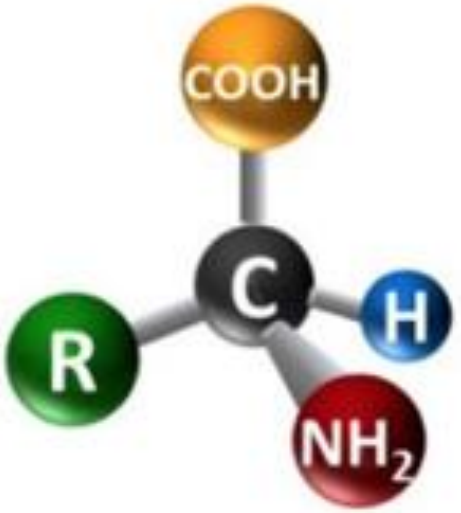
Amino Acids 2



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Nutritional Classification

- Standard amino acids are divided into three types according to the classification based on nutrition and body requirement:

1. Essential amino acids
2. Non-essential amino acids
3. Conditionally essential amino acids

Essential Amino Acids

- Cannot be produced by the body
- Must be supplied through diet
- 8 amino acids: valine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine and tryptophan

Non-essential Amino Acids

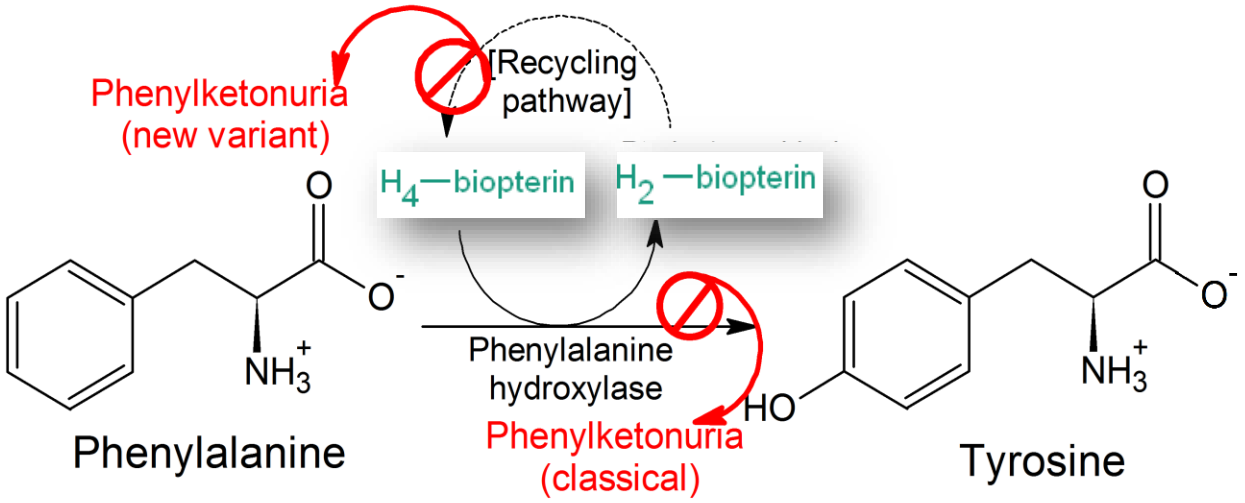
- Can be synthesized by the body
- 9 amino acids: Glycine, alanine, serine, cysteine, aspartic acid, glutamic acid, asparagine, glutamine and proline

Conditionally Essential Amino Acids

- Synthesized in the body in insufficient amounts so should be supplied in diet (requirements are higher than production rate)
- Essential only in certain cases: children, pregnant and lactating women
- 3 amino acids : Histidine, arginine and tyrosine. For example, arginine and histidine are growth promoting factors and during growth are not synthesized in sufficient amounts so essential in growing children, pregnancy and lactation.

Conditionally Essential Amino Acids

- On the other hand, tyrosine is produced from phenylalanine (essential amino acid), so if the diet is deficient in phenylalanine or if an individual is congenitally deficient in an enzyme required to convert phenylalanine to tyrosine (the inherited/ inborn /congenital disease phenylketonuria PKU), tyrosine will be required as well.



