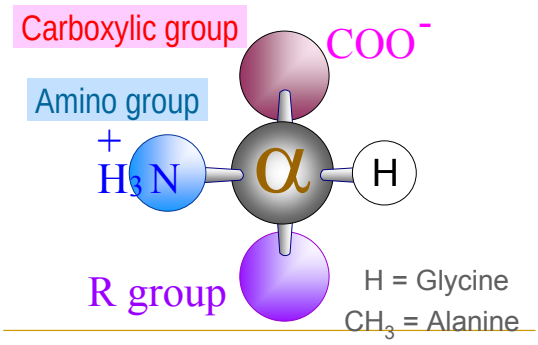
Introduction

- Amino acids are biologically important molecules made from amine ($-NH_2$) and carboxylic acid (-COOH) functional groups, along with a side-chain specific to each amino acid.
- Amino Acids are the building units of proteins.
  - Proteins are polymers of amino acids linked together by what is called " Peptide bond"
- There are about 300 amino acids occur in nature.
  - Only 20 of them occur in proteins.

Structure of Amino Acids

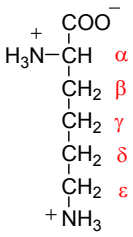
- Each amino acid has 4 different groups attached to α- carbon (which is C-atom next to COOH). These 4 groups are :
  - Amino group,
  - COOH gp,
  - Hydrogen atom and
  - Side Chain (R)

Structure of Amino Acids



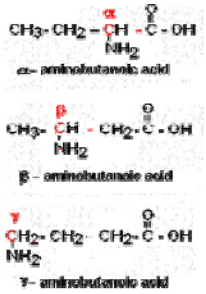
Structure of Amino Acids

- Amino acid carbons are named in sequence using the Greek alphabet (α, β, γ, δ, ε) starting at the carbon between the carboxyl and amino groups.



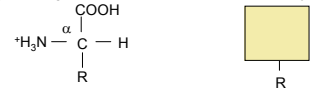
Structure of Amino Acids

Amino acids may be characterized as α, β, or γ amino acids depending on the location of the amino group in the carbon chain.
α are on the carbon adjacent to the carboxyl group.
β are on the 2nd carbon
γ on the 3rd carbon from the carboxyl group



Structure of Amino Acids

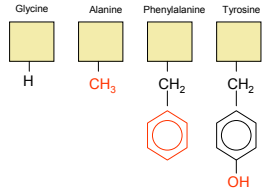
- All amino acids have a common structural unit that is built around the alpha carbon.
  - Lets call this the "core" structure.
- The figure shows the core with one of the bonds on the α-carbon unassigned. A group in this location is represented by the letter R.



- R groups are the only variable groups in the structure.
- Consider R the only unknown and focus on this group to learn the structures.
  - Hence, Rule (1) is amino acids are composed of a core group and an R group.
  - Rule (2) is the R group gives an amino acid its structural identity

