بسم الله الرحمن الرحيم

BioChemistry | FINAL 1

Proteins & Peptides Pt.1

Written by : **Mousa Al-Neimat**

Reviewed by : **Heba Salah**

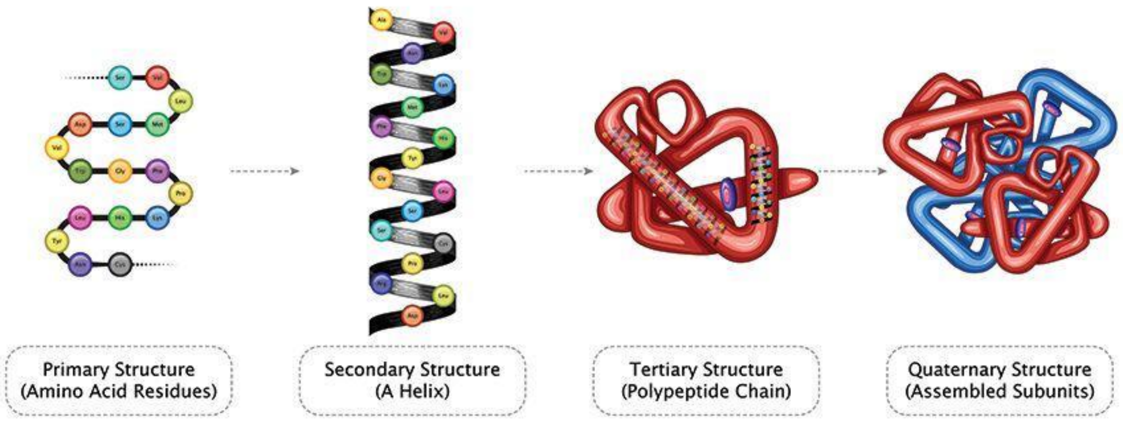
POLYPEPTIDES AND PROTEINS

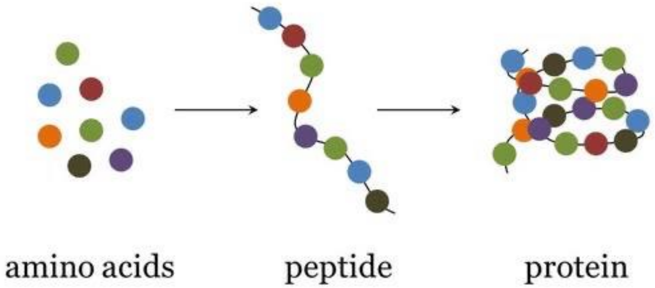
Prof. Nafez Abu Tarboush

Proteins:

- Proteins can change their conformation .
- They are not static (rigid) but **dynamic** in their nature giving huge number of conformations.
- The conformations of a protein that are fully active, which is referred to as the native conformations of that protein.

