

Chapter 5

Protein Structure and Function



Amino Acids and Primary Structure

■ Amino acids

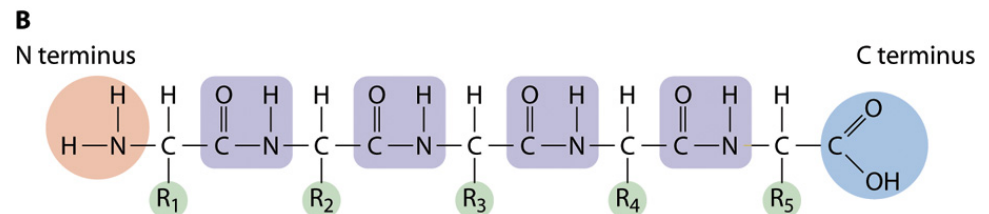
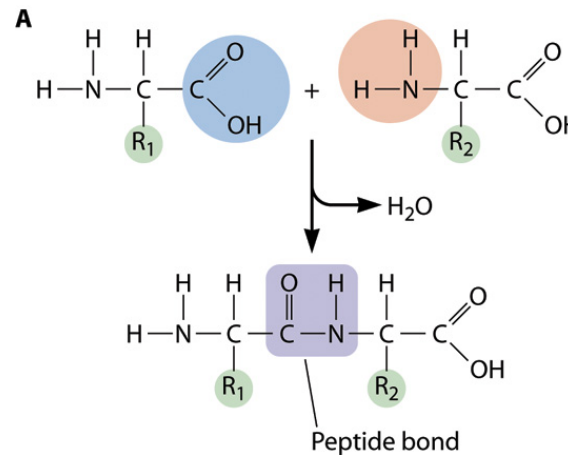
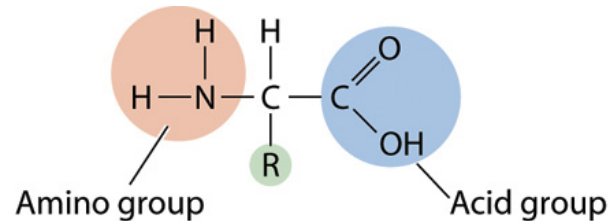
- Amino group
- Carboxyl group
- R group; 20 Side chains

■ Peptide bond

- Between NH_2 and COOH

■ Polypeptide

- A chain of amino acids
- N terminus and C terminus

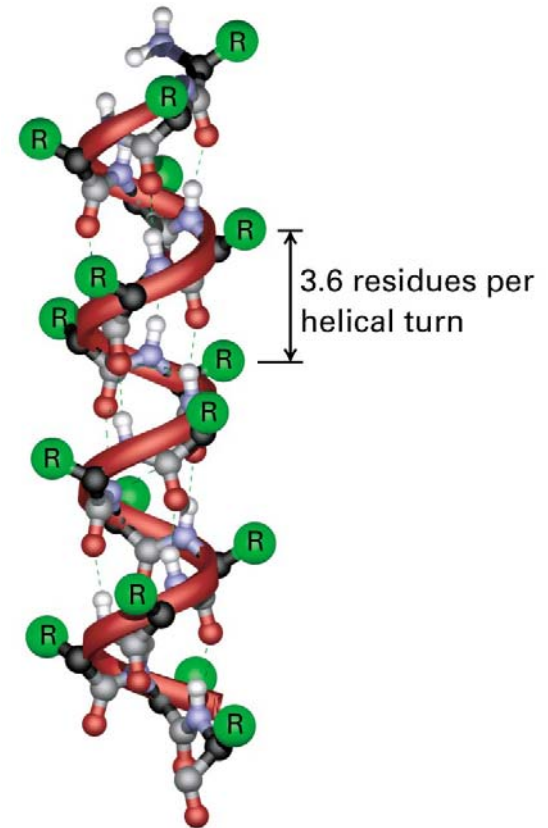
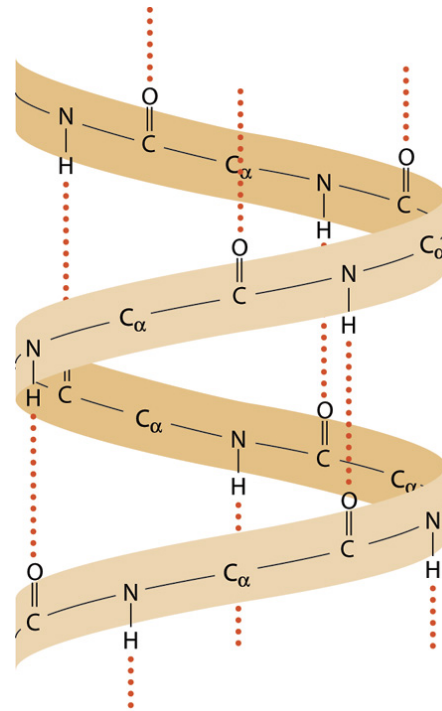


