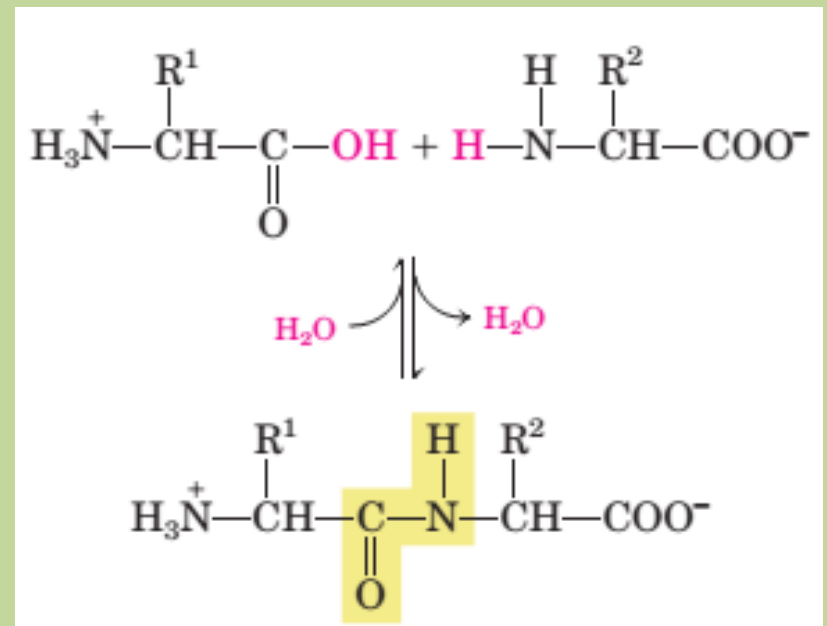


Essential Amino Acid (EAA)

- It can't be synthesized in the body and therefore need to be supplied through diet
- Proper growth and maintenance of the individual
- Ex. **A**rginine, **V**aline, **H**istidine, **I**soleucine, **L**eucine, **L**ysine, **M**ethionine, **P**henylalanine, **T**hreonine, **T**ryptophan
- **Mnemonics** : AV hill, MP TT
- **Semi-essential amino acid**: Adults can synthesize 2 amino acid and not by growing children. Ex: Arginine and histidine
- So in all 8 are essential and 2 semi essential

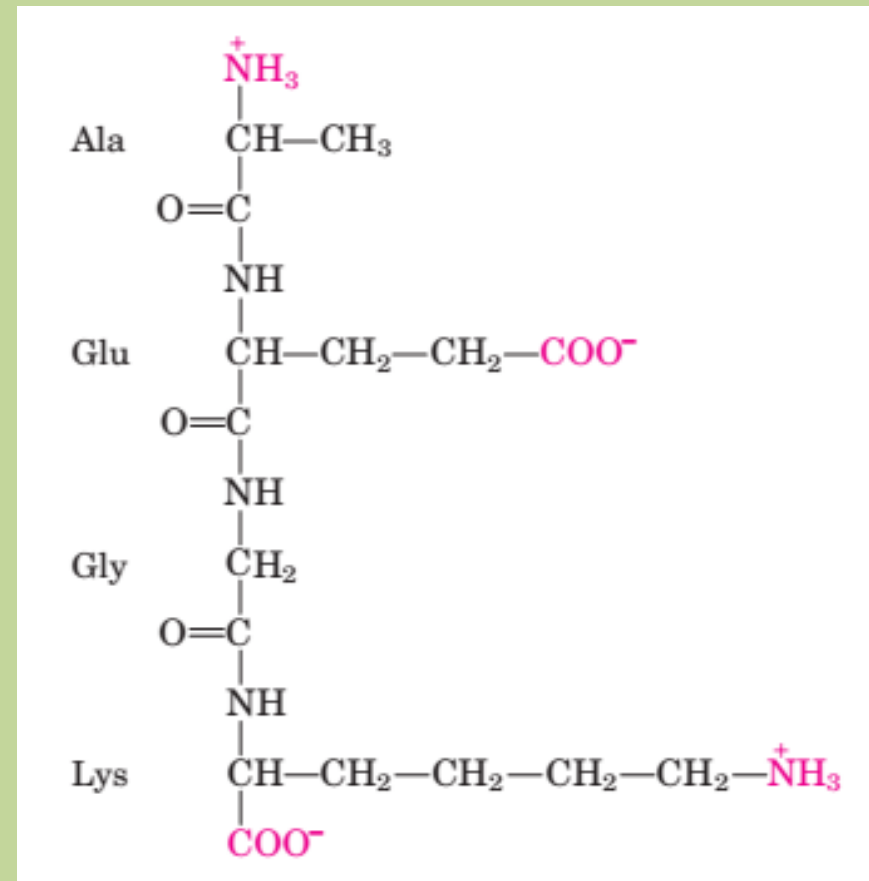
PEPTIDES

- Two AA covalently joined through a substituted amide linkage – **peptide bond**
- **Dehydration** – removal of H_2O
 - OH^- Carboxyl group of one AA
 - H^+ from amino group of another AA
- Example of a **condensation reaction** – common biological reactions



