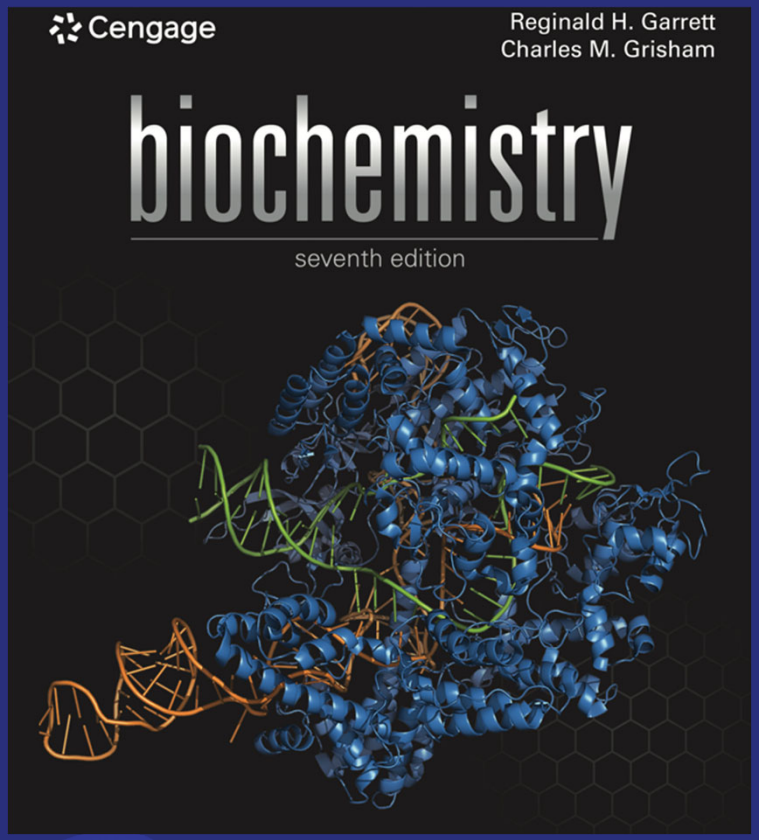
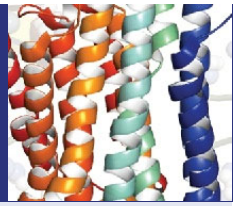


Biochemistry, 7e

Chapter 4: Amino Acids and the Peptide Bond

Cengage

Chapter 4



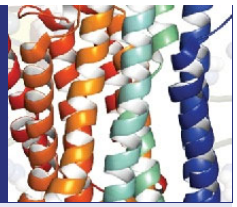
"To hold, as 'twere, the **mirror** up to nature."
William Shakespeare, Hamlet

All objects have mirror images, and **amino acids** exist in **mirror-image** forms.

Only the **L-isomers** of amino acids occur commonly in nature.

Three Sisters Wilderness, Oregon USA

Essential Question



Transcription Translation

DNA ⟶ RNA ⟶ protein

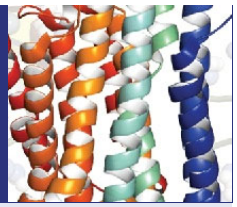
The stunning diversity of the thousands of proteins found in nature arises from the intrinsic properties of only 20 commonly amino acids.

- Why are **amino acids** uniquely suited to their role as the **building blocks of proteins**?

These features includes:

1) The capacity to polymerize
2) Novel acid-base properties
3) Varied structure and chemical functionality in the amino acid side chains
4) Chirality

Outline



4.1 What are the **structures** and **properties** of amino acids?

4.2 What are the **acid-base** properties of amino acids?

4.3 What **reactions** do amino acids undergo?

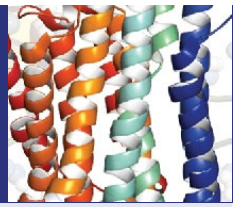
4.4 What are the **optical and stereochemical** properties of amino acids?

4.5 What are the **spectroscopic properties** of amino acids?

4.6 How are amino acid **mixtures separated** and **analyzed**?

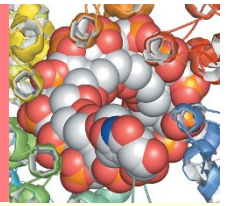
4.7 What is the **fundamental structural pattern** in proteins?

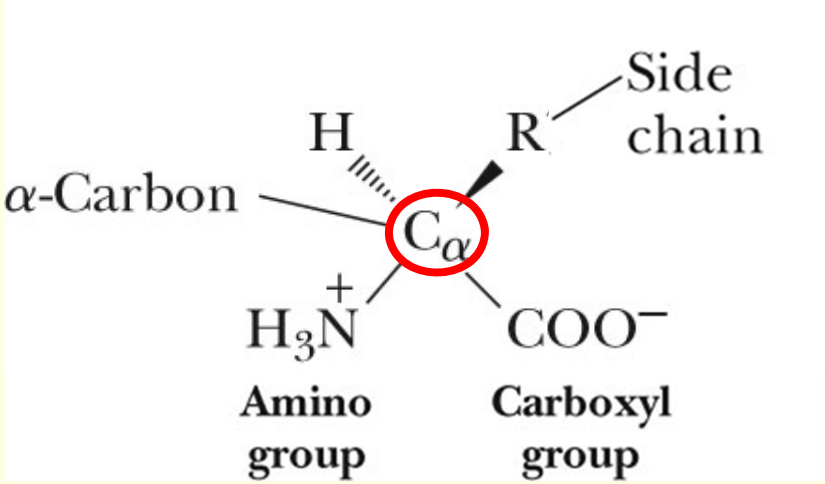
4.1 What Are the Structures and Properties of Amino Acids?

