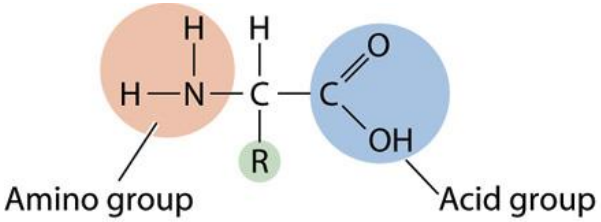
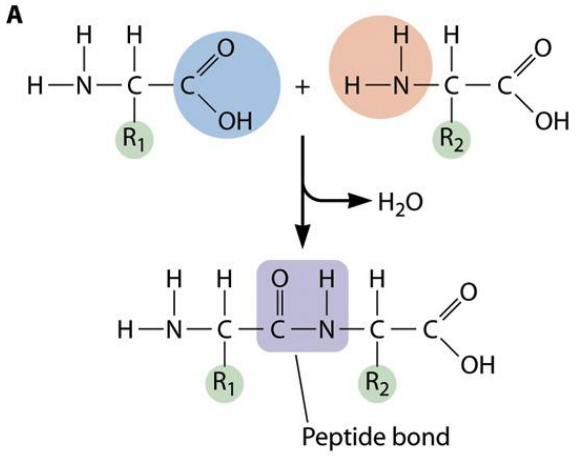
Chapter 5

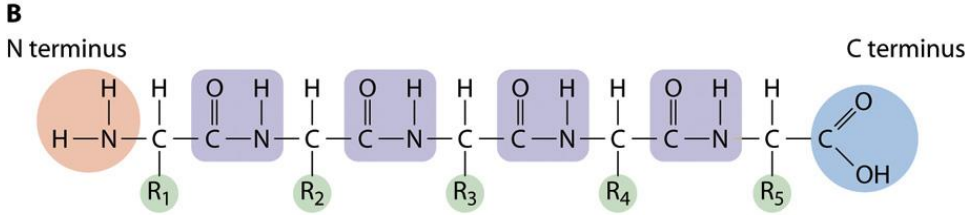
Protein Structure and Function

Amino Acids and Primary Structure

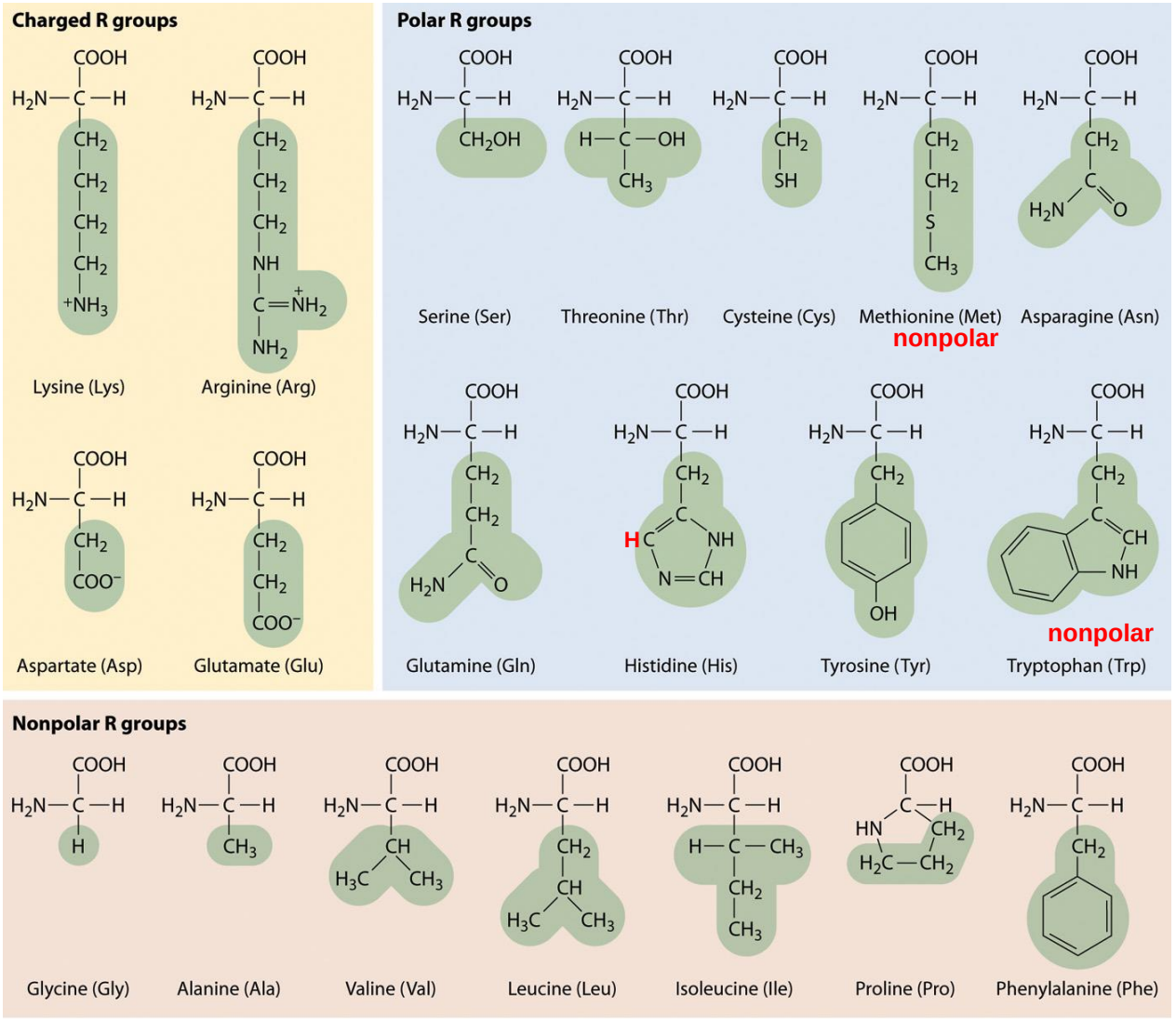
- Amino acids
  - Amino group
  - Carboxyl group
  - R group; 20 Side chains
- Peptide bond
  - Between NH_2 and COOH
- Polypeptide
  - A chain of amino acids
  - N terminus and C terminus