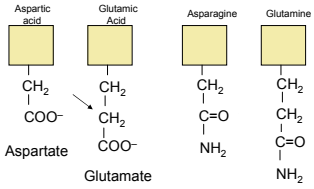
Structure of Amino Acids

Building an R Group

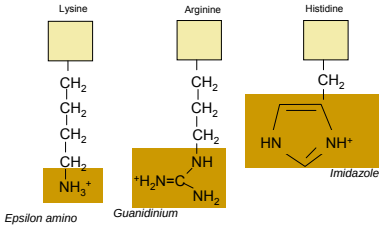


Structure of Amino Acids

Acidic and Amide Amino Acids

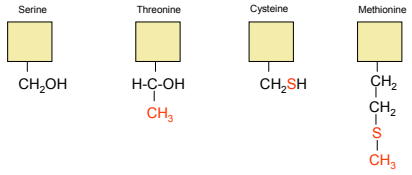


Structure of Amino Acids



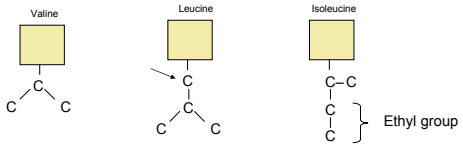
Structure of Amino Acids

Serine,Threonine, Cysteine and Methionine



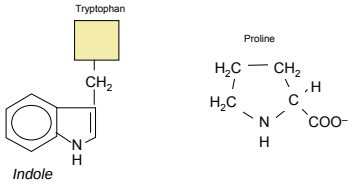
Structure of Amino Acids

Valine, Leucine, Isoleucine



Structure of Amino Acids

Tryptophan and Proline



Classification of Amino Acids

Amino Acids: Classification

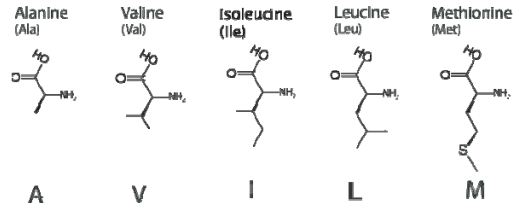
Common amino acids can be placed in five basic groups depending on their R substituents:

- Nonpolar, aliphatic (7)
- Aromatic (3)
- Polar, uncharged (5)
- Positively charged (3)
- Negatively charged (2)

Classification of Amino Acids

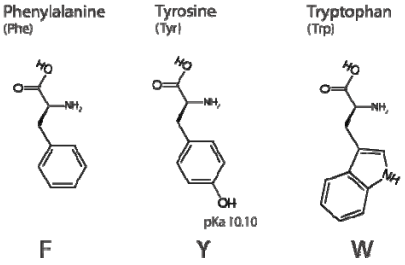
Aliphatic Amino Acids

D. Amino Acids with Hydrophobic Side Chain



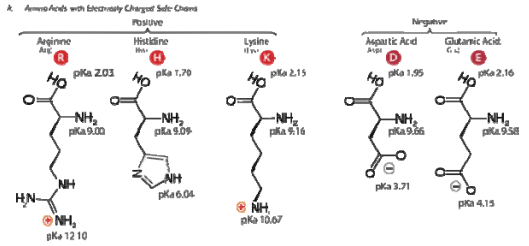
Classification of Amino Acids

Aromatic Amino Acids



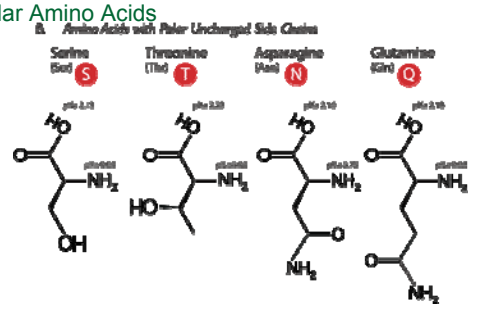
Classification of Amino Acids

Charged Amino Acids



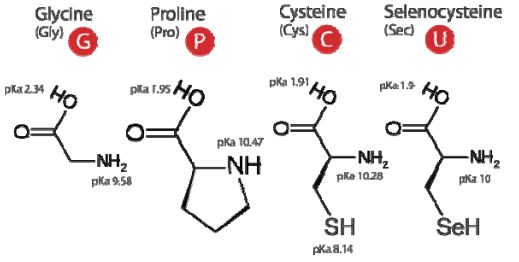
Classification of Amino Acids

Polar Amino Acids



Classification of Amino Acids

Special Amino Acids



Classification of Amino Acids by Polarity

A- Polar amino acids:

- In which R contains polar hydrophilic group so can forms hydrogen bond with H_2O. In those amino acids, R may contain:
  - - OH group : as in serine, threonine and tyrosine
  - - SH group : as in cysteine
  - - amide group: as in glutamine and aspargine
  - - NH_2 group or nitrogen act as a base (basic amino acids): as lysine, arginine and histidine
  - - COOH group (acidic amino acids): as aspartic and glutamic .

