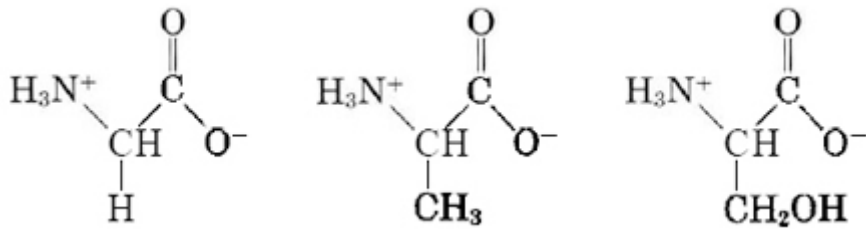


Lecture 2

Amino acids and the Peptide Bond-II

Amino acids the building blocks of proteins can be grouped based on their properties.

The uncharged amino acid residues exist in the zwitterionic form at pH 7. The neutral zwitterionic form means that the amino acid has lost its carboxylic acid proton but the amino group is protonated thus rendering a zero charge for neutral amino acid residues.



Zwitterionic forms of 3 amino acids.

Thus each amino acid possesses at least two pK_a values, since all amino acids have a carboxylate group and an amino group. An additional pK_R value for the R side chain that can ionize exists.

A titration experiment is possible for each amino acid where at least two equivalence points will be obtained. The intermediate point which corresponds to the average of the pK₁ and pK₂ values for an uncharged amino acid is the pI value – the isoelectric point where the amino acid does not possess any charge.

ISOELECTRIC POINT (pI)

Definition: the pH at which a molecule carries no net electric charge

Equilibrium dissociation constant

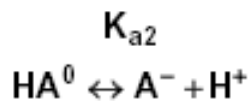
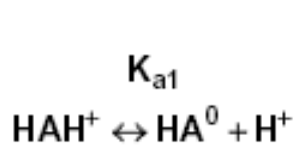
$$K_a = \frac{[H^+][A^-]}{[HA]}$$

Henderson-Hasselbach Equation

$$-\log[H^+] = -\log K_a + \log \frac{[A^-]}{[HA]}$$

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

$$pH = pK_a \quad @ [A^-] = [HA]$$



$$pI = pK_{a1} + \log \frac{[HA^0]}{[HAH^+]}$$

$$pI = pK_{a2} + \log \frac{[A^-]}{[HA^0]}$$

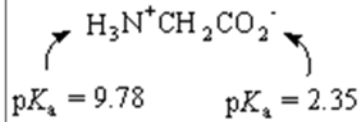
$$2pI = pK_{a1} + pK_{a2} + \log \frac{[HA^0]}{[HAH^+]} + \log \frac{[A^-]}{[HA^0]}$$

$$2pI = pK_{a1} + pK_{a2} + \log \frac{[HA^0]}{[HAH^+]} \frac{[A^-]}{[HA^0]}$$

$$2pI = pK_{a1} + pK_{a2} + \log \frac{[A^-]}{[HAH^+]}; \quad @ pI, [A^-] = [HAH^+]$$