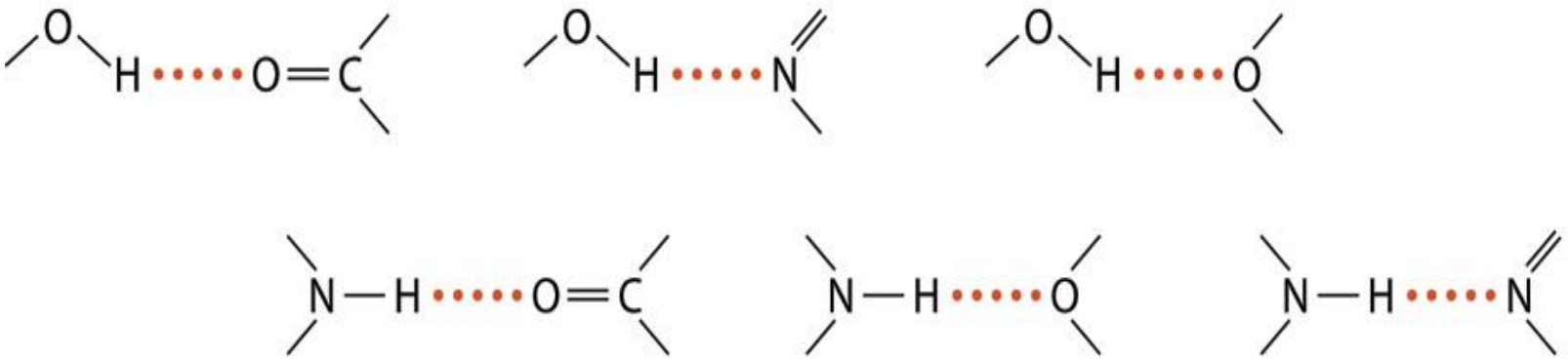
Amino Acids


Charged R groups
Lysine (Lys)
Arginine (Arg)
Aspartate (Asp)
Glutamate (Glu)
Polar R groups
Serine (Ser)
Threonine (Thr)
Cysteine (Cys)
Methionine (Met)
nonpolar
Asparagine (Asn)
Glutamine (Gln)
Histidine (His)
Tyrosine (Tyr)
nonpolar
Tryptophan (Trp)
Nonpolar R groups
Glycine (Gly)
Alanine (Ala)
Valine (Val)
Leucine (Leu)
Isoleucine (Ile)
Proline (Pro)
Phenylalanine (Phe)