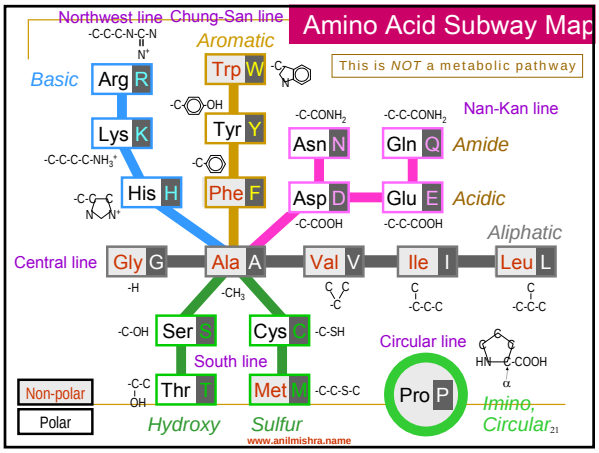
B- Non polar amino acids:

- R is alkyl hydrophobic group which can't enter in hydrogen bond formation.
  - 9 amino acids are non polar
    - glycine, alanine, valine, leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine

Classification of Amino Acids by Polarity

	Acidic	Neutral	Basic
POLAR	Asp	Asn Ser Tyr Cys Gln Thr	Arg His Lys
	Glu	Gly	
NON-POLAR		Ala Ile Val Leu Met Phe Pro	Trp

Polar or non-polar, it is the bases of the amino acid properties.



Optical Activity

- All amino acids show optical activity except for *glycine* , the rest of the amino acids contain at least *one asymmetrical carbon atom*
- What is an asymmetrical carbon atom ?
  - It is a carbon atom that is attached to four different chemical groups (four different substituted groups).
- Why does glycine lack optical activity?
  - Since its" R-group" is a Hydrogen atom thus its α-carbon atom is not asymmetrical.

Optical Activity

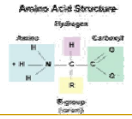
- What does possessing optical activity mean?
  - It means that the amino acid in solution can be present in two isomers;
    - The (dextrarotatory)(+) isomer which has the ability to rotate the plane of polarized light to the right.
    - The (laevorotatory)(-) isomer which has the ability to rotate the plane of polarized light to the left
- So both isomers can rotate the plane of polarized light by the same magnitude but in opposite directions.

Acid – Base Character

- All amino acids contain at least two ionizable groups
  - The α-amino group and
  - The α-carboxylic group
- Some contain an additional acidic or basic group in their side chain ,which are responsible for the amino acids , acid- base behaviour.

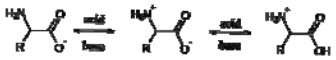
Acid – Base Character

- Amino acids are *amphoteric*:
  - They can react as either an acid or a base.
    - Ammonium ion acts as an acid, the carboxylate as a base.
- Amphoteric properties of amino acids;
  - Amino acids due to the presence of their ionizable α-amino and α-carboxylic group can act sometimes as acids and sometimes as bases depending on the pH of their media .



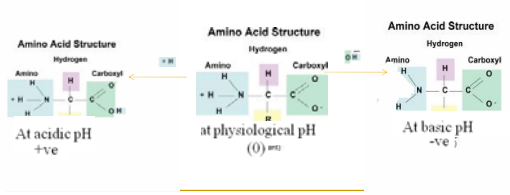
Acid – Base Character

- Majority of amino acids has amphoteric character – functional group –COOH is the reason of acidity and $–NH_2$ group causes basic properties.
- In basic environment AA dissociate proton to form carboxyl anion $–COO^-$.
  - Basic surround defends $–NH_2$ against dissociation.
- In acidic environment AA accept proton to form amonium cation $–NH_3^+$.
  - Acidic environment defends –COOH against dissociation.