POLYPEPTIDES

- Two AA reacts to form **dipeptides**, Three AA can be joined by two peptide bonds to form a **tripeptide** and so on.
- **Oligopeptide:** When a few AA are joined by various peptide linkage
- When many amino acids are joined, the product is called a **polypeptide**.
- **Proteins** may have thousands of amino acid residues



Tetrapeptide

Structures of Protein

- Proteins catalyze metabolic reactions, power cellular motion, and forms structural integrity to hair, bones, tendons and teeth
- Human proteins therefore reflects the sophistication and diversity of their biologic roles
- Therefore maturation of a newly synthesized polypeptide into a biologically functional protein
 - Requires folding into a specific three-dimensional arrangement, or **conformation**

Structures of Protein

- During maturation, **posttranslational modifications** may add new chemical groups or remove it transiently
- Genetic or nutritional deficiencies that impede protein maturation are deleterious to health.
- Ex: *Creutzfeldt Jakob disease, Scrapie, Alzheimer's disease, and bovine spongiform encephalopathy*
- **Scurvy** - nutritional deficiency that impairs protein maturation.

FOUR ORDERS OF PROTEIN STRUCTURE

- The modular nature of protein synthesis and folding are embodied in the concept of orders of protein structure:
 - **Primary structure:** linking amino acid residues in a **polypeptide chain**
 - **Secondary structure:** stable arrangements of amino acid residues giving rise to **recurring structural patterns** into geometrically ordered units; twisting resulting in **α -helix or pleated**
 - **Tertiary structure:** the **three-dimensional** assembly of secondary structural units to form larger functional units
 - **Quaternary structure:** It's the arrangement in space of protein having **two or more polypeptide subunits**

