Notes 10/9

Tuesday, October 09, 2007
10:00 AM

Proteins: Secondary, Tertiary, and Quaternary Structure

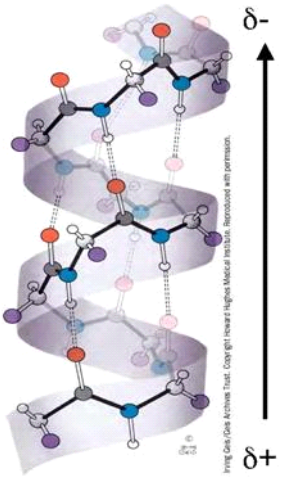
Oct. 9, 2007

Review

- Ramachandran plot shows those regions of phi and psi where there are no steric conflicts
- Amide protons and carbonyl oxygens form H-bonds causing the main chain to adopt a secondary structure
- Alpha-helices, Beta-sheets

Secondary structure refers to the local conformation of backbone

- Helical Structures
- Beta structures
- Non repetitive structures

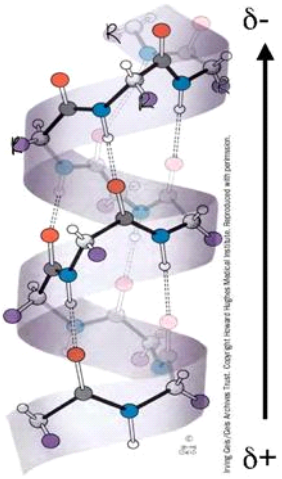


Helices in general

- Can be L or R handed
- Helix itself has a dipole moment
  - Amino end is partially positive
  - Carboxyl end is partially negative
- There are other kinds of helices that can differ in the number of residues per turn, but the geom. of an alpha-helix is most favorable

Review of alpha-helix

- Right-handed when made of L-amino acids
- By definition 3.6 residues per turn
- Intrachain H-bonds are formed between peptide bond elements 4 residues apart
- All H-bonds in alpha-helix are oriented along its axis; R-groups are oriented away from the axis
- Common in fibrous and globular proteins

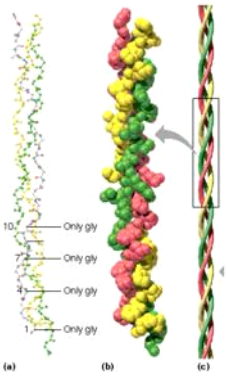


Where you can find alpha-helices

- Alpha keratin
  - Mammals
  - In hair, alpha keratin dimers form L-handed twists
  - It's structure is primarily stabilized by Cys (about 30%)
- Beta keratin
  - Reptiles, birds
  - Stronger than alpha-keratin
  - Combo of alpha-helices and beta-sheets - why, it's stronger

Other kinds of helices exist

- Collagen "coLLLagen" is a R-handed triple helix made of 3 helices that are L-handed
- By definition, the helices in a collagen triple helix are not alpha helices; they have 3.3 residues per turn
- There are many different types of collagen but usually they have
  - Gly-X-Y repeat
  - X often Pro; Y often Hyp
  - But other aa, especially Lys, are present

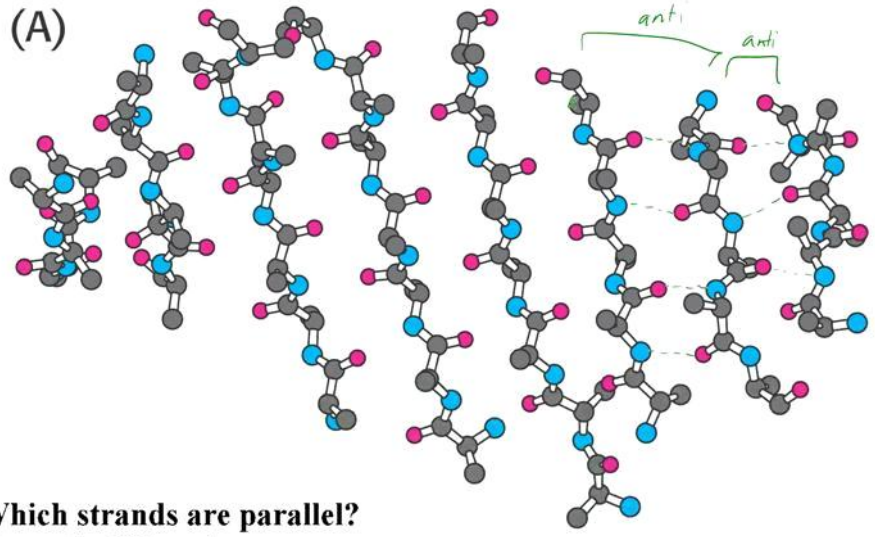


Beta-sheets

- A beta-sheet refers to two or more beta-strands held together by interchain H-bonds
- If strands are both oriented in the same direction the sheet is called a parallel beta-sheet
- If strands are oriented opposite to each other, the sheet is called an anti-parallel beta sheet

