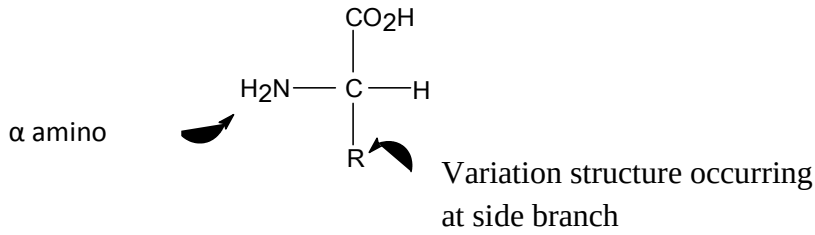
V. AMINO ACIDS, POLYPEPTIDES, AND PROTEIN

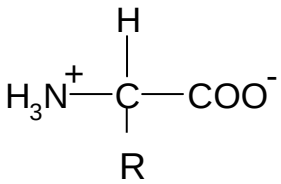
Naturally occurring amino acids has an amino group (NH_2) to the carboxyl group (COOH).



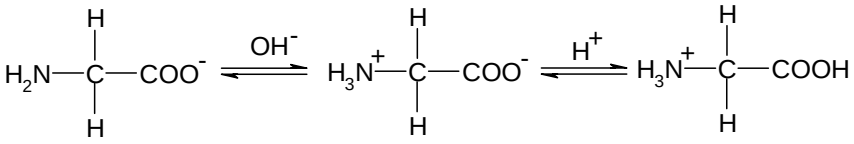
Zwitterions formation

Although the amino acids are commonly shown as containing an amino group and a carboxyl group, H2NCHRCOOH, certain properties, both physical and chemical, are not consistent with this structure:

- On contrast to amines and carboxylic acids, the amino acids are non-volatile crystalline solid which melt with decomposition at fairly high temperatures.
- They are **insoluble in non-polar solvents** like petroleum ether, benzene, or ether and are appreciably **soluble in water**.
- Their aqueous solutions behave like solutions of substances of **high dipole moment**.
- **Acidity and basicity constants are ridiculously low** for –COOH and $–NH_2$ groups. Glycine, e.g., has $K_a = 1.6 \times 10^{-10}$ and $K_b = 2.5 \times 10^{-12}$, whereas most carboxylic acids have K_a's of about 10^{-5} and most aliphatic amines have K_b's of about 10^{-4}.
- All these properties are quite consistent with a **dipolar ion structure** for the amino acids.
- Since it exists as internal salt, known as **zwitterion**,in which **both cation and anion are held together** in the same unit.

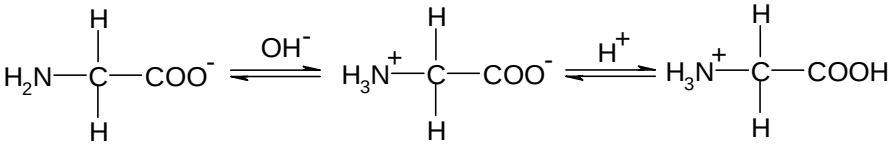


Since the zwitterions are held by strong electrostatic attraction, thus m.p. and b.p. are high. Also, it exerts strong attraction to polar water, so it is highly soluble in water, but insoluble in non-polar solvent. Amino acid with equal number of amino and carboxyl group is neutral when dissolved in water, but in acidic solution, $-COO^-$ group is protonated (I.e. exists as a –COOH), and basic solution, $-NH_3^+$ group is free and exists as an $–NH_2$. Therefore, the acidic group in amino acid is $–NH_3^+$ NOT –COOH. The basic group in amino acid is $-COO^-$ not $–NH_2$.



Isoelectric point and electrophoresis

Amino acids, as a zwitterions, exhibits both acidic and basic properties in aqueous solutions. In aqueous solution, the ion exists in equilibrium with its cationic form and anionic form simultaneously:

