Lecture :.....4.....

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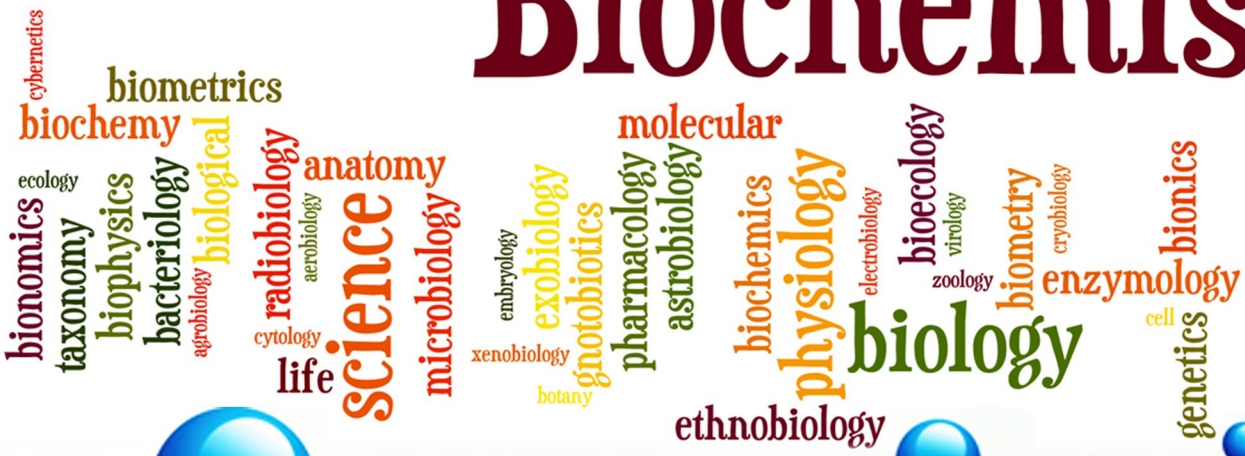
☐ Slide ■ Sheet

Medical Committee
The University of Jordan

Biochemistry



Mousa Suboh

Protein Structures

Protein structure can be divided into four levels based on the complexity of structure (from the simplest to the most complex):

1- Primary
2- Secondary
3- Tertiary
4- Quaternary

Let's start with **the quaternary:**
Quaternary as a structure means that the protein as a whole is composed of more than one polypeptide subunit (polypeptide chains).
E.G: Hemoglobin protein is composed of 4 polypeptide subunits.

The Tertiary structure: Is the overall 3-D structure and arrangement of atoms for one polypeptide chain or a protein that is made of one polypeptide chain. It must be defined and consistent, meaning it has to remain the same

Primary structure:
The whole polypeptide is composed of primary structure which is the order of amino acids starting from the N-terminus to the C-terminus (left to right).

Importance of the primary structure of any protein is determining the overall structure of the protein. Changing one of the amino acids will disrupt the whole 3D structure.

e.g. sickle cell anemia: mutation of the no.6 amino acid from glutamic acid (hydrophilic negatively charged) to valine (hydrophobic non-polar aliphatic) →the presence of valine at the surface of the protein results in clumping and aggregating the hemoglobin molecules in the RBC instead of having individual molecules of Hb you will have an array of molecules interacting with each other at the valine sight which will change the structure of the RBC that will result in clumping of the RBC's themselves and clogging the blood vessels.

Secondary structure:
Localized arrangement of the backbone (nitrogen, alpha carbon and the carbonyl) which results because of the flexibility of rotation within the amino acid (the peptide bond itself doesn't rotate – double bond characteristic) caused by the ability of the phi and psi bonds to rotate so the R-group can be up or down depending on the neighboring amino acid .
Phi → bond between the nitrogen and the alpha carbon
Psi→ bond between the carbonyl and the alpha carbon.

There are common secondary structures that are present in proteins but not all proteins have all of these secondary structures → depends on the primary sequence which determines the secondary and tertiary and quaternary structure.