Do this @ home
. Draw in H bonds
. Point out parallel vs anti parallel

Test yourself

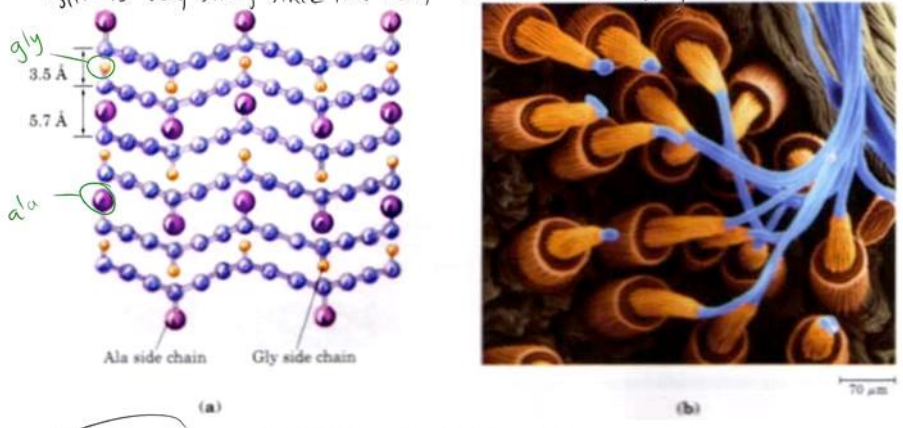


Which strands are parallel?
Draw the H-bonds.
Identify the amino-termini and carboxyl termini.

Fibroin: silk protein

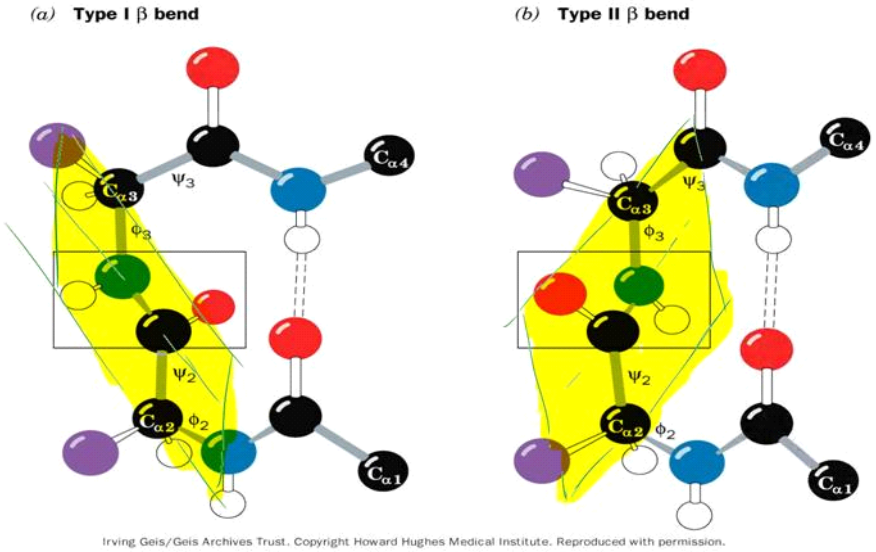
Rich in Ala and Gly that interdigitate (interweave)

Ala and Gly only have Van der Waals forces which adds to strechyness of silk
Silk is very strong since Ala + Gly are small and can tightly back



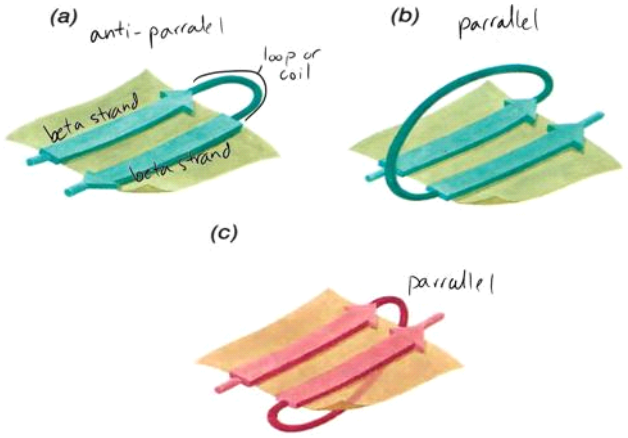
Typo on Oct. 8th slide #8: please change “Beta helix” to “Beta strand”

Nonrepetitive Secondary Structures
Example: Reverse turns in polypeptide chains



Connections between adjacent polypeptide strands in β pleated sheets.