Phenylketonuria

- The accumulated phenylalanine is toxic to brain and can lead to intellectual disability and mental disorders.

Newborn screening program

Amino Acid Derivatives

- The non-standard/ non-proteinogenic amino acids are either not found in proteins (e.g. carnitine and GABA) or are not produced directly by standard cellular machinery (e.g. hydroxyproline)
- Non-standard amino acids that are found in proteins are formed by post-translational modification. These modifications are often essential for the function or regulation of a protein:

1. The **carboxylation** of **glutamate** occurring in proteins involved in blood-clotting cascade allows for better binding of calcium cations
2. The **hydroxylation** of **proline** in collagen protein is critical for maintaining connective tissues

Amino Acid Derivatives

3. The **phosphorylation** of an OH group on **serine**, **threonine** or **tyrosine** introduces a large group with a negative charge that can alter the activity of a protein or enzyme
4. Glycosylation (addition of sugar moieties) stabilizes protein conformation and direct selected proteins to various intracellular organelles (targeting process)

Non-protein Functions

- Some non-standard amino acids are not found in proteins. Examples include the neurotransmitter gamma-aminobutyric acid (GABA)
- Non-standard amino acids often occur as intermediates in the metabolic pathways for standard amino acids (e.g. ornithine and citrulline occur in the urea cycle which is part of amino acid catabolism)
- Many amino acids are used to synthesize other molecules called amino acid derivatives, for examples:

1) **Tryptophan** is a precursor of the neurotransmitter **serotonin**

Non-protein Functions

2) **Tyrosine** is a precursor of the **thyroxin** (thyroid hormone) and the catecholamine neurotransmitters like **dopamine**, **adrenaline** and **noradrenaline**

3) **The** local mediator **histamine** which is released during allergy is derived from the decarboxylation of **histidine**

4) γ-aminobutyric acid **(GABA)** is the major inhibitory NT in brain. It is nonstandard amino acid derived from **glutamate**.

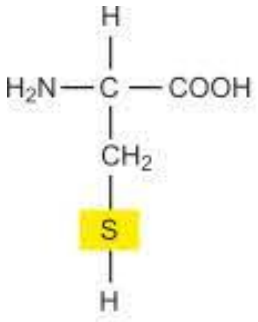
Non-proteinogenic Non-standard

- Nonproteinogenic nonstandard amino acids are derivatives of standard amino acids:
  1. As intermediates during metabolism
  2. Post translational modification process
  3. Other enzymatic reactions

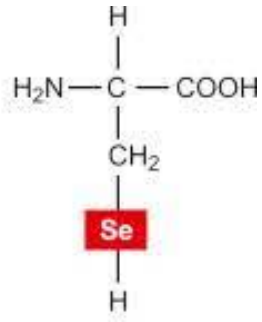
- Nonproteinogenic nonstandard amino acids may have protein role or nonprotein role (they are active by themselves and have a function

Proteinogenic Non-standard

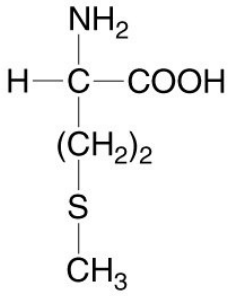
- Proteinogenic nonstandard amino acids are also derivatives of standard amino acids



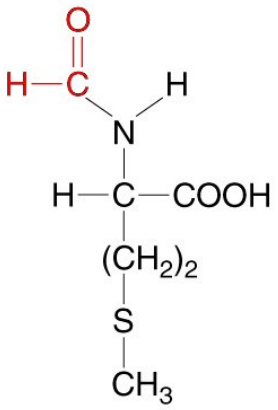
CYSTEINE



SELENOCYSTEINE



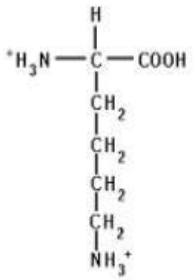
Methionine



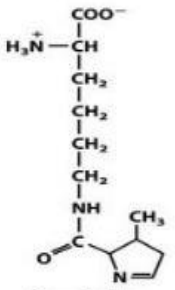
N-Formylmethionine

Lysine V/s Pyrrolysine

- Pyl is similar to Lys, but with an added ***pyrroline ring*** linked the *end of Lys side chain* **(stretching from NH2 toNH)**.