Primary and Secondary Structure

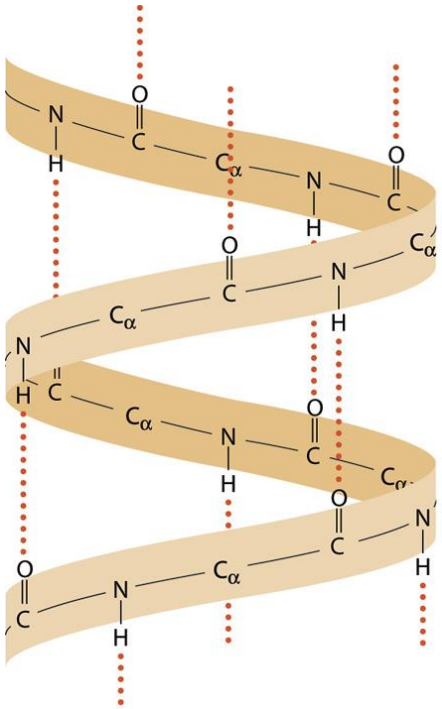
- Primary structure
  - Linear arrangement (sequence) of amino acids
- Secondary structure
  - Core elements of protein architecture
  - Neutralization of partial charges of the peptide backbone by hydrogen bonding
  - Local folding of polypeptide chain
    - α helix, β sheet : 60% of the polypeptide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

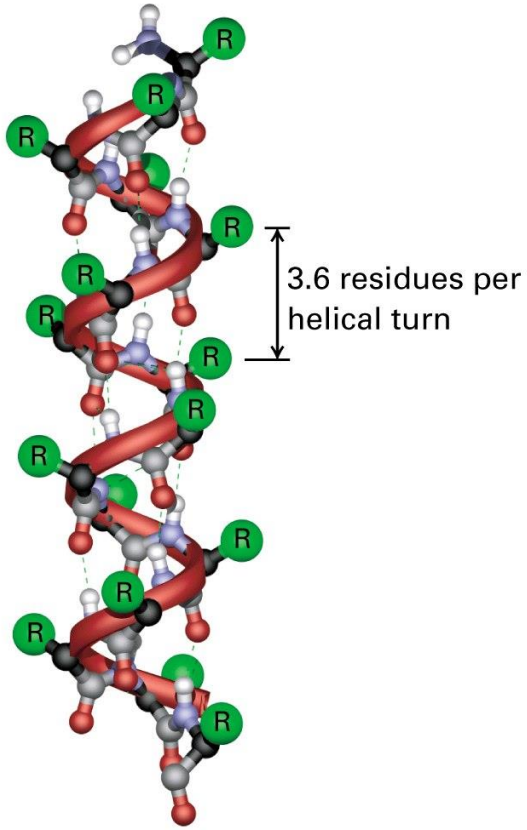
Common Hydrogen Bonds in Biological Systems



