Lecture 13

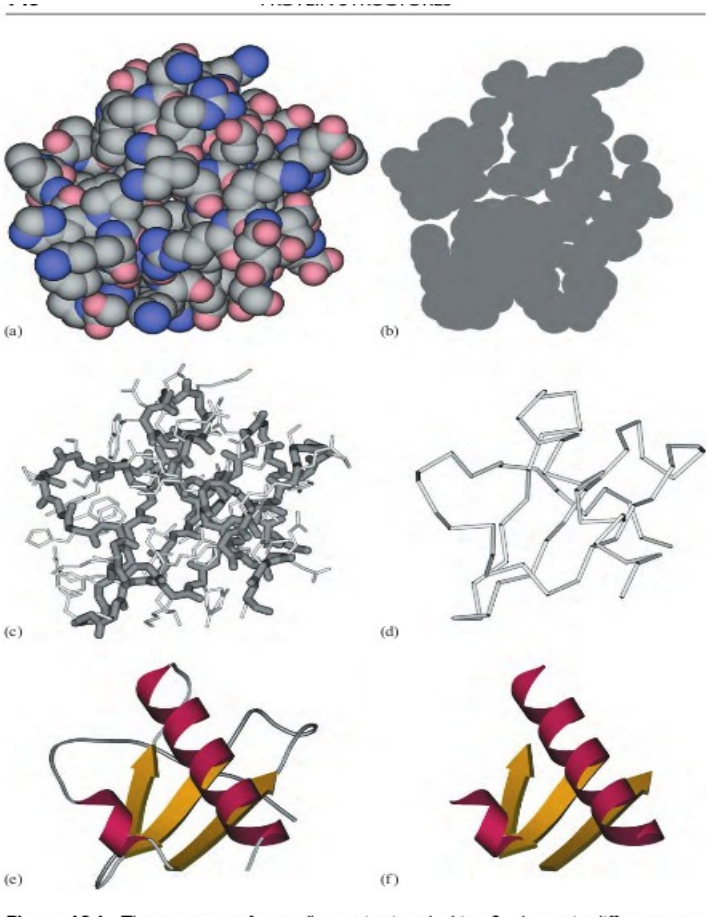
Water Soluble Globular Proteins

Water Soluble Globular proteins

- Best studied group
- Short Chains – 50-150 Residues
- 25-40Å Globule
- Larger Proteins consist of a few globules(domains)

Protein Representation

- Discussing the skeleton(wire model) of proteins
- Ignoring Side chains, orbits of electrons and size of atoms



Special Structure

- Composed of regular secondary structures:
  - Alpha-Helix and β-Sheets
  - Hydrophobic core surrounded by Alpha and β structures
  - Irregular Loops move towards the edge
    - Almost never found in the interior
    - Necessity of peptide groups to maintain H-bonds to water

