**Structure and Hierarchy of Proteins**

**Principles of Protein Structure**

* Proteins are chains of amino acids → sequence determines structure.
* **“Structure = Function”** principle.
* Misfolding → diseases (e.g., Alzheimer’s, prions).
* The protein folding problem: why predicting 3D structure is so challenging.

**Analogy:**

* Protein sequence = list of ingredients.
* Protein structure = final cooked dish (depends on how ingredients are arranged).

**Hierarchy of Protein Structure**

1. **Primary Structure**
   * Linear amino acid sequence.
   * Example: *MVHLTPEEKSAVTAL…* (hemoglobin α-chain).
2. **Secondary Structure**
   * Local folding patterns stabilized by hydrogen bonds.
   * α-helix, β-sheet, turns/loops.
   * Example: helix in myoglobin.
3. **Tertiary Structure**
   * Overall 3D shape (fold).
   * Stabilized by disulfide bonds, ionic interactions, hydrophobic packing.
   * Example: enzyme active site formation.
4. **Quaternary Structure**
   * Assembly of multiple polypeptide chains.
   * Example: hemoglobin = 2 α + 2 β subunits.

**Diagram:**

Primary → Secondary → Tertiary → Quaternary.

**Importance of Protein Structure Prediction**

* Experimental methods: X-ray crystallography, NMR, cryo-EM.
* Computational prediction: homology modeling, threading, *AlphaFold*.
* Applications:
  1. Drug design.
  2. Understanding mutations in disease.
  3. Synthetic biology.

**🧪 Lab Session: Exploring Protein Structures Online**

**Objective:** Visualize real protein structures.

**Steps:**

1. Visit **Protein Data Bank (PDB)**.
2. Search for “Hemoglobin” (PDB ID: 1A3N).
3. Explore 3D view (rotate, zoom).
   * Identify α-helices and β-sheets.
   * Locate heme group.
4. Compare with another protein (e.g., insulin).

Task**:**

* Students sketch the secondary structures they observe in hemoglobin.
* Discuss: *Why do α-helices dominate in oxygen-binding proteins?*

**📝 Quick Review Questions**

1. What are the four levels of protein structure? Give one example for each.
2. How does protein misfolding lead to disease?
3. Why is computational protein structure prediction so valuable?