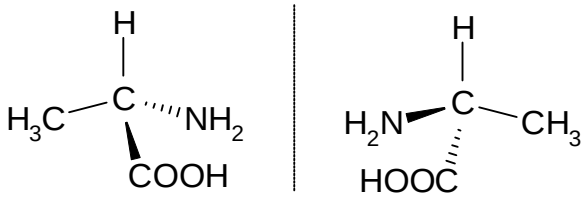


If an **electric field is applied** to an aqueous solution of an amino acid, whether there is a **migration** of the ion or not **depends on the pH** of the solution. In **alkaline** solution, the above equilibrium will shift to the **left** and the concentration of **anion** will **exceed** that of **cation**, and there will be a net migration of the amino acid **towards the positive pole**. In **acidic** solution, the above equilibrium will shift to the **right** and the concentration of **cation** will **exceed** that of **anion**, and there will be a net migration of the amino acid **towards the negative pole**. By **adjusting the pH value** of the aqueous solution of an amino acid, the concentration of cation can be made equal to that of anion, and there will be **no net migration** of the amino acid in an electric field. **The pH value so adjusted** in this case is known as the **isoelectric point** of the given amino acid. **Isoelectric points** are **characteristic of amino acids**. Therefore it is **possible**

to separate different amino acids in a mixture by subjecting the mixture to an electric field and adjusting the pH value, This technique is known as **electrophoresis**.

Optical isomerism

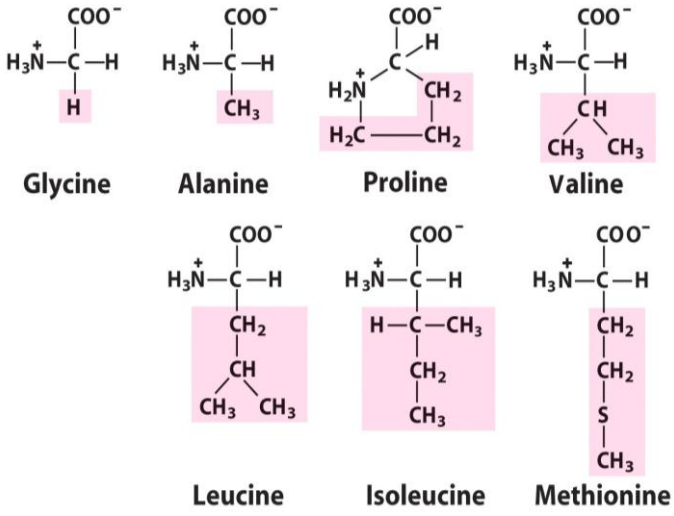
All naturally occurring amino acids **except glycine** possess **chiral / asymmetric** carbon and are optically active.



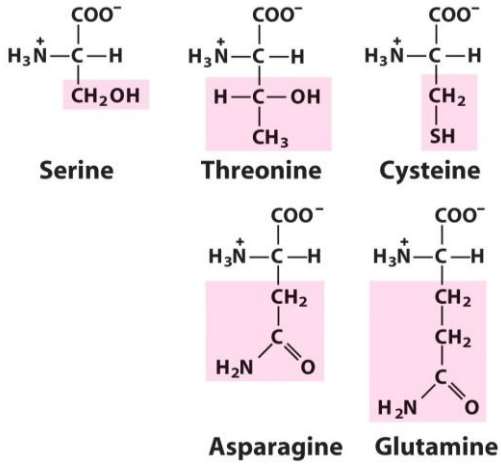
Amino acid are bifunctional and classified as:

a. Neutral: having equal number of amino and carboxyl group.
b. Acidic: two carboxyl and one amino group.
c. Basic: two amino and one carboxyl group.