Primary and Secondary Structure

- Primary structure
 - Linear arrangement (sequence) of amino acids
- Secondary structure
 - Core elements of protein architecture
 - Neutralization of partial charges of the peptide backbone by hydrogen bonding
 - Local folding of polypeptide chain
 - α helix, β sheet : 60% of the polypeptide chain
 - Random coils and U-shaped turn

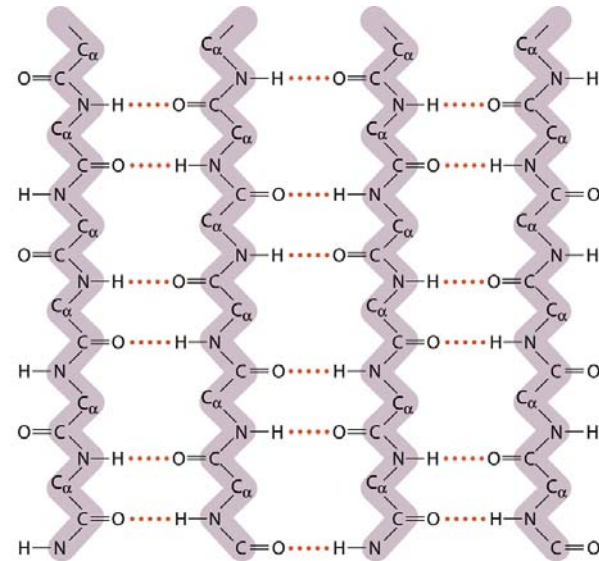
α -Helix

- Hydrogen bond between carbonyl O (n) and amid H (n+4)
- Directionality on the helix : The same orientation of H bond donor
- Side chains point outward :
- Determine hydrophobic or hydrophilic quality

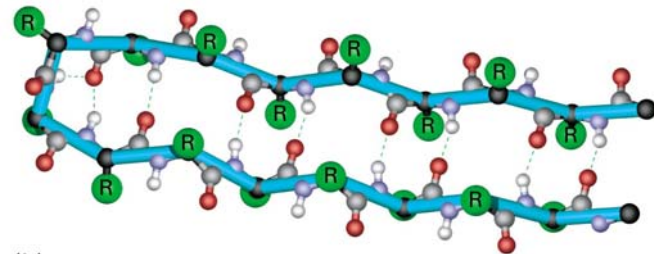


β -Sheet

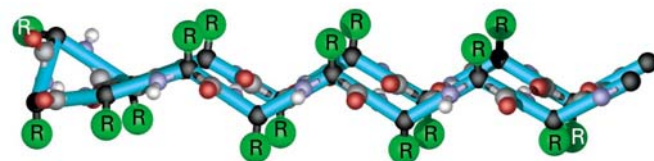
- Laterally packed β strands of 5 to 8 residue
- Hydrogen bonding between β strands \rightarrow β sheet, pleated sheet
- Parallel or antiparallel