usually find these in globular



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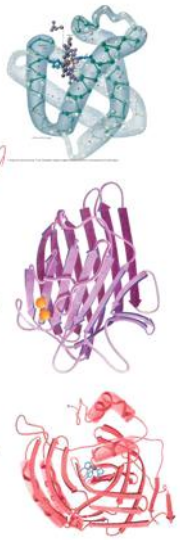
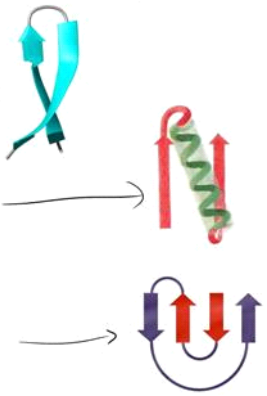
Tertiary Structures

- 3D arrangement, i.e. folding of secondary structures
- Globular proteins may contain alpha-helices and beta-sheets
  - Myoglobin: alpha-helices connected by coils
  - Concavalin: beta-sheets connected by coils
  - Carbonic anhydrase, carboxypeptidase, triose phosphate isomerase contain both alpha-helices and beta-sheets



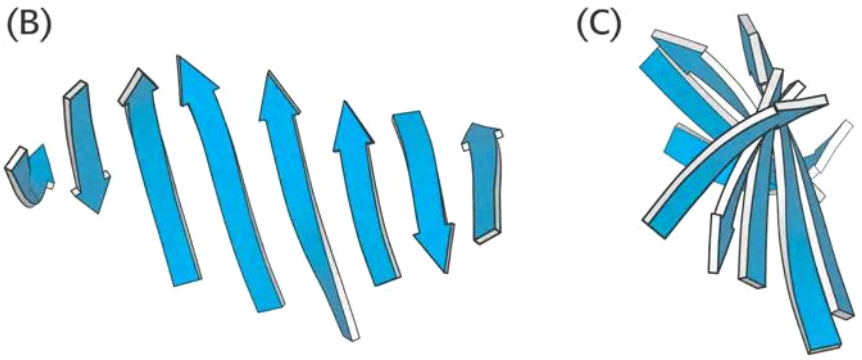
Schematic diagrams of supersecondary structures (a.k.a. motifs) found in globular proteins

- Hairpin β- 2 antiparallel β-strands joined by a loop.
- βαβ motif- two parallel β strands connected by an α-helix
- Greek Key- Two sequentially adjacent hairpin motifs



Tend to twist right

β-sheets in globular proteins make R-handed twists



Tertiary Structure

- Not random; aa sequence dictates structure
- Side chains get involved and interact with
  - each other
  - polypeptide backbone
  - environment
- Interactions stabilize a protein's conformation
  - Covalent bonds (disulfide linkages)
  - Ionic interactions (for example K::::E; S::::K)
  - H-bonds (for ex. S::::N)
  - Hydrophobic interactions (for ex. A::::L)
  - Van der waals forces (for ex. backbone carbonyl::::R-group of Ala)

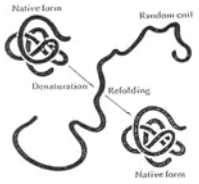
Tertiary Structure

- Native conformation: the specific, 3-D folding pattern for each protein species
- Hydrophobic interactions drive most nonpolar residues (V, L, I, M, F) to the interior of a protein away from water
- Charged groups (R, H, K, D, E) tend to be located on the surface of a protein
- Uncharged polar groups (S, T, N, Q, Y) are usually on the protein surface but also found in the interior where they usually form H-bonds

Quaternary Structure

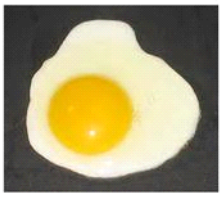
- Proteins are "sticky"--they have polar and nonpolar groups around them---but they don't randomly aggregate
- Some polypeptide subunits come together to form quaternary structures
- Examples: collagen fibrils, hemoglobin, DNA polymerase
- Each polypeptide is a subunit/protomer
- A protein with identical protomers is called a homo-oligomer
- Different protomers = hetero-oligomer

Native and Denatured Conformation of a Protein



- Native: "natural" conformation that is physiologically functional
- When the native conformation is disrupted the protein is referred to as "denatured" form of damage
- Denatured proteins don't function as intended and they are open, random structures
- Stress causes protein denaturation
  - Heat, pH changes, mechanical damage, organic solvents, detergents, change in a solvent's ionic strength, treatment with 6-8 M urea or 2 M guanidine hydrochloride

Examples of protein denaturation at home



- pH change: add acid like lemon to milk and it curdles
- Mechanical damage: beat egg whites and they foam
- Heat change: egg whites harden when cooked
- Detergents: helps get rid of blood stains

What Are the Many Biological Functions of Proteins?

- Many proteins are enzymes
- Regulatory proteins control metabolism and gene expression
- Many DNA-binding proteins are gene-regulatory proteins
- Transport proteins carry substances from one place to another
- Storage proteins serve as reservoirs of amino acids or other nutrients

What Are the Many Biological Functions of Proteins?

- Movement is accomplished by contractile and motile proteins
- Many proteins serve a structural role
- Proteins of signaling pathways include scaffold proteins (adapter proteins)
- Other proteins have protective and exploitive functions
- A few proteins have “exotic” functions