Proteins: 3D-Structure

Chapter 6

(9 / 17/ 2009)

Secondary Structure
- –The peptide group
- –Alpha helices and beta sheets
- –Nomenclature of protein secondary structure

Tertiary Structure

Three Dimensional Protein Structures

Conformation: Spatial arrangement of atoms that depend on bonds and bond rotations.

Proteins can change conformation, however, most proteins have a stable "native" conformation.

The native protein is folded through weak interactions:

a) Hydrophobic interactions
b) Hydrogen-bonds
c) Ionic interactions
d) Van der Waals attractions

There are four levels of protein structure

1. Primary structure
   1° = Amino acid sequence, the linear order of AA's.
   Remember from the N-terminus to the C-terminus
   Above all else this dictates the structure and function of the protein.

2. Secondary structure
   2° = Local spatial alignment of amino acids without regard to side chains.
   Usually repeated structures

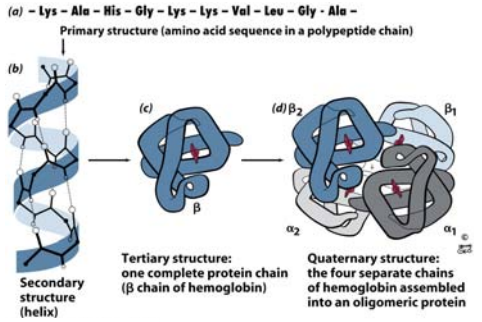
   Examples: α-helix, β-sheets, random coil, or β-turns

3. Tertiary Structure
   3° = the 3-dimensional structure of an entire peptide.
   Great in detail but vague to generalize. Can reveal the detailed chemical mechanisms of an enzyme.

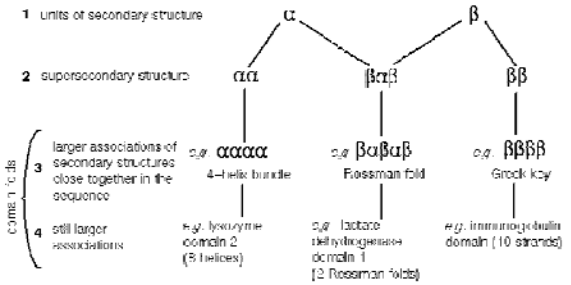
4. Quaternary Structure
   4° two or more peptide chains associated with a protein.

   Spatial arrangements of subunits.

Example of each level of protein structure

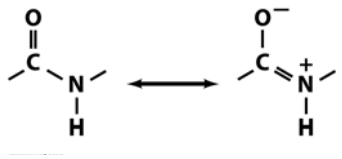


Protein Structure Terminology



The Amide bond

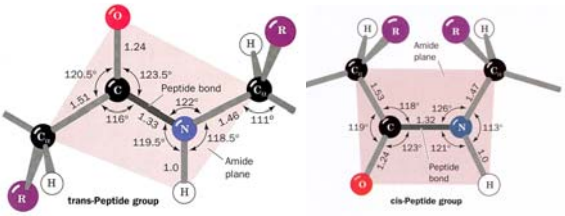
In 1930s-1940s Linus Pauling and Robert Corey determined the structure of the peptide bond by X-ray.



40% double bond character. The amide bond or peptide bond C-N bond is 0.13Å shorter than $C_{\alpha\text{-}N}$ bond.
C=O is .02 Å longer then those for ketones and aldehydes
Planar conformation maximizes pi-bonding overlap
Resonance gives 85 kJ/mol stability when bond is planar!!

Peptide bonds are planar

Resonance energy depends on dihedral/torsional angle (Cα-C-N-Cα)
For peptides, this is the angle between the Cα-C and N-Cα bonds
For a trans peptide bond, the dihedral angle is 180° by definition.
In a cis peptide bond, the dihedral angle is 0° by definition.
Most peptide bonds are trans, 10% that follow proline may be cis
Note: differences between bond angles and bond lengths comparing cis and trans forms of a generic dipeptide.