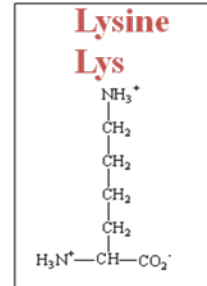
$$pI = \frac{pK_{a1} + pK_{a2}}{2}$$

The Acid-Base Chemistry of the Amino Acids

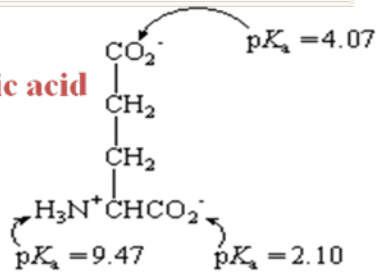


$$\text{pI} = \frac{2.35 + 9.78}{2} = 6.1$$

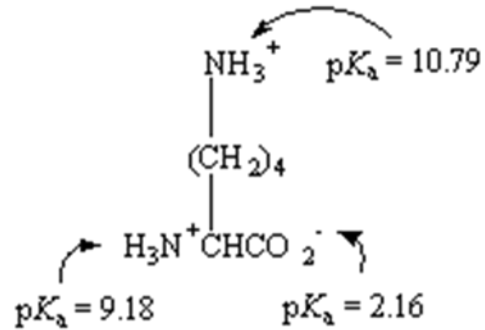
Glycine
Gly



Glutamic acid
Glu

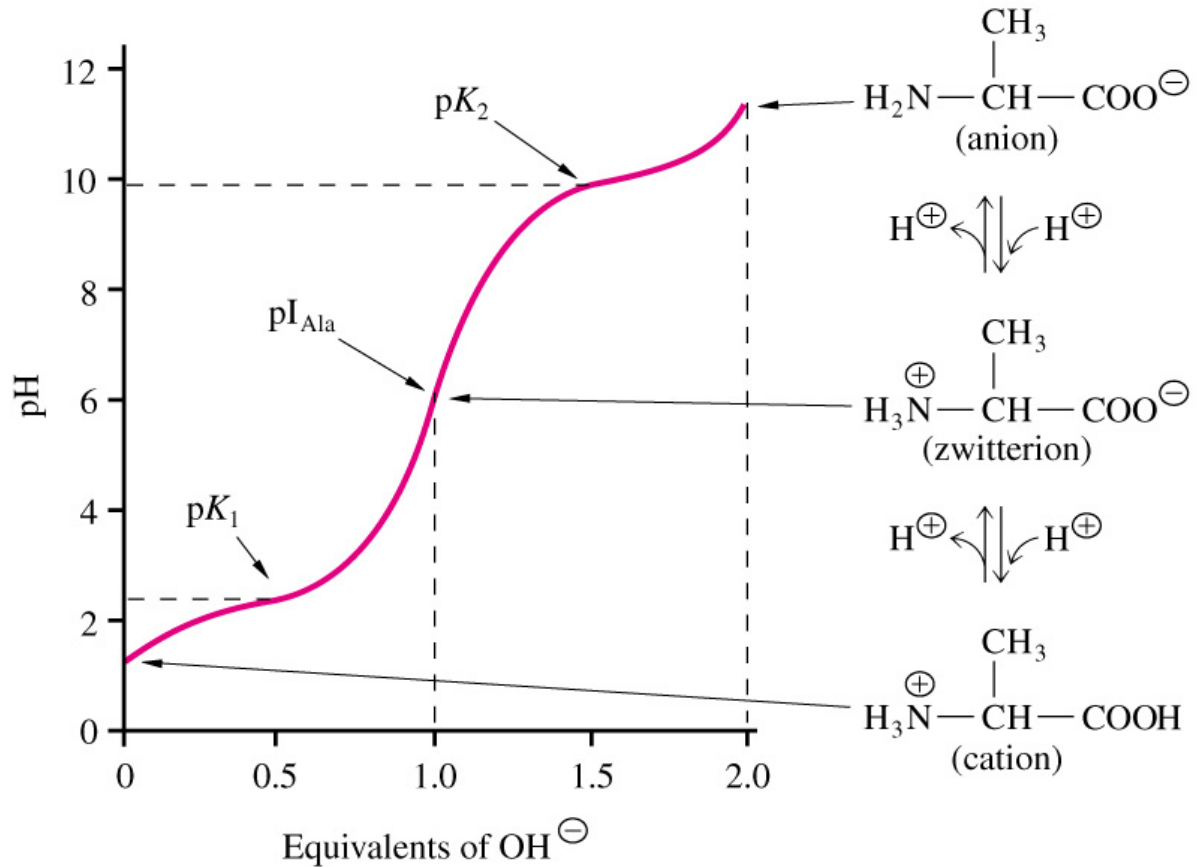


$$\text{pI} = \frac{2.10 + 4.07}{2} = \sim 3.1$$



$$\text{pI} = \frac{9.18 + 10.79}{2} = \sim 10.0$$

For the case of Alanine (Ala or A), we see how this is possible from the graph below.



