❖ QUATERNARY STRUCTURE

- It refers to the spatial arrangement of **subunits** in a protein that consist of **more than one polypeptide chain**
- The subunits are joined together by the same types of **noncovalent interactions** (e.g., hydrogen bonds, ionic bonds, and hydrophobic interactions)
- Subunits either **may function independently** of each other or may work cooperatively, as in hemoglobin.

❖ ⭐ PROTEIN MISFOLDING

- The protein folding sometimes can result in improperly folded molecules.
- These misfolded proteins are **usually tagged and degraded within the cell**. However, this quality control system is not perfect, and intracellular or extracellular aggregates of misfolded proteins can accumulate, **particularly as individual age.**

- **Amyloid disease**
  - **Amyloid,** the accumulation of insoluble fibrous protein aggregates.
  - It has been implicated in neurodegenerative disorders such ad PD and AD.
    - In AD, the dominant component of the amyloid plaque that accumulate is **amyloid β (Aβ)**
      - It is an extracellular peptide containing **40-42 aa residues.**
      - X-ray crystallography and infrared spectroscopy demonstrate a **characteristic β-pleated sheet secondary structure in nonbranching fibrils**
      - It is **neurotoxic** when aggregated in a β-pleated sheet conformation.
      - The Aβ that is deposited in the brain in AD is derived by **enzymic cleavage (by secretases)**
    - In PD, amyloid is formed from **α-synuclein protein**
- **Prion (Proteinaceous Infectious Particle) Diseases**
  - **The prion protein (PrP)** is the causative agent of **transmissible spongioform encephalopathies (TSE),** including **Creutzfeldt-Jakob disease** in humans, **scarpie** in sheep, and **bovin spongioform encephalopathy** in cattle (i.e., "mad cow" disease)
  - The **infectious protein** is designated of **PrP^{Sc}** (Sc = Scarpie);
    - It is **highly resistant to proteolytic degradation** and **tends to form insoluble aggregates of fibrils**
  - **The noninfectious form of PrP^{C} (C = cellular)**
    - It is encoded by the same gene as the infectious agent, it is present in normal mammalian brains on the surface of neurons and glial cells. Thus, **PrP^{c} is a host protein**