بسم الله الرحمن الرحيم

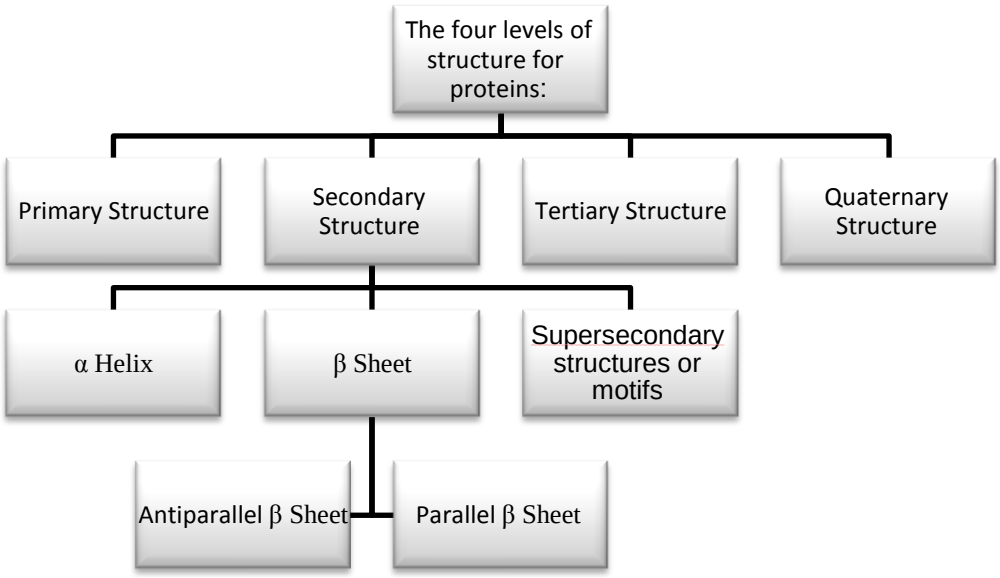
○ Objectives：

1) What are proteins?
2) Four levels of structure (primary, secondary, and tertiary, quaternary).
3) Protein folding and stability.
4) Protein denaturation.(تغير في الخصائص الطبيعية للمادة)
5) Protein misfolding and diseases.

- What are proteins?
  Proteins are polymers of amino acids joined together by peptide bonds.

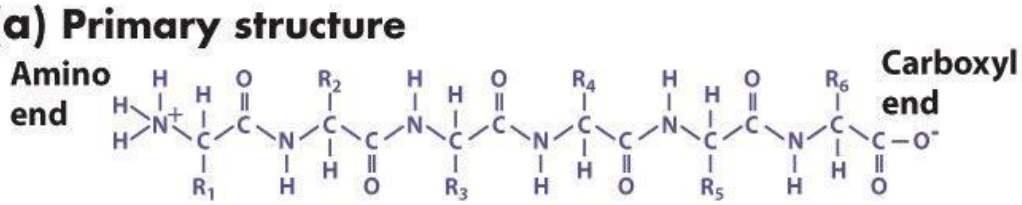
البروتينات: هي عبارة عن عدد من الأحماض الأمينية مرتبطة مع بعضها البعض بـ روابط ببتيدية.

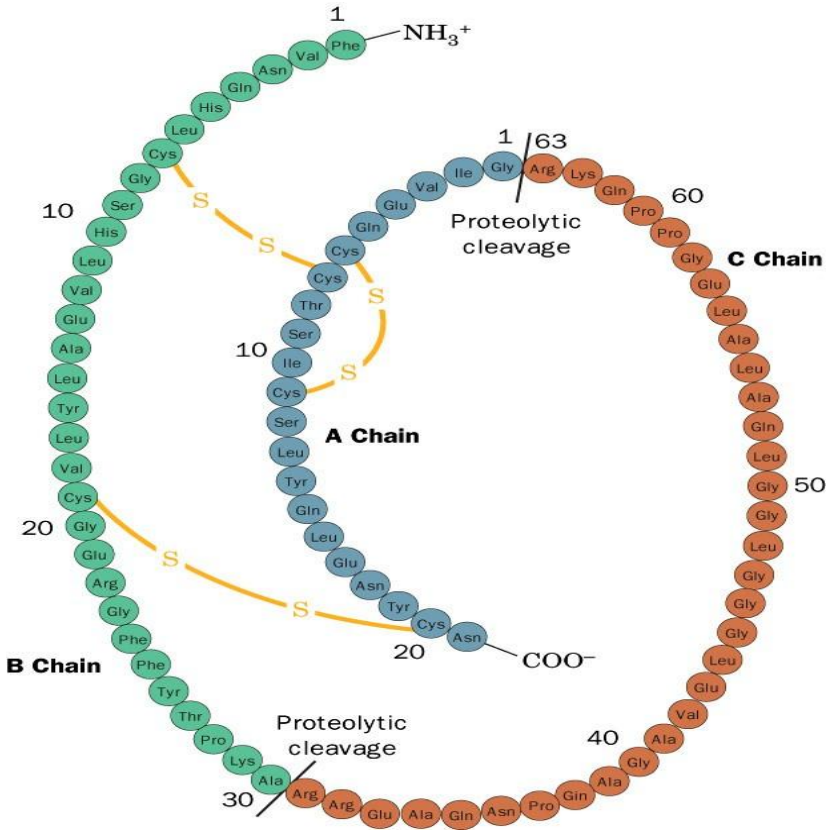
- What are the four levels of structure for proteins?