- Protein has primary, secondary, tertiary and quaternary structures





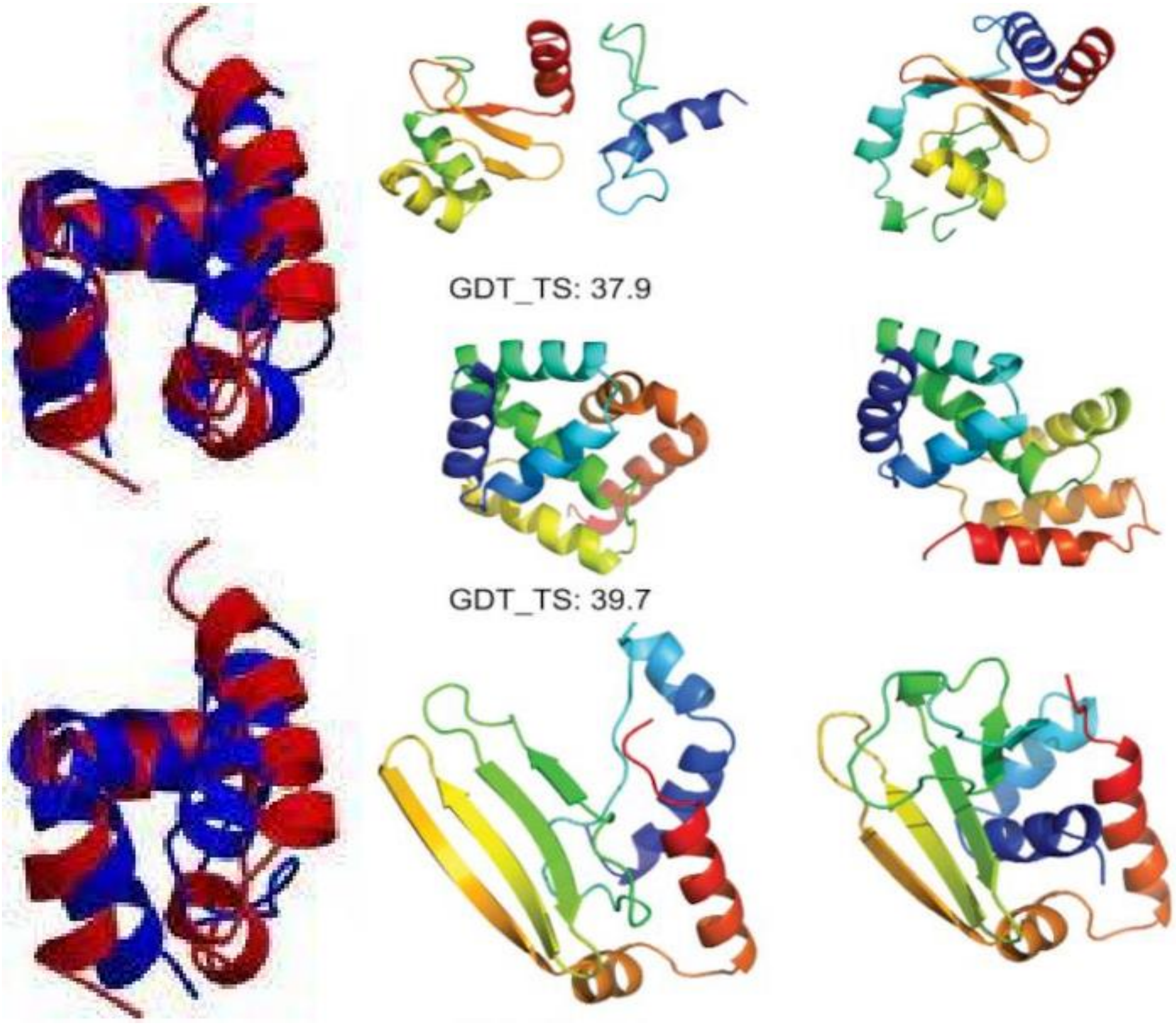
PROTEINS

Why proteins are the most abundant? Because they can exist in different conformations.

- **Native conformation**

~ A protein may have gazillion possibilities of structures, but at least one of these conformations has to be 100% functionally effective, and it's called the native conformation. In some cases, a protein may adopt more than one native conformation, but there must be at least one form that fully carries out its biological function.

-Each protein has a very high number of conformations, that way it's the most abundant macromolecule in our body.



LEVELS OF PROTEIN STRUCTURE

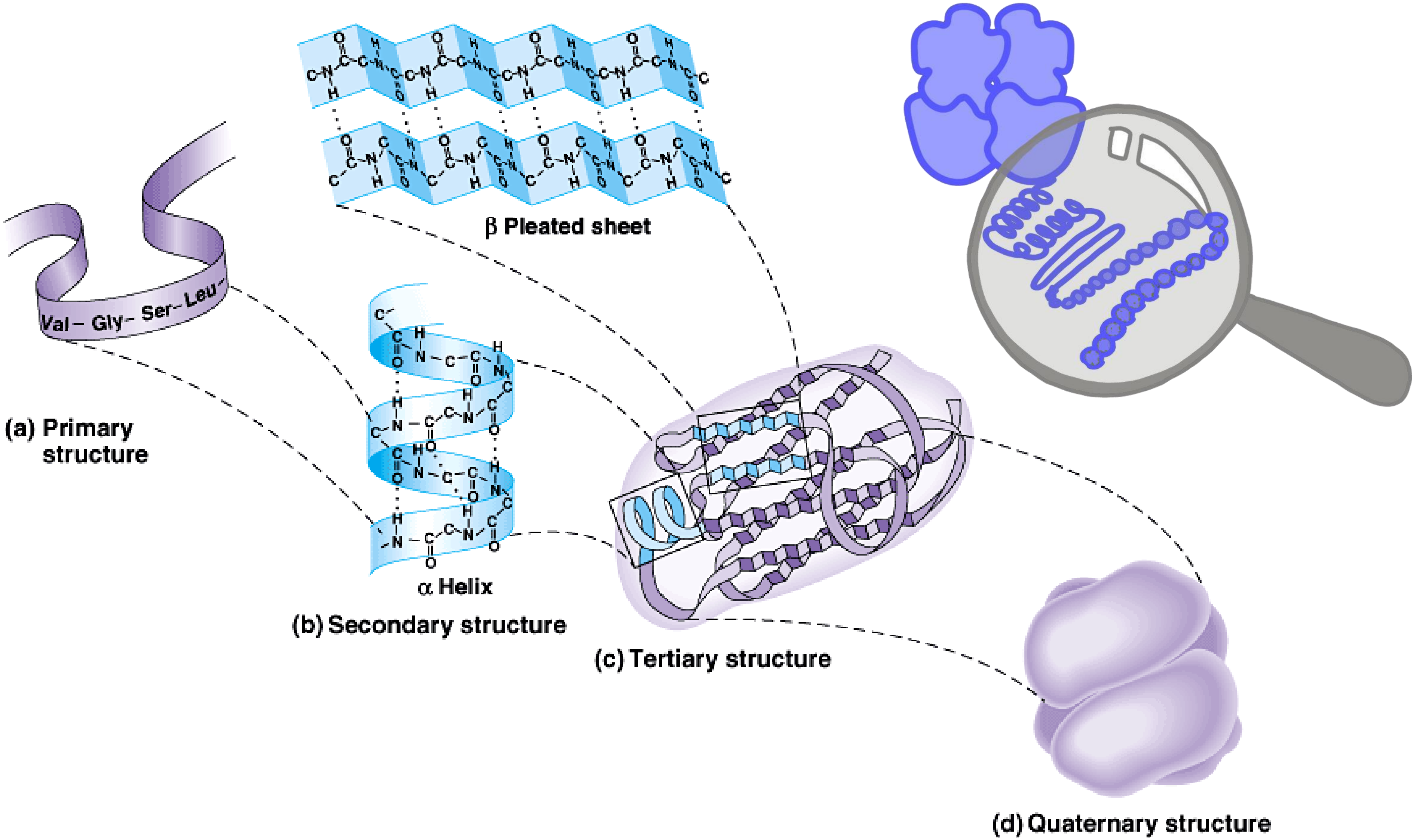
We study the levels of protein structure because each level builds on the previous one. The primary structure (the amino acid sequence) determines how the chain folds into secondary structures (such as α-helices and β-sheets). These fold further into the tertiary structure (the full 3D shape of a single polypeptide). If a protein is made of more than one polypeptide chain, these chains assemble into the quaternary structure. Each level is essential for the next, and together they define the protein's final shape and function.