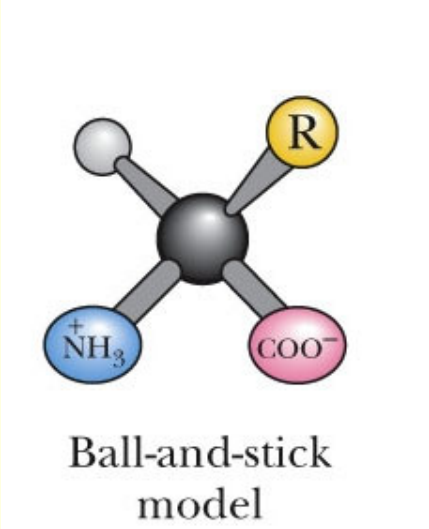


- Amino acids contain a central tetrahedral carbon atom
- There are 20 common amino acids
- Amino acids can join via peptide bonds
- Several amino acids occur only rarely in proteins
- Some amino acids are not found in proteins

4.1a Typical Amino Acid contains a central tetrahedral Carbon Atom







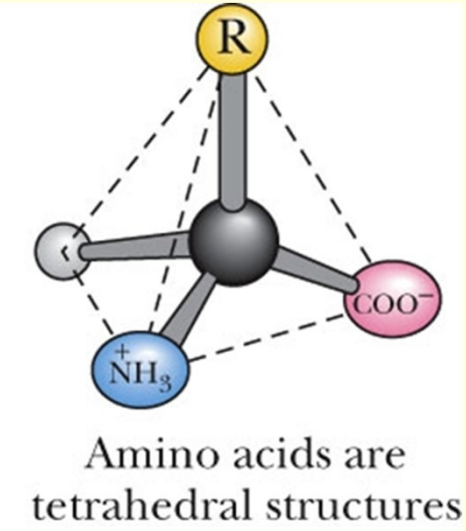
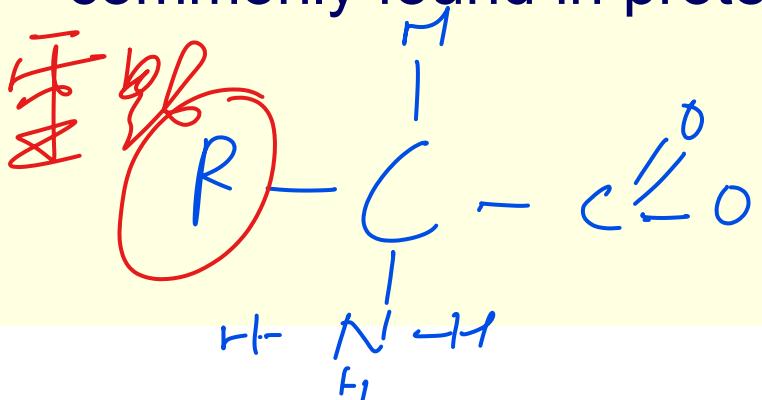


Figure 4.1 Anatomy of an amino acid.

Except for proline and its derivatives, all of the amino acids commonly found in proteins possess this type of structure.



4.1b Amino Acids Can Join vir Peptide Bond.

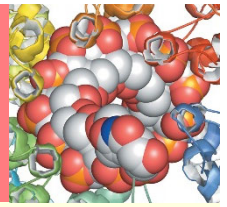
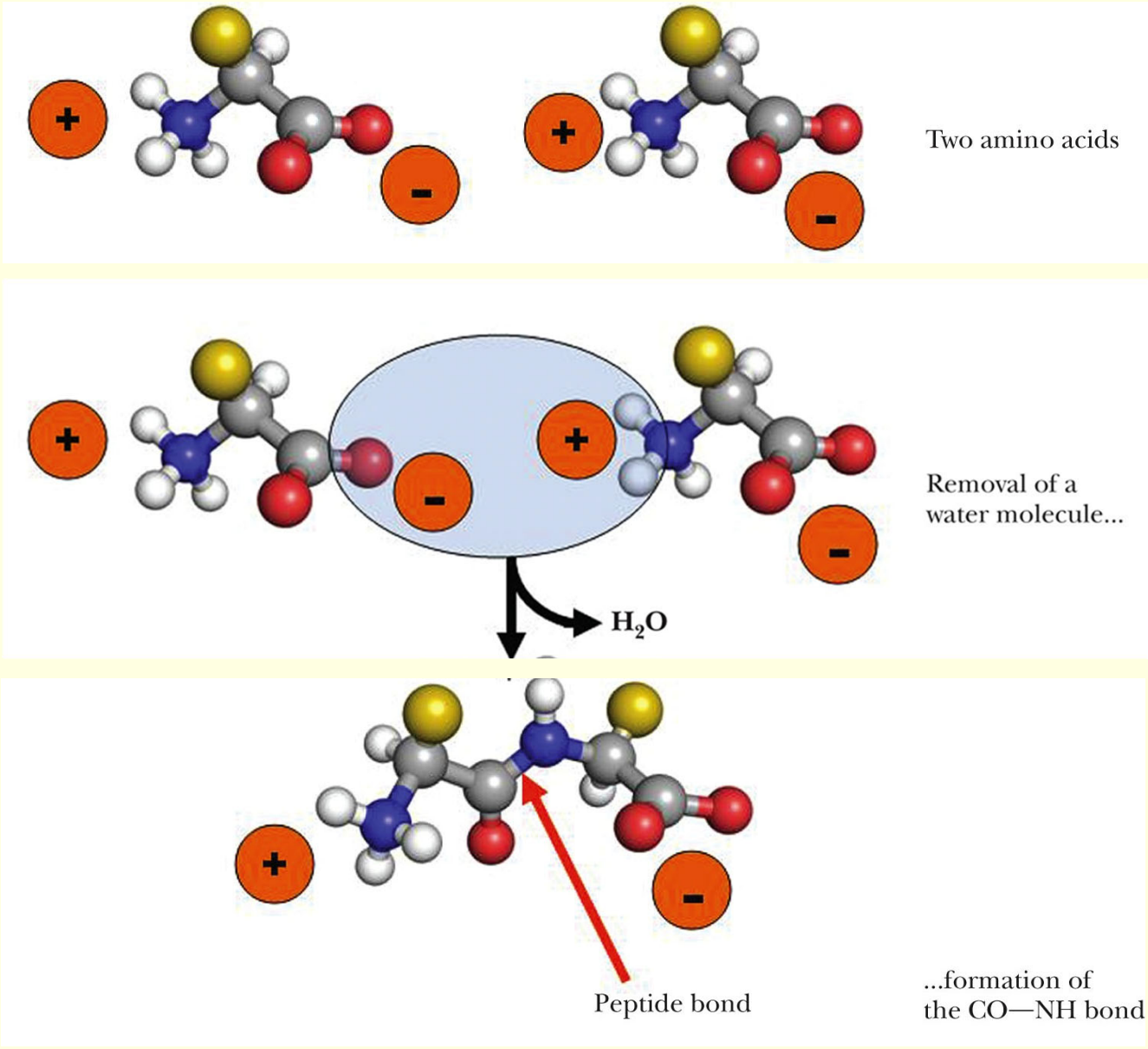
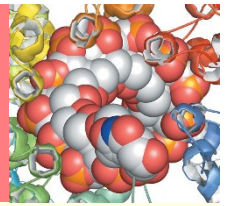


Figure 4.2
Two amino acids can react with loss of a **water** molecule to form a **covalent bond.**

The bond joining the two amino acids is called a **peptide bond**.