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





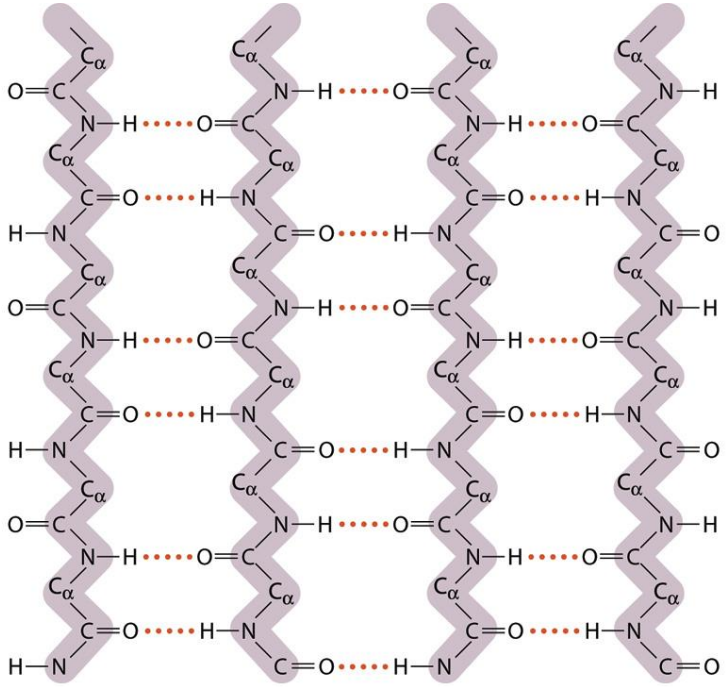
β-Sheet

- Hydrogen bonding between β strands → β sheet,

  pleated sheet

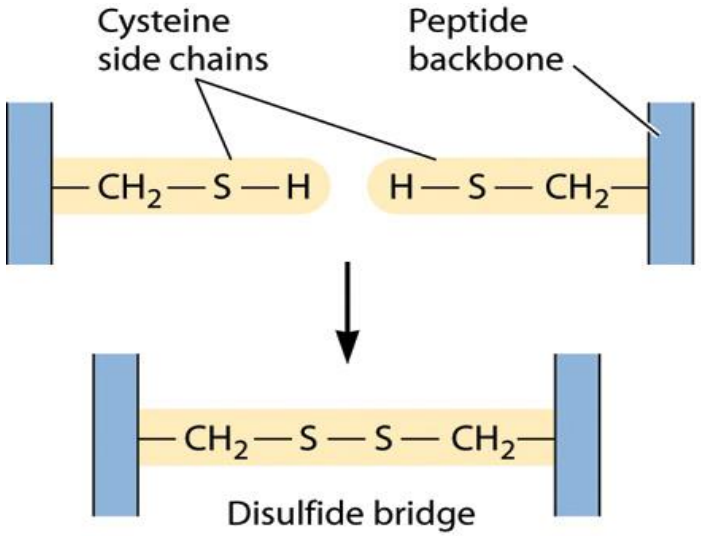
- Usually not flat,

  but twisted



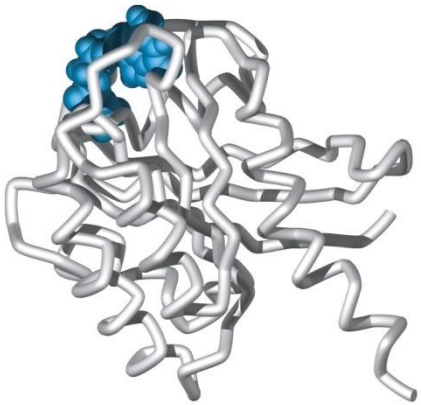
Tertiary Structure

- 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

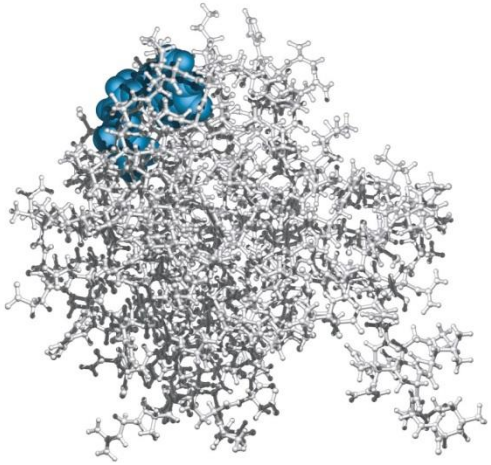


Graphical Representation of the Protein

(a) C_α backbone trace

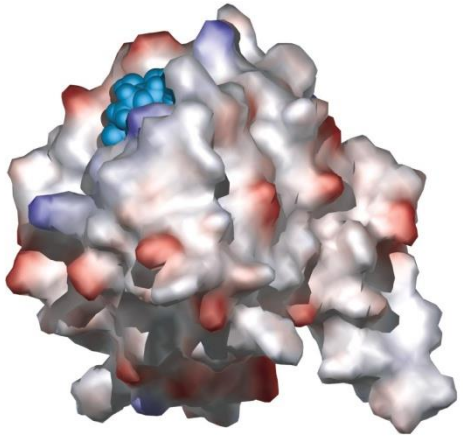


(b) Ball and stick



(c) Ribbons

(d) Solvent-accessible surface

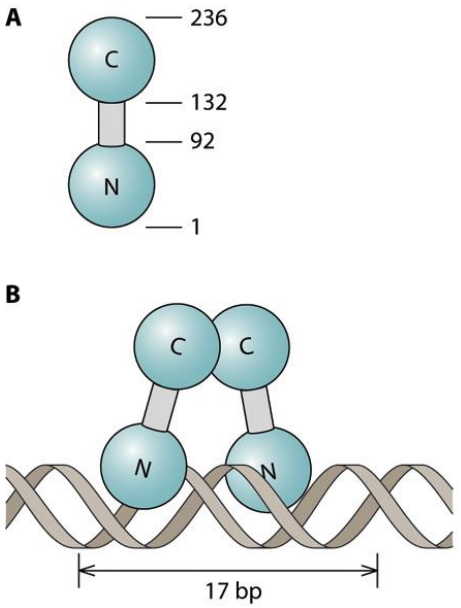


Higher Levels of Structure

- Domains
  - One stable, compact, three-dimensional shape
  - Fundamental units of protein structure and function
    - DNA binding domain, transmembrane domain

