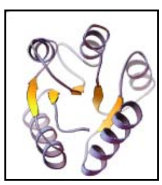
Molecular structures
Proteins

Proteins

- Building blocks of cell structures and motors of cellular activities
- Carry out the program encoded in genes
  - Unique sequence specified by the gene!!!
  - Unique sequence = unique shape = unique function

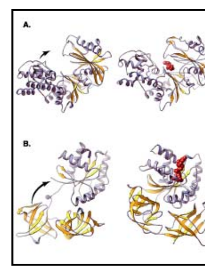
Proteins

- Unbranched (linear) chains of amino acids
- Composed of only 20 amino acids
- Various combinations and lengths
- The shape of protein arises from the 3D structure it assumes due to the noncovalent bonds between regions in the linear sequence (functional domains)

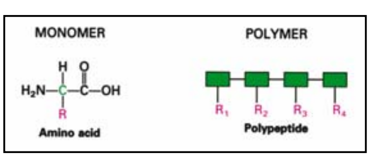


Protein structure determines its function

- In turn, a protein's shape determines the function of that protein
- Only the correctly folded protein can perform its function (native state)



Amino acid structure



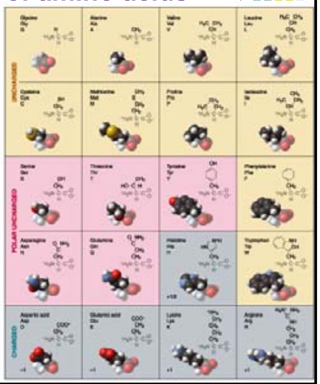
- α carbon bound to four different chemical moieties
  - Amino
  - Carboxyl (or carboxylic acid)
  - Side chain R

Structure of an amino acid

- Side chain is unique to aa
- Determines polarity and properties of aa
  - and thus the tertiary structure of the protein
- 3 main groups of amino acids based on the chemical composition of the side chain

Three main groups of amino acids

- Uncharged
- Polar uncharged
- Charged



Uncharged amino acids

- Poorly interact with water
- Pack inside of the protein structure to avoid aqueous environment
- Like to reside in lipid based plasma membrane (intrinsic membrane proteins)

Uncharged amino acids

- Proline and glycine are stiff
  - Create bending sites
  - Contribute to 3D structure
- Cysteins can form -S-S- (disulfide bonds)
  - S-S covalently link two cysteins and contribute to 3D structure

Polar uncharged amino acids

- Can interact with water by forming hydrogen bonds
- Serine, threonine and tyrosine are preferred places of phosphorylation

Charged amino acids

- Polar groups tend to stick outside of the structure
- Form active pockets and binding sites
- Arg, Lys– main amino acids that contribute to overall charge of a protein

Amino acids can be post-translationaly modified

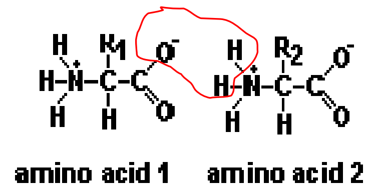
- Phosphorylation
- Methylation
- Hydroxylation
- Formation of –S-S- (disulfide) bonds
- Glycosylation

Polypeptide formation

- Peptide bonds connect amino acids into linear chains
  - Single chemical linkage formed by a dehydration synthesis (condensation reaction) between H_3N group of one aa and COOH group of a second aa
- Forms linear **unbranched** chains
  - Head to tail connection

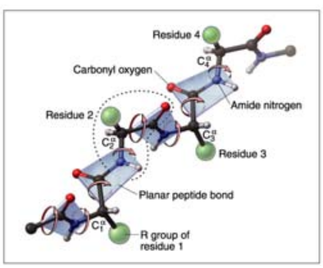
Peptide bond formation

- Two molecules are joined together with the accompanying removal of a molecule of water.



Polypeptide backbone

- Side chains are sticking to the sides
- Peptide bonds are very stiff and flat

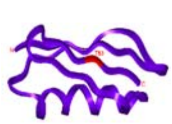


Chains with peptide bonds

- Peptide – less than 20-30 AAs
- Polypeptide – less than 4000 AAs does not assume 3D structure
- Protein – peptide or polypeptide that assumes a 3D structure

Protein folding

- 3D structure (conformation) is determined solely by the sequence of amino acids
  - Interactions between aa
  - If you change aa in a mutation or posttranslational modification you change the shape and function
  - Conformational changes are basis for the function



Four levels of structure determine the shape of proteins

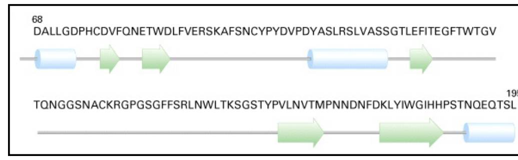
- Primary – sequence - the linear order of amino acids
- Secondary – localized organization of the polypeptide chain
  - α helix
  - β sheet (two or more b strands)
  - Omega loop