- **Primary structure**: the number, type, and sequence of amino acid residues
- **Secondary structure**: the localized organization of parts of a polypeptide chain
- **Tertiary structure**: the three-dimensional structure and/or arrangement of all the amino acids residues of a polypeptide chain.
- The tertiary structure is the final structure for polypeptide that consists of only one polypeptide chain.
- Some proteins are made of multiple polypeptides crosslinked (connected) with each other. These are known as multimeric proteins.
- **Quaternary structure** describes the number and relative positions of the subunits in a multimeric protein
- The Quaternary structure is the final shape of protein that contains of more than one polypeptide chain.

Protein structure levels describe how the protein is built through different types of bonding between amino acids — starting from peptide bonds in the primary structure to more complex interactions in the secondary, tertiary, and quaternary structures.

Each protein must go through different levels of structural organization, similar to the process of building a house. The amino acids act like the foundation of the house – they are the basic building blocks. As these amino acids start to interact with nearby ones, they fold into localized patterns, forming the secondary structure, which can be compared to the walls of the house.

Then, the entire chain continues to fold into a unique three-dimensional shape, creating the tertiary structure, similar to assembling all parts of the house into a complete and functional building. In some cases, multiple protein chains come together, forming the quaternary structure, just like connecting different sections or wings of a complex building.


Val – Gly – Ser – Leu
(a) Primary structure
β Pleated sheet
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

PRIMARY STRUCTURE (sequence of amino acids).

- It is unfolded in shape.

- The next structural levels of protein depends on the primary structure (cuz the primary structure is composed of sequence of amino acids that are going to interact with each other through ~>hydrogen bonds, hydrophobic interactions between side chines and electrostatic interactions ,these interactions that are determined by the sequence of amino acid will determine the foldings and twisting of the polypeptid

- For example, if the sequence includes hydrophobic amino acids like tryptophan they will tend to cluster together inside the protein, away from water, forming hydrophobic interactions. On the other hand, if the sequence includes polar or charged amino acids like aspartic acid, they will not form hydrophobic interactions and will lead to a different folding pattern.

- Ultimately, the final shape — and thus the function — of the protein is always determined by the sequence of amino acids in its primary structure.

- Hemoglobin is a protein composed of 4 subunits (two identical
- α-polypeptide chains and two identical β polypeptide chains):

- α → binds to oxygen firstly (harder).
- β → binds to oxygen secondly (Easier).

So, these subunits have the same function which is binding to oxygen but since β is has relatively low affinity for binding to oxygen compared to α subunit, α subunit bind firstly to oxygen making binding of β subunit to the oxygen atom easier, and binding of the second β subunit to oxygen easier than the first.

1.the α subunits have high affinity for binding to oxygen so they bind to oxygen.

2.binding of α subunits to oxygen causes a conformational change in the shape of hemoglobin —-> which results it becomes easier for β to bind to oxygen.

Q: Why do we need Hemoglobins?

A:To transfer Oxygen (binding & releasing).

Q:Why doesn’t oxygen simply diffuse in the blood plasma instead of being transported by hemoglobin, considering that producing a large amount of hemoglobin in red blood cells would require high ATP consumption? What makes the use of hemoglobin more critical or efficient than relying on passive diffusion of oxygen through plasma alone although oxygen is diffusible in water (can be dissolved in water) ?

A:The area that the blood is susceptible to oxygen is too small, so we need haemoglobin to pick up oxygen.

-Hemoglobin gives oxygen to other molecules that have higher affinity for oxygen (Myoglobin).

- Myoglobin is the protein that picks up oxygen from Hemoglobin in every cell in our body. (It is present in high concentrations in the muscles due to their high oxygen need for movement).

- -Myoglobin exists in the cytoplasm and delivers oxygen to mitochondria, where it is taken up by a protein with even higher oxygen affinity – for use in the electron transport chain.

The journey of oxygen begins in the air, passes into the lungs, and then enters the blood, where it binds specifically to hemoglobin. From there, oxygen is delivered to tissues, where it is picked up by myoglobin. Myoglobin is a protein that facilitates the storage and transport of oxygen within muscle cells and other tissues.

WHAT IS PRIMARY STRUCTURE?

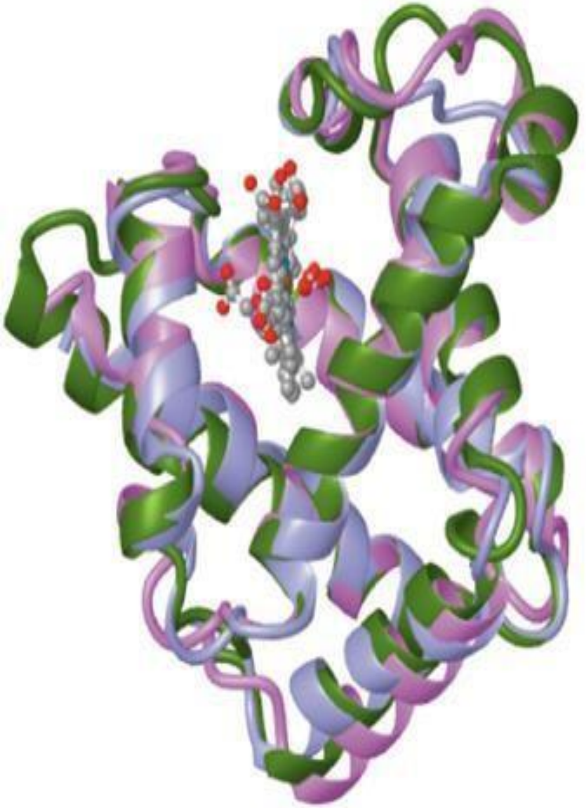
- The primary structure of a protein determines the other levels of structure