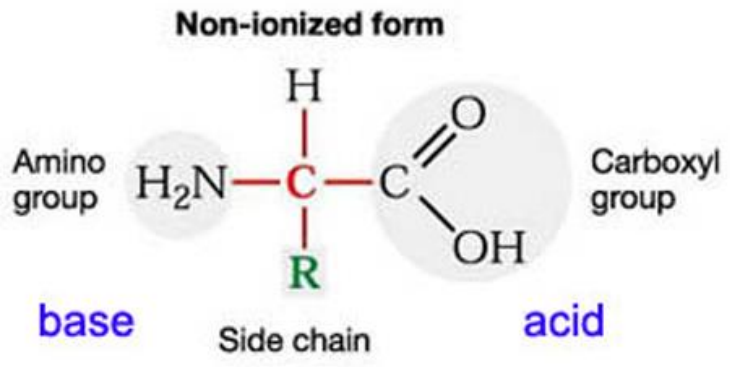
Lysine

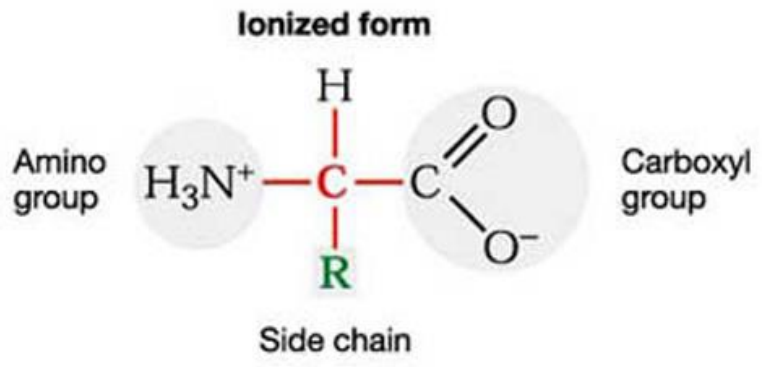


Pyrrolysine

Amphoteric property of Amino Acids

- Amino acids are amphoteric molecules (ampholytes) having both acidic (-COOH) and basic ($-NH_2$) groups
- α-amino acids are ionized in aqueous solutions with the ionization state is dependent on the pH value