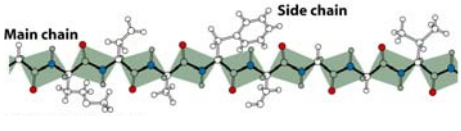


Torsion angles

Rotation or dihedral angles

C_α-N	ϕ	phi
C_α-C	ψ	psi

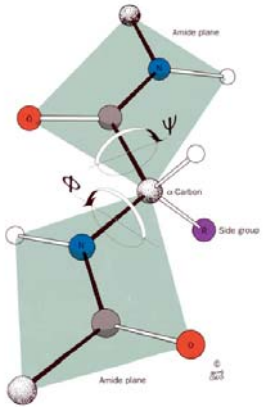
When a peptide chain is fully extended the angles are defined as 180° or -180° (these are the same).
At 180°, one gets a staggered conformation - (all trans) i.e. ethane



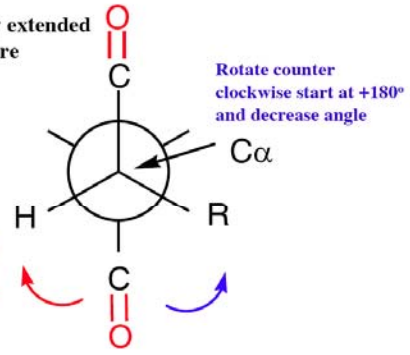
Note: alternating C=O pointing in opposite directions.

When viewed down the Cα–N axis, rotation to the right or clock wise increases the angle of rotation.

Must start with the fully extended form which is defined as 180° or -180°



Start with fully extended protein structure

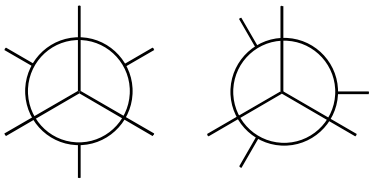


Rotate counter clockwise start at +180° and decrease angle

Rotate clockwise start at -180° and increase angle

This is Cα-N bond or phi angle, Φ

Ethane can exist as staggered or eclipsed conformation



Staggered gauche

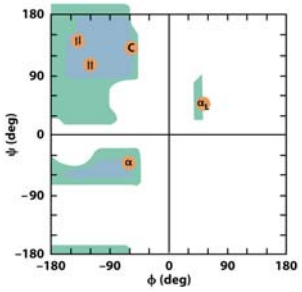
There is a 12 kJ/mol penalty in energy for an eclipsed geometry
Bulky amino acid side chains have a much higher energy penalty.
There are a few favored geometries which the protein backbone can fold

If all $\phi + \psi$ angles are defined then the backbone structure of a protein will be known!!

These angles allow a method to describe the protein's structure and all backbone atoms can be placed in a 3D-grid with an X, Y, Z coordinates.

Ramachandran diagram

If you plot ψ on the Y-axis and ϕ on the X-axis, you will plot all possible combinations of ϕ, ψ.

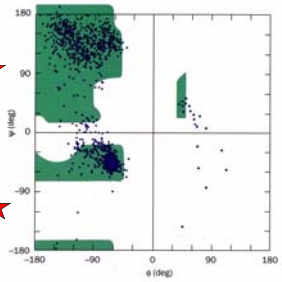


You must know the different regions of the Ramachandran diagram.
That is, you must be able to identify them on an exam, given the figure.
See next slide!

Secondary structure can be defined by ϕ and ψ angles

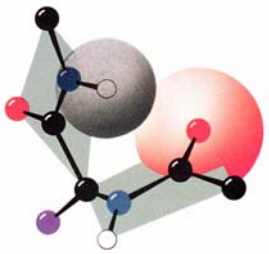
	Φ	Ψ
α-helix right-handed	-57	-47
↑↑ β-sheet	-119	113
↓↑ β-sheet	-139	135
3_{10} helix	-49	-26
collagen	-51	153

Repeating local protein structure determined by hydrogen-bonding helices and pleated sheets.