4.1c There are 20 Common Amino Acids



*We should know **names**, **structures**, **pK_a** values, **3-letter** and **1-letter** codes*

a) **Non-polar** amino acids MILF WA YV

b) **Polar**, uncharged amino acids STNQ

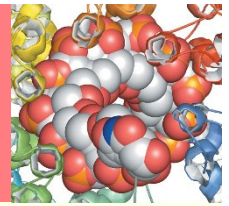
c) **Acidic** (酸性) amino acids HKR

d) **Basic** amino acids DE

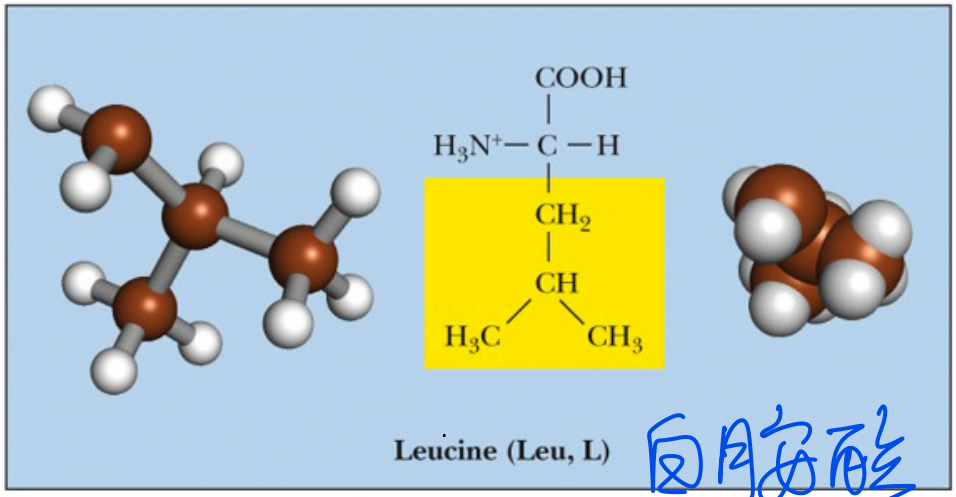
GCUP

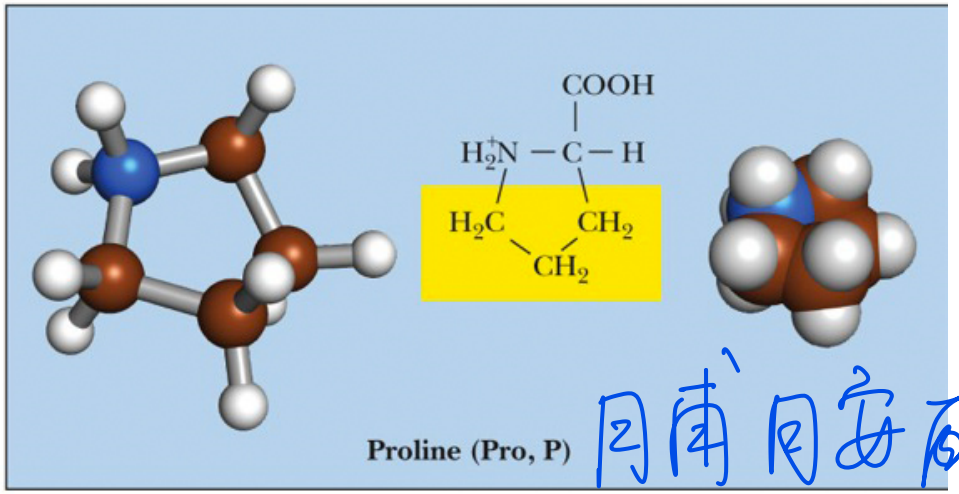
Figure 4.3 The 20 amino acids that are building blocks of most proteins can be classified as (a) nonpolar (hydrophobic); (b) polar, neutral; (c) acidic; or (d) basic.
The side chain R group is highlined in yellow Protonated (low pH)form

