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Structure, Classification and Functions of Proteins

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ABSTRACT: Proteins are very large molecules composed of basic units called amino acids. Proteins contain carbon, hydrogen, oxygen, nitrogen, and sulphur. Protein molecules are large, complex molecules formed by one or more twisted and folded strands of amino acids. Proteins are highly complex molecules that are actively involved in the most basic and important aspects of life. These include metabolism, movement, defense, cellular communication, and molecular recognition. Positive negative attractions between different atoms in the long amino acid strand cause it to coil on itself again and again to form its highly complex shape. Folded proteins may combine with other folded proteins to form even larger more complicated shapes. The folded shape of a protein molecule determines its role in body chemistry. Structural proteins are shaped in ways that allow them to form essential structures of the body. Collagen, a protein with a fibre shape, holds most of the body tissues together. Keratin, another structural protein forms a network of waterproof fibres in the outer layer of the skin. Functional proteins have shapes that enable them to participate in chemical processes of the body. Functional proteins include some of hormones, growth factors, cell membrane receptors, and enzymes.

KEYWORDS: proteins, shapes, structure, types, functions, classification, enzymes, hormones

I. INTRODUCTION

Protein molecules are large, complex molecules formed by one or more twisted and folded strands of amino acids. Each amino acid is connected to the next amino acid by covalent bonds.^{1,2}

1. **Primary (first level)** – Protein structure is a sequence of amino acids in a chain.
2. **Secondary (secondary level)** – Protein structure is formed by folding and twisting of the amino acid chain.
3. **Tertiary (third level)** – Protein structure is formed when the twists and folds of the secondary structure fold again to form a larger three dimensional structure.
4. **Quaternary (fourth level)** – Protein structure is a protein consisting of more than one folded amino acid chain.

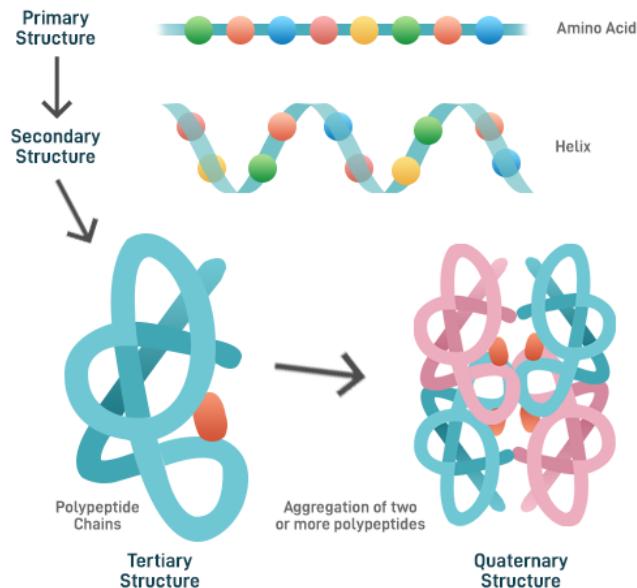
Proteins can bond with other organic compounds and form “mixed” molecules. For example, glycoproteins embedded in cell membranes are proteins with sugars attached. Lipoproteins are lipid-protein combinations.^{3,4}

Nucleic Acids

The two forms of nucleic acid are deoxyribonucleic acid and ribonucleic acid. The basic building blocks of nucleic acids are called nucleotides. Each nucleotide consists of a phosphate unit, a sugar and a nitrogen base. DNA nucleotide bases include adenine, thymine, guanine and cytosine. RNA uses the same set of bases, except for the substitution of uracil for thymine.

Nucleotides bind to one another to form strands or other structures. In the DNA molecule, nucleotides are arranged and twisted, and a double strand called a double helix. The sequence of different nucleotides along the DNA double helix is the “master code” for assembling proteins and other nucleic acids.^{5,6}

PROTEIN STRUCTURE



Primary structure

In the primary structure of proteins, the polypeptide chain consists of a sequence of amino acids. This primary structure has a unique protein structure. The primary structure of this level contains mainly amino acids which are present anywhere in the chain. Peptide bonds are present in the primary structure of the protein. If two amino acids are there to form a chain of proteins it is called a dipeptide bond. Similarly, if three amino acids are ready to form a link it is called tripeptide.^{7,8}

Characteristics of peptide bond:

- A peptide bond is rigid and planar
- It is not able to charge but it is polar.
- It has a partial double bond character.