1 5 10 15

Myoglobin	gly-----leu-ser-asp-gly-glu-trp-gln-leu-val-leu-asn-val-trp-gly-lys-
β-chain hemoglobin	val-his-leu-thr-pro-glu-glu-lys-ser-ala-val-thr-ala-leu-trp-gly-lys-
α-chain hemoglobin	val-----leu-ser-pro-ala-asp-lys-thr-asn-val-lys-ala-ala-trp-gly-lys-val-
ζ-chain hemoglobin	met-ser-leu-thr-lys-thr-glu-arg-thr-ile-ile-val-ser-met-trp-ala-lys-ile-
γ-chain hemoglobin	met-gly-his-phe-thr-glu-glu-asp-lys-ala-thr-ile-thr-ser-leu-trp-gly-lys-val-

Zinc Finger Domain 1

Human GATA2	ECVNCGATATPLWRRDGTGHYLCNACGLYHKMNGQNRPLIKPKRRLSAARRAGTCCANCQ	353
Mouse GATA2	ECVNCGATATPLWRRDGTGHYLCNACGLYHKMNGQNRPLIKPKRRLSAARRAGTCCANCQ	353
Zebrafish Gata2a	ECVNCGATSTPLWRRDGTGHYLCNACGLYHKMNGQNRPLIKPKRRLSAARRAGTCCANCQ	329
Zebrafish Gata2b	ECVNCGATSTPLWRRDGTGHYLCNACGLYHKMNGQNRPLIRPKRRLSASRRAGTCCANCQ	323



- α-Globin (blue)
- β-Globin (violet)
- Myoglobin (green)

- All proteins that function in aqueous environments, such as the cytoplasm or blood, should be globular in shape. For example, alpha-globin, beta-globin, and myoglobin each have their own distinct 3D structures, but they all perform the same function —>binding and releasing oxygen. Because they share this function, it makes sense that their overall structures are more or less similar. This reflects the principle that structure is closely related to function. Since a protein's 3D structure is determined by its amino acid sequence, the parts of the sequence responsible for the protein's function – especially regions like the oxygen-binding site – are often highly conserved.

SICKLE CELL HEMOGLOBIN (HBS)

- In hemoglobin, each beta subunit is positioned diagonally, and each alpha subunit is also diagonal to the others. On the surface of each beta subunit, there is a negatively charged amino acid, Glutamic acid, which causes the beta subunits to repel each other. This repulsion ensures that even when two hemoglobin molecules come close to each other, their beta subunits do not stick together, keeping each hemoglobin molecule soluble and functional inside red blood cells.

- The problem occurs when valine replaces glutamic acid on the surface of the beta subunit. When hemoglobin molecules come close to each other, the hydrophobic valine residues stick together, causing hemoglobin to aggregate. These aggregates are no longer soluble and begin to precipitate inside red blood cells. This precipitation distorts the cell into a sickle shape, which can partially block blood vessels, leading to reduced blood flow and ultimately hypoxia (oxygen deficiency in tissues).

- -> Hypoxia causes severe pain, known as a sickle cell crisis.

- Since it is a genetic disorder, there is no definitive cure. Treatment focuses on managing symptoms.

- Patients are often given morphine to control pain. However, long-term use may lead to addiction, making it difficult to determine whether the patient is experiencing true pain or seeking the drug due to dependence.

- This disease is common in Gulf countries, mainly due to the high rate of consanguineous marriages, which increases the risk of inheriting genetic disorders like sickle cell disease.

- Note: Although sickle cell disease is not common in Jordan, it is important for healthcare professionals here to understand and recognize it, in case they encounter such a case in the future

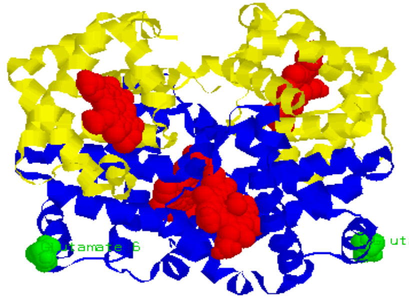
SICKLE CELL HEMOGLOBIN (HBS)

- It is caused by a change of amino acids in the 6th position of β globin (Glu to Val)
- The mutation results in:

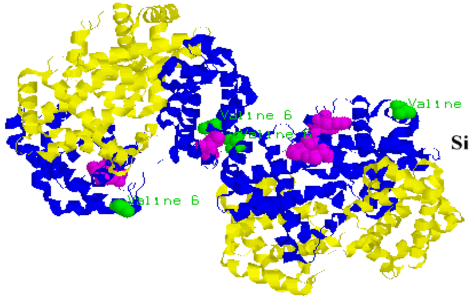
1) arrays of aggregates of hemoglobin molecules,

2) deformation of the red blood cell, and

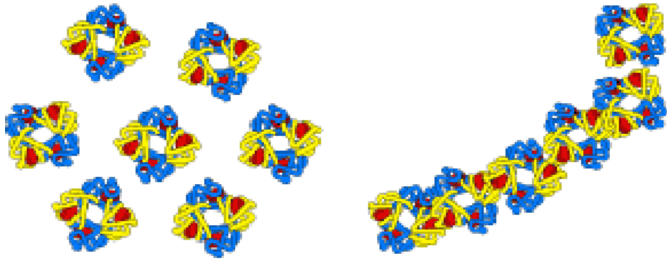
3) clotting in blood vessels and tissues