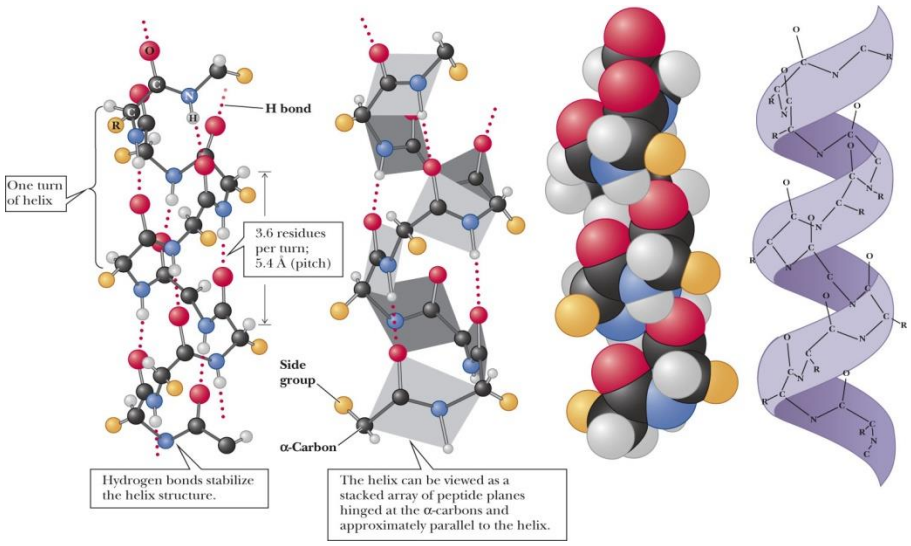
Secondary structures are:

1- Alpha helix
2- Beta - pleated sheet
3- Turns
4- Loops

1- Alpha helix:

It's a helical, rod-like a spring → 3.6 A.A. per turn

The distance (the pitch) between an amino acid at a point and another amino acid at the same point -but above it- is 5.4 Angstroms.



*hydrogen bonding between the backbone (not R-groups) helps stabilize the secondary structures →LINEAR (straight) hydrogen bonds within the alpha helix (being straight strengthens these bonds and helps stabilize the secondary structure too) are between the oxygen from the carbonyl and the hydrogen linked to the nitrogen.

*certain amino acids <u>DO NOT</u> exist in the alpha helices such as:

1-**Glycine →** because it's too small which would disrupt the smooth flow of the alpha helix.

2-**Proline →** exists at the end of the alpha helices and break it to start another structure because it has a rigid structure and no rotation around the psi bond in addition that it can't form hydrogen bonds because it doesn't have a hydrogen bond donor.

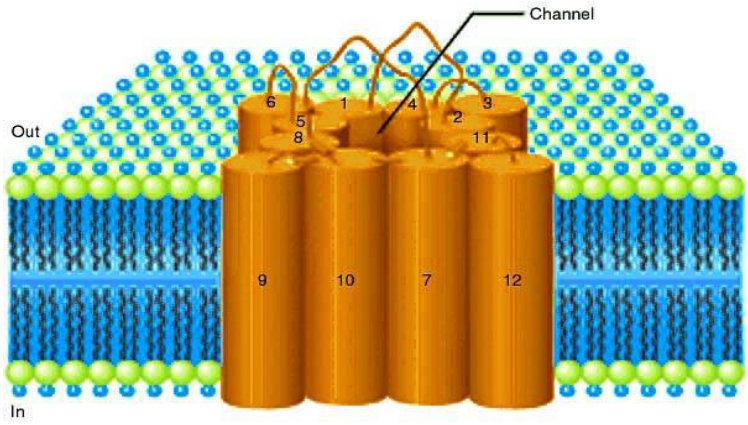
3- **Close proximity of charged amino acids with similar charges** (e.g. you have arginine and lysine on top of each other will result in repulsion between the two positive charges).