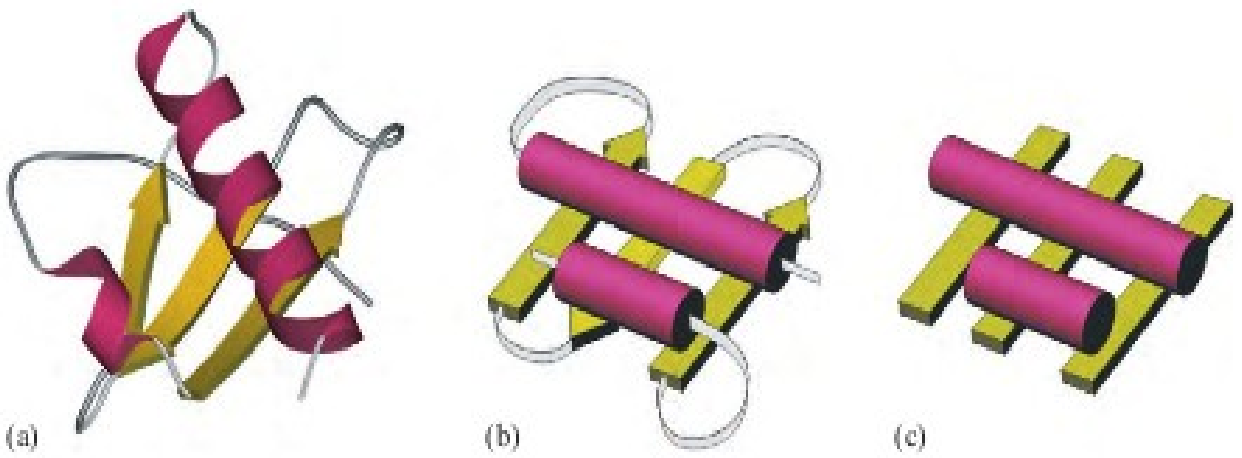
Subdivision of Globular Proteins

- Classification of small proteins
- Characterized by structural features of main chain
  - Pure Alpha or β proteins or a combination of both
- Large proteins can contain a mix of these structures.

- Interested in:
  - Architecture of packing of alpha and β structural segments into a globule
  - Pathway taken by chain through the globule
    - Topology of the protein globule
- Ignore:
  - Differences in size
  - Orientation
- Focus on:
  - Secondary structures(folding Patterns)

Packing of segments into a globule

- Look at secondary structures
- Ignoring loops connecting the structures
- Simplifying – Get rid of detail to classify the main points of the globule

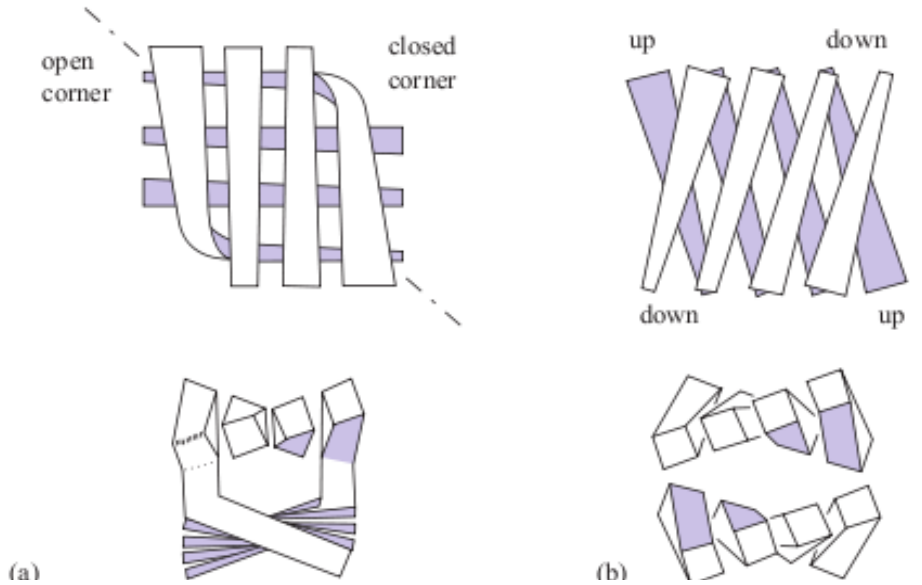


Architecture of β proteins

- Two or more β-sheets stacked on top of each other
- Antiparallel β structure predominates
- Proteins made of asymmetric Aas, β-strands are twisted
  - 25 degree angle between strands
  - Right hand twist
- β strands H-bond together in propeller-like assembly

