A simple method for instructing protein structure for medical students: a case review

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ABSTRACT

In the process of learning basic biochemistry, as in any other area, much extra class work is required for students before basic concepts, such as those concerning protein structure and properties, are firmly settled. To reach this end we have developed a simple instruction method to teach protein structure in biochemistry courses for medical students. The objectives of this method are to illustrate some aspects of protein structure; to allow students to gain competence by learning a number of biochemical and molecular biology teaching techniques easy enough to carry out to ensure a successful outcome; and to allow students to become skilled in processing, presenting and discussing data obtained directly by themselves, or furnished by the instructor. The method of this paper can be successfully used to illustrate, explain and characterize most of the physical and chemical properties of proteins.

Key Words *PROTEIN SPECIAL STRUCTURE, ILLUSTRATIVE TEACHING TECHNIQUE*

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Introduction

The proteins' structure had a direct influence of their function (1). The linear sequence of amino acid residues in a polypeptide chain determines the three-dimensional configuration of a protein; the structure of a protein in turn determines its function (2). Proteins play a major role in forming cellular structure and determine the physical characteristics of the cell (3). All living processes are in some way or another regulated by proteins. There is a close relation between structure and function (4) and a detailed study of protein structure enables us to understand how a macromolecule works. The basic concept of biochemistry and molecular biology is frequently taught at the beginning of the first semester of undergraduate medical course here at Babol University of Medical Sciences (5). Medical students often find basic biochemical subjects hard to digest since they deemed it irrelevant to clinical practice. It is therefore reasonable that the students are not interested in learning this kind of biological concept.

On the other hand, in the process of learning fundamentals of biochemistry, as in any other area, much extra class work is required for students before they form a sound understanding of basic concepts such as those related to protein structure and protein spatial configuration. It is evident that any effort at the part of instructors to facilitate tangible illustration of protein structure will be most welcomed by the students.

Given the abundance of topics to be covered and the limited class time, instructors must be creative and flexible to provide such facilitations.

To provide the medical student with an effective tool helping in understanding protein structural and spatial configuration, we devised a new method to illustrate the amino acid and protein structure. The following is a thorough description of this new method.

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Amino acid structure

To learn amino acid structure twenty different

colored papers are used for twenty essential amino acids. Twenty main models of amino acids were made by some pieces of thick colored paper and thread. Different colors were selected for -COOH, -NH, α-Carbon and R groups. Each atom of H, O, C, and N are stained by a different marker. Polar, nonpolar, negative and positive charged side chains of amino acids, hydrophobic and hydrophilic amino acid residues are more tangibly presented through this model in comparison to two-dimensional illustration de- picted in standard textbooks. Rotation around α carbon in a number of amino acid residues and no rotation in others such as proline was better emphasized through this model.

Peptide, Polypeptide and Protein Structure

To show peptide and polypeptide linkage, the models of the amino acid residues were linked together with thread. To illustrate peptide, polypeptide and protein structure and the way amino acid residues are bound to each other, students simply connected amino acid residues together by a strand of thread. Structure of oligopeptide, polypeptide and proteins were demonstrated by less than 10 amino acid residue, 100 amino acid residue and more than 100 amino acid residues, respectively. The students worked with 10 to over 100 amino acids and made oligopeptides, polypeptides and proteins. This simple work, made them more familiar with amino acid residue varieties in the structure of the proteins. Also, they learned about N and C terminals and numbering of amino acids and their sequences in proteins. For instance, they made insulin with the models of the amino acid residues. Moreover, they learned about the function of some proteins. They have gotten familiar with protein structure and have experienced a kind of cooperative work.

Primary Structure of Proteins

The amino acid sequence along a polypeptide chain is known as the primary structure of the protein. To illustrate the primary structure of protein, as it was mentioned before, peptide bound of amino acid residues have been connected by strands of thread. Amino acid residues were linked together to show a peptide junction in primary structure. Demonstration of the flexibility of protein structure could be easily accomplished because of the elasticity of thread. So, students were introduced to the arrangement of amino acid residues in the primary structure of proteins.