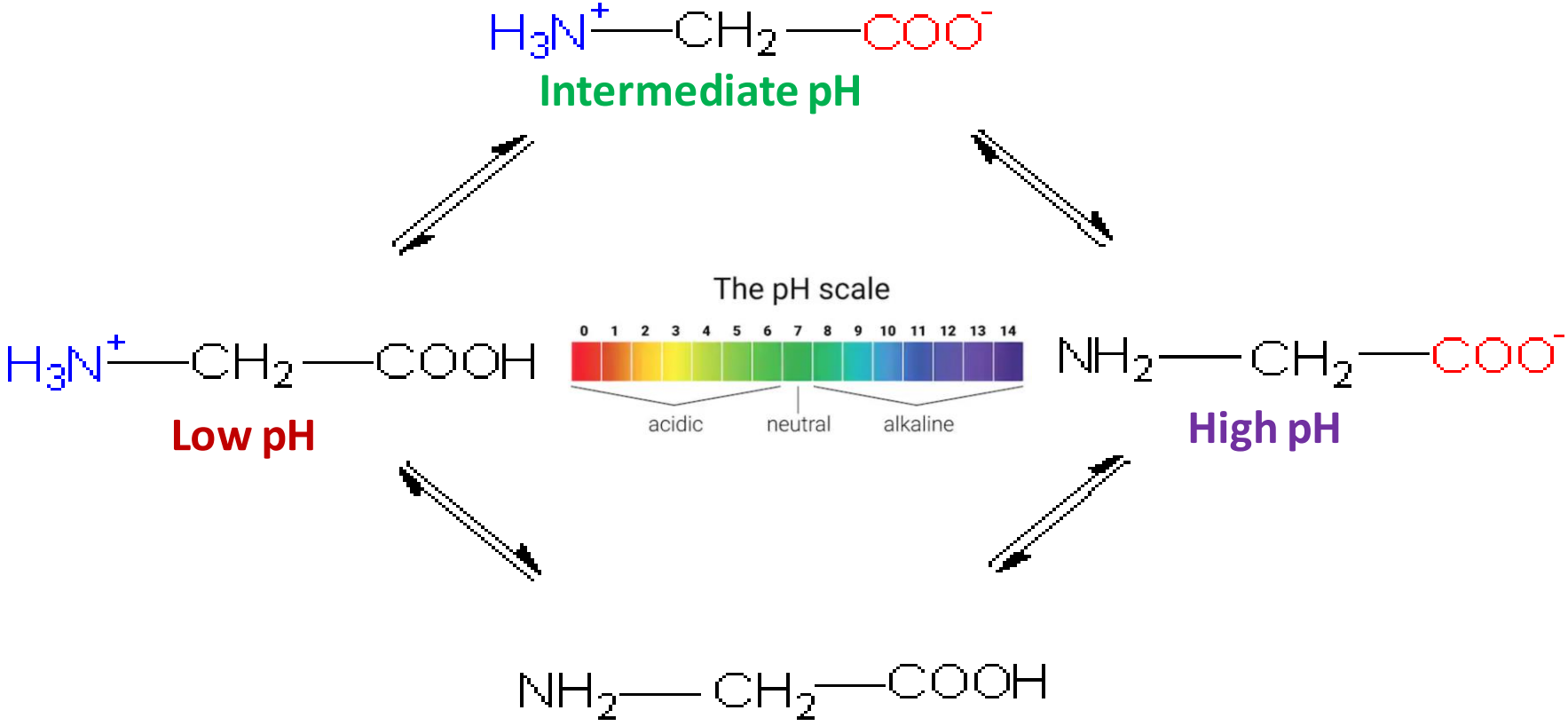




which group is ionized depends upon the pH

Ionization of Amino Acids

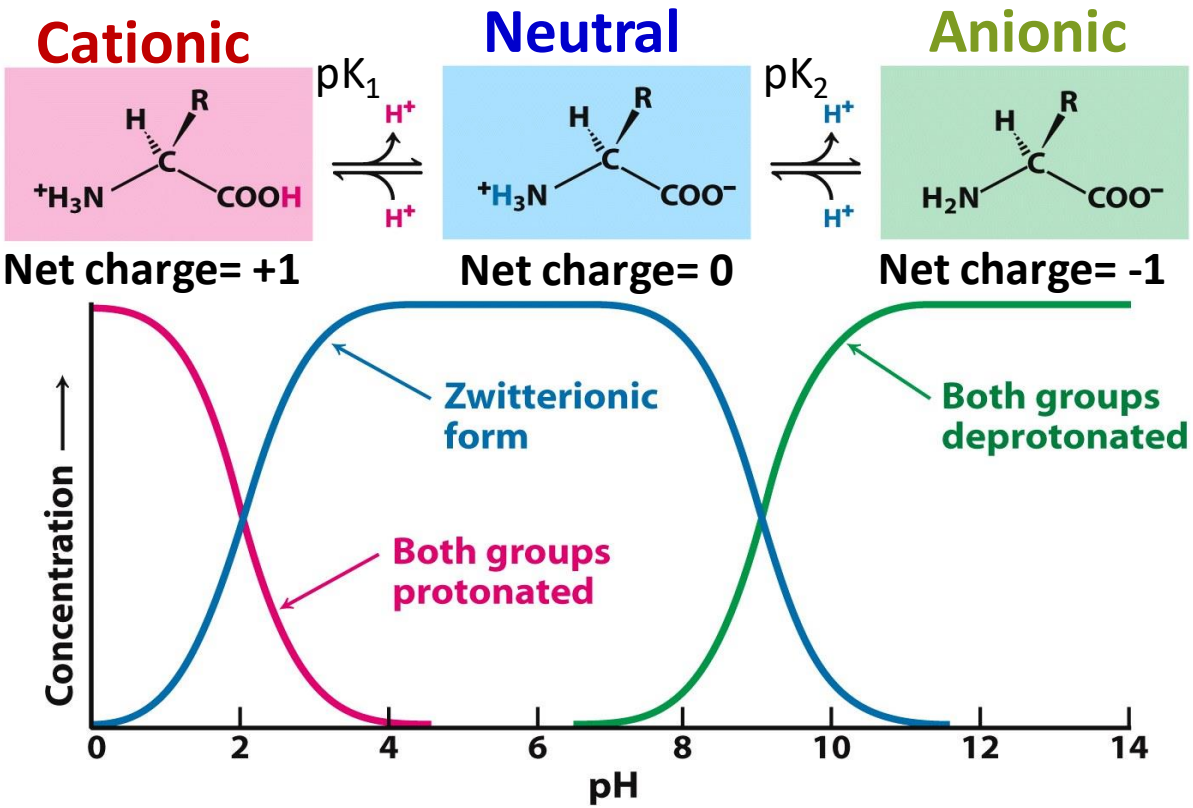
- At very low pH values, these groups are fully protonated and at very high pH values, these groups are deprotonated. At intermediate pH, both are ionized