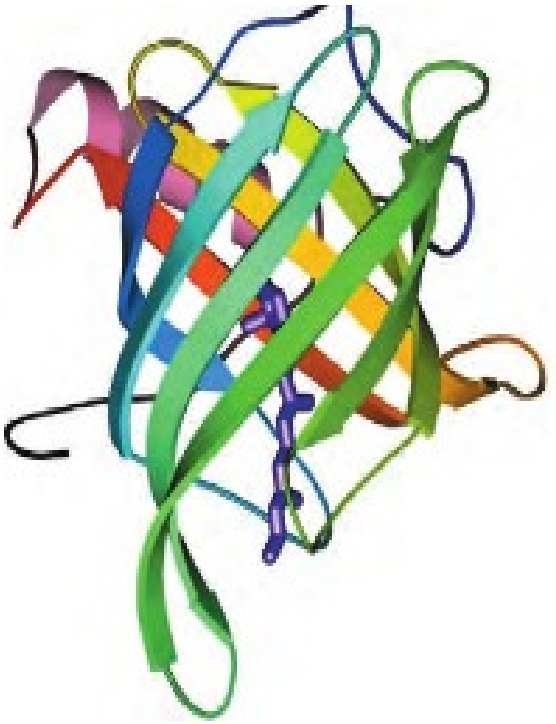
Packing Types

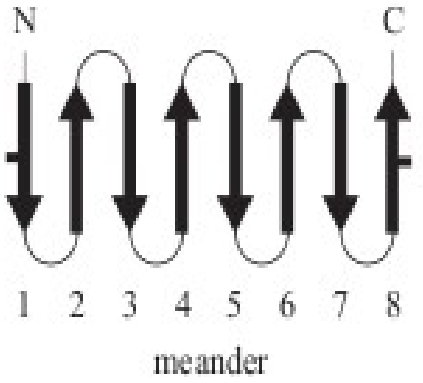
- Orthogonal Packing – 90 degrees between sheets
- Aligned Packing - (-)30 degrees between sheets



Orthogonal Packing

- B strands twisted, slightly bent
- Resembles a cylinder (β-Cylinder, β-Barrel)
- Anti-parallel strands
- Opposite sides of barrel H-Bonds are broken
- Closed corner β-Sheets come together, chain passes from one sheet to next with 90 degree bend
- At open corner β sheets spread apart
  - Filled with Alpha Helices or loops