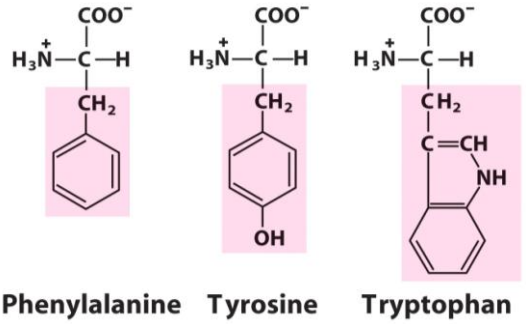
Hydrophobic, neutral, aliphatic



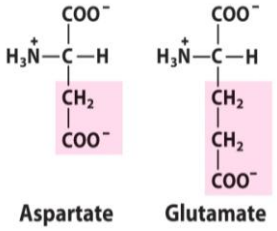
Hydrophilic, neutral, typically H-bond



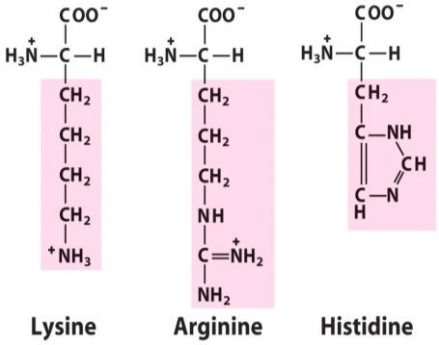
Bulky, neutral, polarity depend on R



- Acidic
  - R group = carboxylic acid
  - Donates H^+
  - Negatively charged



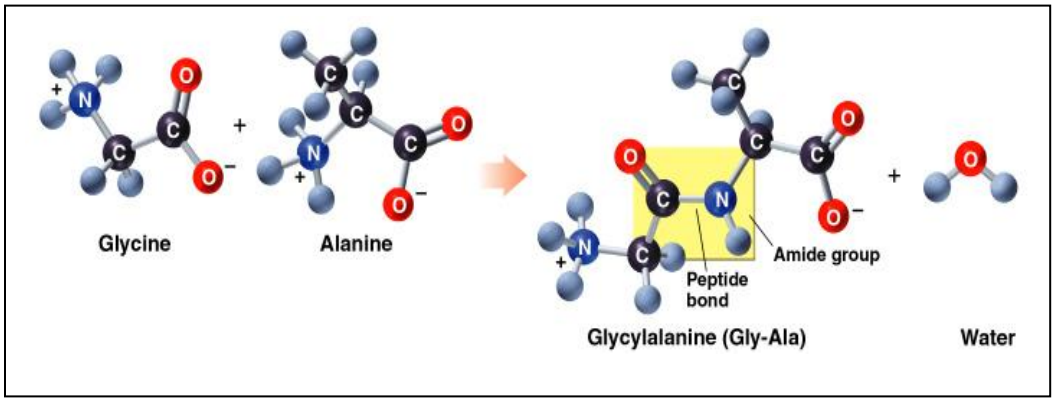
- Basic
  - R group = amine
  - Accepts H^+
  - Positively charged



Polypeptides

- Linear polymers (no branches)
- AA monomers linked head to tail
- Terminal residues:
  - Free amino group (N-terminus),Draw on left
  - Free carboxylate group (C-terminus),Draw on right
- pK_a values of AAs in polypeptides differ slightly from pK_a values of free AAs

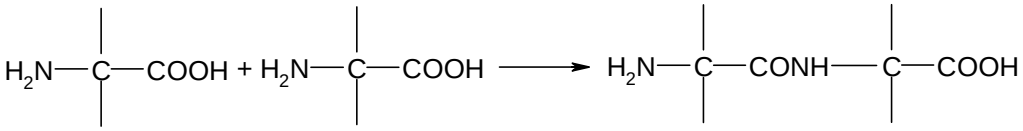
- Name from the free amine (NH_3^+)
- Use *-yl* endings for the names of the amino acids
- The last amino acid with the free carboxyl group (COO^-) uses its amino acid name



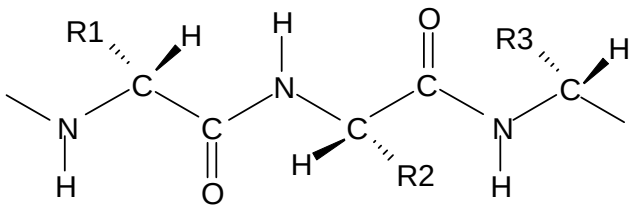
- Draw the structural formula of each of the following peptides.
  i. Methionylaspartic acid
  ii. Alanyltryptophan
  iii. Methionylglutaminyllysine
  iv. Histidylglycylglutamylalanine

Proteins

Proteins are high molecular weight compounds composing of α-amino acids linked through amide formation between the carboxyl group of one acid and α-amino group of the next. The linkage is called peptide linkage.



A molecular weight of 10,000 is suggested as limit for polypeptides, while the molecular weight of protein can reach millions. The side chains of proteins molecule or polypeptide chain may associate together to give a special shape.



It can be brought about by refluxing protein with acid e.g. H_2SO_4 or by base e.g. $Ba(OH)_2$, or by enzyme into a mixture of amino acid. The study of the amino acids so formed gives some information to the structure of their protein. Analysis of amino acids is by chromatogram. The spots are made visible by spraying the chromatogram with ninhydrin. The R_f value is then found and check against data book.

Protein sequencing

- Analysis of primary structure
- In general, proteins contain > 40 residues
- Minimum needed to fold into tertiary structure
- Usually 100-1000 residues
- Percent of each AA varies
- Proteins separated based on differences in size and composition
- Proteins must be pure to analyze, determine structure/function