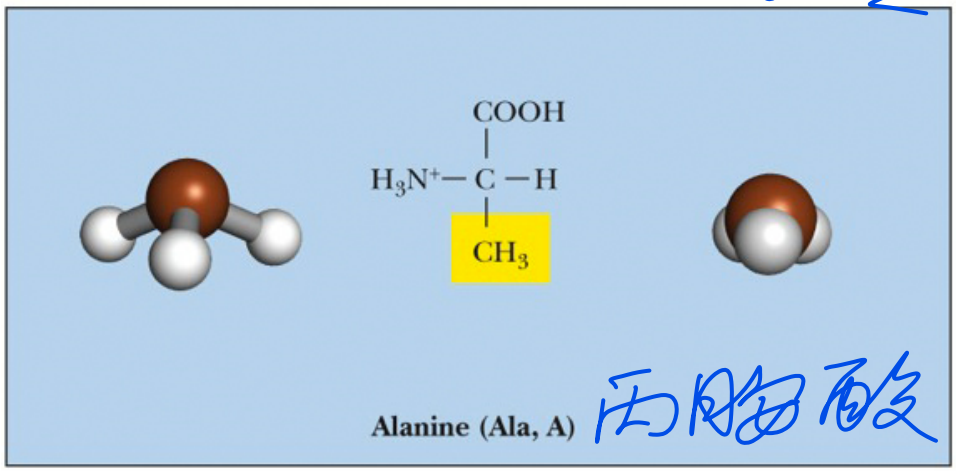
The 20 Common Amino Acids



Nonpolar (hydrophobic) amino acids







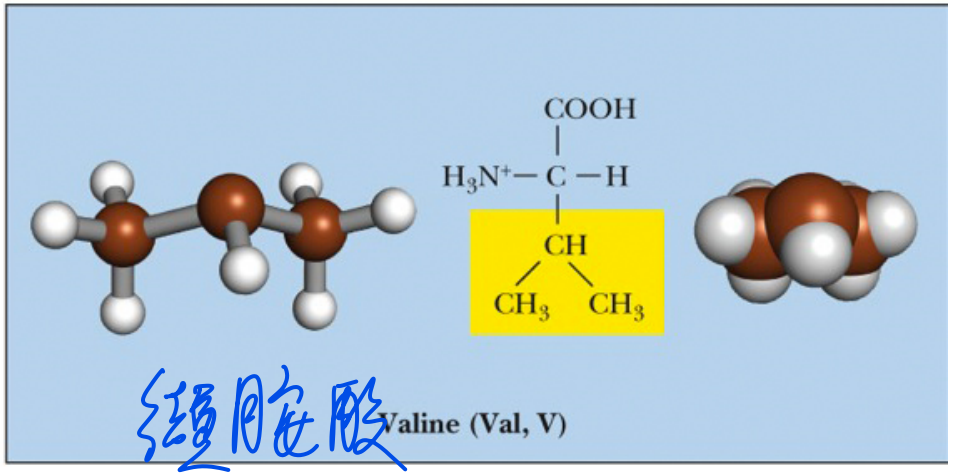
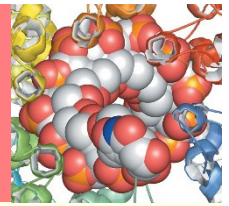
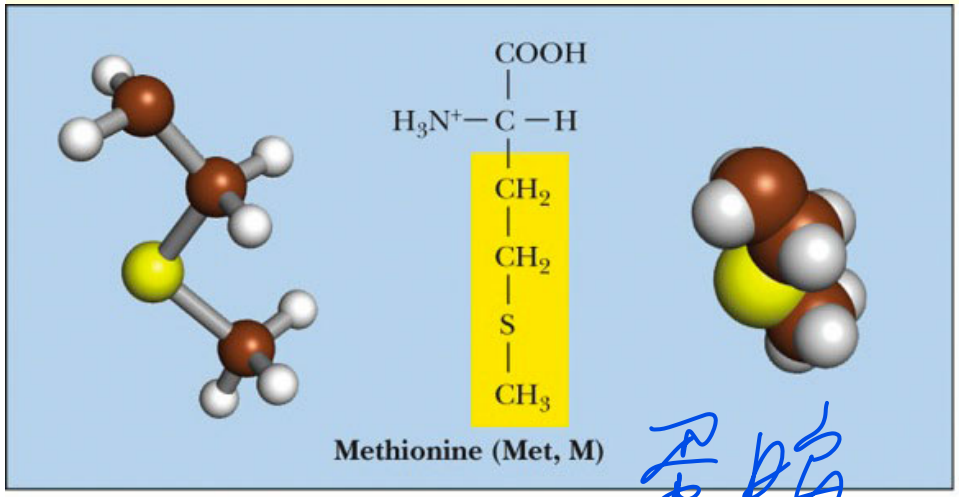


Figure 4.3 The 20 amino acids that are building blocks of most proteins can be classified as (a) nonpolar (hydrophobic); (b) polar, neutral; (c) acidic; or (d) basic.
The side chain R group is highlighted in yellow. Protonated (low pH) form

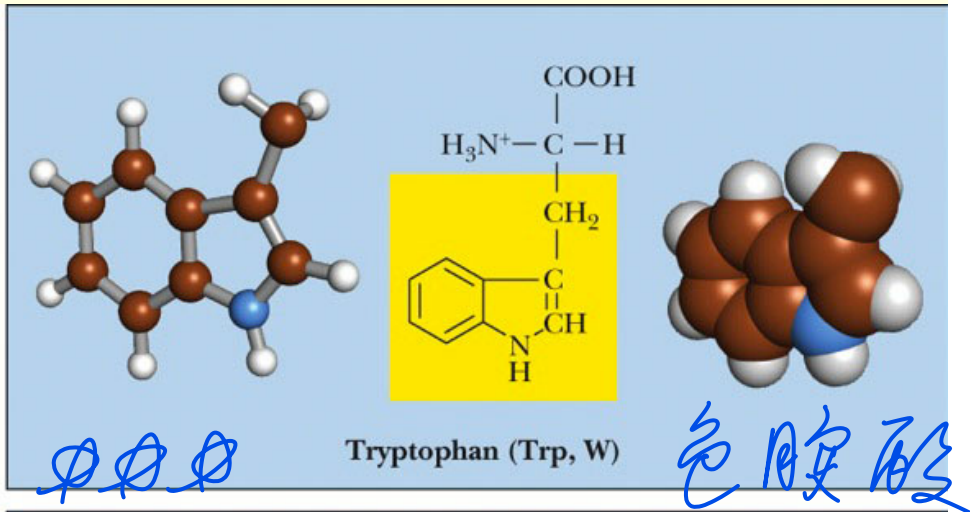
The 20 Common Amino Acids



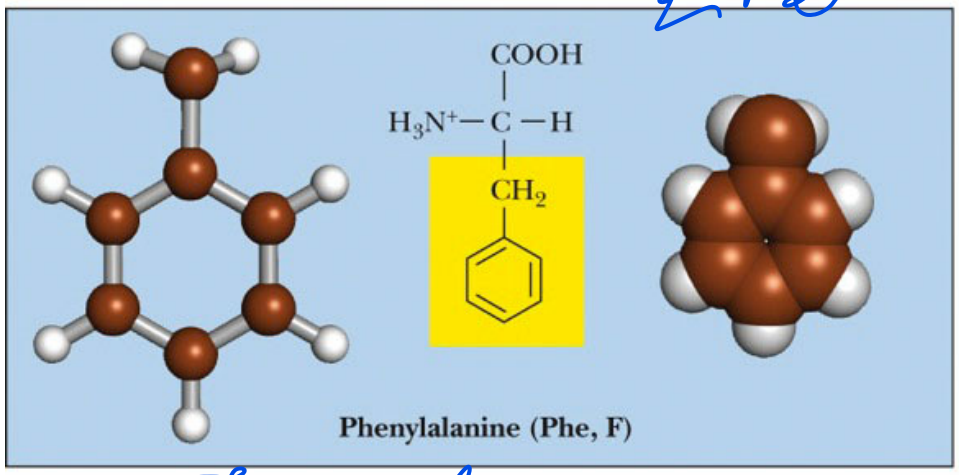
Nonpolar (hydrophobic) amino acids



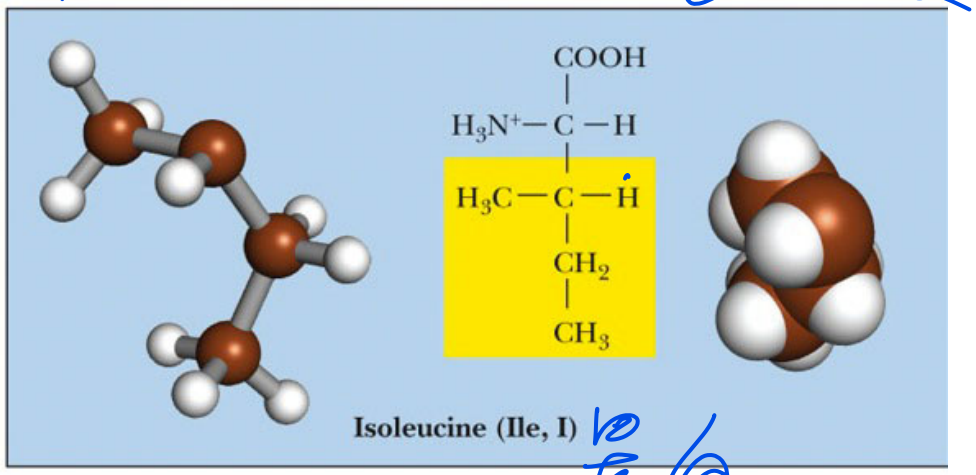
Methionine (Met, M)