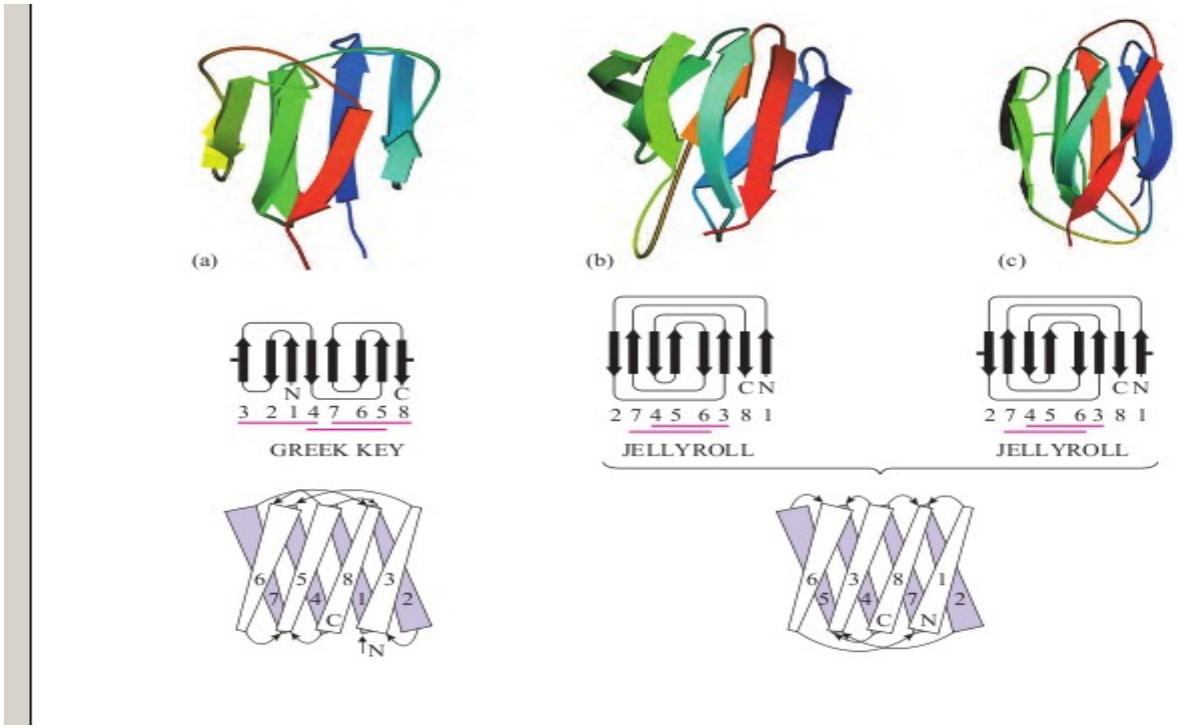




meander

Aligned Packing

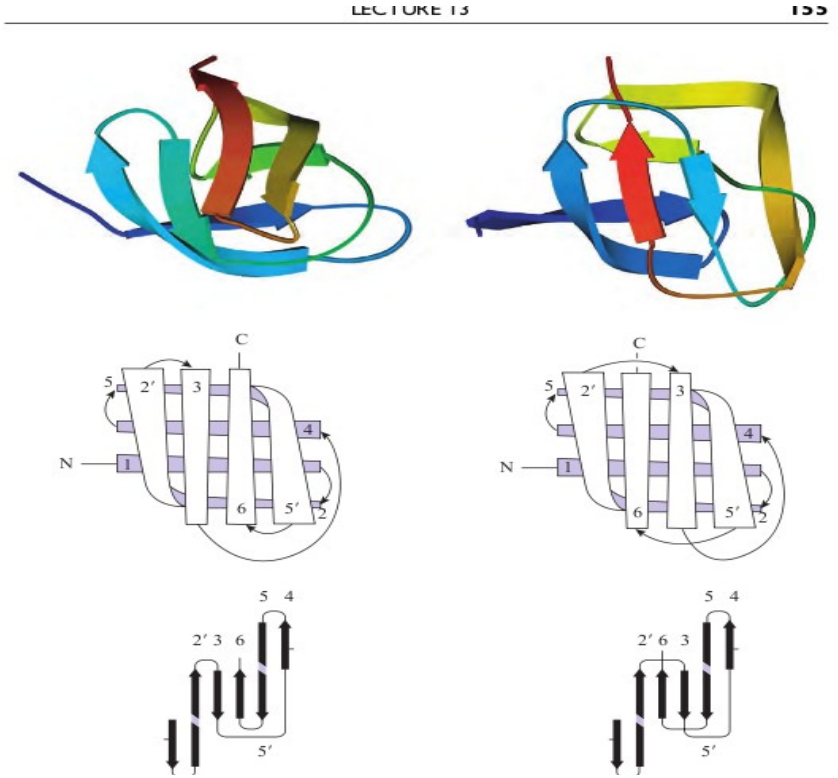
- Non bent sheets with propeller twist
- B-Sandwich
- Ends have irregular loops



- The same packing of structural segments can form in various paterns of chain folding
- Core of the fold remains unchanged