- Primary Structure:
  It is the linear sequence of amino acids.

عبارة عن ترتيب معين متتابع خطي من الأحماض الأمينية.





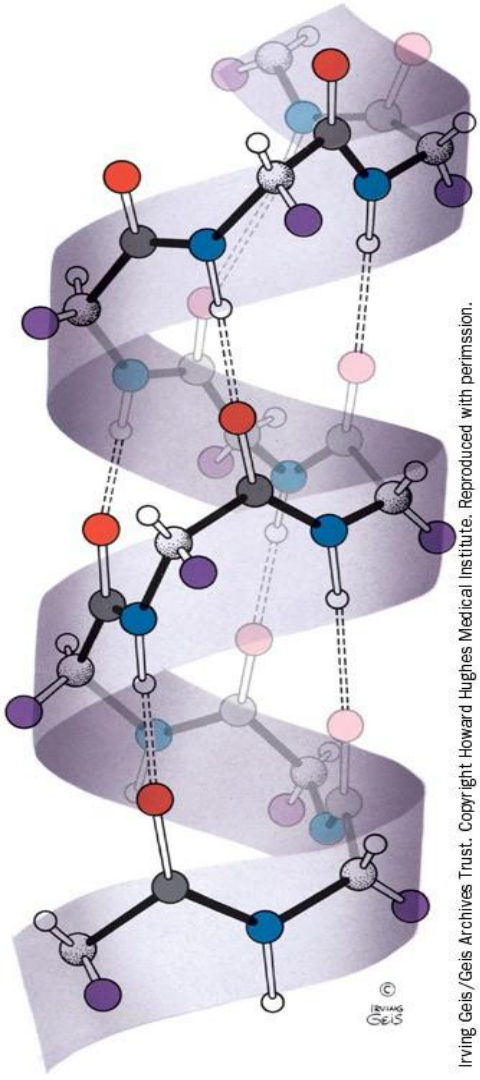
Primary structure of proinsulin

- Secondary Structure:
- It is the local three-dimensional arrangement of a polypeptide backbone.
- Excluding the conformations (3D arrangements) of its side chains.
- It comes from primary but you can make it like 3D.
- Hydrogen bounding in secondary structure make it Helix or sheet.

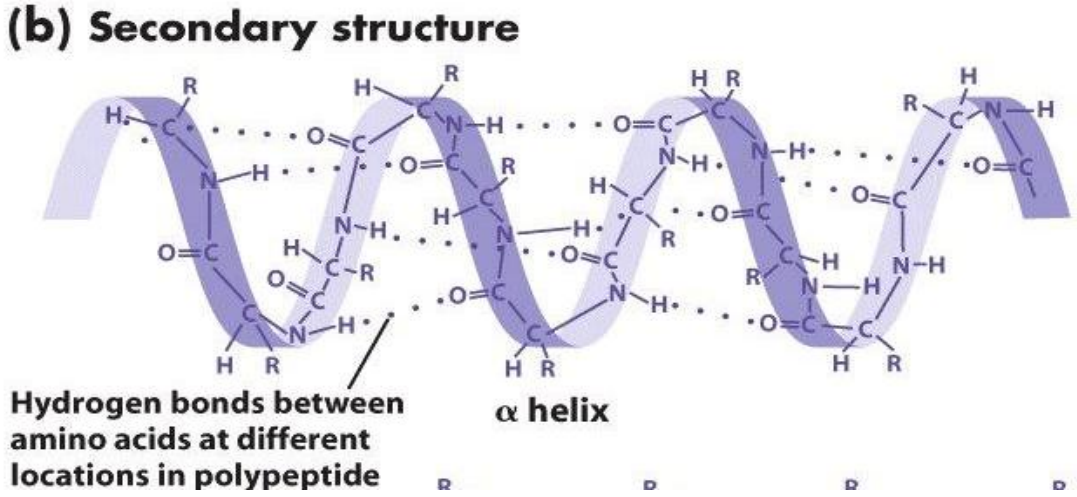
1) α Helix :

- A helix is right-handed.(عكس عقارب الساعة)

- It has 3.6 residues (amino acids) per turn.
- The helix is stabilized by hydrogen bonding between carboxylic group and 4_{th} N–H group.
- The amino acid side chains point outward and downward from the helix.
- The core of the helix is tightly packed; its atoms are in van der Waals contact.



