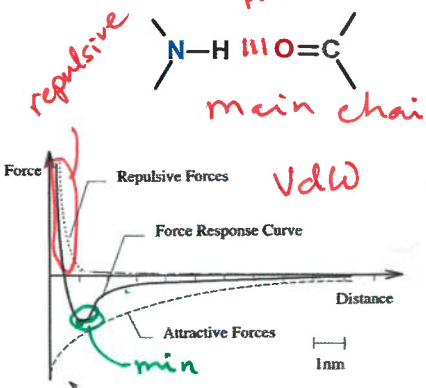
Lecture 7: Secondary Structure:

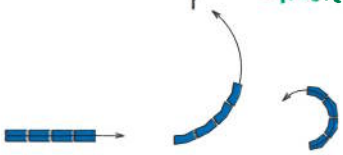
Goals:

- Why are peptide bonds planer and usually *trans*.
- Why H-bonding and van der Waals restrict secondary structures.
- Ramachandran plot & van der Waals
- Geometrical properties of secondary structures



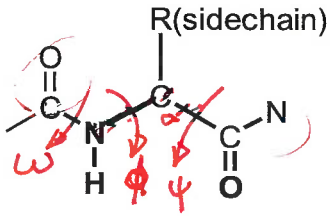
Regular Secondary Structure:

- Local conformation of **mainchain** atoms.
- Each residue within a secondary structural element has essentially the same geometrical shape due to similar bond angles.
- The repeating geometrical properties of the subunits will result in a three-dimensional shape if the units are laid end to end:
  - Rectangular blocks will generate a linear shape.
  - Curved blocks will generate curved shapes, helices in three dimensions.

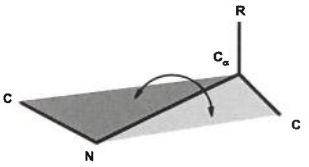


The "shape" of each amino acid depends on the conformation of the bonds within a residue:

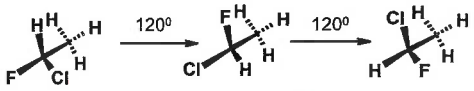
ω (omega) - peptide bond
Φ (Phi), the bond between N and C_α
Ψ (Psi), the bond between C_α and C.



The rotational angle around a bond is specified as the angle between two planes that share the bond. The two planes that are used to specify the phi angle are shown on the right

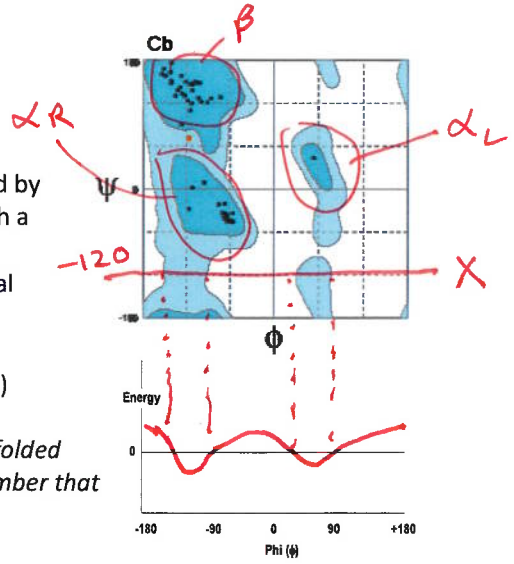


In the case of a simple molecule, such as a 1-chloro-1-fluoroethane three different conformations are generally considered stable for free rotation about a single bond.



***Reflection**: How many different conformations could the backbone atoms of one residue in a protein assume, assuming free rotation around all three bonds (C-N, N-Cα, Cα-C)?*

$3 \times 3 \times 3 = 27 \Rightarrow 3$



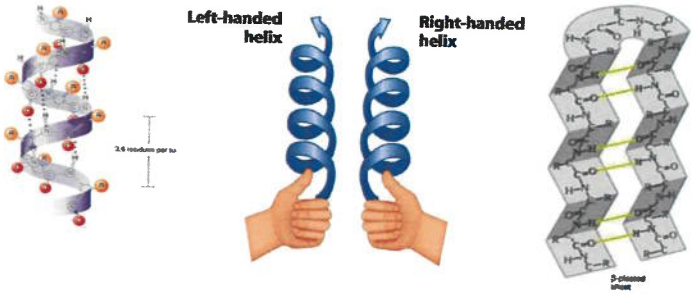
The conformations that are experimentally observed can be visualized by plotting the Φ (Phi) and Ψ (Psi) angles in a two-dimensional plot. Such a plot is called a **Ramachandran Plot:**

- The horizontal and vertical axes represent the phi and psi torsional angles of a residue.
- A single point in the plot represents ***one*** residue in the protein.
- The colored regions (which are different for different amino acids) represent regions of low (favorable) energy.