Normal Hemoglobin

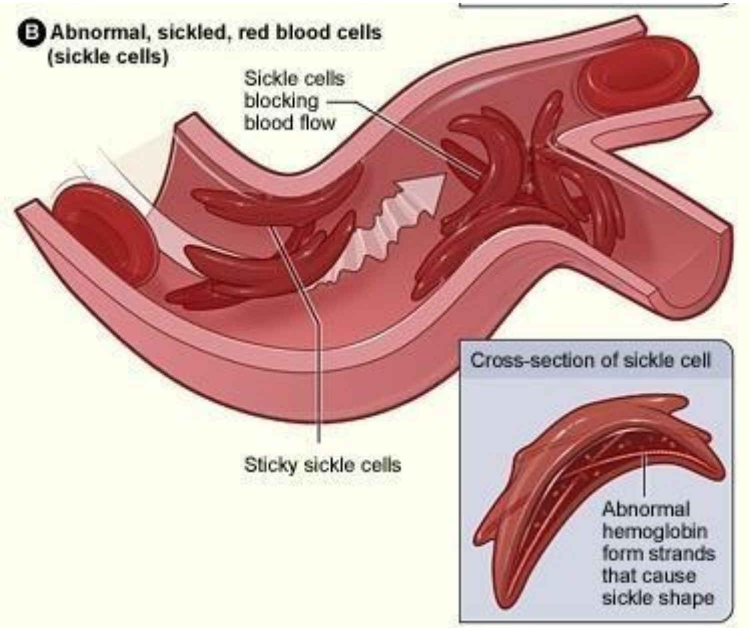


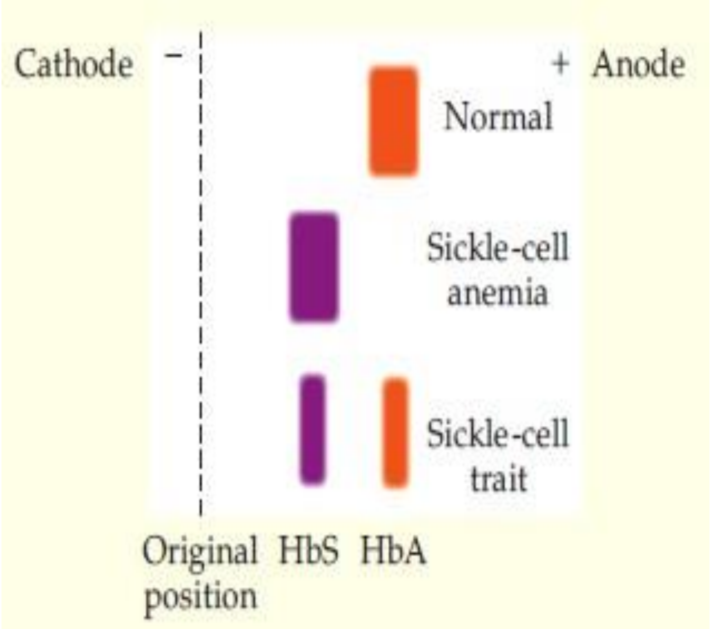
Sickle Hemoglobin

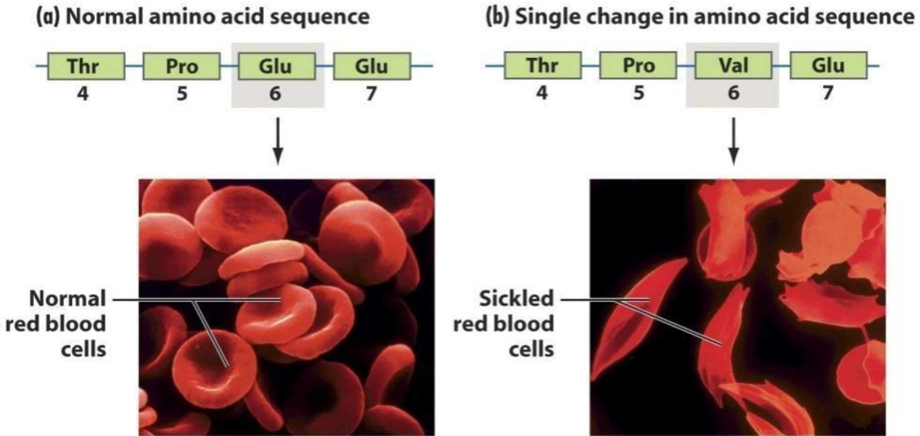


NORMAL HEMOGLOBIN

CLUMPED HEMOGLOBIN







SECONDARY STRUCTURE

Interactions between the backbones of amino acids cause nearby regions of the polypeptide chain to fold toward each other, forming hydrogen bonds. These hydrogen bonds stabilize secondary structures such as α-helices and β-sheets.

- Their diversity is limited, why?

The secondary structure formation depends on the formation of hydrogen bonding between the backbone of amino acid which means that it is limited and not diverse since we only have amino group and carbonyl group in the back bone that can interact with each other and the are the same in all amino acids so the Change in the amino acids won't create any diversity in the secondary structure, and the only secondary structures that can be formed are:

- α-helix and β-sheets and some others.

Explanation in other words at the next slide:

SECONDARY STRUCTURE

–> Why is their diversity limited?

Secondary structure formation depends on hydrogen bonding between the backbone of amino acids. This is limited because the backbone only contains an amino group (-NH) and a carbonyl group (C=O), which are the same in all amino acids.
Therefore, changing the amino acid side chains does not significantly affect the types of secondary structures that can form.