(a)



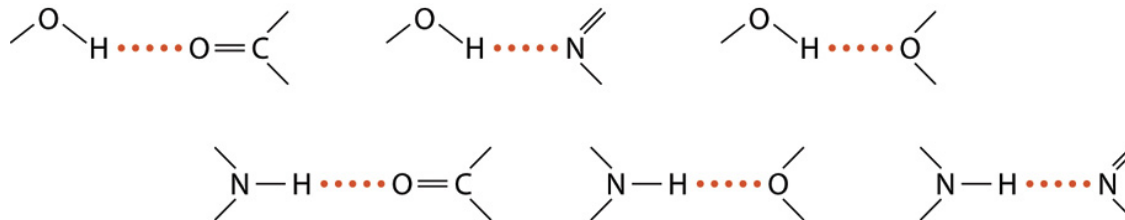
(b)



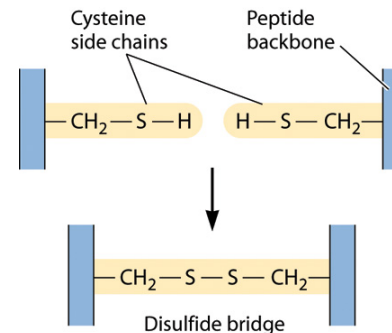
Tertiary Structure

■ Tertiary structure

- Overall folding of a polypeptide chain
- Stabilization
 - weak interaction
 - Hydrophobic interaction between nonpolar side chains
 - Hydrogen bond between polar side chains and peptide bonds