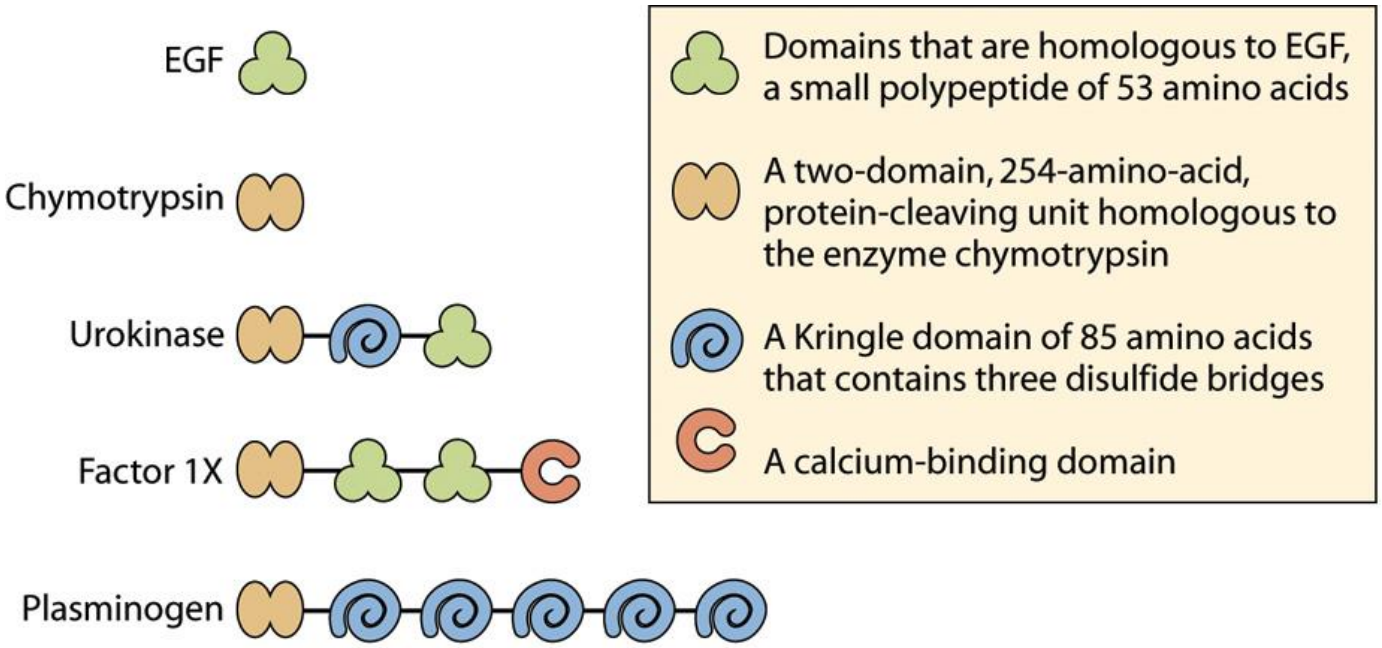
  - e.g. lambda repressor (236 aa)
    - N terminal domain : DNA binding
    - C terminal domain :

      Interaction with C terminal domain of another molecule (dimerization)