The main types of secondary structures are:

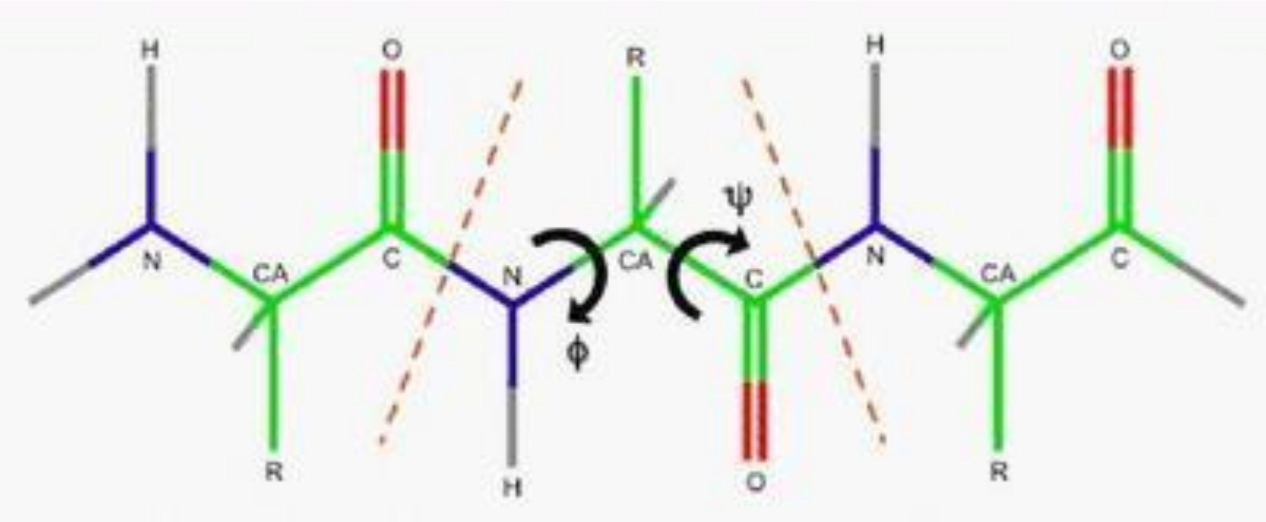
1) α-helix 2) β-sheet

3) and a few others (e.g., turns and loops).

**There is much greater variety in tertiary structure compared to secondary structure because it involves interactions not only between the backbone atoms but also between amino acid side chains (R-groups).

WHAT IS IT? HOW IS IT CAUSED?

- The two bonds within each amino acid residue freely rotate
  - the bond between the α-carbon and the amino nitrogen
  - the bond between the α-carbon and the carboxyl carbon
- A hydrogen-bonded, local arrangement of the backbone of a polypeptide chain
- Polypeptide chains can fold into regular structures such as:
  - Alpha helix
  - Beta-pleated sheet
  - Turns
  - Loops



THE α .HELIX

- The alpha helix is a helical secondary structure stabilized by hydrogen bonds between the carbonyl oxygen of one amino acid and the amide hydrogen of another amino acid four residues ahead . These hydrogen bonds are not perfectly linear but follow the natural twist of the helix. This results in approximately 3.6 residues per turn and a vertical rise (pitch) of 5.4 Å per full turn. We mention these values to emphasize that the alpha helix is a periodic and highly ordered structure with specific geometric parameters — a helical shape with precise, repeating measurements.

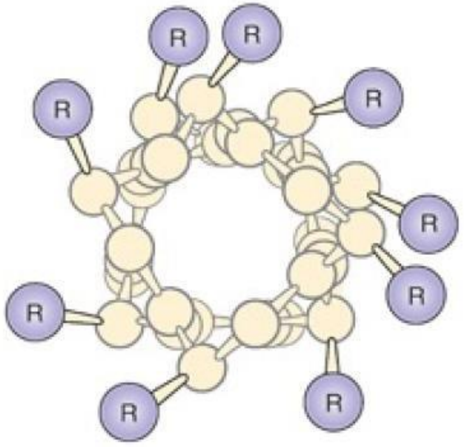
- The α-helix is a helical structure that resembles a spring. When viewed from above, the side chains (R-groups) project outward from the helix. They cannot fit inside the helix without disrupting its regular pattern. If side chains were forced inside, the structure might still be helical, but it would no longer be a true α-helix, because the precise geometric parameters and hydrogen-bonding pattern of the α-helix would be disturbed.

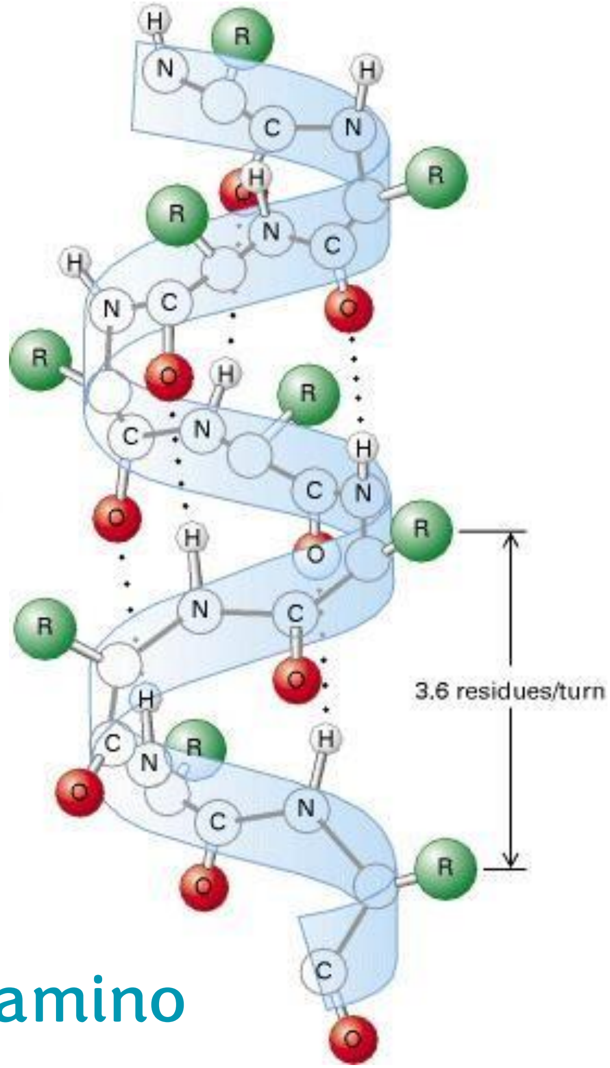
- If this structure becomes disrupted it may still appear helical, but it can no longer be considered a true alpha helix, as any major deviation from its characteristic parameters disrupts its identity.
-