***Reflection:** Which regions of the Ramachandran plot are observed in folded proteins? How does this number of conformations compare to the number that you would obtain with free rotation about all three bonds?*

The Ramachandran plot shows that most of the residues in a protein fall into three possible "shapes". These shapes are:

- A single right-handed helical geometry, called an α-helix.
- The mirror image of the helix, but left-handed.
- Linear strands, called β-strands, forming a multi-strand sheet.



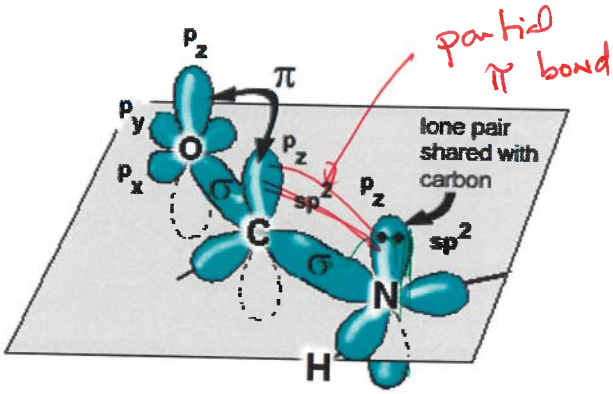
***Question**: Why are there only three possible "shapes", free rotation about all three bonds should give us 27 possible shapes.*

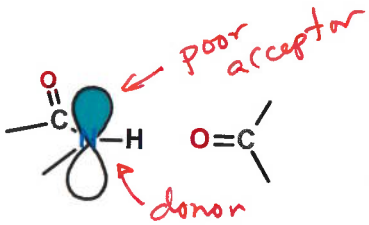
Conformational Freedom of Proteins – one bond at a time:

C_{i-1} - N (Peptide bond):

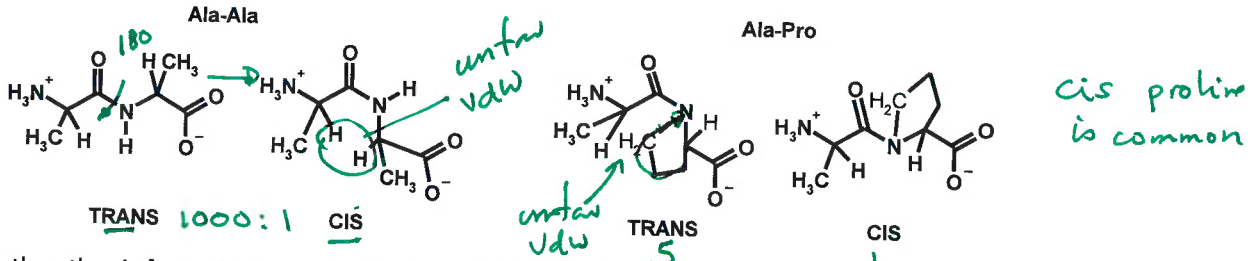
The four atoms that make up this bond are planar due to the hybridization properties of the carbonyl carbon and the nitrogen (both sp_2). In addition, free rotation about the bond is **not** possible since the p_z orbitals of oxygen, carbon, and nitrogen form a delocalized system. Rotation about the peptide bond would break the interaction between the p_z orbital of the nitrogen and carbon atoms and is therefore unfavorable. The peptide bond is said to be a "partial double bond".

- **The N-H group** within the peptide bond can only act as a hydrogen bond donor. The partial negative charge on the nitrogen is delocalized over the entire conjugated system so it is not energetically favorable for it to accept a hydrogen bond (a similar argument applies to the NH group on Trp sidechain, and Asn and Gln sidechains).





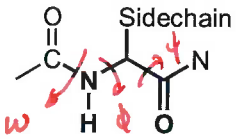
Cis and trans Peptide Bonds: Two possible orientations of the peptide bond that maintain the p_z interaction between the carbon and nitrogen are possible. They are related by a 180° flip of the peptide bond, giving two possible conformations, the ***trans*** form and the ***cis*** form. For most peptide bonds, the trans form is ~1000 more



stable than the cis form. The exception is for peptide bonds involving proline, in which the ratio is reduced to 5:1.

