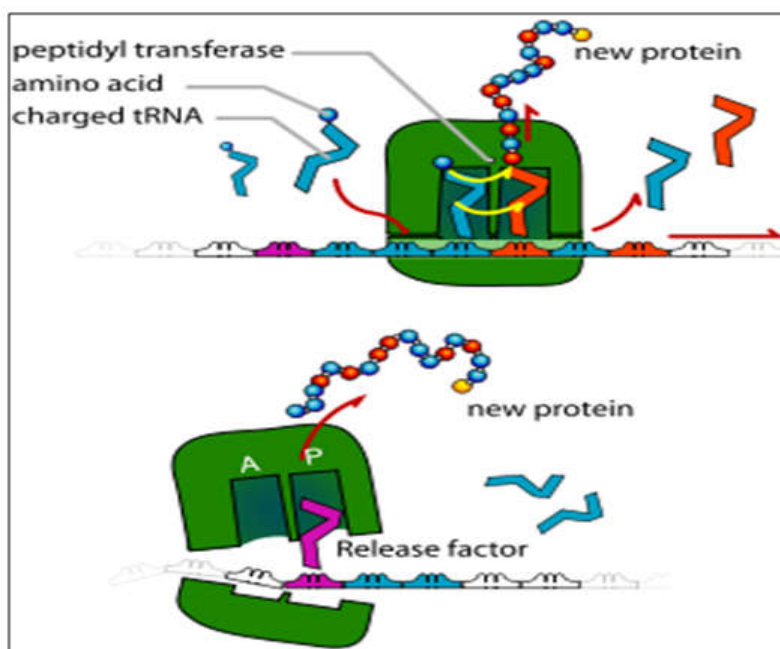


Fig. 5. Mechanism of the termination of translation [11]

2.2.3 Termination

The last step in protein biosynthesis occurs with help of one of the three stop codons that enter the A site. The tRNA molecules not bind to these codons, so the peptide and tRNA in the P site become hydrolyzed, and finally releasing the polypeptide into the cytoplasm. The large and small subunits of the ribosome become ready for the next round of translation [13].

3. FOLDING OF POLYPEPTIDES AND MODIFICATION OF PROTEINS

Once a polypeptide chain has been synthesized, it can go through additional conformational processes. The polypeptide chain folds down to adopt a specific structure that enables the protein to perform its specific functions. Folding of polypeptide chain due to the interactions between the amino acids. It can bind to other polypeptides or to different types of molecules, such as lipids or carbohydrates [14]. Proteins have different levels of structural organization; primary, secondary, tertiary, and quaternary (Fig. 6) [1].

3.1 Primary Structures

A simple polypeptide chain with a specific sequence of amino acids linked by covalent bonds called the primary protein. The primary structure of a protein is encoded by a gene. Therefore, any change in the gene sequence can change the primary structure of the protein and all subsequent levels of the protein structure, which ultimately changes its overall structure and function. The primary structure is maintained by the covalent peptide bonds. Insulin is an example of a protein with a primary structure (Fig. 7) [15].

3.2 Secondary Structures

When the primary structure of a protein folds through hydrogen bonds, electrostatic bonds, hydrophobic interactions, and Van der Waals forces within the polypeptide chain, it forms a structure known as the secondary structure of the protein. There are different types of secondary structures of proteins, such as α -helical structures (such as hemoglobin , myoglobin, myosin, and keratins), β -Sheet structure (such as fibroin, chymotrypsin (Fig. 8), ribonuclease and cytochrome c), and β -Turn (myohemerytherin) [1].