FOUR ORDERS OF PROTEIN STRUCTURE

Primary structure



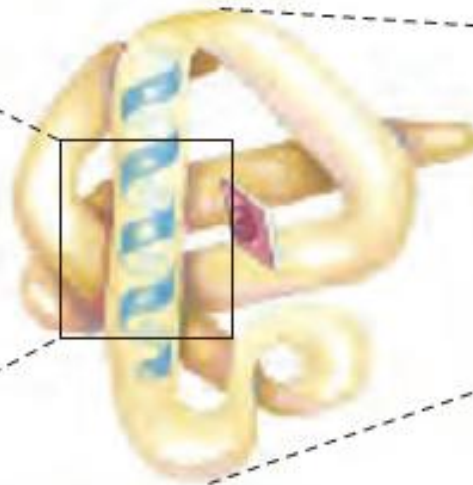
Amino acid residues

Secondary structure



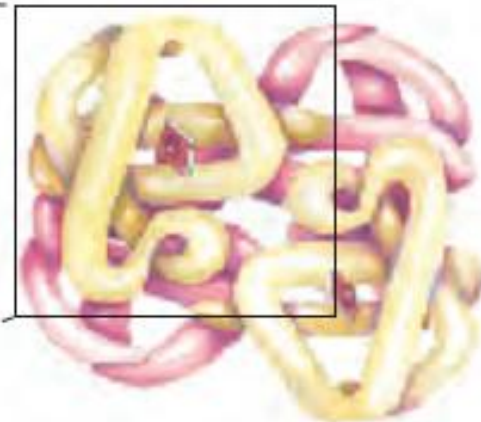
α Helix

Tertiary structure



Polypeptide chain

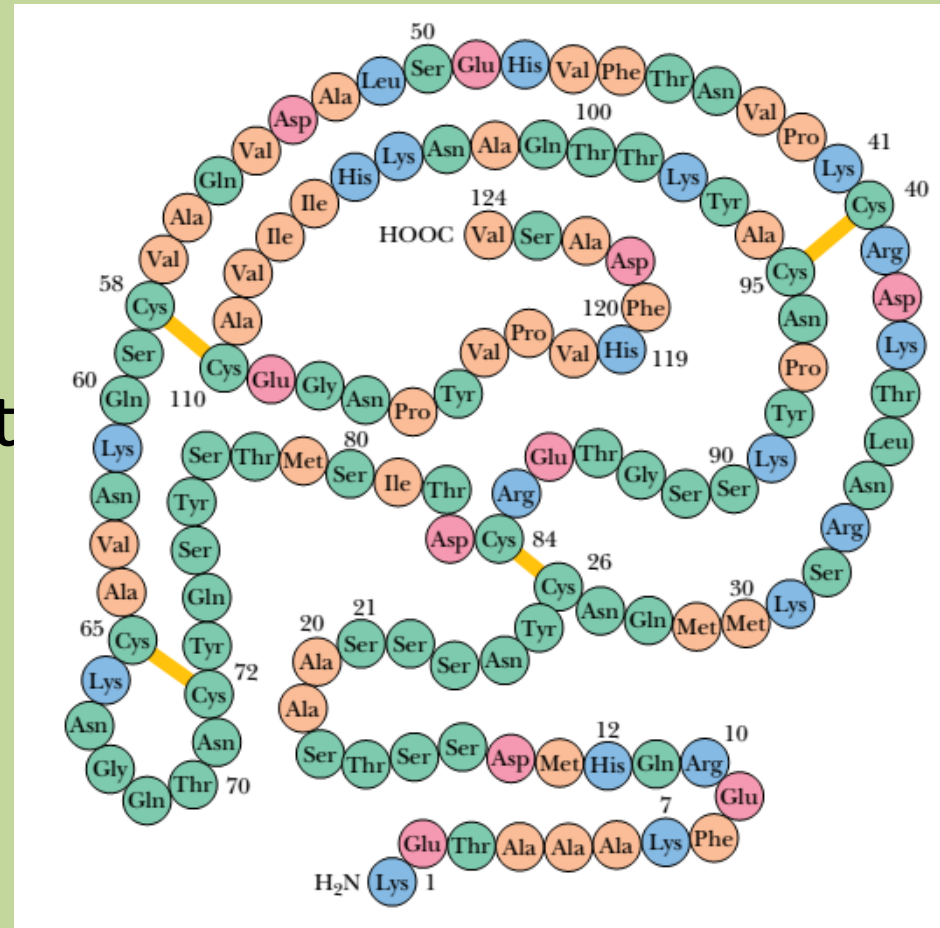
Quaternary structure



Assembled subunits

PRIMARY STRUCTURE

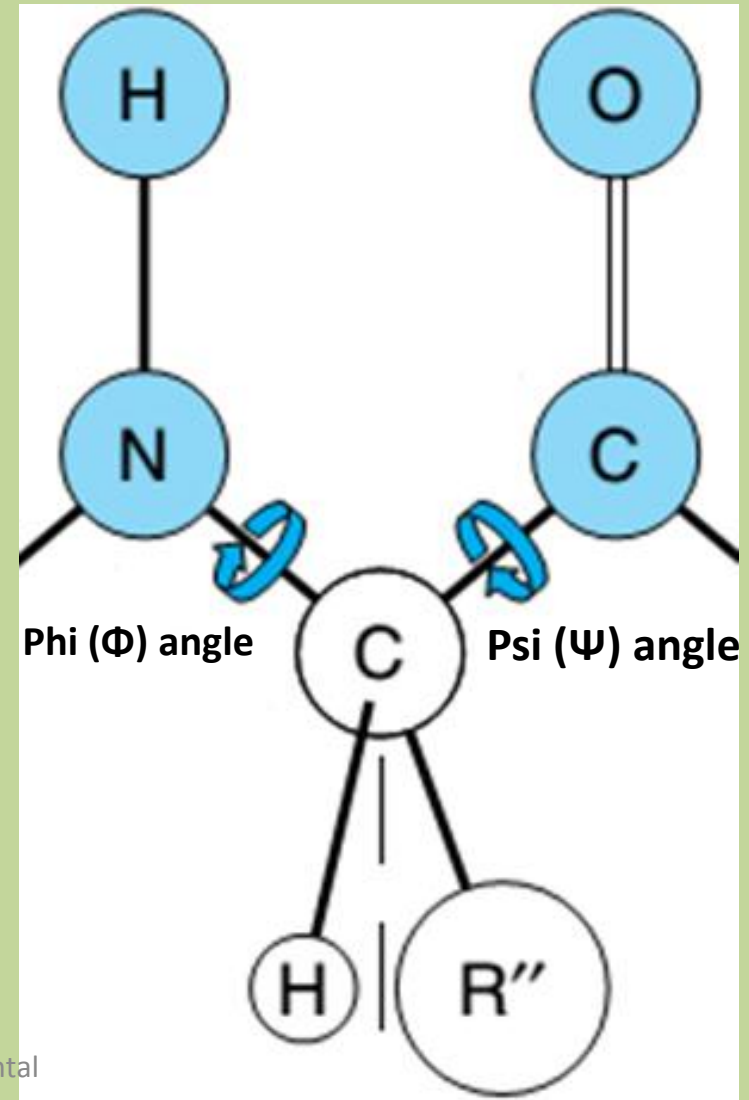
- Primary (1°) structure
- Each protein has a distinctive number and sequence of amino acid residues
- This determines how it folds up into a unique three-dimensional structure
- This in turn determines the function of the protein