Secondary structure

This secondary structure is formed by the H-bonds. This secondary structure is formed mostly with the alpha helix and beta pleated sheets. Example: Myoglobin. There are some types of secondary structure^{9,10}

- Alpha Helix
- Beta plated sheet
- Strand
- Loops

Tertiary structure

The tertiary structure of proteins is in the form of a 3Dimentional structure of the monomeric and multimeric structures. Three dimension structure of a polypeptide is simply called the tertiary structure of the protein. This tertiary structure is because of the lowest energy and greatest stability state of the polypeptide chain. The tertiary structure came from folding secondary structure of the protein.^{11,12}

Functions of Tertiary structure:

- It has a unique function like interacting with other molecules.

Quaternary structure

The quaternary structure of proteins is in the form of a 3Dimensional structure of macromolecules which is a combination of individual polypeptide chains. This quaternary structure is also formed from a special combination of tertiary structures. Quaternary structure is also known as oligomeric proteins. Example: Hemoglobin

Functions of quaternary structure:

- It helps in the chromosome replication process.

- It helps in metabolism

Importance

- Protein helps in maintaining good shape and fit for our body.
- Protein repairs the body's damaged tissues.
- Protein is used to build bones, skin, and muscles.

Classification

Classification of proteins is based on the

- Based on the shape
- Based on Constitution
- Based on the Nature of molecules^{13,14}

Based on shape

- Fibrous protein
- Globular proteins

Based on the constitution

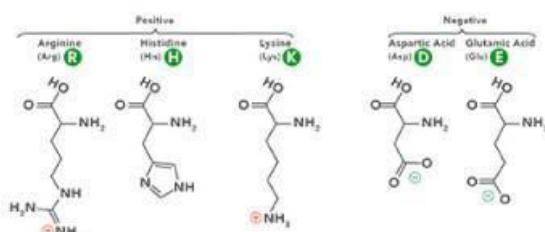
- Simple proteins
- Conjugated proteins

The basic unit of protein-amino acids:

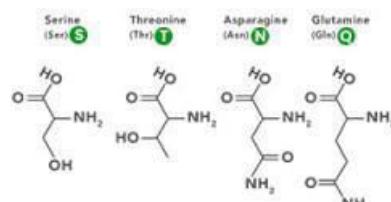
Amino acids are the basic structural unit of protein. Amino acids consist of the carbon atom, a carboxyl group (COOH), and a hydrogen atom.

Amino acids are classified as follows

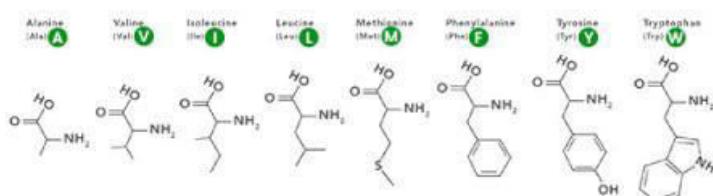
A. Amino Acids with Electrically Charged Side Chains



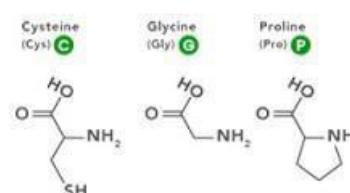
B. Amino Acids with Polar Uncharged Side Chains



D. Amino Acids with Hydrophobic Side Chains



C. Special Cases



- **Aromatic:** Tyrosine, Tryptophan, Phenylalanine.
- **Positively charged:** Lysine, Arginine, Histidine.
- **Negatively charged:** Aspartate, Glutamate.
- **Nonpolar, aliphatic:** Leucine, Methionine, Isoleucine.