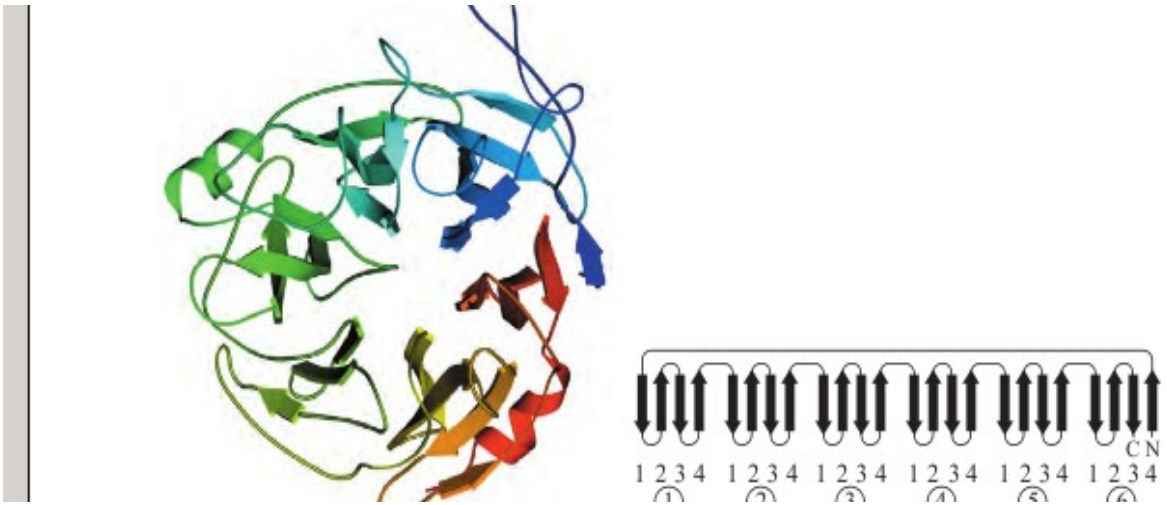
Orthogonal Packing β Sheets

- Other Common Architectures
  - Two different chain topolgies(paths taken by chain
    - a)chymotrypsin b)pepsin



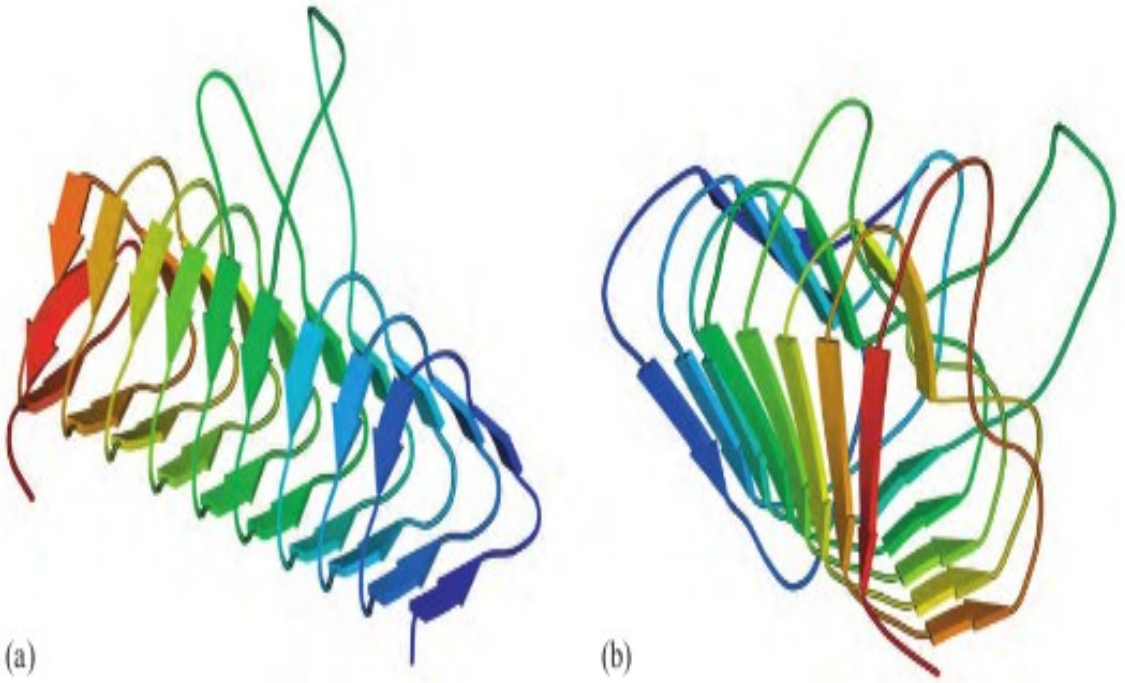
- Other Common Architectures

- Multiblade Propeller
  - Neuraminidase propeller
  - 6 sheets form β sandwich
  - Super cylinder built of β sandwiches



Other Common Architectures

- B – Prisms (β-Helix)
- 3 parallel β sheets
- Chain passes from one sheet to the next
- Chain coils around the axis and forms a right handed helix(parallel strands) or left handed helix(rare) usually joining β strands in other proteins
- Parallel β Structures are rare
- Different conformations
  - Energetically Unstable



(a) (b)

Anti Parallel β Strands

- Mostly due to the architecture of β hairpins
- Pathways of loops connecting β segments start and finish on same edge of fold
- Loops connect ends of β segments that are close
- B segments adjacent in the chain are not parallel and form anti-parallel β hairpins