Bovine Pancreatic Ribonuclease A

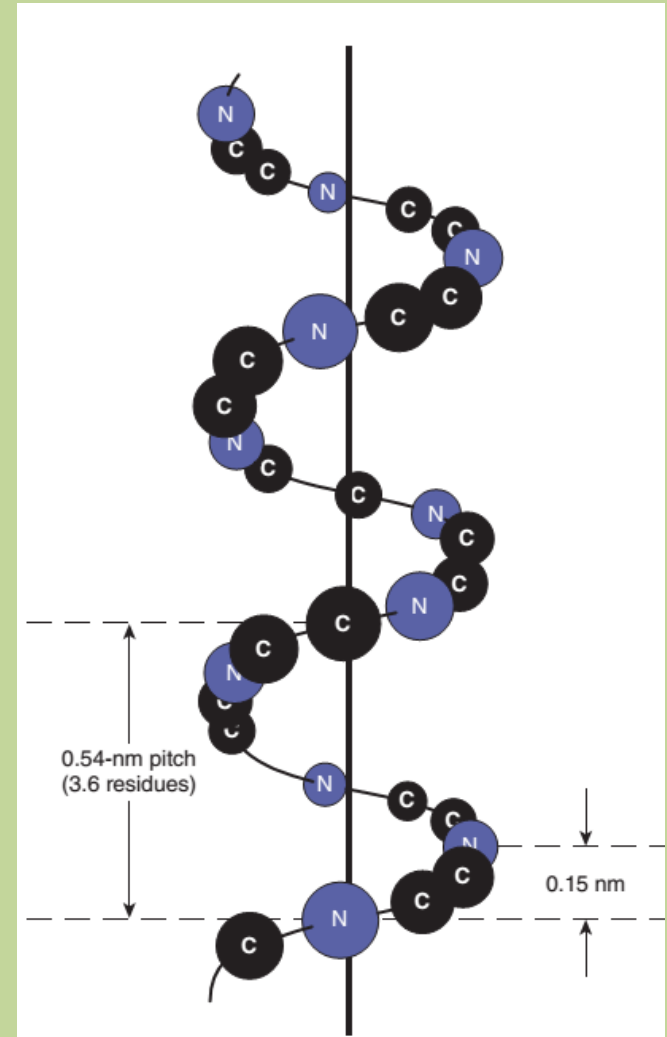
SECONDARY STRUCTURE

- 2° structures
- Polypeptide chain can arrange itself into characteristic **helical or pleated segments**
 - Given by Pauling and Corey
 - **hydrogen bonding** interactions between adjacent amino acid residues
- Free rotation is possible about only two of the three covalent bonds of the polypeptide backbone
 - α -carbon ($C\alpha$) to the carbonyl carbon ($C\omega$) bond
 - $C\alpha$ to nitrogen bond