Functions

Enzymatic protein

The function of enzymatic protein:

- It accelerates the metabolic process in our cells.
- It also accelerates the metabolic process in stomach digestion, liver functions, and blood clotting.^{15,16}

Hormonal protein

The function of hormonal protein

- Hormonal proteins are protein-based chemicals secreted by endocrine glands.
- By using hormonal protein each hormone affects particular cells in the body.

Structural protein

The function of structural protein

- Structural proteins are very important for the body because they are fibrous proteins.
- It helps in developing muscles, bones, skin, and cartilage.^{17,18}

Defensive protein

The function of defensive protein

- These defensive proteins help in developing antibodies for attacking.
- These antibodies are developed in white blood cells to attack bacteria.

Storage protein

The function of storage protein

- Storage protein stores minerals like potassium.
- Storage protein contains ovalbumin and casein found in milk, and egg whites.

Transport protein

The function of transport protein

- Transport protein called calbindin which is useful for absorption of calcium from intestinal walls.
- Transport proteins carry important materials to the cells of the body.^{19,20}

Receptor protein

- It controls the substances which enter and leave the cells.

Contractile protein.

The function of contractile protein

- It helps in regulating the strength, speed of the heart, and muscle contractions.
- Contractile proteins cause heart complications if the heart produces severe contractions.^{21,22}

II.DISCUSSION

Proteins were recognized as a distinct class of biological molecules in the eighteenth century by Antoine Fourcroy and others, distinguished by the molecules' ability to coagulate or flocculate under treatments with heat or acid.^[1] Noted examples at the time included albumin from egg whites, blood serum albumin, fibrin, and wheat gluten.

Proteins were first described by the Dutch chemist Gerardus Johannes Mulder and named by the Swedish chemist Jöns Jacob Berzelius in 1838.^{[2][3]} Mulder carried out elemental analysis of common proteins and found that nearly all proteins had the same empirical formula, C₄₀₀H₆₂₀N₁₀₀O₁₂₀P₁S₁.^[4] He came to the erroneous conclusion that they might be composed of a single type of (very large) molecule. The term "protein" to describe these molecules was proposed by Mulder's associate Berzelius; protein is derived from the Greek word πρώτειος (proteios), meaning "primary",^[5] "in the lead", or "standing in front",^[6] + -in. Mulder went on to identify the products of protein degradation such as the amino acid leucine for which he found a (nearly correct) molecular weight of 131 Da.^[4] Prior to "protein", other names were used, like "albumins" or "albuminous materials" (Eiweisskörper, in German).^[7]

Early nutritional scientists such as the German Carl von Voit believed that protein was the most important nutrient for maintaining the structure of the body, because it was generally believed that "flesh makes flesh."^[8] Karl Heinrich Ritthausen extended known protein forms with the identification of glutamic acid. At the Connecticut Agricultural Experiment Station a detailed review of the vegetable proteins was compiled by Thomas Burr Osborne. Working with Lafayette Mendel and applying Liebig's law of the minimum in feeding laboratory rats, the nutritionally essential amino acids were established. The work was continued and communicated by William Cumming Rose. The understanding of proteins as polypeptides came through the work of Franz Hofmeister and Hermann Emil Fischer in 1902.^{[9][10]} The central role of proteins as enzymes in living organisms was not fully appreciated until 1926, when James B. Sumner showed that the enzyme urease was in fact a protein.^[11]

The difficulty in purifying proteins in large quantities made them very difficult for early protein biochemists to study. Hence, early studies focused on proteins that could be purified in large quantities, e.g., those of blood, egg white, various toxins, and digestive/metabolic enzymes obtained from slaughterhouses. In the 1950s, the Armour Hot Dog Co. purified 1 kg of pure bovine pancreatic ribonuclease A and made it freely available to scientists; this gesture helped ribonuclease A become a major target for biochemical study for the following decades.^[4]

Linus Pauling is credited with the successful prediction of regular protein secondary structures based on hydrogen bonding, an idea first put forth by William Astbury in 1933.^[12] Later work by Walter Kauzmann on denaturation,^{[13][14]} based partly on previous studies by Kaj Linderstrøm-Lang,^[15] contributed an understanding of protein folding and structure mediated by hydrophobic interactions.