State of glycine ionization in an acidic and an alkaline solution

Amino Acids as Zwitterions

- Zwitterions (dipolar molecules) have charged —NH_3^+ and COO^- groups (both groups are ionized). Zwitterion is neutral as it carries + and - charges



Isoelectric Point (pI)

- Isoelectric point is the pH at which a particular molecule carries no net electrical charge (overall charge = zero)
- At pI, zwitterion is the dominant form of the amino acids

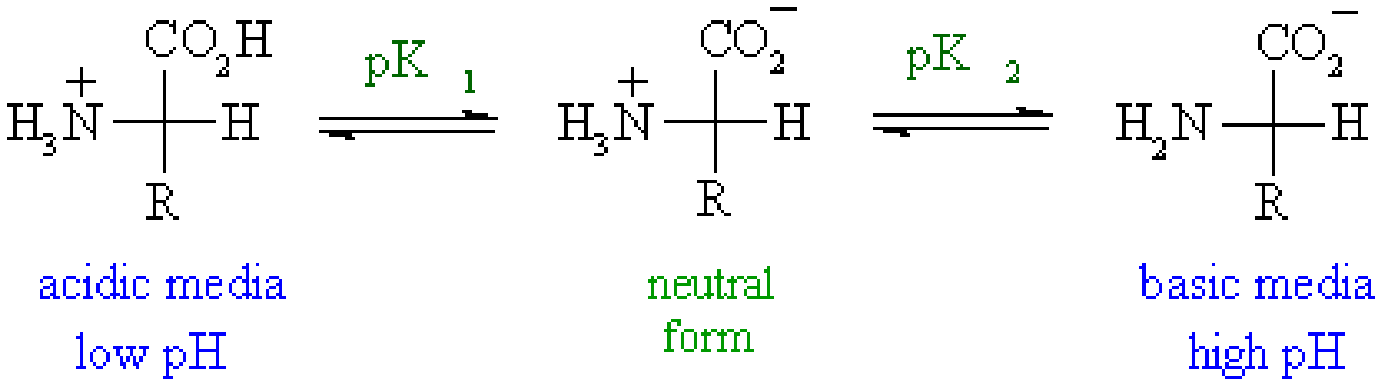
$$pI = \text{average of } pK\text{'s} = \tfrac{1}{2}\,(pK_1 + pK_2)$$

Note: pK = -log [K] where K is the dissociation constant of a weak acid or base

Isoelectric Point (pI)

- For example, the simplest amino acid glycine has $pK_1 = 2.34$ and $pK_2 = 9.6$