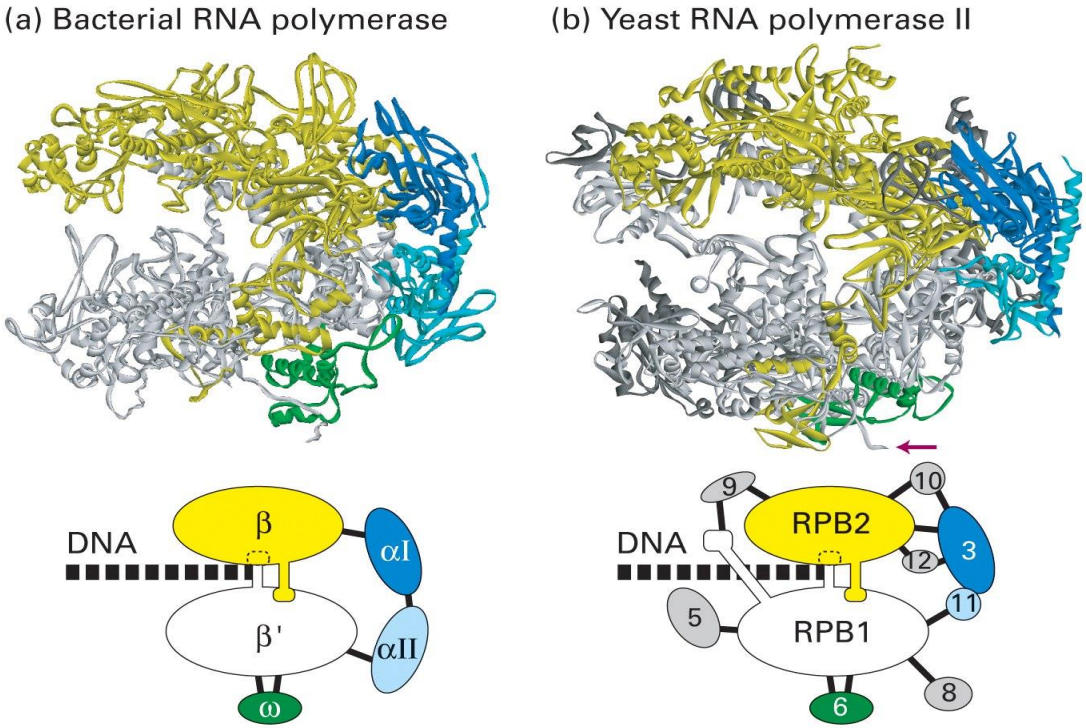
Modular Proteins

- New proteins by combination of functional domains
- Biotechnological application using recombinant DNA technology