The first protein to be sequenced was insulin, by Frederick Sanger, in 1949. Sanger correctly determined the amino acid sequence of insulin, thus conclusively demonstrating that proteins consisted of linear polymers of amino acids rather than branched chains, colloids, or cyclols.^[16] He won the Nobel Prize for this achievement in 1958.^[17]

With the development of X-ray crystallography, it became possible to sequence protein structures.^[18] The first protein structures to be solved were hemoglobin by Max Perutz and myoglobin by John Kendrew, in 1958.^{[19][20]} The use of computers and increasing computing power also supported the sequencing of complex proteins. In 1999, Roger Kornberg succeeded in sequencing the highly complex structure of RNA polymerase using high intensity X-rays from synchrotrons.^[18]

Since then, cryo-electron microscopy (cryo-EM) of large macromolecular assemblies^[21] has been developed. Cryo-EM uses protein samples that are frozen rather than crystals, and beams of electrons rather than x-rays. It causes less damage to the sample, allowing scientists to obtain more information and analyze larger structures.^[18] Computational protein structure prediction of small protein domains^[22] has also helped researchers to approach atomic-level resolution of protein structures. As of 2017, the Protein Data Bank has over 126,060 atomic-resolution structures of proteins.^[23]

III.RESULTS

Proteins are assembled from amino acids using information encoded in genes. Each protein has its own unique amino acid sequence that is specified by the nucleotide sequence of the gene encoding this protein. The genetic code is a set of three-nucleotide sets called codons and each three-nucleotide combination designates an amino acid, for example AUG (adenine–uracil–guanine) is the code for methionine. Because DNA contains four nucleotides, the total number of possible codons is 64; hence, there is some redundancy in the genetic code, with some amino acids specified by more than one codon.^[30] Genes encoded in DNA are first transcribed into pre-messenger RNA (mRNA) by proteins such as RNA polymerase. Most organisms then process the pre-mRNA (also known as a primary transcript) using various forms of Post-transcriptional modification to form the mature mRNA, which is then used as a template for protein synthesis by the ribosome. In prokaryotes the mRNA may either be used as soon as it is produced, or be bound by a ribosome after having moved away from the nucleoid. In contrast, eukaryotes make mRNA in the cell nucleus and then translocate it across the nuclear membrane into the cytoplasm, where protein synthesis then takes place. The rate of protein synthesis is higher in prokaryotes than eukaryotes and can reach up to 20 amino acids per second.^[34]

The process of synthesizing a protein from an mRNA template is known as translation. The mRNA is loaded onto the ribosome and is read three nucleotides at a time by matching each codon to its base pairing anticodon located on a transfer RNA molecule, which carries the amino acid corresponding to the codon it recognizes. The enzyme aminoacyl tRNA synthetase "charges" the tRNA molecules with the correct amino acids. The growing polypeptide is often termed the nascent chain. Proteins are always biosynthesized from N-terminus to C-terminus.^[30] The size of a synthesized protein can be measured by the number of amino acids it contains and by its total molecular mass, which is normally reported in units of daltons (synonymous with atomic mass units), or the derivative unit kilodalton (kDa). The average size of a protein increases from Archaea to Bacteria to Eukaryote (283, 311, 438 residues and 31, 34, 49 kDa respectively) due to a bigger number of protein domains constituting proteins in higher organisms.^[35] For instance, yeast proteins are on average 466 amino acids long and 53 kDa in mass.^[27] The largest known proteins are the titins, a component of the muscle sarcomere, with a molecular mass of almost 3,000 kDa and a total length of almost 27,000 amino acids.^[36]

The best-known role of proteins in the cell is as enzymes, which catalyse chemical reactions. Enzymes are usually highly specific and accelerate only one or a few chemical reactions. Enzymes carry out most of the reactions involved in metabolism, as well as manipulating DNA in processes such as DNA replication, DNA repair, and transcription. Some enzymes act on other proteins to add or remove chemical groups in a process known as posttranslational modification. About 4,000 reactions are known to be catalysed by enzymes.^[46] The rate acceleration conferred by enzymatic catalysis is often enormous—as much as 10^{17} -fold increase in rate over the uncatalysed reaction in the case of orotate decarboxylase (78 million years without the enzyme, 18 milliseconds with the enzyme).^[47]

The molecules bound and acted upon by enzymes are called substrates. Although enzymes can consist of hundreds of amino acids, it is usually only a small fraction of the residues that come in contact with the substrate, and an even smaller fraction—three to four residues on average—that are directly involved in catalysis.^[48] The region of the enzyme that binds the substrate and contains the catalytic residues is known as the active site.