Some amino acids can disturb the alpha helix. Proline breaks the alpha helix structure because it has a ring that makes it unable to form hydrogen bonds. Glycine is very small and flexible, which makes the helix unstable. Also, if there are two negative charges close to each other, or a very large side chain, these can also break or bend the helix.

THE α-HELIX

- It has very minute measurements.
- 3.6 amino acids per turn.
- Since bond is not from the first of an amino acid to the first of amino acid it is from the N atom at amino group and carbonyl group, each one of them is not at the first or end of the amino acid exactly.
- The pitch of the helix (the linear distance between corresponding points on successive turns) is 5.4 Å
- It is very stable!
- Avoiding steric hindrance





- In secondary structure of polypeptide, the backbone of amino acids interacts with each other.
- Hydrogen bonds between carbonyl group & amino group happens every 4 amino acids. (One with four and two with five).

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	-	-	Some changes have been made.
V1 → V2			

رسالة من الفريق العلمي:

جميعُنا يحتاج إلى تلك اليد الحنونة، إلى مكان حيث لا يفكر بما يفعل فقط يسلم نفسه لارادة صاحب تلك اليد الحنونة، أتعلم ما أخافه؟
إلا يكون لي مكان اذهب إليه!
هل تعلم معنى إلا يكون للإنسان مكان يذهب إليه؟
كانا مُمسكَينِ بأَيْدِي بَعضِهِما البَعْضِ، مُتَشابِكَتَيْنِ كما تَتَشابَكُ أَغْصانُ الأَشْجارِ.
كان يَشْعُرُ بِالدِّفْءِ مِنْ تِلْكَ اليَدِ الحَنونَةِ النّاعِمَةِ، رَغْمَ أَنَّ الجَوَّ كانَ بارِدًا جِدًّا، إِلَّا أَنَّهُ لَمْ يَشْعُرْ بِشَيْءٍ سِوى الدِّفْءِ؛ يَدُ والِدَتِهِ "مِيلِيسا" كانَتْ كَالشَّمْسِ الَّتي تُمْطِرُ الدِّفْءَ عَلى نَباتاتِها.

ومَعَ أَخْذِ الشَّمْسِ مَوْقِعَها في مُنْتَصَفِ السَّماءِ، وَإِطْلاقِ أَشِعَّتِها لِتُعانِقَ كُلَّ مَنْ يَقِفُ خارِجًا في هٰذا الوَقْتِ الحارِّ، كانَ النّاسُ، وَخُصوصًا عُشّاقُ المالِ، يَسْتَعِدّونَ لِفِعْلِ أَكْثَرَ مِنَ اللّازِمِ مِنْ أَجْلِ بَعْضِ التَّخْفيضاتِ التِّجارِيَّةِ عَلى مُنْتَجاتٍ لَنْ يَسْتَخْدِمُوها، فَتَدافَعوا في الأَسْواقِ، وَنَسُوا كُلَّ ما يُمَيِّزُهُمْ عَنِ الحَيَواناتِ، بَلْ أَصْبَحوا أَشَدَّ شَراهَةً مِنْها.

كانَ يَخافُ أَنْ تُفْلِتَ أُمُّهُ يَدَهُ، وَيَغْرَقَ بَيْنَ أَمْواجِ البَشَرِ الَّذِينَ نَسُوا كَرامَتَهُمْ، وَتَدافَعوا مِنْ أَجْلِ خُصوماتٍ كاذِبَةٍ.
فَكَّرَ في نَفْسِهِ: "لَنْ يَحْدُثَ ذٰلِكَ..."، لَكِنَّهُ كانَ خائِفًا مِنْ أَنْ يَحْدُثَ. كانَ يَسْتَخْدِمُ ما يُسَمِّيهِ "اِسْتراتِيجِيَّةَ العَكْسِ"، حَيْثُ يَقولُ لِنَفْسِهِ عَكْسَ ما يَخْشاهُ كَيْ يَهْدَأَ.

وَلَكِنْ، عِنْدَ اجْتِياحِ النّاسِ لِلسّوقِ عِنْدَ الظُّهْرِ، لَمْ يَعُدْ يَسْتَطيعُ رُؤْيَةَ والِدَتِهِ.
ظَلَّتْ يَداهُما مُتَشابِكَتَيْنِ كَالأَغْصانِ... وَلَكِنْ، حَتّى الأَغْصانُ تَتَقَطَّعُ.

كانَ كُلُّ ما يَشْغَلُهُ: "أَلّا تُفْلِتَ يَدُها يَدِي... لَنْ تُفْلِتَنِي! لا... لَنْ تُفْلِتَنِي!"