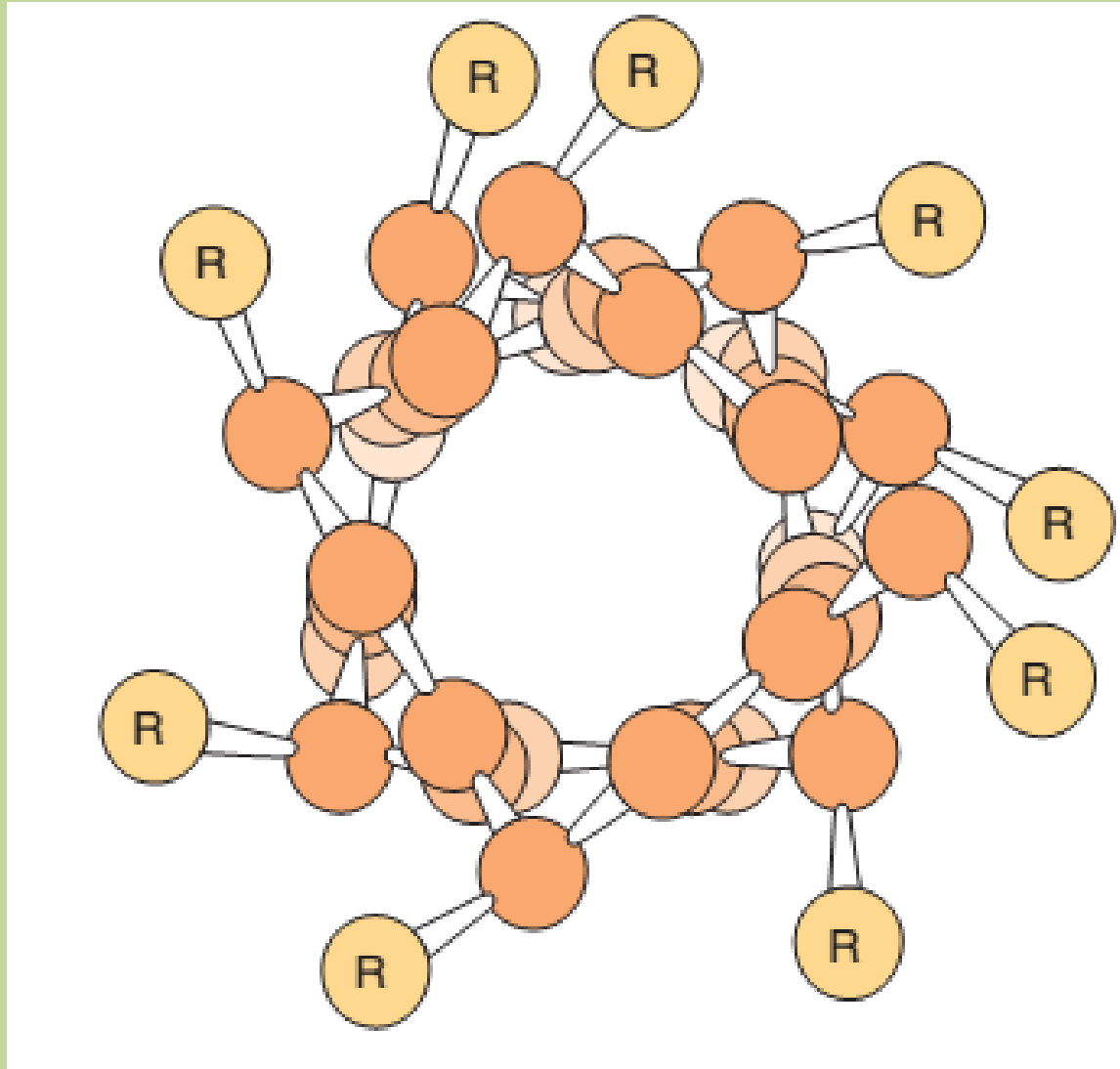


SECONDARY STRUCTURE : Alpha Helix

- α helix is twisted by an equal amount about each α -carbon
- With a phi angle of approx. -57° and a psi angle of approx -47°
- Complete turn of the helix contains an average of 3.6 aminoacyl residues
- Distance it rises per turn (**pitch**) is 0.54 nm
- **R groups** of each aminoacyl residue in an α helix **face outward**

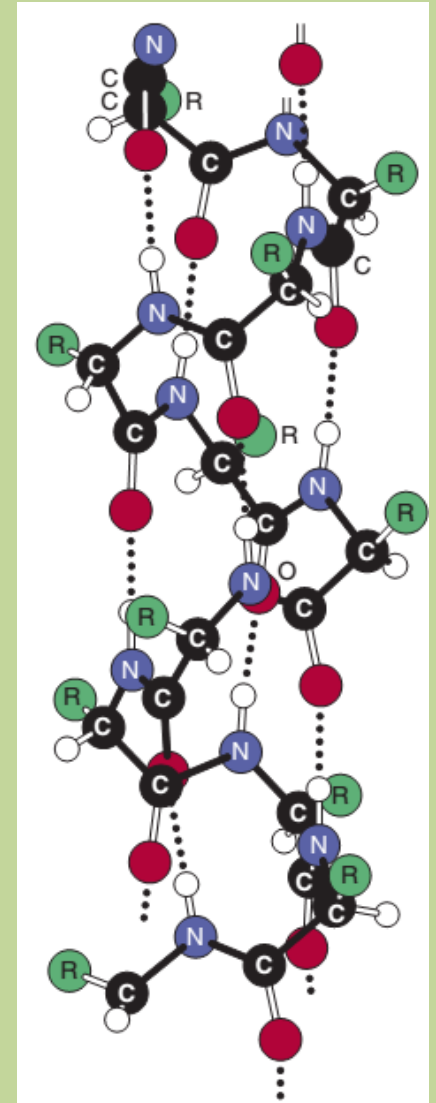


View down the axis of an α helix



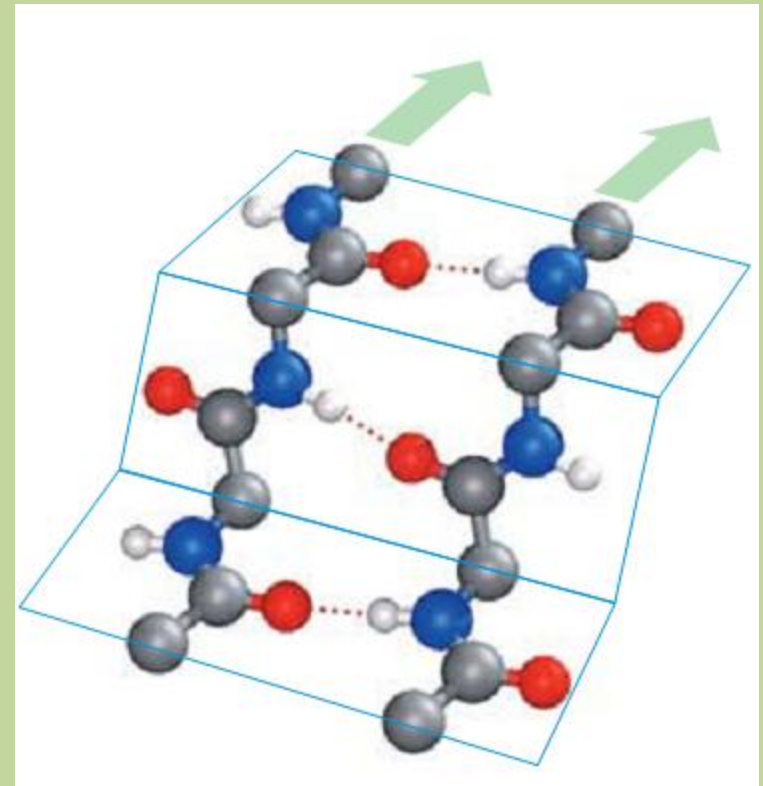
SECONDARY STRUCTURE : Alpha Helix

- **Stability** of an α helix arises primarily from **hydrogen bonds**
- Between the **oxygen** of **carbonyl** and the **hydrogen** atom of **nitrogen** of the **4th residue** down the polypeptide chain
- Supplemented by **van der Waals interactions**