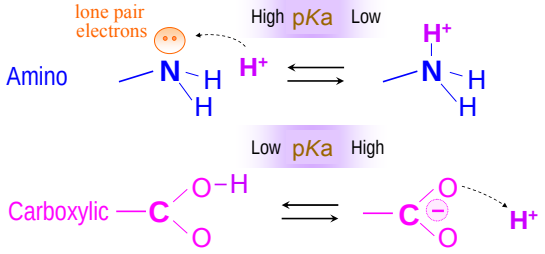
Acid – Base Character

- In solutions more basic than the pH of the amino acid, the amino group $—NH_3^+$ in the amino acid donates a proton.
- In solution more acidic than the pH of the amino acid, the carboxylic group COO- in the amino acid accepts a proton.
- Thus behaving sometimes as an acid and other times as a base depending on the pH of the solution.



Acid – Base Character

Proton : abundant and small, affects the charge of a molecule



Ampholyte contains both positive and negative groups on its molecule

Acid – Base Character

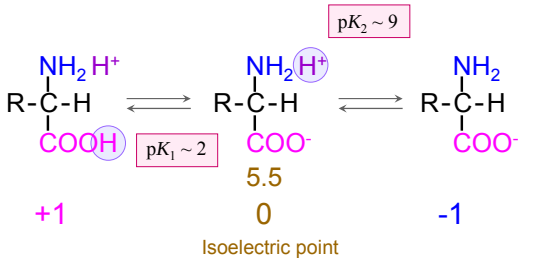
- Amino acids exist as a zwitterion: a dipolar ion having both a formal positive and formal negative charge.
  - All neutral amino acids are present in the Zwitterions form at physiological pH (around 7.4) the carboxyl group will be unprotonated and the amino group will be protonated.
    - Ionization of the $–NH_2$ and the –COOH group
    - Zwitterion has both a + and – charge
    - Zwitterion is neutral overall

$NH_2–CH_2–COOH \longrightarrow H_3N^+–CH_2–COO^-$

glycine **Zwitterion of glycine**

Acid – Base Character

Acidic environment Neutral environment Alkaline environment



pK_a Values

TABLE 4.1 pK_a Values of Common Amino Acids

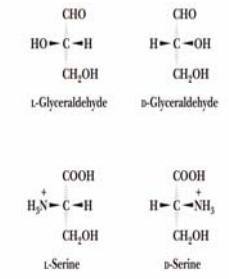
Amino Acid	α-COOH pK_a	α-NH_3^+ pK_a	R group pK_a
Alanine	2.4	9.7	
Arginine	2.2	9.0	12.5
Asparagine	2.0	8.8	
Aspartic acid	2.1	9.8	3.9
Cysteine	1.7	10.8	8.3
Glutamic acid	2.2	9.7	4.3
Glutamine	2.2	9.1	
Glycine	2.3	9.6	
Histidine	1.8	9.2	6.0
Isoleucine	2.4	9.7	
Leucine	2.4	9.6	
Lysine	2.2	9.0	10.5
Methionine	2.3	9.2	
Phenylalanine	1.8	9.1	
Proline	2.1	10.6	
Serine	2.2	9.2	~13
Threonine	2.6	10.4	~13
Tryptophan	2.4	9.4	
Tyrosine	2.2	9.1	10.1
Valine	2.3	9.6	

Physical Properties

- Amino acids are mainly *water soluble* which is explained by its polarity and the presence of charged groups. They are soluble thus in polar solvents and not soluble in non-polar solvents.
- They have a high melting point reflecting the high energy needed to break the ionic forces maintaining the crystal lattice.
- It is important to note that the general properties of amino acids is shared by all the amino acids and is in many cases contributed by its α-amino and α- carboxyl group . Amino acids can posses other specific properties dictated by they unique side chain.