Dirigent proteins are members of a class of proteins that dictate the stereochemistry of a compound synthesized by other enzymes.^[49]

Many proteins are involved in the process of cell signaling and signal transduction. Some proteins, such as insulin, are extracellular proteins that transmit a signal from the cell in which they were synthesized to other cells in distant tissues. Others are membrane proteins that act as receptors whose main function is to bind a signaling molecule and induce a biochemical response in the cell. Many receptors have a binding site exposed on the cell surface and an effector domain within the cell, which may have enzymatic activity or may undergo a conformational change detected by other proteins within the cell.^{[29]:251–81}

Antibodies are protein components of an adaptive immune system whose main function is to bind antigens, or foreign substances in the body, and target them for destruction. Antibodies can be secreted into the extracellular environment or anchored in the membranes of specialized B cells known as plasma cells. Whereas enzymes are limited in their binding affinity for their substrates by the necessity of conducting their reaction, antibodies have no such constraints. An antibody's binding affinity to its target is extraordinarily high.^{[30]:275–50}

Many ligand transport proteins bind particular small biomolecules and transport them to other locations in the body of a multicellular organism. These proteins must have a high binding affinity when their ligand is present in high concentrations, but must also release the ligand when it is present at low concentrations in the target tissues. The canonical example of a ligand-binding protein is haemoglobin, which transports oxygen from the lungs to other organs and tissues in all vertebrates and has close homologs in every biological kingdom.^{[30]:222–29} Lectins are sugar-binding proteins which are highly specific for their sugar moieties. Lectins typically play a role in biological recognition phenomena involving cells and proteins.^[50] Receptors and hormones are highly specific binding proteins.

Transmembrane proteins can also serve as ligand transport proteins that alter the permeability of the cell membrane to small molecules and ions. The membrane alone has a hydrophobic core through which polar or charged molecules cannot diffuse. Membrane proteins contain internal channels that allow such molecules to enter and exit the cell. Many ion channel proteins are specialized to select for only a particular ion; for example, potassium and sodium channels often discriminate for only one of the two ions.

IV.CONCLUSIONS

Most microorganisms and plants can biosynthesize all 20 standard amino acids, while animals (including humans) must obtain some of the amino acids from the diet.^[42] The amino acids that an organism cannot synthesize on its own are referred to as essential amino acids. Key enzymes that synthesize certain amino acids are not present in animals—such as aspartokinase, which catalyses the first step in the synthesis of lysine, methionine, and threonine from aspartate. If amino acids are present in the environment, microorganisms can conserve energy by taking up the amino acids from their surroundings and downregulating their biosynthetic pathways.

In animals, amino acids are obtained through the consumption of foods containing protein. Ingested proteins are then broken down into amino acids through digestion, which typically involves denaturation of the protein through exposure to acid and hydrolysis by enzymes called proteases. Some ingested amino acids are used for protein biosynthesis, while others are converted to glucose through gluconeogenesis, or fed into the citric acid cycle. This use of protein as a fuel is particularly important under starvation conditions as it allows the body's own proteins to be used to support life, particularly those found in muscle.^[88]

In animals such as dogs and cats, protein maintains the health and quality of the skin by promoting hair follicle growth and keratinization, and thus reducing the likelihood of skin problems producing malodours.^[89] Poor-quality proteins also have a role regarding gastrointestinal health, increasing the potential for flatulence and odorous compounds in dogs because when proteins reach the colon in an undigested state, they are fermented producing hydrogen sulfide gas, indole, and skatole.^[90] Dogs and cats digest animal proteins better than those from plants, but products of low-quality animal origin are poorly digested, including skin, feathers, and connective tissue.^[90]