12 proteins except for Gly and Pro

Steric hindrance between the amide hydrogen and the carbonyl



$\Phi = -60^{o}$ and $\Psi = 30^{o}$

Helices

A repeating spiral, right handed (clockwise twist) helix
pitch = **p**

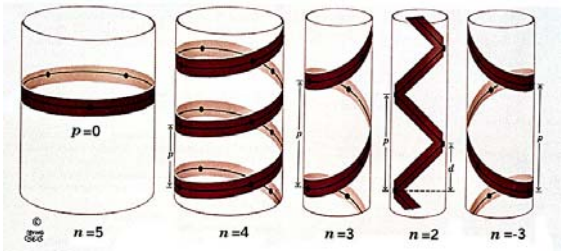
Number of repeating units per turn = **n**

d = p/n = Rise per repeating unit (**d**istance)

α-helix is right-handed – point your thumb up and curl your fingers on your right hand for α-helix.

Several types α, 2.2_7 ribbon, 3_{10} , π-helices, or the most common is the α-helix.

Examples of helices



The α-helix

The most favorable Φ and Ψ angles with little steric hindrance.

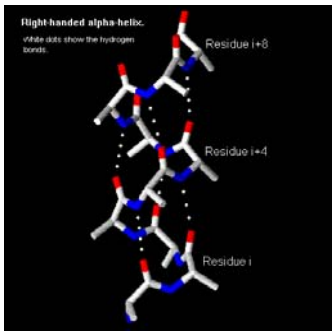
Forms repeated hydrogen-bonds.

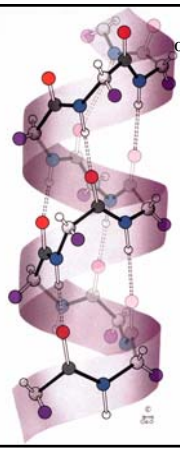
- **N = 3.6 residues per turn**
- **P = 5.4 Å (What is the d for an α-helix?) d=p/n=5.4Å/3.6=1.5**

The C=O of the n^{th} residue points towards the N-H of the $(N+4)^{th}$ residue.

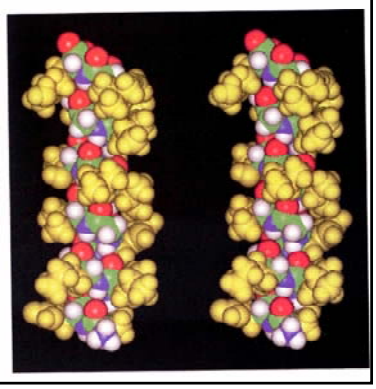
The N ····· H ····· O hydrogen-bond is 2.8 Å and the atoms are 180° in plane. This is almost optimal with favorable Van der Waals interactions within the helix.

α-helix





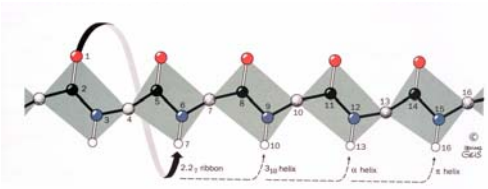
α-helix formed by 1-5 (n+4th), N-H…O H-bond



The N_m nomenclature for helices

N = the number of repeating units per turn

M = the number of atoms that complete the cyclic system that is enclosed by the hydrogen bond.