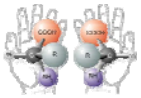
Stereochemistry of Amino Acids

- All common AA except glycine are chiral at the α-carbon atom.
  - L-amino acids predominate in nature and are the only ones used in ribosomal protein synthesis.
  - D,L-nomenclature is based on D- and L-glyceraldehyde.

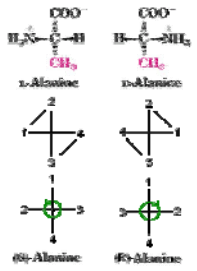


Stereochemistry of Amino Acids

- AA are optically active molecules and asymmetry of their mirror images is not superimposable (except in the case of glycine where the R-group is hydrogen)

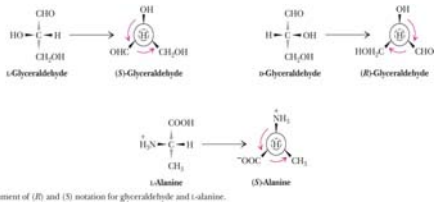


- according new IUPAC nomenclature L- D- forms were replaced for (S)- and (R)- system



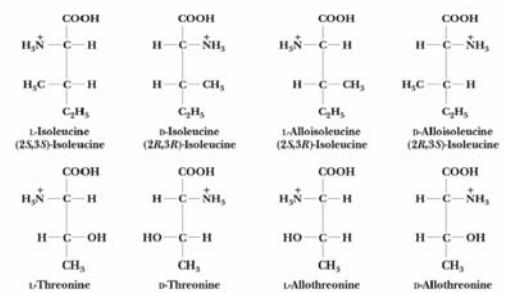
Stereochemistry of Amino Acids

- R,S-nomenclature system is more convenient, since amino acids like isoleucine and threonine (with two chiral centers) can be named unambiguously.



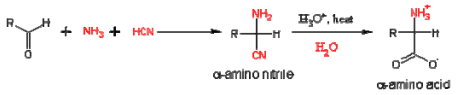
▲ The assignment of (*R*) and (*S*) notation for glyceraldehyde and L-alanine.

Stereochemistry of Amino Acids



Synthesis of Amino Acids

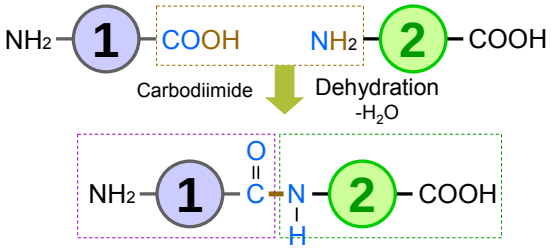
- The Strecker synthesis



Reactions of Amino Acids

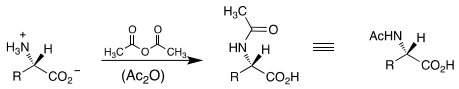
Peptide Bond Fomation

- Amide bond formed by the –COOH of an amino acid and the –NH2 of the next amino acid
- Amino acids are connected head to tail



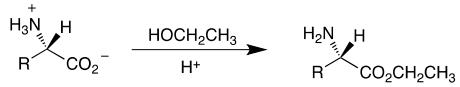
Reactions of Amino Acids

- **Acylation Reactions.**
  - The amino group reacts with acetic anhydride.



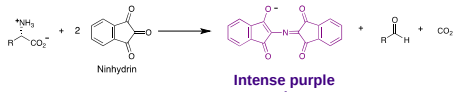
Reactions of Amino Acids

- **Esterification Reactions.**
  - The carboxylic acid group can undergo Fischer esterification



Reactions of Amino Acids

- **Reaction with Ninhydrin.**
  - Primary amines react with ninhydrin



Intense purple color

Reactions of Amino Acids

- **Disulfide linkage** – conversion of cysteine to cystine is like a conversion of thiols to disulfides by mild oxidizing agents. This conversion can be reversed by mild reducing agents.
- Disulfide bonds stabilize protein structure by providing cross-link.