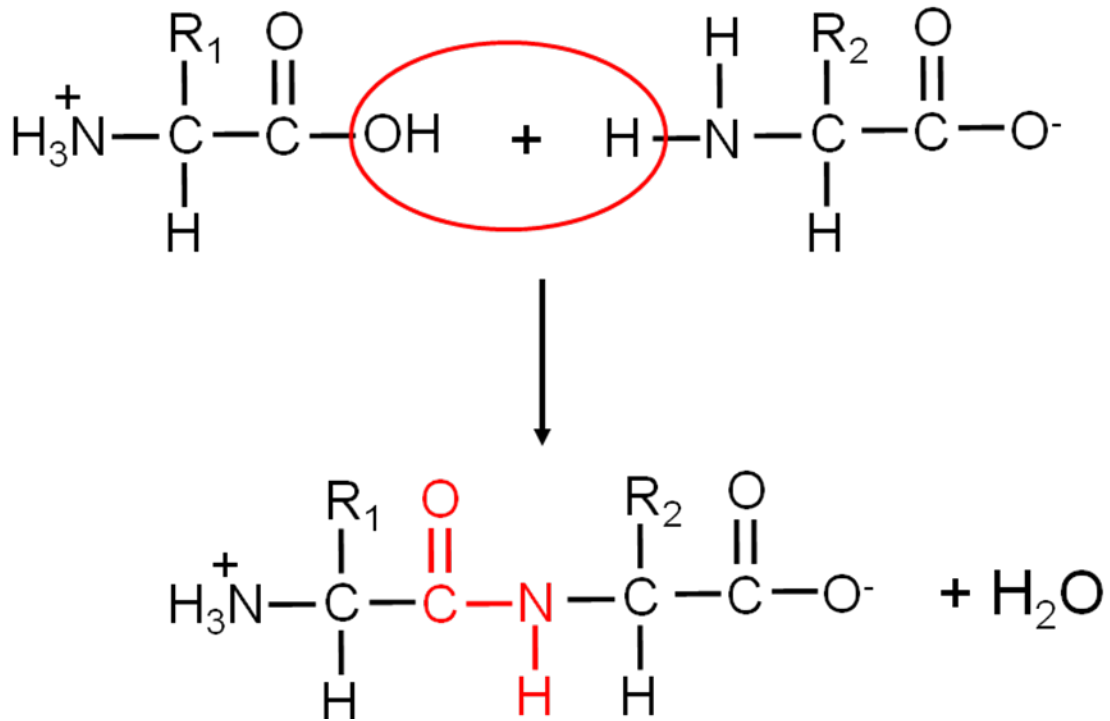
pI (isoelectric point) = the pH at which the number of positive and negative charges on the molecules is equal (i.e. no net charge).

Proteins are made up of chains of these amino acids that are linked together by peptide bonds to form a polypeptide chain.

What is a peptide bond?

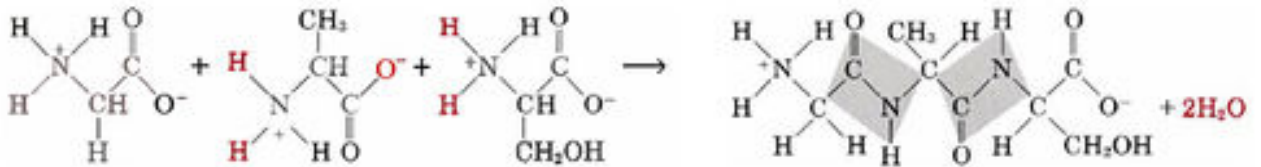
The connection between two amino acids occurs through a peptide bond. The peptide bond is formed by the condensation of amino acids with the elimination of water.

Proteins are called polypeptides because they contain many such peptide bonds.

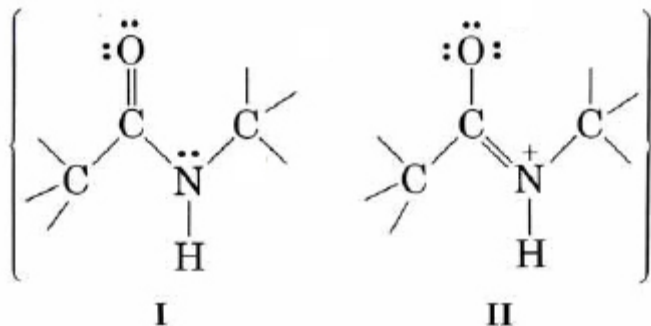


The peptide bond has several important features that are important for protein structure and function. The peptide bond has a partial double bond character because of the lone pair present on the Nitrogen atom of the peptide bond.

This could be extended further to connect more amino acid residues:

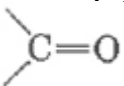
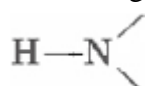


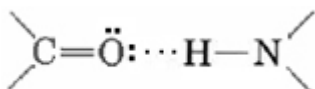
Let us see what other properties exist for the peptide bond.



In the structure above, there is a double bond between the carbon and the nitrogen atoms. This imparts a rigidity to this bond thus restricting its rotation because the bonds involving the C and N atoms must lie in the same plane. This renders a planar structure often referred to as the peptide plane.