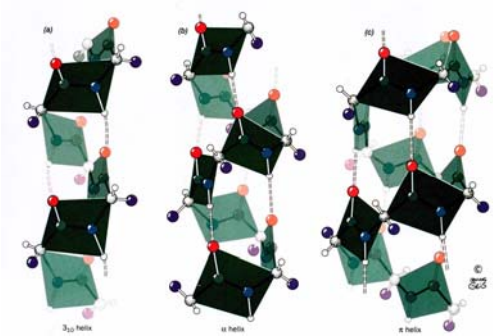


The 2.2_7 Ribbon

- **Atom (1) -O- hydrogen-bonds to the 7th atom in the chain with an N = 2.2 (2.2 residues per turn)**

3_{10}-helix

- **Atom (1) -O- hydrogen-bonds to the 10th residue in the chain with an N= 3.**
- **Pitch = 6.0 Å occasionally observed but torsion angles are slightly forbidden. Seen as a single turn at the end of an α-helix.**
- **Π-helix 4.4_{16} 4.4 residues per turn. Not seen!!**



Beta structures

- Hydrogen-bonding between adjacent peptide chains.
- Almost fully extended but have a buckle or a pleat.
  Much like a Ruffles potato chip

Two types

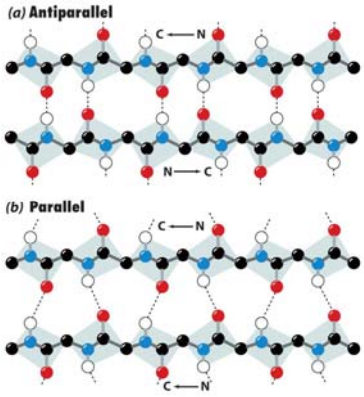
Parallel Antiparallel

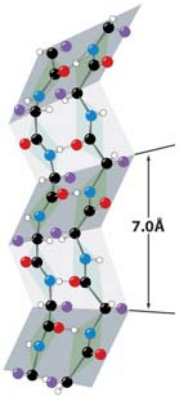
7.0 Å between pleats on the sheet

Widely found pleated sheets exhibit a right-handed twist, seen in many globular proteins.

Sheet facts

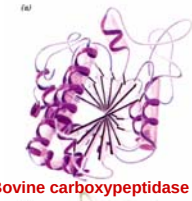
- **Repeat distance is 7.0 Å**
- **R group on the Amino acids alternate up-down-up above and below the plane of the sheet**
- **2 - 15 amino acids residues long**
- **2 - 15 strands per sheet**
- **Avg. of 6 strands with a width of 25 Å**
- **parallel less stable than antiparallel**
- **Antiparallel needs a hairpin turn**
- **Tandem parallel needs crossover connection which is right handed sense**





- β-pleated sheet, 2 β-strands
- Typically 2 to >22 strands
- Each strand may have up to 15 AAs
- Average length is 6 AAs

Two proteins exhibiting a twisting β sheet



The twist is due to chiral L-amino acids in the extended plane.

This chirality gives the twist and distorts H-bonding.

A little tug of war exists between conformational energies of the side chain and maximal H-bonding.

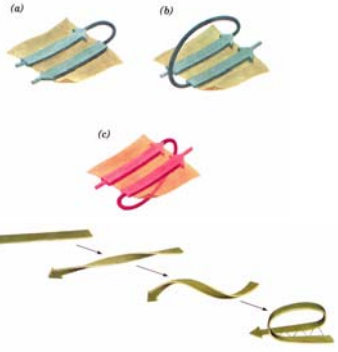
These structures are not "static" but breathe and vibrate with a change in structure due to external circumstances.

Bovine carboxypeptidase

Triose phosphate isomerase

Connections between adjacent β sheets

Topology



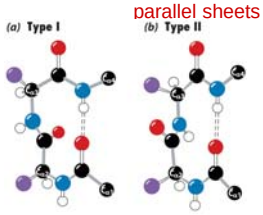
Non-repetitive regions

Turns - coils or loops

50% of structure of globular proteins are not repeating structures

β-bends

type I and type II: hairpin turn between anti-parallel sheets



Type I $\phi_2 = -60^o, \psi_2 = -30^o$

$\phi_3 = -90^o, \psi_3 = 0^o$

Type II $\phi_2 = -60^o, \psi_2 = 120^o$

$\phi_3 = 90^o, \psi_3 = 0^o$

Lecture 9
Tuesday 9/22/09
Exam 1 review