Tryptophan (Trp, W)



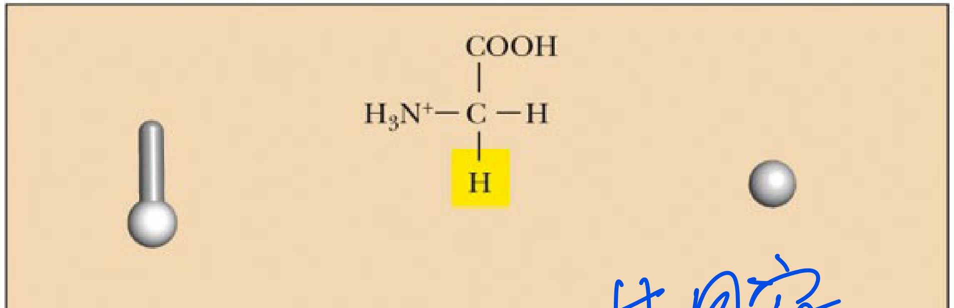
Phenylalanine (Phe, F)



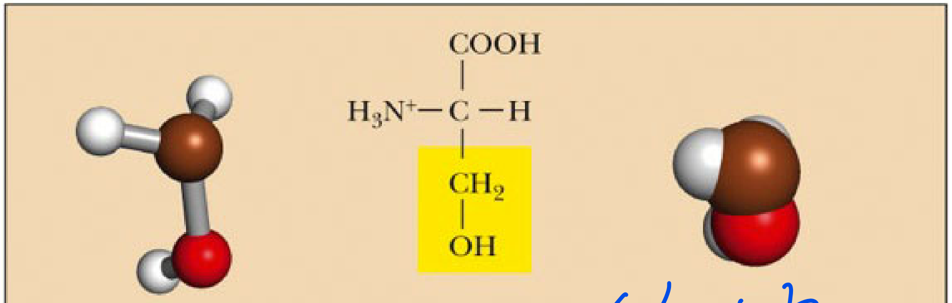
Isoleucine (Ile, I)