4- **Amino acids with branches at the β-carbon atom (valine, threonine, and isoleucine)**

**amphipathic alpha helices:

Is an alpha helix that has from one side non-polar hydrophobic a.a and on the other side a hydrophilic charged a.a

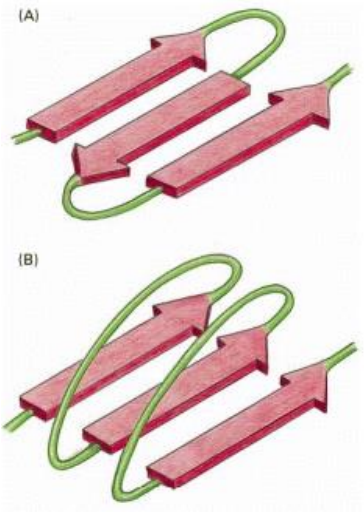
Exist mainly in proteins that form channels in the plasma membrane to pass charged ions that are repulsed by the hydrophobic membrane → the channel is made of several alpha helices that create a hole in the middle (to the outside you have the non-polar amino acids exposed to the fatty acid and to the inside you have the polar charged a.a that attract the charged ions)



2- Beta-pleated sheet:

Made up of multiple beta strands (beta strand has a zigzag structure with R-groups extending outwards - as in the alpha helix) on top of each other → stabilized by hydrogen bonds

*Beta – pleated sheet can be found in two forms: parallel and anti parallel



- Parallel: same direction beta strands → each amino acid can form two hydrogen bonds with **two different** amino acids that are separated by another amino acid.
- Anti parallel : opposite direction beta strands → each amino acid can form two hydrogen bonds with the **ONLY ONE** other amino acid (more stable)

*β sheets can form between many strands, typically 4 or 5 but as many as 10 or more Such β sheets can be purely antiparallel, purely parallel, or mixed .

*amino acids can disrupt beta strands particularly proline.

*Valine, threonine and Isoleucine tend to be present in β-sheets.

3- Turns:

*It exist to connect different secondary structures

* Composed of only four amino acids → two of them are proline and glycine → proline creates a kink and glycine fits in a small position in the turn.

* Turns are stabilized by hydrogen bonding between amino acid **no.1** and **no.4** the rest are not involved in any hydrogen bonding.

4- Loops:

*Don't have a regular structure

*They connect secondary structures like turns but they **are larger** than turns.

****super secondary structure**:

Region that has a collection of multiple secondary structures and they are 2 types:

1- **Motifs**: repetitive secondary structure, small (20 a.a), they may not indicate a certain function but they may indicate a certain structure for a protein. (Check slide 27 and 28 to know types of motifs). They have to be repetitive, not separated by any other structure. Are mainly found in DNA binding proteins along with other proteins. Another more complex motif is the immunoglobulin fold, such as antibodies and the folds are found in their antigen binding sites.

2-**domains**

Tertiary structure:

Is the overall 3-D structure and arrangement of atoms for one polypeptide chain or a protein that is made of one polypeptide chain. It must be defined and consistent, meaning it has to remain the same, (not random, well organized). (Check slide 30 for more definitions).

Zooming into the tertiary structure you would find localized arrangement of specific structures (e.g. helical structure) which is part of the 3D structure of the protein (secondary structures).

*ways to look at tertiary structures: (slide 31)
-ball and stick→ a ball for every atom
-trace structure→ shows only the backbone (no R-groups and no side chains)

-ribbon structure→represent the alpha helices (ribbon) and the beta strands (arrows)
-cylinder structure→represent the alpha helices (cylinder) and the beta strands (arrows)
- Space filling structure.
-protein surface map→ shows the external structure of the protein.

**what determines the tertiary structure of a protein?

The set of chemical forces:

1- Non-covalent interactions (H-bonds, hydrophobic interactions, Van Der Waals interactions, and the electrostatic interactions)

2- Covalent bonds

-Non-covalent interactions:

*H-bonds: between polar **R-groups** (remember that the secondary structure is stabilized by H-bonds within **the backbone**). They can occur between amino acids and the surrounding environment.

*Charged-charged interactions (electrostatic interactions or salt bridges): e.g. between lysine (positively charged) and glutamic acid (negatively charged).

*Charged-dipole interactions: between the charged group and surrounding environment (water)

*Van der Waals: the weakest and the most dynamic interactions are due to the temporary clustering of electrons in one side → having so many of them in a protein form a very strong force in the protein.

ومن يتهيب صعود الجبال يعش أبد الدهر بين الحفر

دعوات صادقة من قلوبكم بأن نلتقي في جنان الخلد.

تحياتي ..

سرى خليل أبوسليم