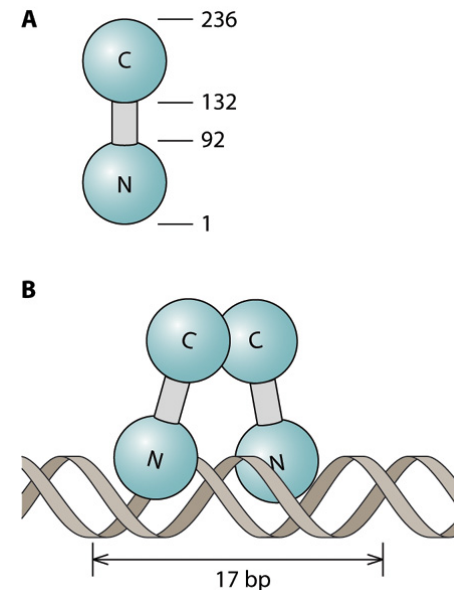
• Disulfide bond formation



Higher Levels of Structure

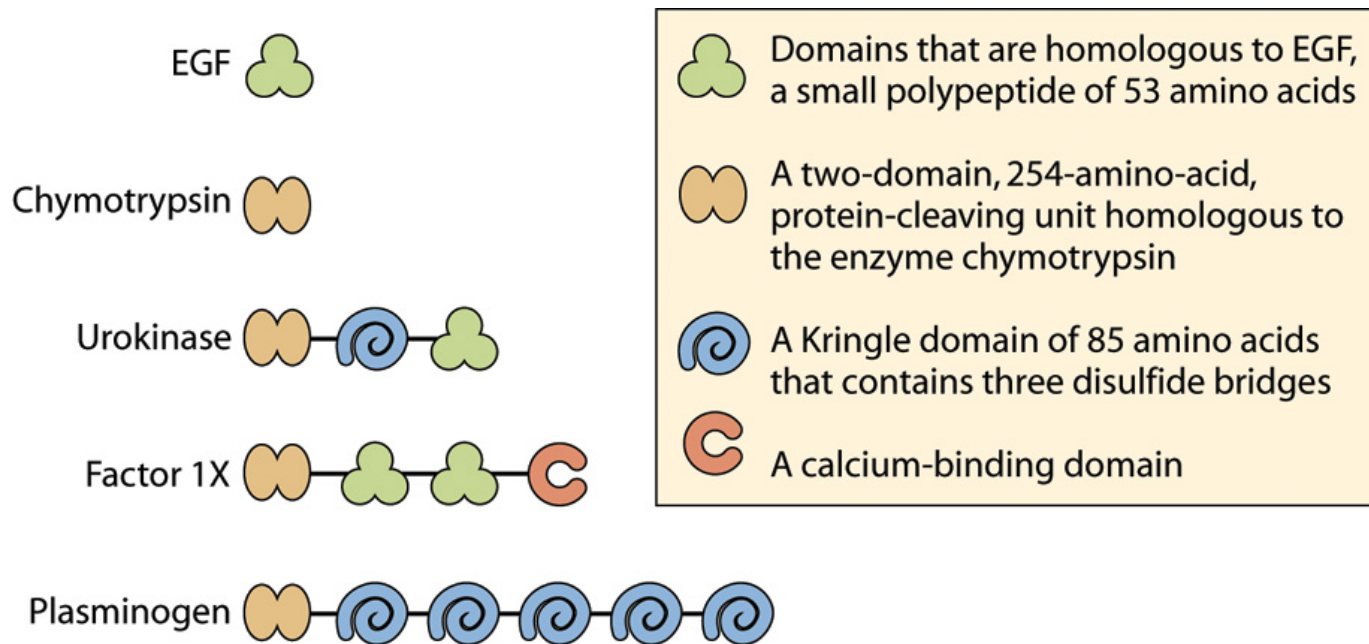
■ Domains

- Completely folded region of polypeptide
- Fundamental units of protein structure and function
 - Structural feature:
 - proline-rich, acidic
 - Functional feature:
 - DNA binding, membrane
- e.g. lambda repressor (236 aa)
 - N terminal domain : DNA binding
 - C terminal domain : Dimerization
 - Interaction with C terminal domain of another molecule



Modular proteins

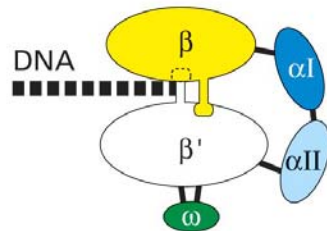
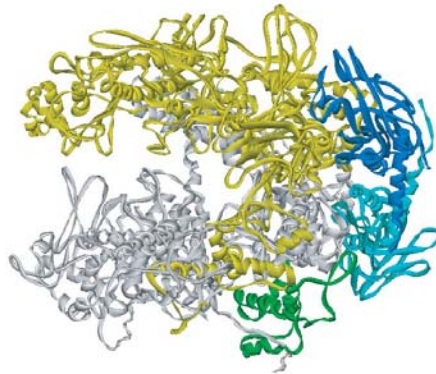
- New proteins by combination of functional domains
- Biotechnological application



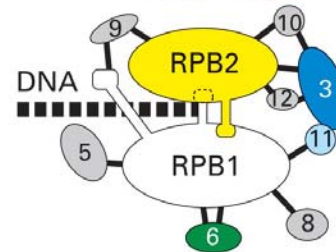
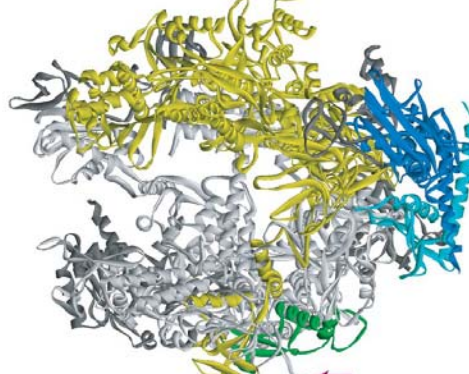
Quaternary Structure

- Association of multiple polypeptide chains
 - Lambda repressor : dimer
 - E. coli RNA polymerase : Five polypeptide chains