The 20 Common Amino Acids

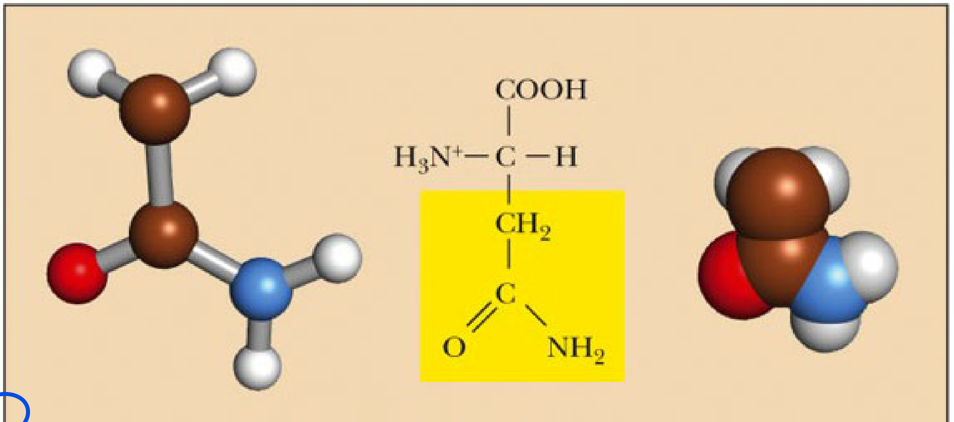
Polar, uncharged amino acids



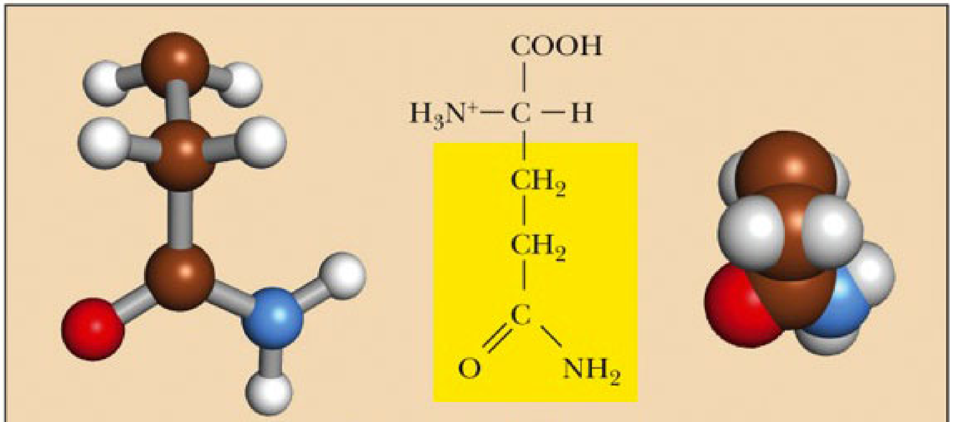
Glycine (Gly, G) 甘氨酸



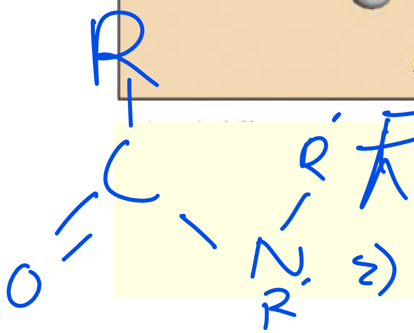
Serine (Ser, S) 丝氨酸



Asparagine (Asn, N) 天门冬酰胺

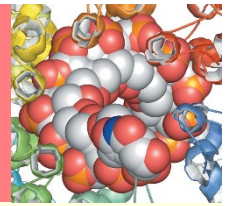


Glutamine (Gln, Q) 谷氨酰胺

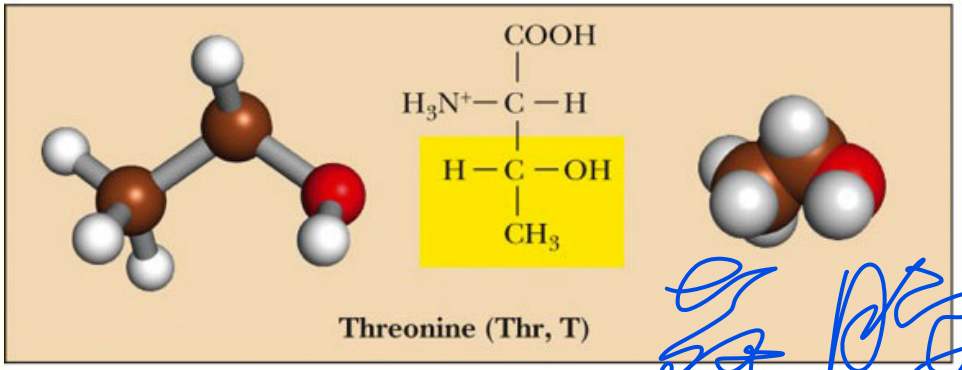


⇒ R' = H

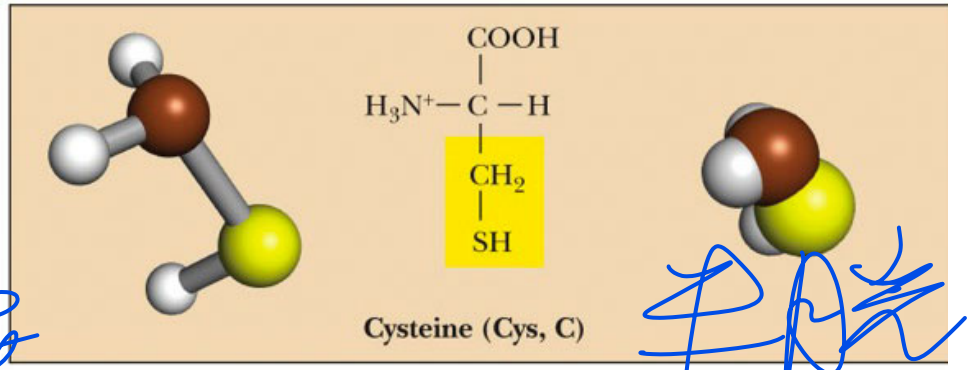
The 20 Common Amino Acids



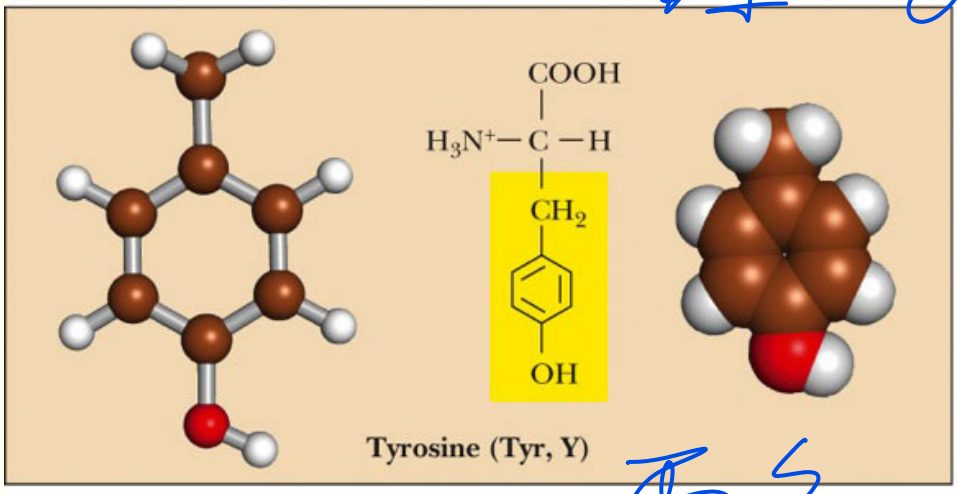
Polar, uncharged amino acids



Threonine (Thr, T)



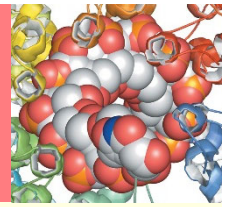
Cysteine (Cys, C)



Tyrosine (Tyr, Y)

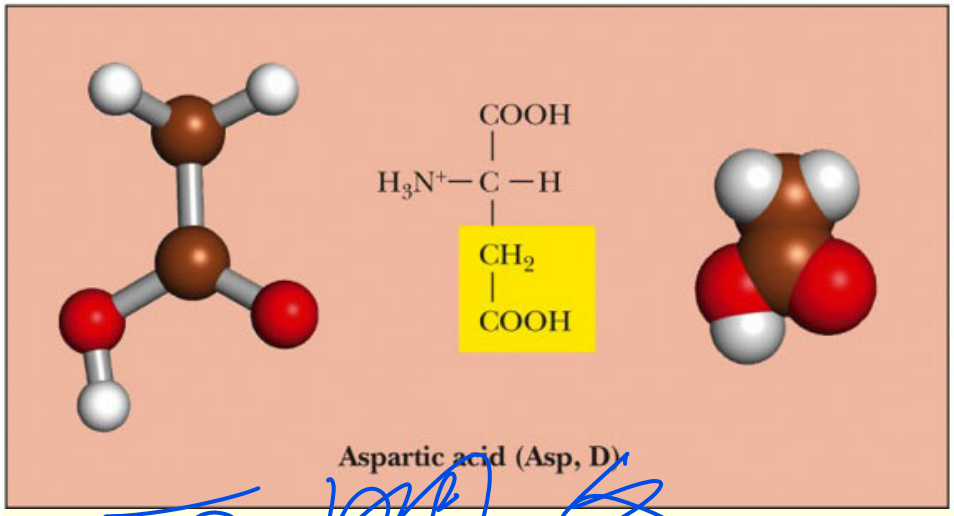
proline

The 20 Common Amino Acids

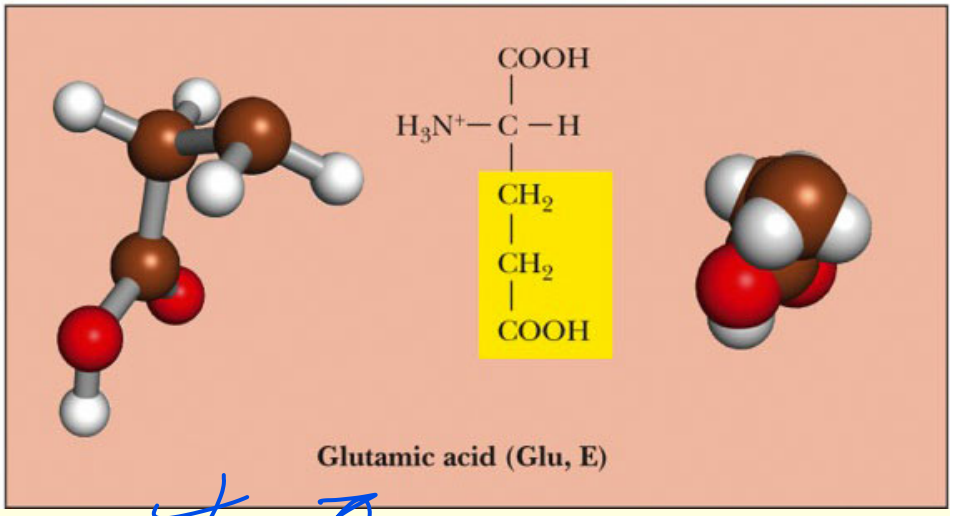


Acidic amino acids

(c) Acidic



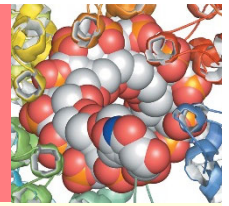
Aspartic acid (Asp, D)