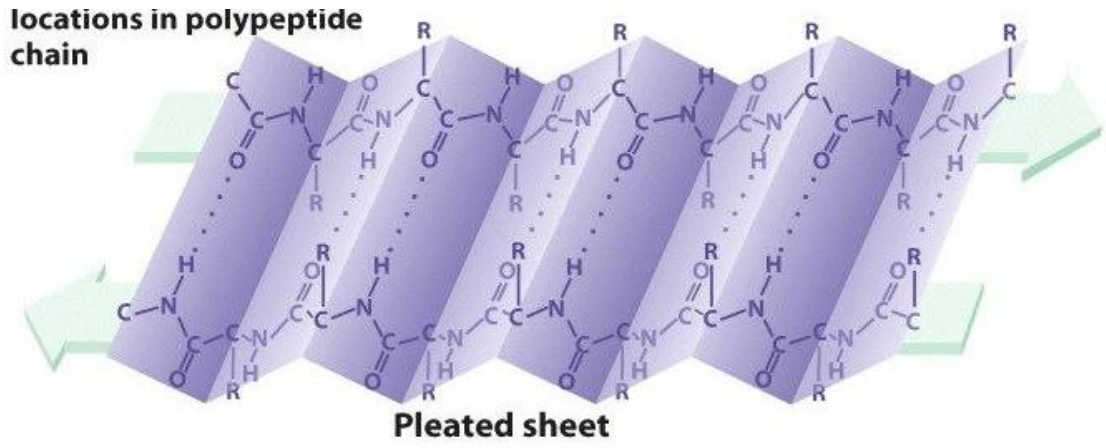
The right-handed α helix



2) β Sheet :

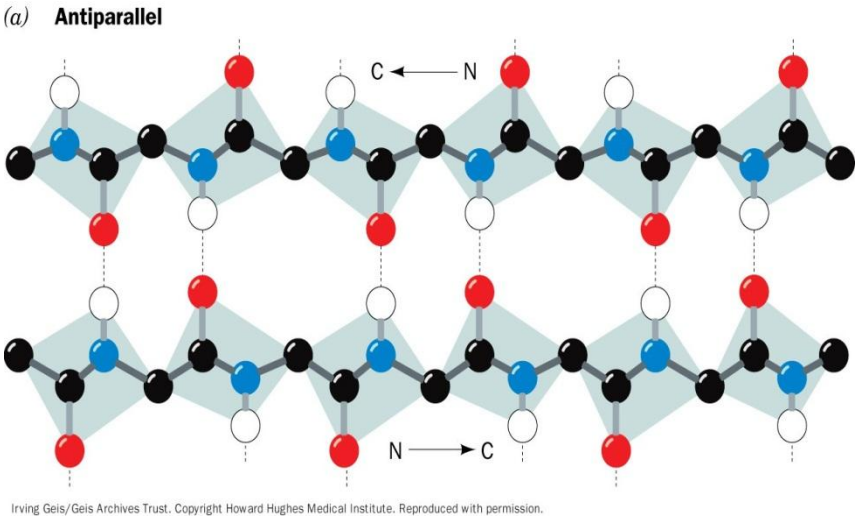
- Two or more polypeptide chains form hydrogen bonding with each other.
- Also called pleated sheets.
- They appear as folded structures with edges.

- تتكون من العديد من الروابط الببتدية مكونة روابط هيدروجينية تربطها مع بعضها البعض.
- تسمى أيضاً بـ الشييت المطوية.