SECONDARY STRUCTURE : Beta Sheet

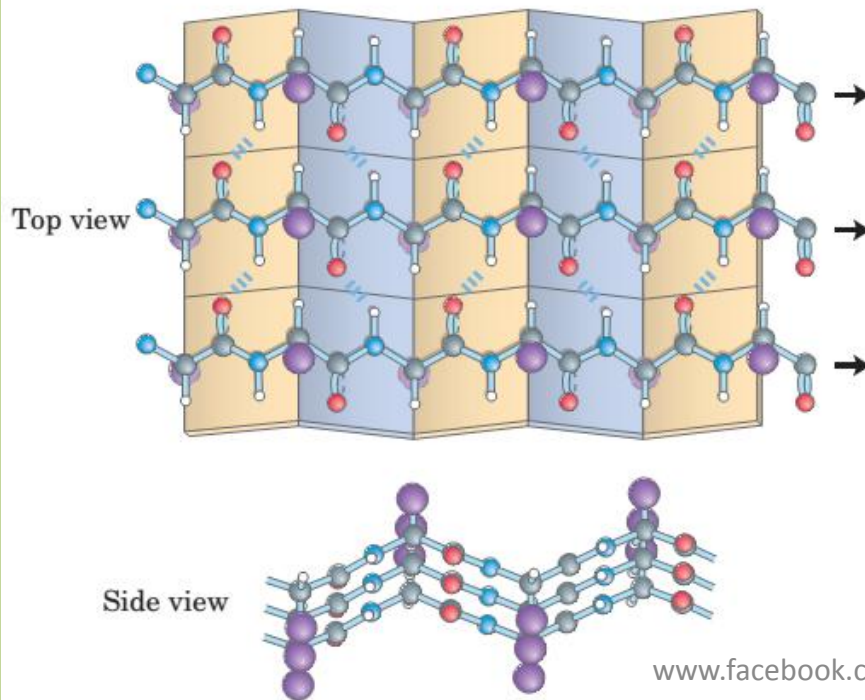
- Extended conformation of polypeptide chains
- Viewed edge-on, form a zigzag or pleated pattern in which the **R groups of adjacent residues** point in **opposite directions**
- **Stability** from **hydrogen bonds** between the **carbonyl oxygens** and **amide hydrogens** of peptide bonds - **adjacent segments** of β sheet



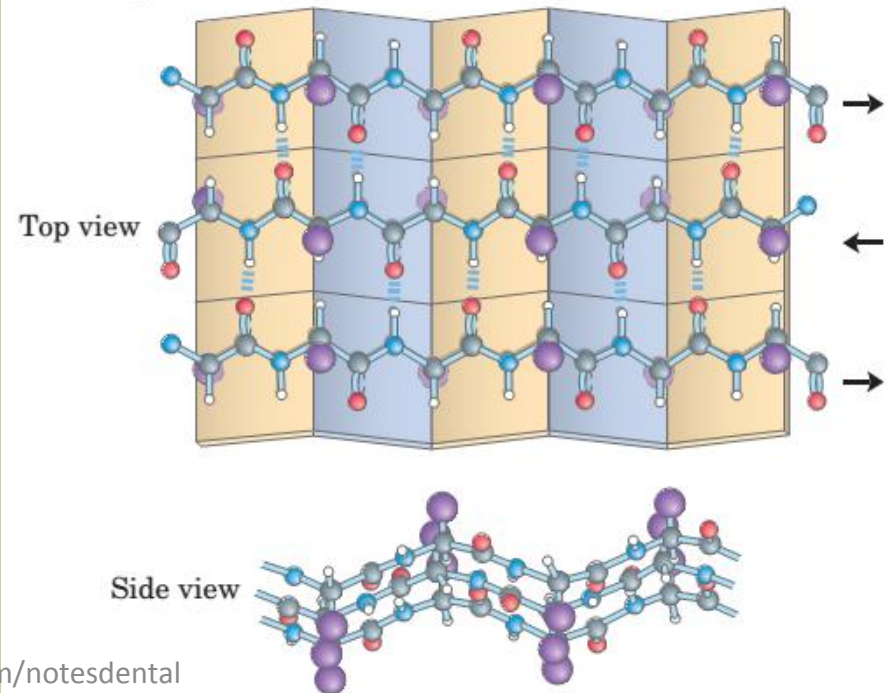
SECONDARY STRUCTURE : Beta Sheet

- **Parallel:** polypeptide chain proceed in the same direction amino to carboxyl
- **Antiparallel:** they proceed in opposite directions