Secondary structure of proteins

α-Helices and β-Pleated sheets present the secondary structure. α-helices and β-Pleated sheets are regularly repeating secondary structures formed by hydrogen bonds between the carboxyl of one peptide bond and the (-NH) of another peptide bond in a protein. In α-Helix, each carboxyl of a peptide bond forms a hydrogen bond with the (-NH) of another peptide bond from amino acid residues farther along the chain. The formation of these hydrogen bonds makes a right-handed helix that contains 3.6 amino acid residues in each turn. The side chains of the amino acid residues extend outward from the central axis of the rod-like structure. The α-Helix is disrupted by proline residues, in which the amine agent impose geometrical constraints, and by regions in which numerous amino acid residues have β-Pleated sheets. β-Pleated sheets may be formed by hydrogen bonds between two extended polypeptide chains or between two regions of a single chain. The sheets are parallel if the chains run in the same direction or anti-parallel if they run in opposite directions. Some fibrous proteins, such as silk fibrin, consist almost entirely of β-Pleated sheets. Globular proteins may contain regions β-Pleated sheets that are formed in areas where the chain folds back on itself. Hydrophobic amino acid residues tend to collect in the interior side of globular protein where they repelling water, while hydrophilic residues are usually found on the surface where they interact with water. The types of interactions between amino acid residues that produce the three-dimensional shape of protein includes: hydrophobic interactions, electrostatic interactions, hydrogen bonds, and disulfide bonds. Using strands of thread for amino acid connection, students applied colored springs to show the connection between H and N atoms. The students connected the carbon of one amino acid to the nitrogen of another. Also, they produced a linkage between H, N and /or O atoms with a spring wire and showed hydrogen bound in the second structure of proteins as well as α-Helix and β-Pleated sheet. The internal and external hydrogen bound, α-helix and β-Pleated sheet structure were tangibly outlined for the students.

Tertiary Structure of Proteins

Other forces producing the three-dimensional conformation of a protein include electrostatic and hydrophobic interactions and hydrogen and disulfide bonds. The tertiary structure of a protein refers to its overall three-dimensional conforma-

tion. It is produced by interactions between amino acid residues that may be located at a considerable distance from each other in the primary sequence of the polypeptide chain. In addition to using strand of thread for amino acid connection (peptide chain) and colored spring for hydrogen bound between H and N atoms, students used colored wire to show the effect of positive and negative side chain. The students used colored wires to show effects of side chain and compression and decompression of amino acid residues.

They experienced the effect of side chains by pressing and releasing amino acid residues. The spatial structures of proteins were also clearly presented for students through this method.

Quaternary Structure of Proteins

Quaternary structure refers to the spatial arrangement of subunits in a protein that consists of more than one polypeptide chain. The subunits are joined together by the same types of bonds that join various segments of a single chain to form its tertiary structure. Hemoglobin is an example of a protein in which the amino acid sequence and three-dimensional structure have been extensively studied and correlated with its function. The structure of hemoglobin consists of four polypeptide chains (two α and two β chains), each containing a molecule of heme. The α and β chains of HbA are similar in three-dimensional configuration to each other and to the single chain of muscle myoglobin, although their amino acid sequences differ. There are eight regions of α-Helix in each chain. The nonpolar amino acids are in the interior and the charged amino acids are on the surface. Heme fits into a crevice in each globin chain near two histidine residues. The iron in the heme ring binds to one histidine and the other histidine stabilizes the ferrous form of iron. As previously shown two strands of amino acid residues were linked with plastic springs, to show salt bridges or disulfide links. To show the quaternary structure of proteins a molecule of hemoglobin and myoglobin were selected and compared. As previously demonstrated four chains of hemoglobin were connected to each other by four colored strands of thread as a bridge, whereas only one chain was used for myoglobin. Also, they compared hemoglobin and myoglobin structures as quarternary and tertiary structure of proteins respectively. To demonstrate hemoglobin they stick four envelopes on an A4 paper sheet and put a button in each of the envelopes that represented iron (Fe). Moreover, they put an envelope on a square sheet and with the help of a button, they tried to show the iron on the myoglobin chain and then they linked the button to the other one to show oxygen-iron linkage and that each myoglobin carries a heme, an iron and oxygen molecule. Also, to show the position of oxygen, a colored button sticks outside the envelopes. Then by using a strand of thread, these two buttons were connected to each other. Therefore, it has been shown that, hemoglobin contains four envelopes (heme), four Iron atoms and four oxygen atoms whereas myoglobin molecules contain only one envelope (heme), one iron atom and one oxygen atom.

Discussion

Hydrogen bonds, disulfide bonds, sheets and helices and subunit interactions were illustrated in a tangible way for the students by themselves. Also, students were equipped with a method that enables them to closely examine amino acid, oligopeptide, polypeptide and protein structures. The method presented here offers particular advantages for teaching protein structure to medical students. In our experience with this method students show grate interest and participate in team work enthusiastically. To assess the extent of this method effectiveness in students' understanding protein structure further studies is needed.

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