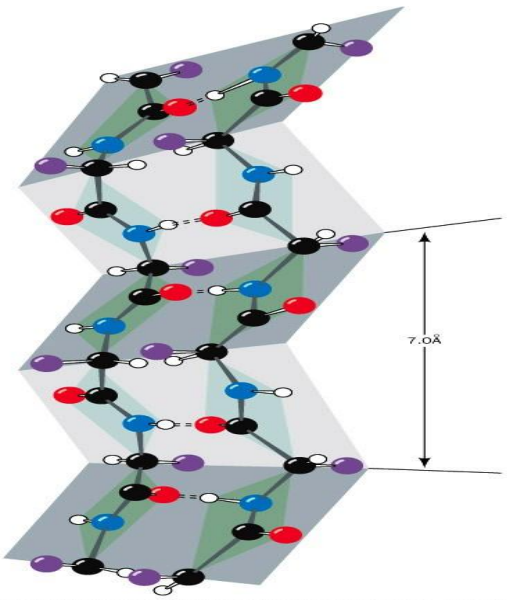


A. Antiparallel β sheets:

- Two or more hydrogen-bonded polypeptide chains run in opposite direction.(متوازيان وبعكس الاتجاه)
- Hydrogen bonding is more stable.



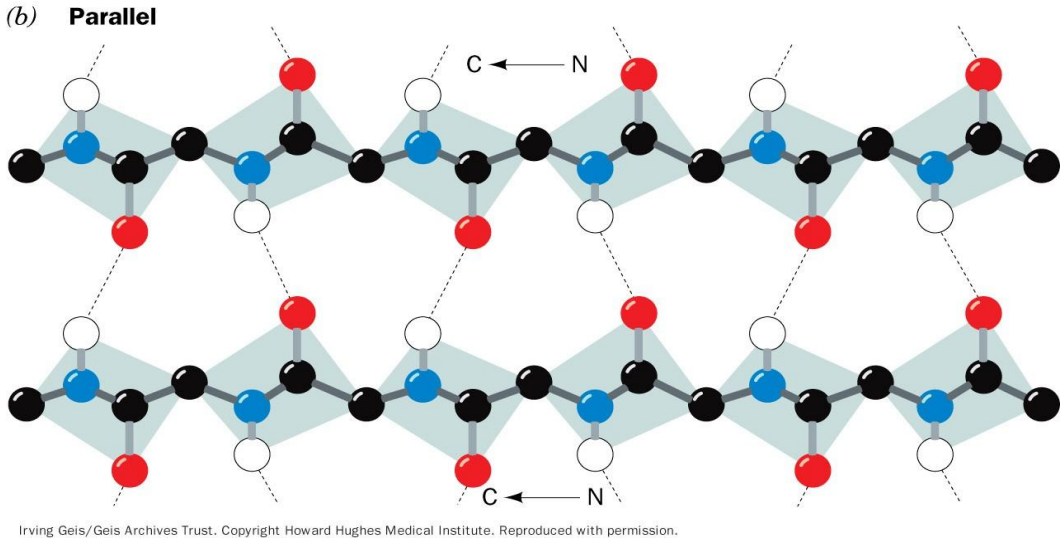
β pleated sheets. (a) The antiparallel β pleated sheets



A two-stranded β antiparallel pleated sheet

B. Parallel b sheets:

- Two or more hydrogen-bonded polypeptide chains run in the same direction.(متوازيان وبنفس الاتجاه)
- Hydrogen bonding is less stable (distorted) (أقل ثباتاً من السابقة).



β pleated sheets. (β) The parallel b pleated sheets.

- Other secondary structures:

✓ Turns (reverse turns).
✓ Loops.
✓ b bends.
✓ Random coils.

- Supersecondary structures or motifs:
- βαβ motif: α helix connects two β sheets (الفا هيلكز متصلة مع 2 بيتا شييت)
- β hairpin: reverse turns connect antiparallel β sheets.

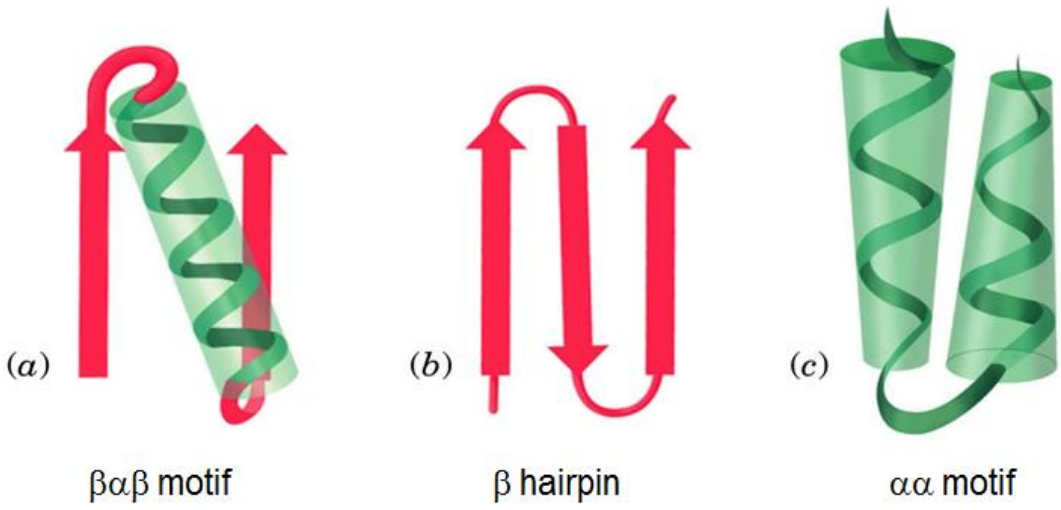
(وجود أكثر من بيتا شيت من النوع الغير متوازي مع بعضهم البعض على شكل منعطفات).