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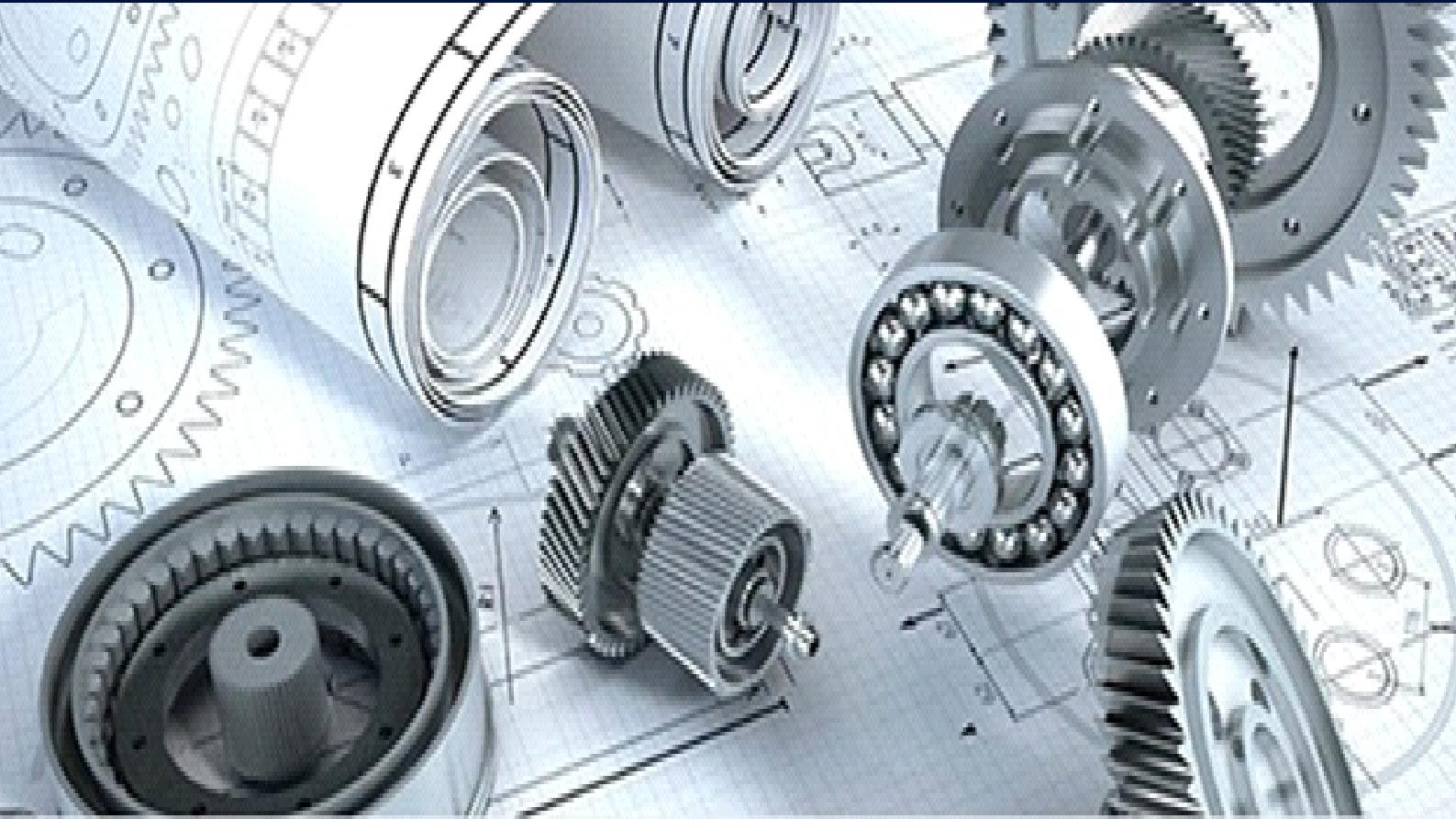
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