***Reflection**: Why is the trans form lower in energy?*

N - C_α & C_α - C Bonds: There is free rotation about *both* of these bonds. Since both the phi and psi bonds are free to rotate, a total of 9 (3x3) different stable pairs of phi and psi angles should be observed. However, there are only three pairs, each of which correspond to a secondary structure:



1 x 3 x 3 = 9

Φ = -60°, and Ψ = -45°	**α-helix, right handed**
Φ = +60°, and Ψ = +45°.	**α-helix, left handed**
Φ = -120°, and Ψ = 125°.	**extended, β-structure**

Ψ and Φ torsional angles are the *same* for *each* residue within the element of secondary structure. In these structures, each peptide bond is rigid and planar and in the *trans* conformation.

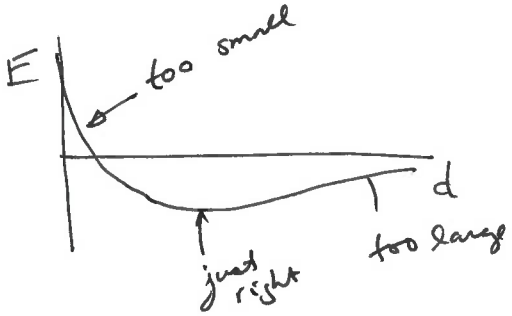
***Reflection**: Why are there only three – what limits forming the other six? What forces are stabilizing, and which are destabilizing?*

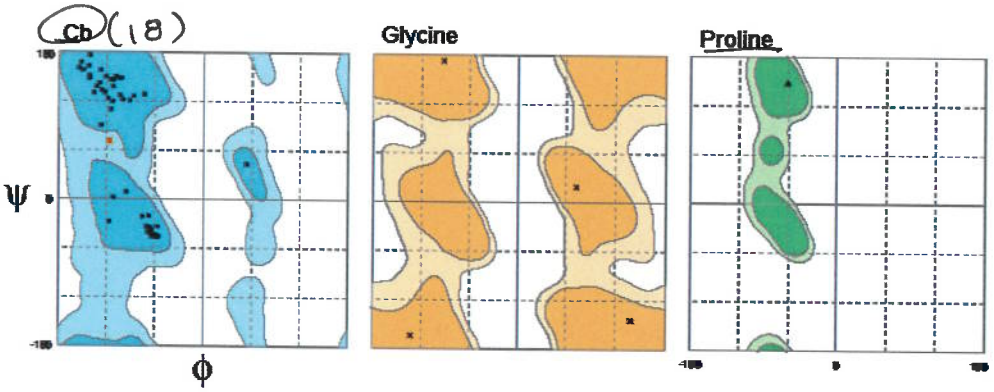
Forces
- ✓ H-bond
- VdW (dipole-dipole)
- ~~Hydrophobic~~
- ~~Electrostatic~~

Hydrogen bonding in Helices: *Use the paper strips to form an H-bonded helix. Compare yours to your neighbor's – are they the same?*

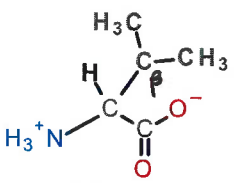
Conclusions:

- H-bonds stabilize
- VdW select. one helix

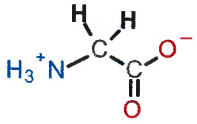




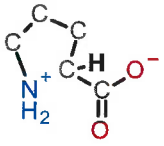
- Residues with a C_β show three low energy regions in the plot, β, α_R, and α_L.
- Glycine residues can assume a larger range of Ψ and Φ torsional angles. Gly can exist in regular secondary structure as well as adopt other conformations. *Why?*
- Proline residues can only assume a smaller range of Ψ and Φ torsional angles. *Why?*



Valine



Glycine



Proline

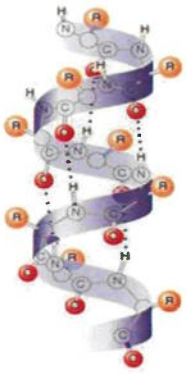
Properties of Regular Secondary Structure:

α-Helix Structures (Φ = -60°, Ψ = -45°) — same ϕ & ψ each residue

_____ residues/turn

pitch = 5.4 Å/turn

rise/residue = 1.5 Å



- H-bonds || to helix axis.
- Sidechains point outwards
- Right handed
- There is a repeating hydrogen bonding pattern within the helix, you will discover what that is on the problem set.

Beta Structures (Φ = -120°, Ψ = 125°)

- H-bonds perpendicular to direction of strands.
- β-Sheets
  Parallel or anti-parallel
- Sidechains point up and down, above and below the sheet, alternating on a single strand, all on one side across a row of residues in the sheet.