- αα motif: two α helices together.

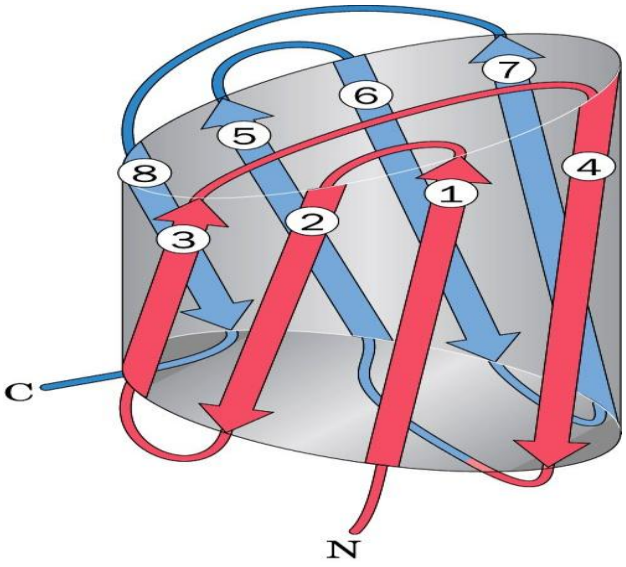
(2ألفا هيلكز متصلين مع بعضهما البعض)

- β barrels: rolls of β sheets.

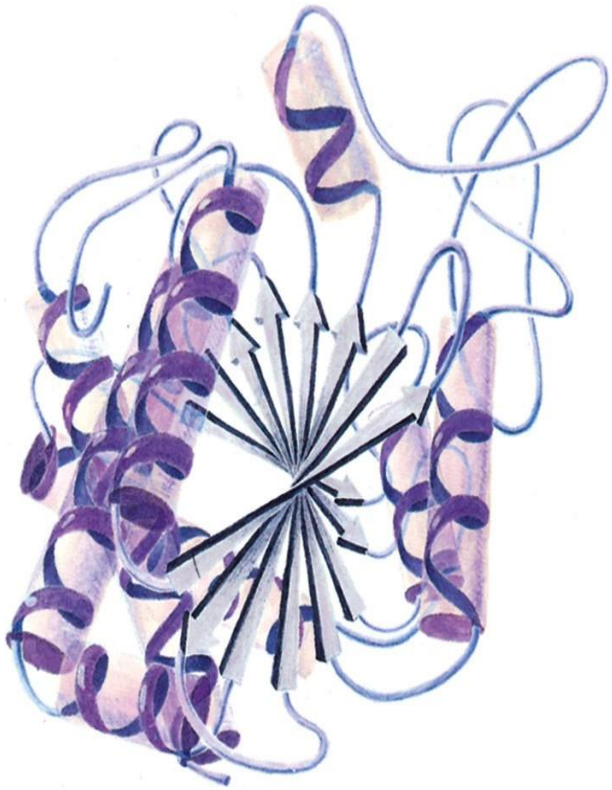
(كأنه برميل من البيتا شييت)