Four levels of structure

- Tertiary: the overall, three-dimensional arrangement of the polypeptide chain
  - Domains
- Quaternary: the association of two or more polypeptides into a multi-subunit complex
  - Macromolecular structures

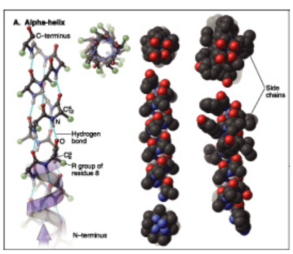
Primary structure of hemagglutinin

- Primary – sequence of amino acids



Secondary structure: the α helix

- Spiral structure
- Strong hydrogen bonds
- Packing of α -carbons with the rotation

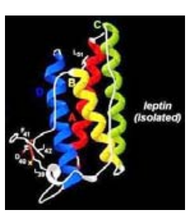


Secondary structure: the β sheet

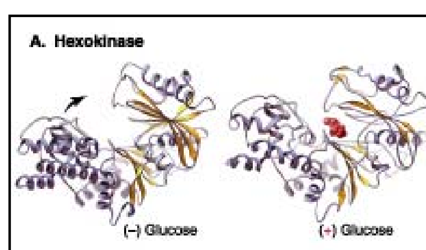
- A planar structure composed of alignments of two or more β strands
- Group is bound by hydrogen bonds
- Can be antiparallel or parallel
  - Antiparallel are more stable
  - Parallel tend to be buried inside the protein

Tertiary structure

- Packing of secondary structures
- Tertiary structure of the protein results from hydrophobic interactions and disulfide bonds
- Decides about protein function
- Form protein motifs and functional domains



Tertiary structure

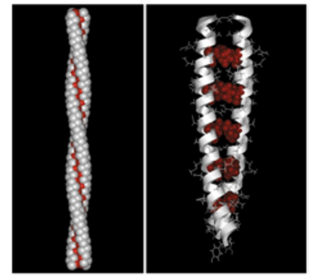


Tertiary structure – protein motif

- Defined by specific combinations of secondary structures that have a particular topology and is organized into a characteristic 3D structure
- Ex:
  - Coiled coil
  - Helix loop helix
  - Zinc finger

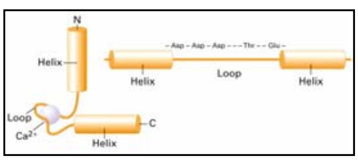
A coiled-coil motif

- Formed by two or more helices wound around one another
- Responsible for dimerization



Helix-loop-helix motif

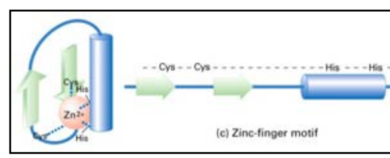
- Occurs in many calcium binding proteins



- Loop forms a ring around Ca^{2+} ion
- Important for Ca^{2+} binding/sensitivity

Zinc-finger motif

- Present in proteins that bind nucleic acids
- Zn^{2+} ion is held between a pair of β strands and α helix

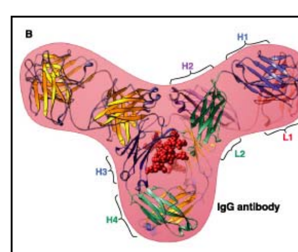


Domains

- Functional not structural modules
  - Kinase domain
  - Immunoglobulin domain
- Can be formed by parts of secondary structures very distant from each other
- Activity of the protein is localized to a particular domain

Modular nature of the proteins

- In a protein domains become functional modules



Summary

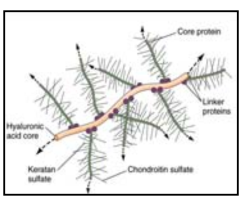
- A protein is a linear polymer of AA linked by peptide bonds
- There are 3 groups of AAs based on the properties of the side chain
- The sequence of the protein determines its 3D structure that in turn determines its function

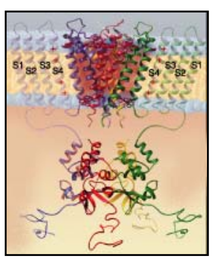
Summary

- Secondary structure of the protein assumes two most prevalent forms: α helix and β sheet
- Combinations of secondary structures give rise to specific motifs or domains
- Tertiary structure determines protein function

Quaternary structure of macromolecules proteins, carbohydrates etc.

- Several molecules form one functional unit
  - Ex. K+ channel
  - Proteoglycans





Quaternary structure of macromolecules

- Form by self-assembly
- Do not require template
- Association rarely involves enzymatic reactions
- Physical properties of parts determine the mechanism of assembly and final shape of the complex

Forces to keep quaternary structures together

- If it is self-assembly it is also self-disassembly
- Subunits are held together by
  - Hydrophobic effect
  - Hydrogen bonds
  - Electrostatic interactions
  - Perfect fit between complementary surfaces

Advantages of multiunit complexes

- Conservation of the genome
- Small subunits are easier to synthesize without errors
- Elimination of “mistakes”
- Recycling
- Opportunities for regulation