(b) Parallel



(a) Antiparallel

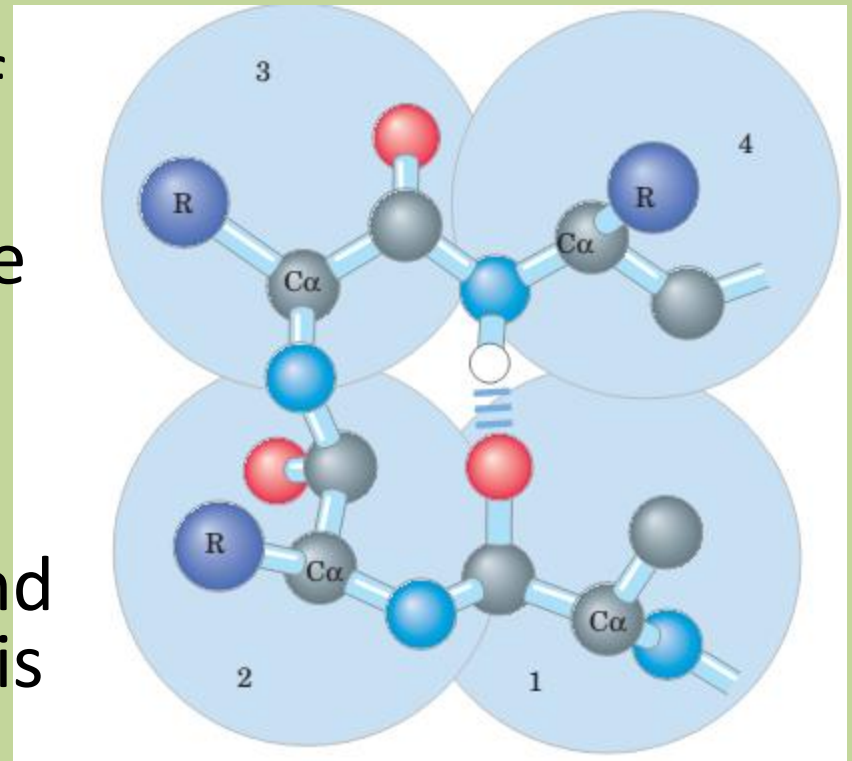


Loops & Bends

- Short segments of amino acids that join two units of secondary structure – 3-4 units
- **Globular proteins** - compact folded structure
- Nearly **one-third** of the amino acid residues are in turns or loops where the polypeptide chain reverses direction
- The structure is a 180° turn involving four amino acid residues

Loops & Bends

- **Carbonyl oxygen of the first residue forms a hydrogen bond with the amino-group hydrogen of the fourth residue**
- The **peptide groups** of the central two residues do **not** participate in any **hydrogen bonding**
- **Gly** (small and flexible) and **Pro** (readily assume the cis configuration) residues often occur in turns



Loops & Bends

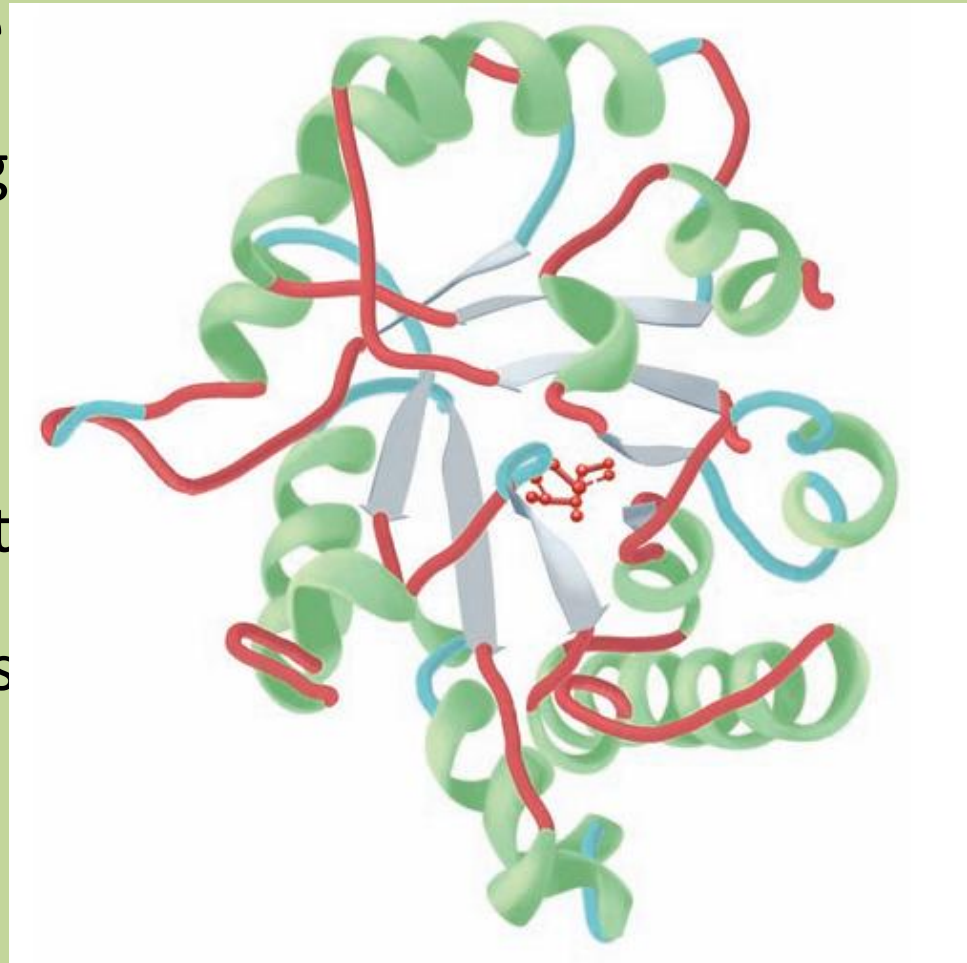
- Generally found on the surface of a protein
- γ -turn - less common is the, a **three residue turn** with a **hydrogen bond** between the **first and third** residues.