Another important aspect of the peptide bond is the possibility of hydrogen bonding

between the oxygen on the  carbonyl group and the hydrogen on an  group that could be close to one another or even further along the chain.



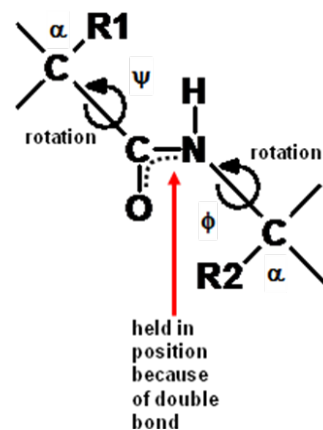
Thus the structure of the peptide bond exhibits a double bond character that leads to a coplanar nature.

However, rotation about the single bonds is feasible resulting in different conformational possibilities.

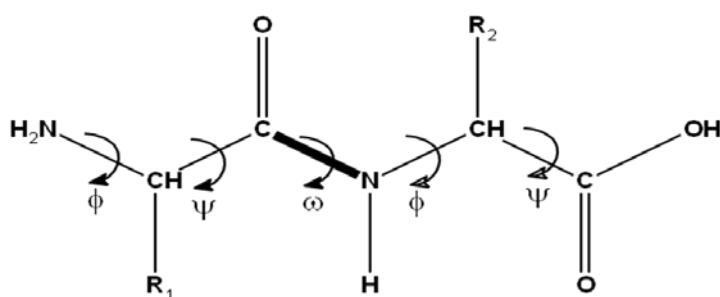
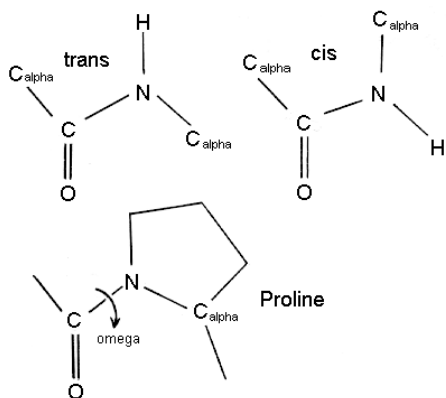
These are called the torsion angles and have definitions corresponding to the atoms considered in the formation of the dihedral angle.

These are:

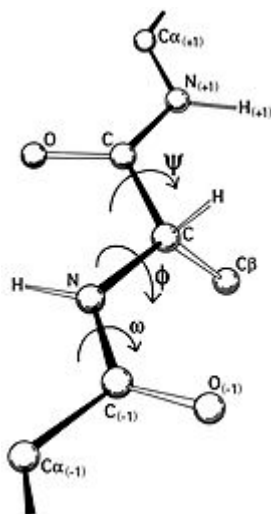
- phi (ϕ)** torsion angle around N-CA bond
- psi (ψ)** torsion angle around CA-C bond
- omega (ω)** peptide bond; *trans* ~180 degrees, *cis* ~0



Rotation about the peptide bond, referred to as the omega (ω) angle can adopt a *cis* or a *trans* configuration. The *cis* peptide bond is not very common since the bulk of the side chains may not permit it. It is possible for the imino acid proline to easily adopt this configuration.



It can be seen that free rotation is possible around certain bonds – however, there are limitations due to steric reasons as well as backbone geometrical constraints. We will learn about these later when we look at protein structure.



The side chain R groups are also free to rotate and as a result of these degrees of freedom, the protein molecule can adopt a large number of conformations in three-dimensional space. We will learn about these later when we understand structural aspects of proteins.

The character of the side chain has considerable influence on the conformation of the polypeptide chain. Much like the hydrocarbon tails of fatty acid molecules, hydrophobic amino acid side chains tend to avoid water.

These normally interact with other nonpolar groups to form the core of globular proteins. We will see what we mean by a globular protein when we study more about protein structure. In globular proteins, most hydrophobic residues are embedded within the molecule. Hydrophilic side chains are found to occupy positions on the outer surface. This permits favorable interactions with the surrounding water molecules.

Hydrogen bonds and dipole forces attract these water molecules and help solubilize the globular proteins. Thus the important properties of amino acids that affect the structure of proteins are:

- Hydrophobicity
- Size
- Charge
- Secondary structure preference
- Aromaticity

Other Special characteristics:

- bridge forming by cysteines,
- rigidity of prolines,
- flexibility of glycines