Schematic diagrams of supersecondary structures



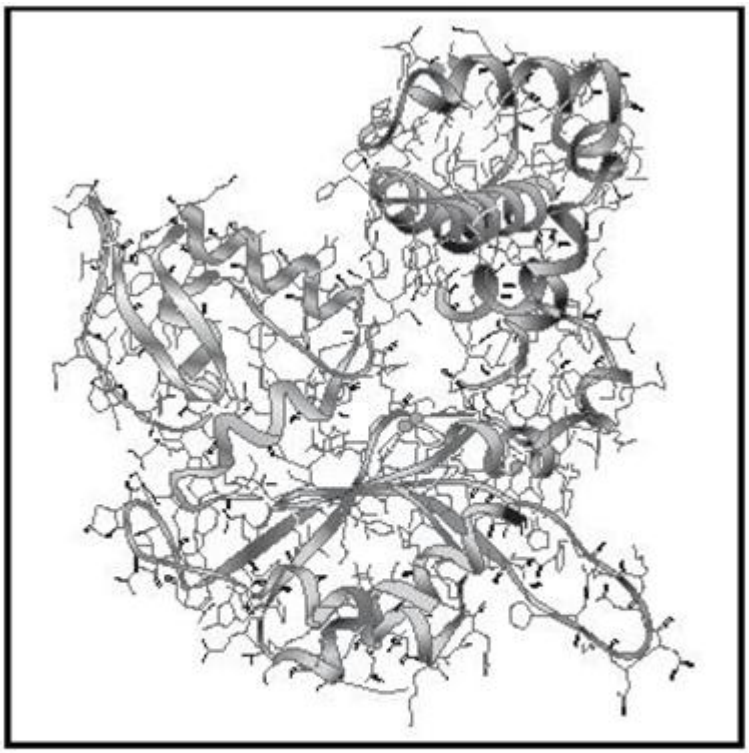
β barral



Secondary structure of proteins
(a-helix, b-sheets, loops, turns, random coils)

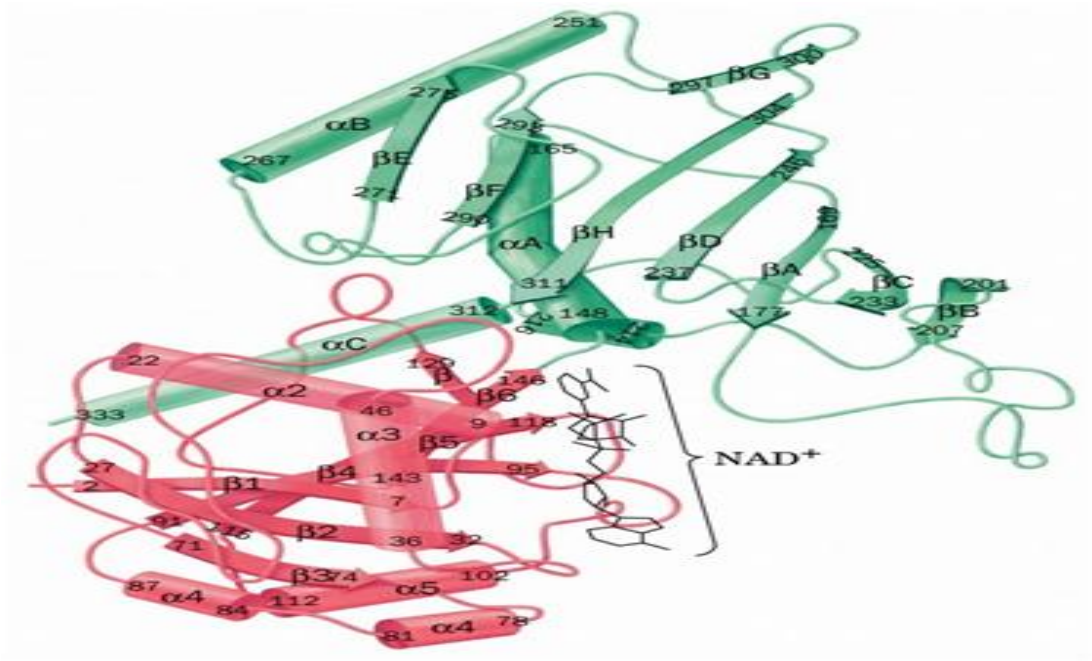
- Tertiary Structure:

- It is the three-dimensional structure of an entire polypeptide chain including side chains.
- It is the folding of secondary structure (a helix and b sheets) and side chains.
- Primary structure+ secondary structure+ side chains (too much).
- Helices and sheets can be combined to form tertiary structure.
- Also we can say the tertiary structure is (domain).

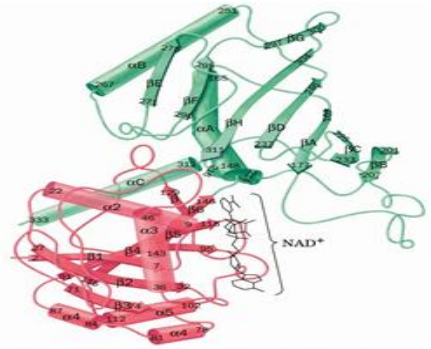


Tertiary structure of proteins
(Secondary structure + side chains)