$$pI = \tfrac{1}{2}(pK_1 + pK_2)$$
$$= \tfrac{1}{2}(2.34 + 9.6)$$
$$= 5.97$$

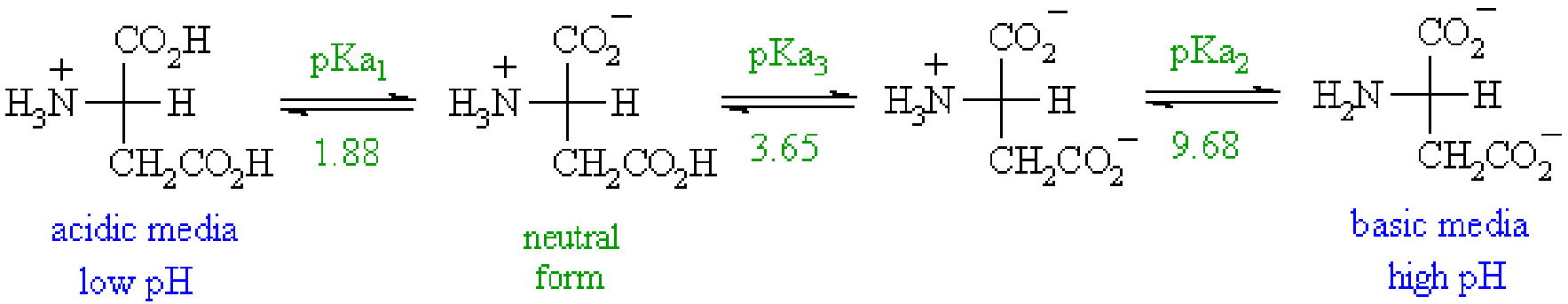


pI of Acidic and Basic Amino Acids

- For the acidic and basic amino acids which contain an ionizable "**R**" group in their side chains, pI calculation is different from those with neutral side chains

1. Acidic side chain: zwitterion exists at more acidic conditions when the extra –ve has been neutralized

$$pI = \tfrac{1}{2} (pK_1 + pK_3)$$



pI of Acidic and Basic Amino Acids

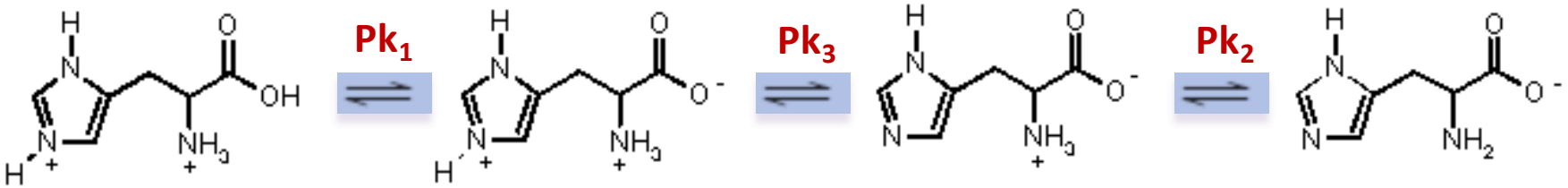
- For example, the aspartic acid which has $pK_1 = 1.88$, $pK_3 = 3.65$ and $pK_2 = 9.68$

$$pI = \tfrac{1}{2}(pK_1 + pK_3)$$
$$= \tfrac{1}{2}(1.88 + 3.65)$$
$$= 2.77$$

pI of Acidic and Basic Amino Acids

2. Basic side chain: zwitterion exists at more basic conditions when the extra +ve has been neutralized

$$pI = \tfrac{1}{2} (pK_2 + pK_3)$$



For example, histidine which has $pK_2 = 6.00$, $pK_3 = 9.17$

$$pI = \tfrac{1}{2} (pK_2 + pK_3)$$
$$= \tfrac{1}{2} (6.00 + 9.17)$$
$$= 7.59$$

pKa values of Amino Acids

The pK values for the α-carboxyl, α-amino groups and side chains

Amino acid	pK_1	pK_2	pK_R
Alanine	2.4	9.9	-
Arginine	1.8	9.0	12.5
Asparagine	2.1	8.7	-
Aspartate	2.0	9.9	3.9
Cysteine	1.9	10.7	8.4
Glutamate	2.1	9.5	4.1
Glutamine	2.2	9.1	-
Glycine	2.4	9.8	-
Histidine	1.8	9.3	6.0
Isoleucine	2.3	9.8	-

Amino acid	pK_1	pK_2	pK_R
Leucine	2.3	9.7	-
Lysine	2.2	9.1	10.5
Methionine	2.1	9.3	-
Phenylalanine	2.2	9.3	-
Proline	2.0	10.6	-
Serine	2.2	9.2	-
Threonine	2.1	9.1	-
Tyrosine	2.2	9.2	10.5
Tryptophan	2.5	9.4	-
Valine	2.3	9.7	-