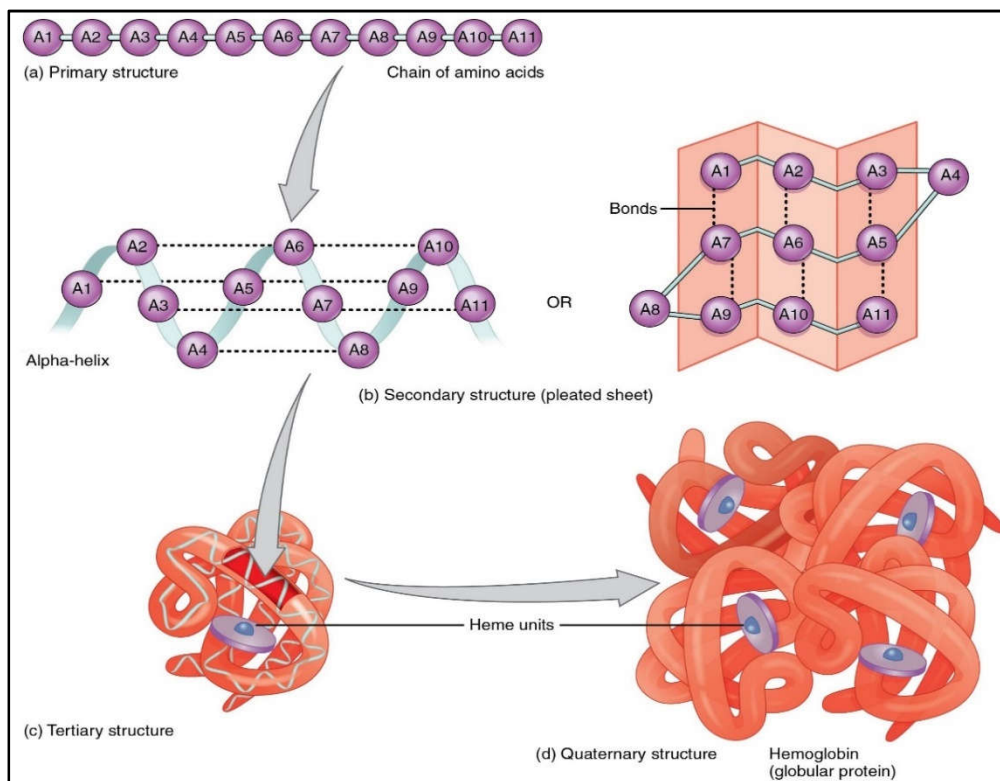


Fig. 6. Primary, secondary, tertiary, and quaternary structure of protein

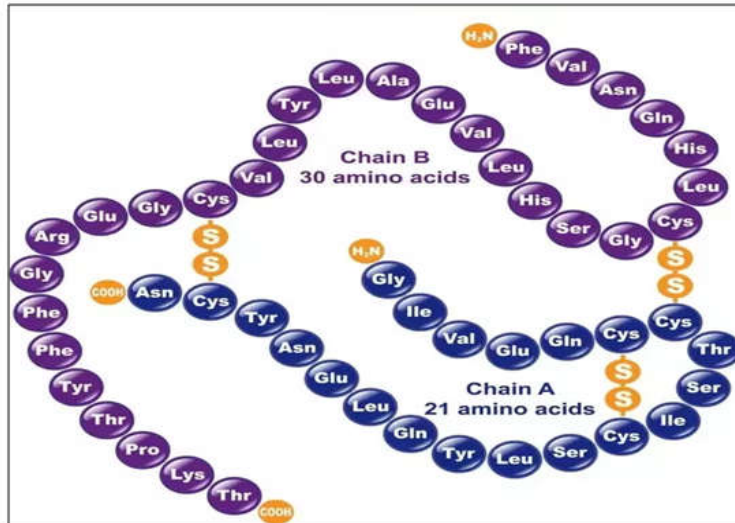


Fig. 7. Insulin primary structure protein [16]

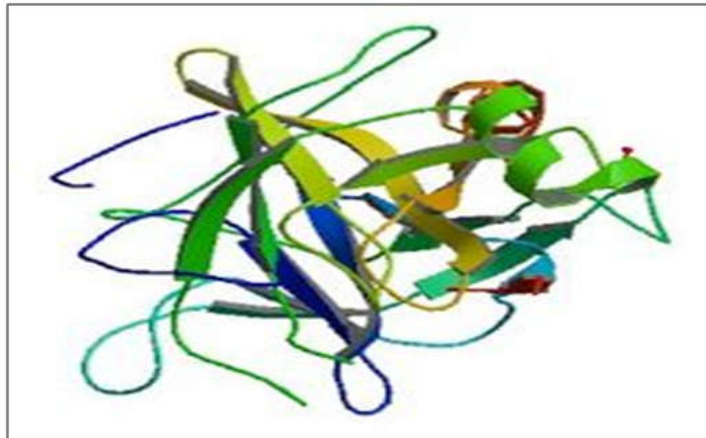


Fig. 8. Secondary structure of chymotrypsin [17]