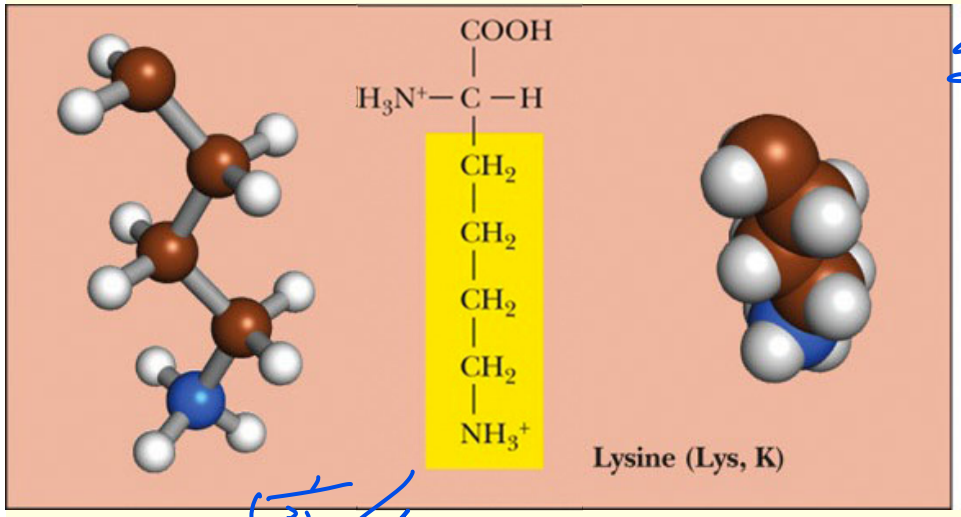
Glutamic acid (Glu, E)