Quaternary Structure

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



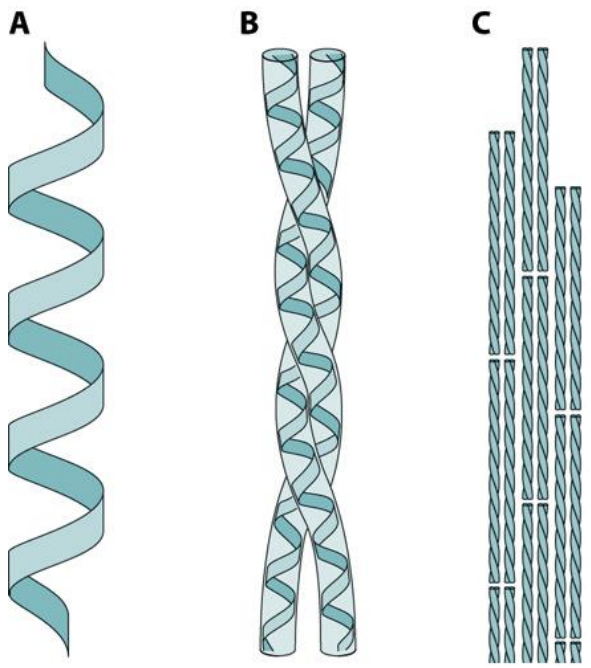
Disruption of Protein Structure

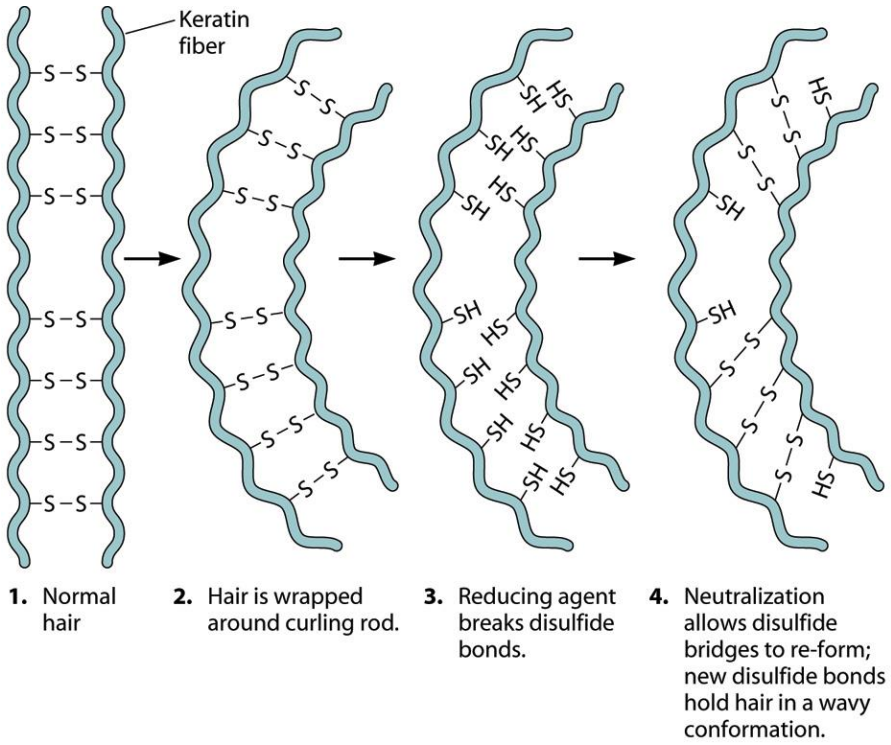
- Factors disrupting protein structure
  - Heat, extreme pH, organic solvent, detergent
- Denaturation
  - Complete unfolding of amino acid chain
  - Sometimes irreversible : e.g. boiled egg
  - Melting temperature (T_m)
    - Denaturation temperature for a given protein
    - Depending on protein structure
      - Proteins from organisms living at high temperature
      - 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
      - – Forming fibers by hydrophobic interactions
    - Disulfide bonds
      - – The more S-S bonds the harder the structure
      - – Permanent hair wave
        - » Reducing of disulfide bond → Generation of new disulfide bond

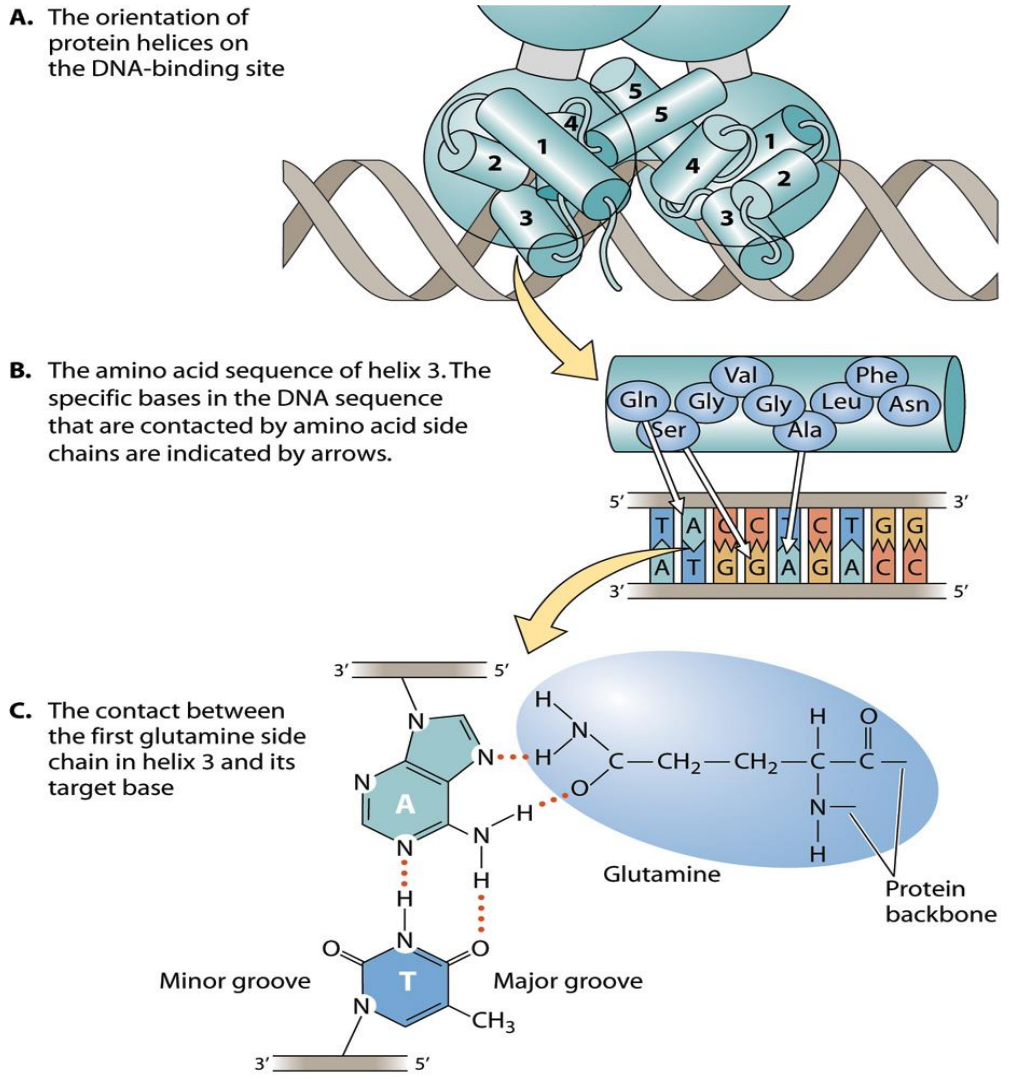
Examples of Protein Structure and Function