وَلكِنْ، ما كانَ يَخْشاهُ حَدَثَ.
كانَ طُولُهُ طَبيعيًّا لِطِفْلٍ في الحادِيَةَ عَشْرَةَ، وَلَكِنَّهُ بَدا قَزَمًا وَسْطَ الزِّحامِ، وَتَلاعَبَتِ الأَجْسادُ بِجَسَدِهِ الصَّغيرِ كَما تَتَلاعَبُ أَمْواجُ البَحْرِ بِقارِبٍ خَشَبِيٍّ صَغيرٍ في لَيْلَةٍ عاصِفَةٍ.

رسالة من الفريق العلمي:

وَكانَ خُروجُهُ مِنْ بَيْنِ النّاسِ أَشْبَهَ بِمُعْجِزَةٍ حَمِدَ اللهَ عَلَيْها.
جَلَسَ بِجانِبِ أَحَدِ الأَسْواقِ الَّتِي لَمْ يُتَدافَعْ عَلَيْها النّاسُ، وَجَلَسَ يَبْكِي وَحِيدًا، حَزينًا، حَتّى أَنَّ عَيْنَيْهِ طَغى عَلَيْهِما اللَّوْنُ الأَحْمَرُ.

وَفَجْأَةً، قاطَعَ شَلالَ دُموعِهِ يَدٌ ناعِمَةٌ أَمْسَكَتْ بِرَقَبَتِهِ العارِيَةِ بِقُوَّةٍ...
وَسَمِعَ صاحِبَةَ اليَدِ تَقولُ بِصَوْتٍ دافِئٍ:
"لا تَبْكِ... لا تَبْكِ يا صَغيرِي... والِدَتُكَ لَنْ تَتْرُكَكَ أَبَدًا."

العبرة:

نظن احيانًا أننا قادرون على العيش بمفردنا، قادرون على ان نكمل الطريق بأنفسنا لكننا بالنهاية بشر.. بشر ضعفاء خلقنا شعوبًا وقبائل لنتعارف وفضل بعضنا على بعض في الرزق ليتخذَ بعضنا بعضًا سُخريا، فنحن بحاجة إلى بعضنا البعض في الحياة وعلى قدر ما ترى ان هذا بديهي فإنه مهم الذكر في عصرٍ انتشرت به الفردانية والنظرة المادية للأمور والنظرة للإنسان على انه رقم وليس على ان العالم الأكبر انطوى به، وعلى ذكر الأرقام والفردانية، ان كنت ممن غُسلت عقولهم بان الرجل بما يملك من مال والأنثى بما تملك من جمال، فاني أدعوك لان تفكر خارج حدود الصندوق الذي وضعك الإعلام به، هل هذه المقارنة التي تقارن بها البشر عادلة في اصلها ؟ أي ان مقارنة النساء بالجمال هي مقارنة غير عادلة لمقارنتك عنصرًا لا طاقة للمقارن به وبحكمك عليه بناءً على هذا فأنت كمن حكم على بريء بالاعدام، ومقارنة الرجال بناءًا على المال هي مقارنة غير عادلة أيضا، فكم من رجل ولد غنيًا، وماذا لو كانوا كلهم فقراء في بدايتهم ثم منهم من بقي فقيرًا ومنهم من اصبح غنيًا هل تجوز المقارنة؟ سأجيب عن هذا السؤال بسؤال، هل توافرت لهم نفس الظروف الفيزيائية والنفسية نفسها؟ كلا والف كلا، فلا يمكن ان تجتمع الظروف نفسها في تجربة شخصين مختلفين وحتى ان اجتمعت فسننظر إلى نية كل منهم في اتخاذه للقرار -وهذه عند علام الغيوب-

ومن الجانب الديني لو نظرنا إلى مقياس التفاضل عند الله لوجدنا انه التقوى، قال تعالى: (وجعلناكم شعوبا وقبائل لتعارفوا إن أكرمكم عند الله أتقاكم).

وقال الرسول صلى الله عليه وسلم: (إذا خطب إليكم من ترضون دينه وخلقه فزوجوه إلا تفعلوا تكن فتنة في الأرض وفساد كبير) فلم يقل من ترضون ماله أو جماله لانه المال دون تقوى الله لا فائدة له والجمال لا يدوم فمن أراد الجمال مل.

رسالة من الفريق العلمي:

ولكن من قد يكون هذا الشخص الذي تشكي له همك وحزنك؟ أيكونُ أخًا أو أُختًا، صديقًا أو صديقةً. زوجًا أو زوجة؟
كم اود اخبارك بأن لا تشكوا همك إلا لله، ولكن نفس الإنسان ترغب عادة إلى إنسان بجانبها.. إلى كتف تبكي عليه، وان تشكي همك لخلق الله بما يسمى بالفضفضة ليس من نقص الإيمان بل هو من الطبيعة البشرية التي خلقنا الله عليها، فقد شكى لبشرٍ من هو خير مني ومنك الرسول محمد صلى الله عليه وسلم عندما رأى جبريل في غار حراء عاد إلى امنا خديجة بنت خويلد رضي الله عنها، فكانت له خير الزوجة فطمئانته ونصحته ولم تدعه يعاني وحدة بعد ما أصابه الخوف.
وإن لم تكن كتفًا يبكي عليها من تحب، فلا تتوقع أن يكون لك كتفٌ تبكي عليه، وإن لم تكن سندًا لمن حولك فلا تتعجب إن سقطت ولم تجد من يسندك.

وتذكّر:
تلك اليد التي أفلتتك مرة، لا يعني انها تعمدت ذلك.

من كتابٍ قادمٍ : (العالم كما أراه / موسى النعيمات)