Tertiary Structure

- Entire 3-dimensional conformation of a polypeptide
- Beside H bond, sulfide bond (-S-S), ionic interaction and hydrophobic bond
- Consists of helices, sheets, bends, turns, and loops— assemble to form **domains**
- Domain is a section of protein structure - perform a particular chemical or physical task
 - binding of a substrate or other ligand
 - anchor a protein to a membrane
 - interact with a regulatory molecules

Single domain:triose phosphate isomerase

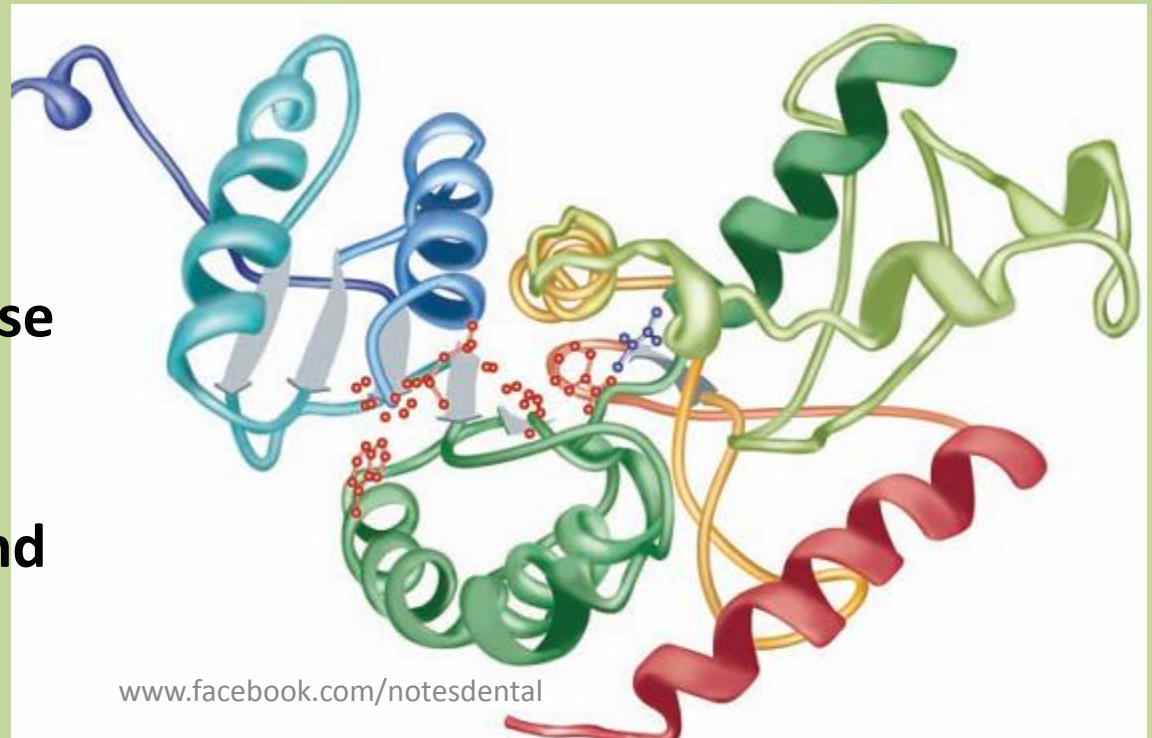
- Enzyme triose phosphate isomerase complexed with the substrate analog 2-phosphoglycerate (red)
- Elegant and symmetrical arrangement of alternating β sheets (light blue) and a helices (green), with the β sheets forming a β -barrel core surrounded by the helices



Tertiary Structure

- **Single domain** - triose phosphate isomerase, myoglobin
- **Two domains** - lactate dehydrogenase, quinone oxidoreductase
- A polypeptides with 200 amino acids normally consists of two or more domains

Tetrameric enzyme lactate dehydrogenase with the substrates NaDh (red) and pyruvate (blue) bound



Quaternary Structures

- Majority of proteins are composed of single polypeptide chains
- Some of protein consists of 2 or more polypeptide chain which may be identical or different
- Such protein are termed as **oligomers** and poses quaternary structures.
- When it consists of 2 polypeptides - **dimers**
- **Homodimers** contain two copies of the same polypeptide chain, while in a **heterodimer** the polypeptides differ