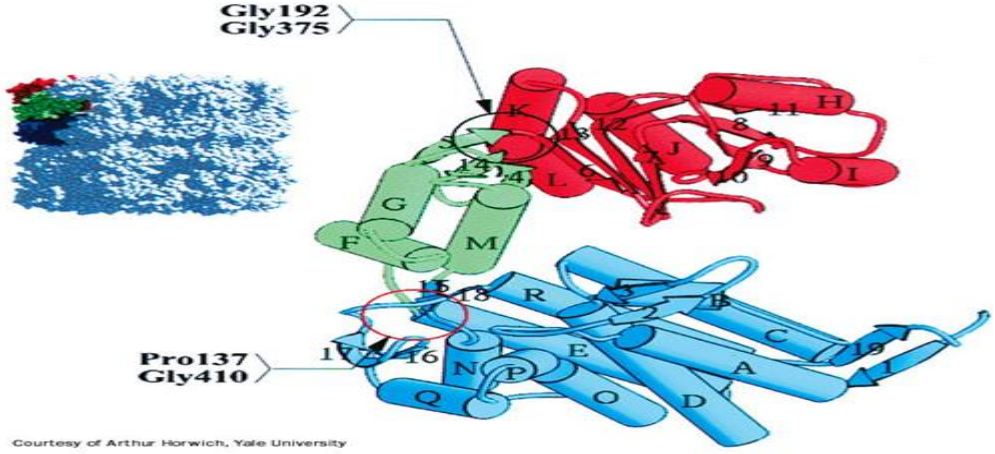
- What is the Domain?
- Polypeptide chains (>200 amino acids) fold into two or more clusters known as domains.
- Domains are units that look like globular proteins (تشبه البروتينات الكروية).
- Domains are parts of protein subunits.
- بمعنى آخر الدومين هو نفسه tertiary structure .



One subunit with two domains

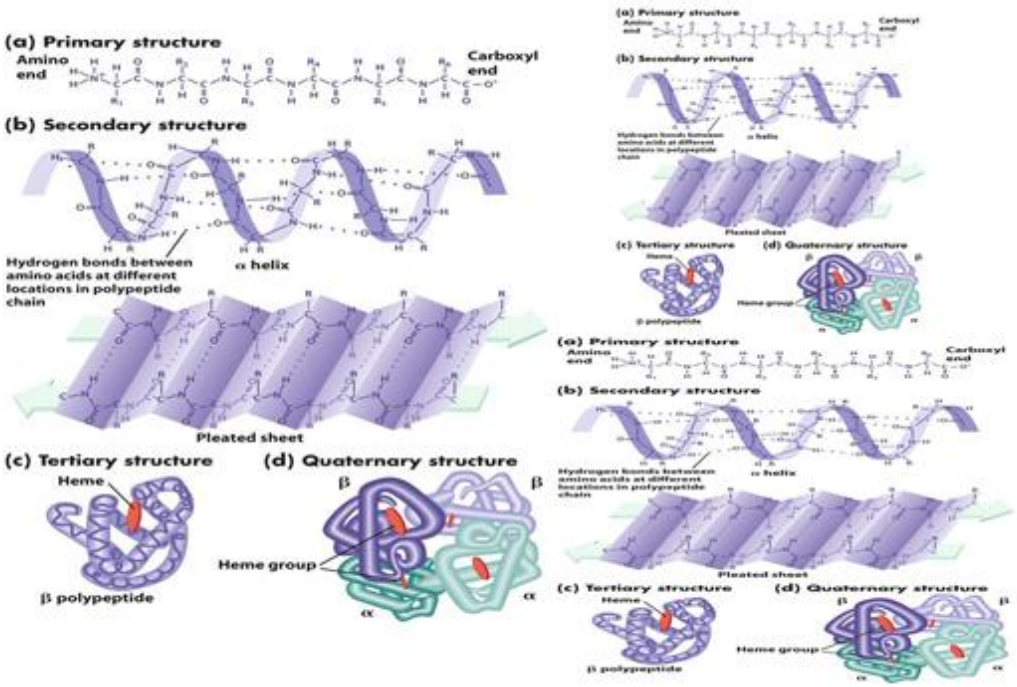


One subunit of the enzyme glyceraldehyde-3-phosphate dehydrogenase from *Bacillus stearothermophilus*