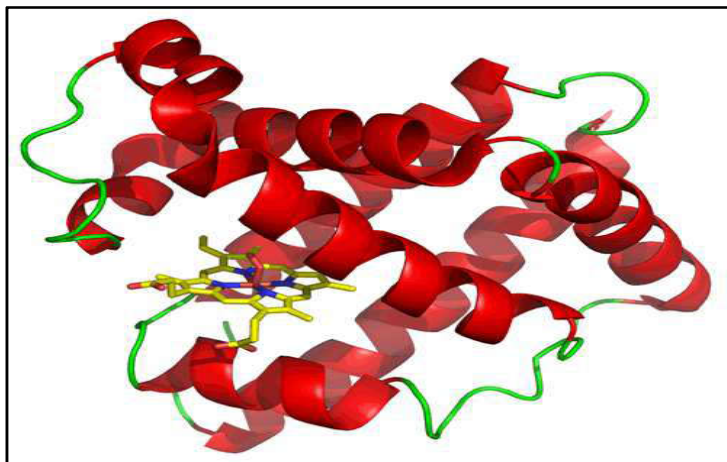


Fig. 9. Tertiary structure of myoglobin [18]

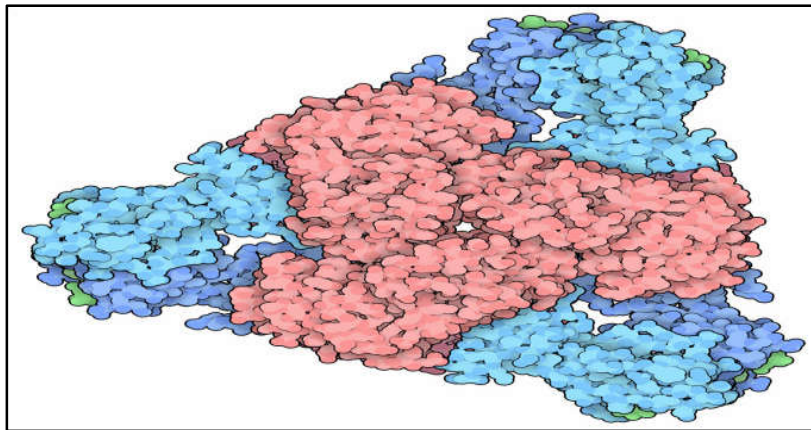


Fig. 10. Quaternary structure of aspartate transcarbamylase [19]

3.3 Tertiary Structure

When secondary structure undergoes tertiary folding, this leads to formation of a tertiary structure. The tertiary structure is stabilized by wide range of interactions, such as disulfide crosslinking, hydrogen bonding, hydrophobic interactions, electrostatic interactions, and Van der Waals interactions. Collagen and myoglobin are an example of tertiary structure proteins (Fig. 9) [1].

3.4 Quaternary Structure

The proteins that contain two or more distinct polypeptide chains or subunits, which may be the same or different. The three-dimensional shape of these protein subunits is described as quaternary structures. These subunits or polypeptide chains can be similar or different, creating homogeneous or heterogeneous quaternary structures. Hemoglobin proteins have a heterogeneous quaternary structure because they consist of 2 α chains and two β chains. Likewise, aspartate transcarbamylase has twelve polypeptide chains or subunits (six catalytic and six regulatory) arranged in the form of two catalytic trimers and three regulatory dimers (Fig. 10) [1].

4. CONCLUSION

Proteins have essential functions in living organisms. Proteins not only serve as structural materials, but they are also involved in regulation, transport, defense, and catalysis of metabolism. Some proteins are multifunctional; they have at least two seemingly independent functions. Proteins can also be divided into categories according to their similarity, their shape, and composition. Biochemists have

identified four levels of protein structure. The primary sequence of amino acid is determined by genetic information. As the polypeptide chain folds, the local folding patterns form the protein's secondary structure. The three-dimensional shape that a polypeptide takes is called tertiary structure. Proteins consisting of two or more polypeptides have a quaternary structure.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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