

Secondary Structure

α helix

Discovered by Linus Pauling

- 2 Nobel prizes.
- Discovered folding while sick in bed!
- Treated poorly as a result of his anti-nuclear stands - 2nd prize
- Pushed high doses of vitamin C

The helix is a right handed twist of the backbone - notice when we are looking at this the side groups are NOT considered

Notice where the amino acids are.

Hydrogen bonding occurs between the carbonyl and the amino group four residues away. The bonding takes place within the same chain.

Used on most soluble proteins.

A run of proline residues lead to breaking the helix structure. Why?

Specifics on helical descriptions:

Pitch: the vertical distance per turn. Think of a screw, if you turned a screw one turn this is how far the screw would penetrate

n = residues per turn. This depends on the helix. If it is stretched out ($n=2$) if it is compressed ($n=12$) the most stable is 3.6 or nearly 4 amino acids per turn. This is where the best H bonding can occur. (think of the alignment of the donor and acceptor)

nth residue: This means any residue in the helix as a reference point

nth + 4 residue: Indicates the residue 4 positions in with n taken as the first. The + sign does not mean add 4 residues to n, just you are looking at a residue 4 amino acids away from the nth residue.



n_m : n refers to the residue position, m is the number of atoms in the loop formed by hydrogen bonding. The α helix has an n_m of 4_{13m}

β Pleated sheet

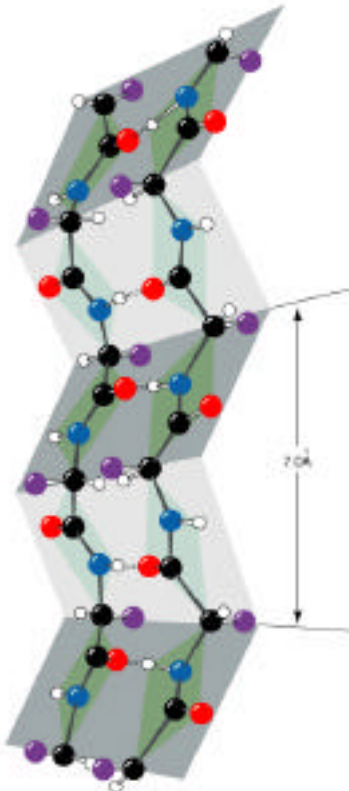


Figure 6-10. Pleated appearance of a β sheet. [Figure copyrighted © by Irving Gels.]

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Formed when the peptide chain is lined up side by side. This is an extended formation of the backbone

The structure is stabilized by hydrogen bonds between two different chains

- $-C=O$ and $-NH$
- Same donors and acceptors as in the helix but not within the same chain

Each strand of the β pleated sheet is from 6 to 15 residues

2 arrangements of sheets parallel and anti parallel. Look at the N to C terminus directions

H bonding within 3 residues can disrupt the sheets - causes bend or turn in the chain.

the chain.

Anti parallel conformations are stronger - alignment of H bonding.

- Often found in silk

R groups can interact - glycine and alanine

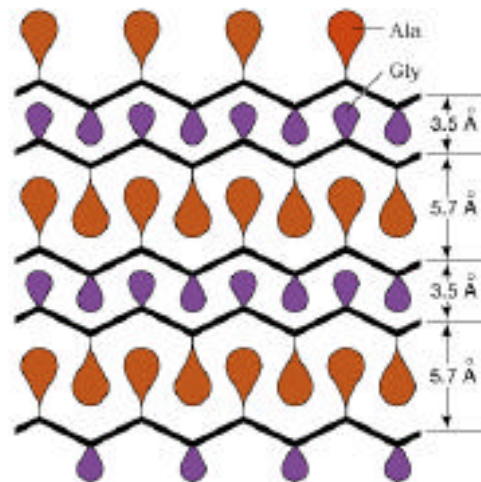


Figure 6-16. Schematic side view of silk fibroin β sheets. [Figure copyrighted © by Irving Gels.]

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Unique structure of collagen

A special helical protein

- biological significance - fibrous, structural component
- Three types, I is found in bones, tendons and skin, II in collagen and III in blood vessels
- Very different amino acid sequence from alpha helices
- 3 residues / turn

- 1/3 amino acids are glycine – sequence = Gly X Y
- Glycine R group face inside others outside
- up to 30% are proline or hydroxyproline - important for maintaining secondary structure
- hydroxyprolines involved in H bonding of three strands together
- helical structure formed by three left handed helices twisted to form a right handed superhelix (gives strength)
- hydrogen bonding between 3 helices (thus the glycine)
- covalent bonding of lysine between strands

Collagen Related Disease

- Loss of flexibility with age is likely due to increased amount cross-linked collagen compared to younger tissue
- Scurvy – problems with sea voyages, lack of food other than salted meats.
 - Symptoms include, swollen gums, loose teeth, small black-and-blue spots on the skin, and bleeding from small blood vessels are among the characteristic signs of scurvy.
 - Caused when vitamin C (ascorbic acid) is lost from diet
 - Vit C is needed to keep iron reduced in the active site of prolyl hydroxylase. This is the enzyme responsible for conversion of proline to hydroxyproline. The H bonding of hydroxyproline is vital for the connective protein's function
 - In 1795, the British Royal Navy provided a daily ration of lime or lemon juice to all its men. English sailors to this day are called "limeys", for lime was the term used at the time for both lemons and limes.
- Several heritable diseases result from mutations in the collagen
 - Brittle Bone Disease – results from a Gly-Ala mutation – Consider the consequences of this mutation, both in the protein's triple helix and the strength of the bone!
 - Marfan's Syndrome and Ehler's-Danlos syndromes - inherited disorder of connective tissue which affects many organ systems, including the skeleton, lungs, eyes, heart and blood vessels. All resulting from various mutation in collagen and other fibril associated proteins, ultimately affecting the structure and molecular interaction.

Tertiary structure

overall final 3 D shape of a protein assumes
 aa side chain interactions responsible for 3 D structures
 hydrophobic interactions
 salt bridges

hydrogen bonds (know donors and acceptors)
sulfhydryl bonds

Domain – an amino acid segment of folded protein showing conformational integrity. OR ...

Can be made of the whole protein or just part of the protein.
Often coded by their own section of DNA (exon)

Quaternary structure

- proteins with 2 or more peptide chains or subunits can be different or identical subunits
- loss of quaternary or tertiary (native) structure is called denaturation. Examples include
 - Heat – to unravel the folding by adding energy – eg. egg whites
 - Detergent – interfere with hydrophobic interactions
 - Changes in pH - ionization of R groups
 - Reducing agents – chemicals which break sulfhydryl bonds by changing the redox state of cys amino acids.

Prions and protein folding

Protein misfolding can cause a serious problem with prions

- infectious diseases
- Scrapie and bovine spongiform encephalopathy
- normal form of a protein is shortened by 1/3
- shortened protein is insoluble and forms into long polymers
- insoluble protein collects in lysosomes but not degraded (all due to change in structure)
- Normal and mutated protein is cleaved post translationally, meaning the gene is not altered
- Treatment to degrade DNA has little effect while protein treatment stopped transmission in mouse
- Still not clear if protein alone can cause disease
- How did this affect the beef industry in Great Britain?