One subunit with three domains

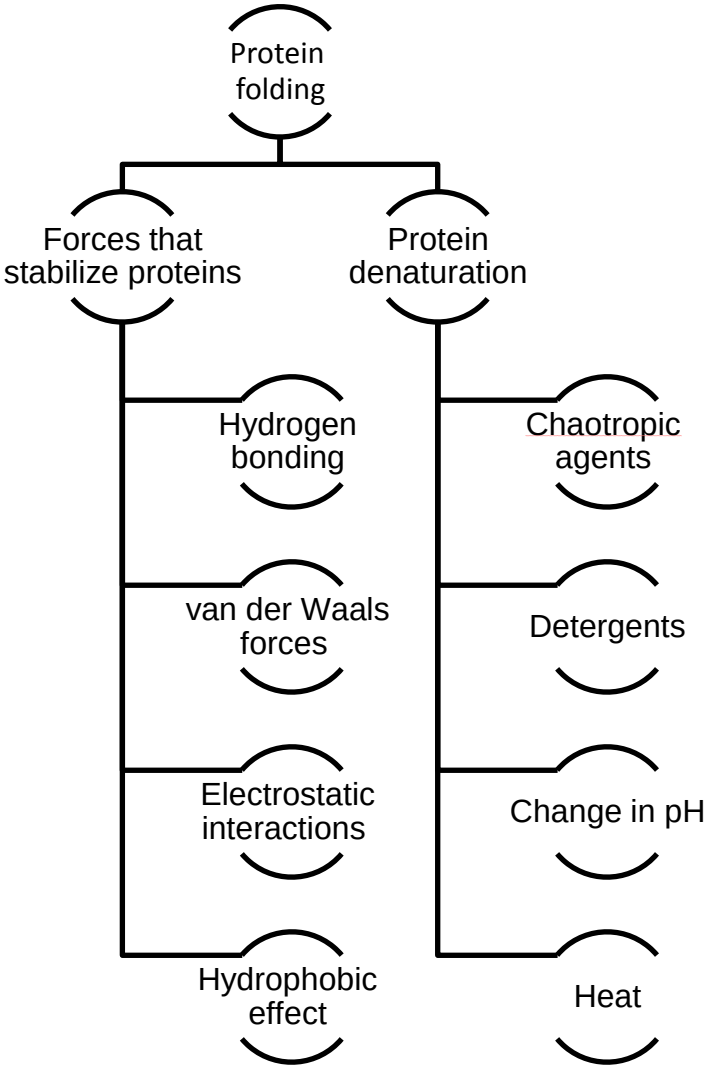
- Quaternary Structure:
- Many proteins contain two or more polypeptide chains.
- Each chain forms a three-dimensional structure called subunit.
- It is the 3D arrangement of different



- What is Hemoglobin?
  - Hemoglobin is a globular protein (بروتين كروي).
  - A multisubunit protein is called oligomer
  - Composed of $\alpha_2\beta_2$ subunits (4 chains, 4 subunits) (2 ألفا , 2 بيتا)

- Two same subunits are called protomers.

❖ Protein folding:



❖ Forces that stabilize protein structure:

❖ القوى التي تساعد على استقرار التركيب البروتيني :

1. Hydrophobic effect:
   - Nonpolar groups to minimize their contacts with water.
   - Nonpolar side chains are in the interior of a protein.

- (المجموعات الغير قطبية والتي تقلل من الاتصال بالماء وموجودة في داخل البروتين)

2. Hydrogen bonding.
3. Electrostatic interactions (ion pairing):
    - Between positive and negative charges.

- التفاعلات التي تكون بين الجزيئات المتعادلة وعادة ما تكون تفاعلات ضعيفة.

4. van der Waals forces (weak polar forces):
    - ❖ Weak attractive or repulsive forces between molecules.

❖ التجاذب الضعيف بين الجزئيات.

- ❖ Protein denaturation:
    - Denaturation: A process in which a protein looses its native structure.
- ✓ Factors that cause denaturation:
- Heat: disrupts hydrogen bonding.
- Change in pH: alters ionization states of aa.
- Detergents: interfere with hydrophobic interactions.
- Chaotropic agents: ions or small organic molecules that disrupt hydrophobic interactions.

❖ Protein misfolding:

- Every protein must fold to achieve its normal conformation and function.
- Abnormal folding of proteins leads to a number of diseases in humans.

- كل بروتين يحصل له إنطواء لكي يتمكن من أداء مهمته بشكل صحيح لكن قد يحصل له إنطواء غير طبيعي يؤدي إلى إصابة الانسان بعدد من الامراض.

1) Alzheimer's disease:
    - β-amyloid protein is a misfolded protein
    - It forms fibrous deposits or plaques in the brains of Alzheimer's patients.

2) Creutzfeldt-Jacob or prion disease:

- Piron protein is present in normal brain tissue.
- In diseased brains, the same protein is misfolded.
- Therefore it forms insoluble fibrous aggregates that damage brain cells.

- يوجد في جسم الانسان وبالتحديد في نسيج المخ الـPiron , إذا حصل لهذا البروتين Misfold يحصل هذا المرض ويكون مجموعة من الالياف الغير قابلة للذوبان والتي تقوم بإتلاف المخ .

انتهى☺