(a) Bacterial RNA polymerase



(b) Yeast RNA polymerase II



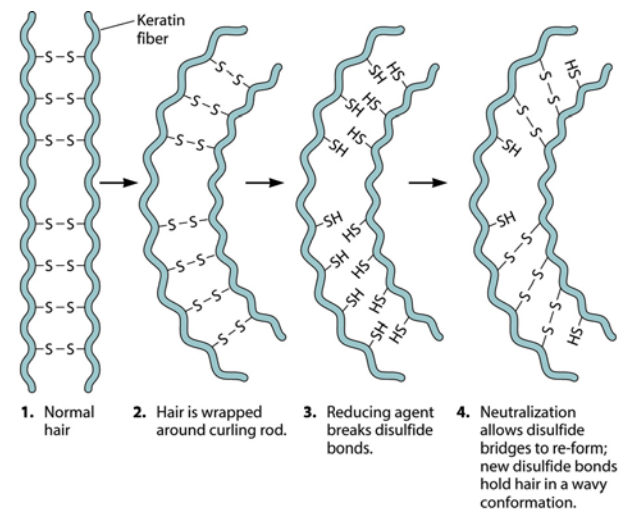
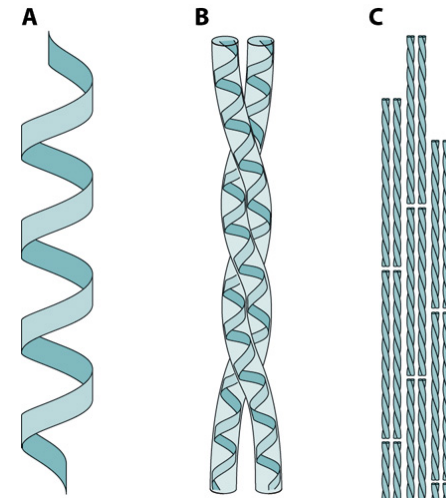
Disruption of Protein Structure

- Factors disrupting protein structure
 - Heat, extreme pH, organic solvent, detergent
- Denaturation
 - Complete unfolding of amino acid chain
 - Sometimes irreversible : e.g. boiled egg
 - Melting temperature (T_m)
 - Denaturation temperature for a given protein
 - Depending on protein structure
 - Proteins from organisms living in thermal vents have high T_m
 - Disulfide bridge increases protein stability

Examples of Protein Structure and Function

■ Keratin

- Structural protein for hair, wool, feathers, nails, scales, hooves, horns, skin
- Very strong and water insoluble
 - Hydrophobic alpha helices
 - Long α -helix with hydrophobic amino acids (A, I, V, M, F)
 - Forming fibers by hydrophobic interactions
 - Disulfide bonds
 - The more S-S bonds the harder the structure
 - Permanent wave
 - » Reducing of disulfide bond \rightarrow Generation of new disulfide bond

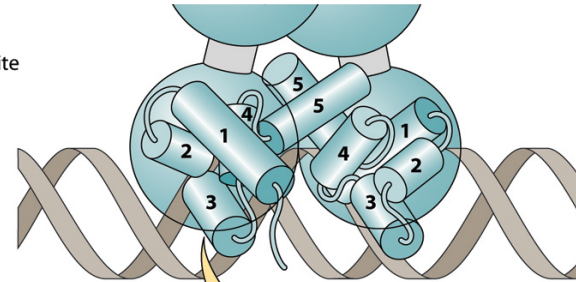


Examples of Protein Structure and Function

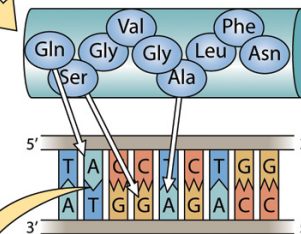
■ Lambda Repressor

- Binding of N-terminal domain helix 3 to specific bases within the DNA binding sequence