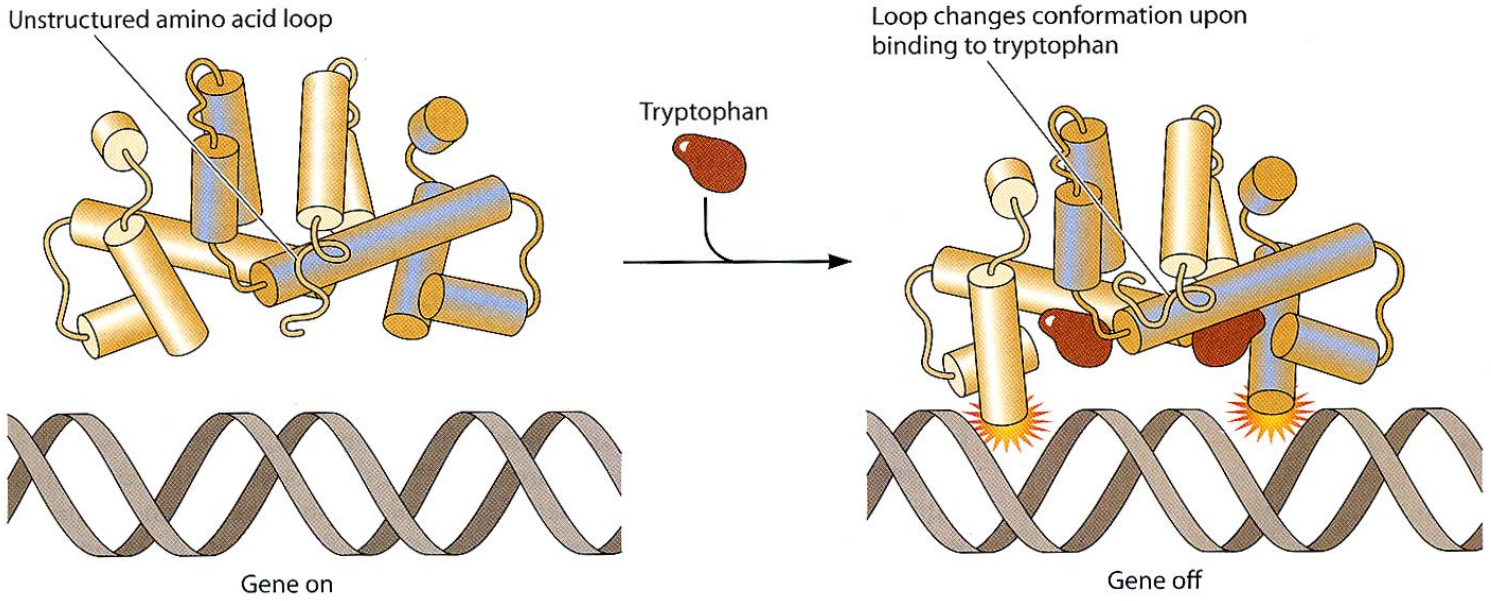
Lambda Repressor

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



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 the expression of genes involved in Trp synthesis



Predicting Protein Structure

- It is difficult to predict three dimensional structure from the amino acid sequence
- Compare 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
    - Introduction of mutations into protein

      →change of protein function

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