Anti-parallel β Hairpins

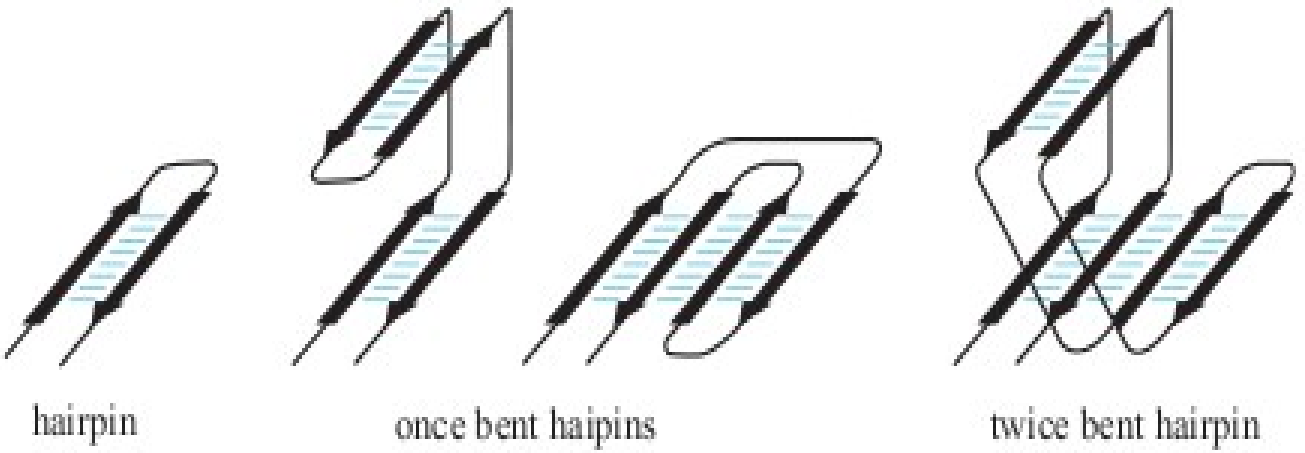
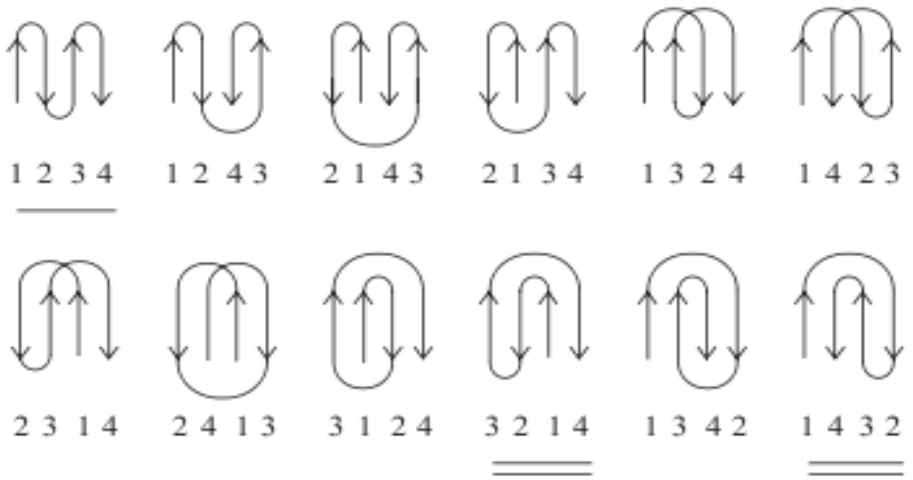


Figure 13.13. Antiparallel β-hairpins.

Architectures

- Overlapping/crossing of loops is rare
  - Energetically unfavorable (Additional bend)
    - Most abundant Configurations of β sheets formed by a continuous chain
      - Meander
      - 2 Greek Keys



Architectures

- Meander
  - Name of a winding river in Greece
  - Adjacent strands on the chain are adjacent in space and linked with H-Bonds
- Greek Key
  - 4 Strands adjacent in chain are anti-parallel
  - H-bonds between 1st and 4th strands
  - 2nd and 3rd strands usually belong to another sheet