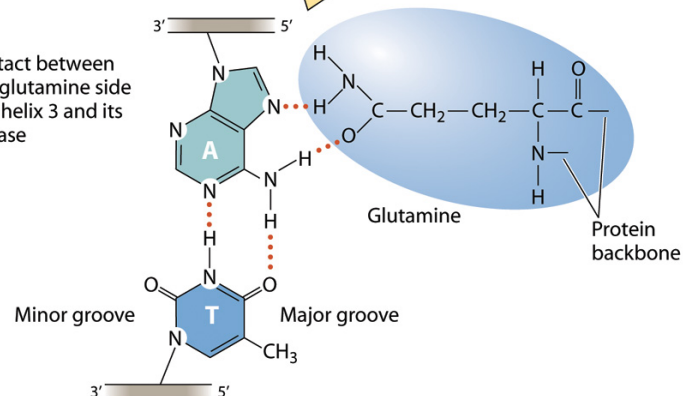
A. The orientation of protein helices on the DNA-binding site



B. The amino acid sequence of helix 3. The specific bases in the DNA sequence that are contacted by amino acid side chains are indicated by arrows.



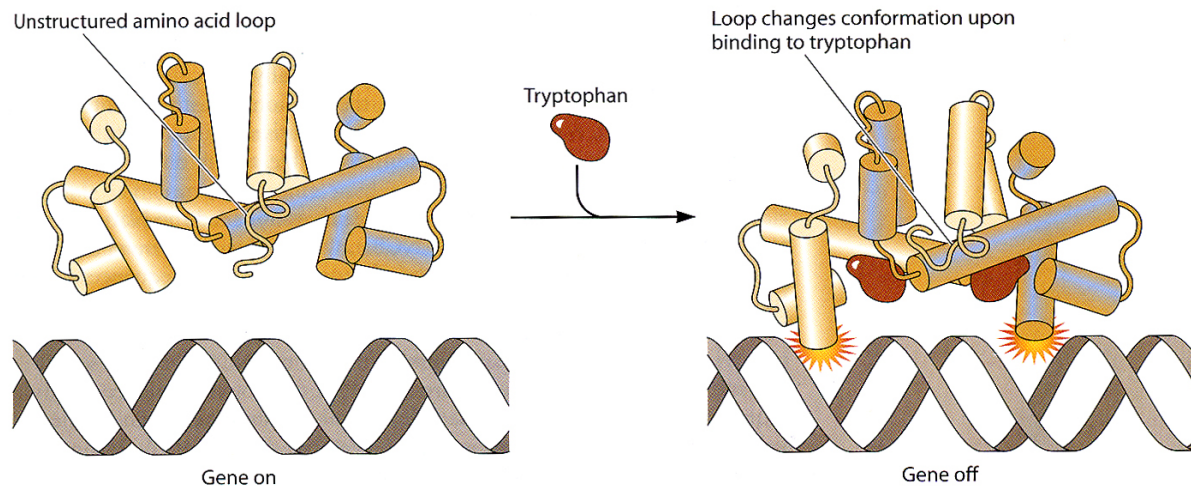
C. The contact between the first glutamine side chain in helix 3 and its target base



Examples of Protein Structure and Function

■ Trp Repressor

- If plenty of Trp in the cytosol
- Binding of Trp into Trp Repressor and change the conformation
- Trp repressor binds to DNA and represses expression of genes involved in Trp synthesis



Predicting Protein Structure

- It is difficult to predict three dimensional structure from the amino acid sequence
- Comparison to other proteins with known function or structure
 - Easy access of information through public database
 - NCBI (National center for Biotechnology Information) run by National Institutes of Health (NIH)
 - <http://www.ncbi.nlm.nih.gov>
 - Testing structure-function prediction
 - Using molecular biological tools

Protein Engineering

- Manipulation of protein's amino acid sequence to change its function or properties
- Chemical manufacturing
 - Develop enzymes more suitable for industrial applications
 - Increasing enzyme stability
 - e.g. bacteriophage lysozyme: introduce S-S bond to increase heat resistance
 - Proteases in detergent