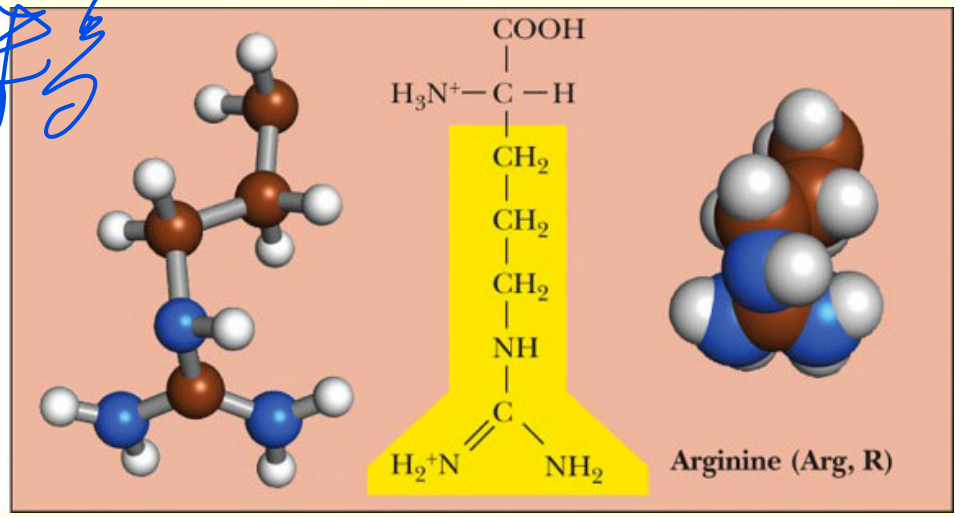
have a net negative charge at pH 7.0

The 20 Common Amino Acids

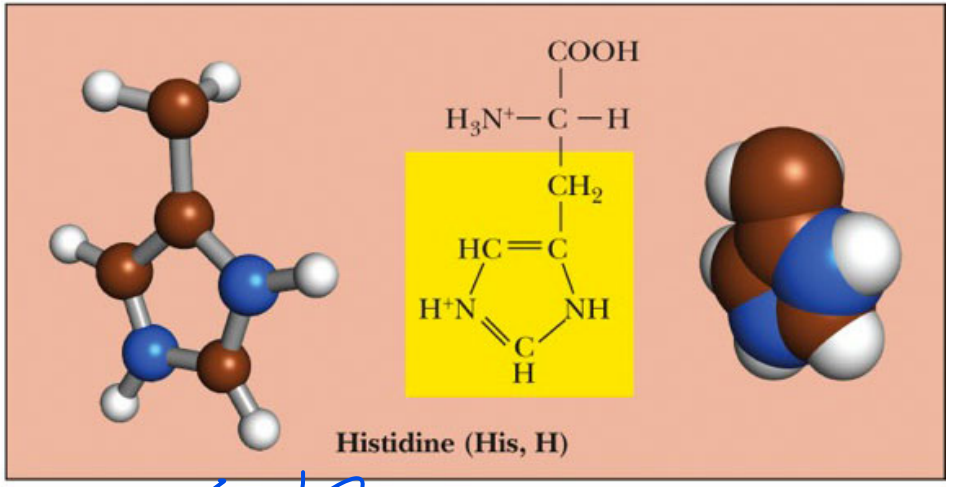


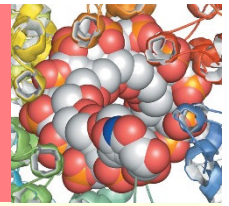
Basic amino acids

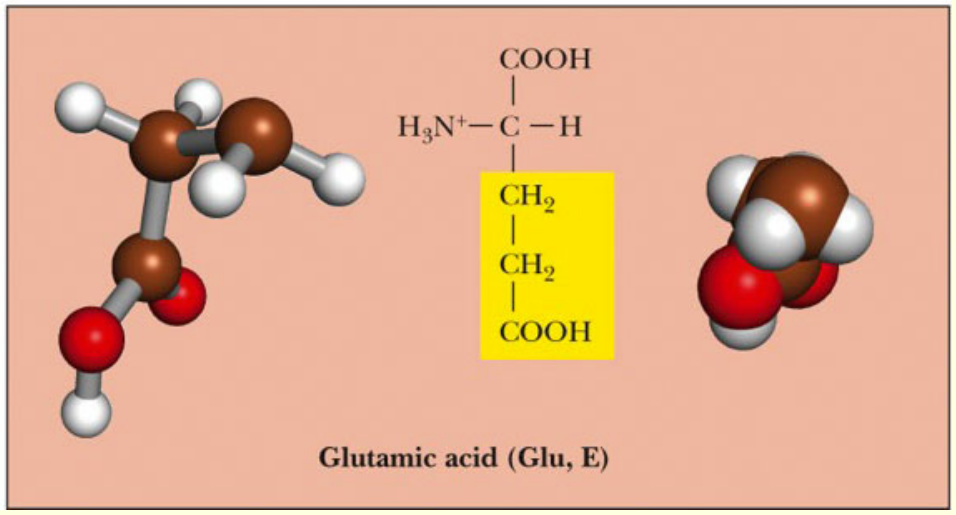


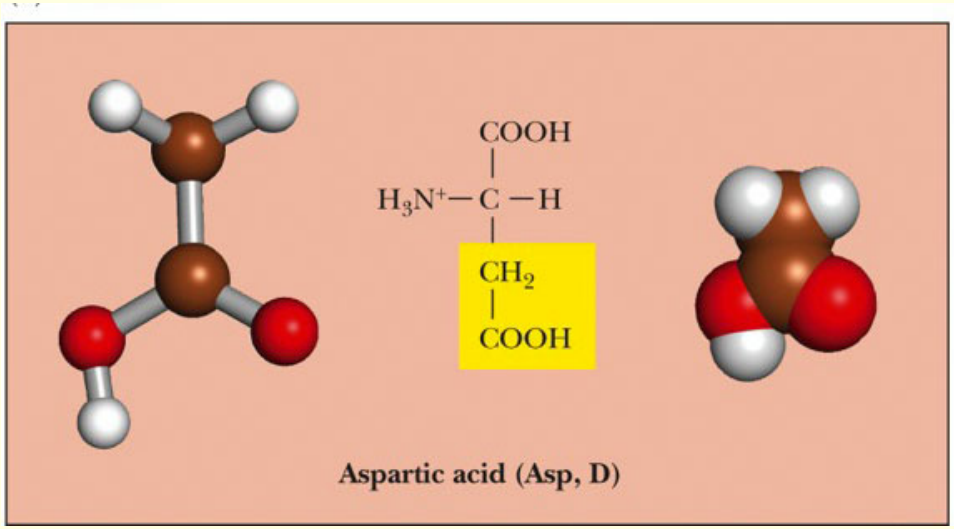


have a net positive charge at neutral pH









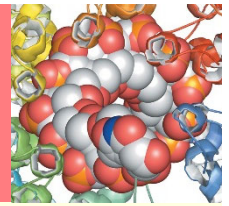
Glutamate

deprotonated form
H^+ removed,
anionic form
陰離子形式 glutamate

Aspartate

deproteonated form
H^+ remoced
anionic form
陰離子形式Aspartate

4.1d Are there other ways to classify Amino Acids?



Hydrophobic:

- Ala
- Gly
- Ile
- Leu
- Phe
- Pro
- Val

Hydrophilic:

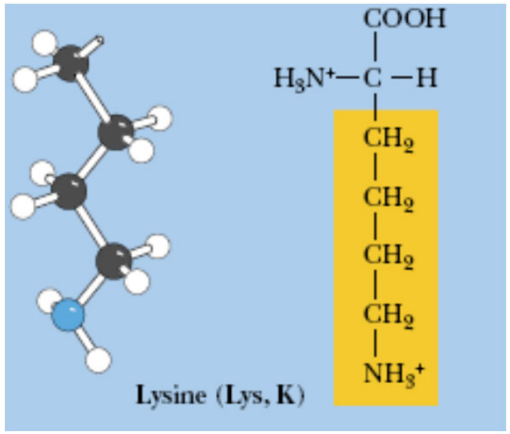
- Arg
- Asn
- Asp
- Cys
- Glu
- Gln
- His
- Ser
- Thr

Amphipathic:

- Lys
- Met
- Trp
- Tyr

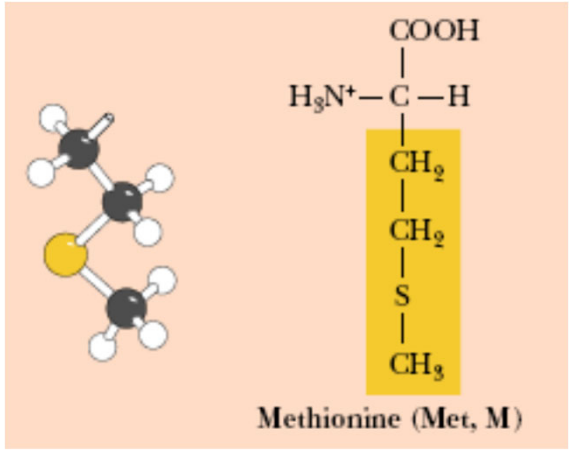
Amphipathic aa

- **Lysine**
- R consists of aliphatic side chain,
- which can Interact with hydrophobic aa in protein
- an amino group is normally charged at neutral pH.

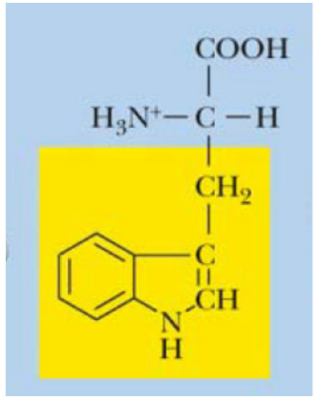


Methionine

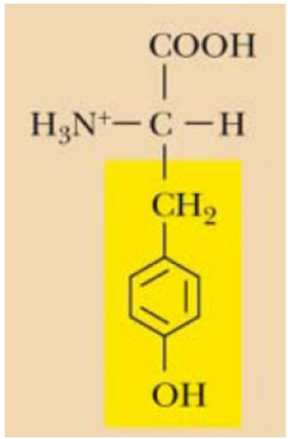
The least polar of the amphipathic aa, Thioether sulfur can be an effective metal ligand in protein.



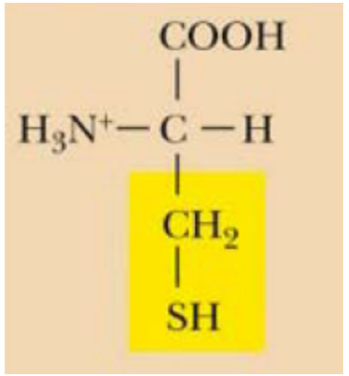
Tryptophine



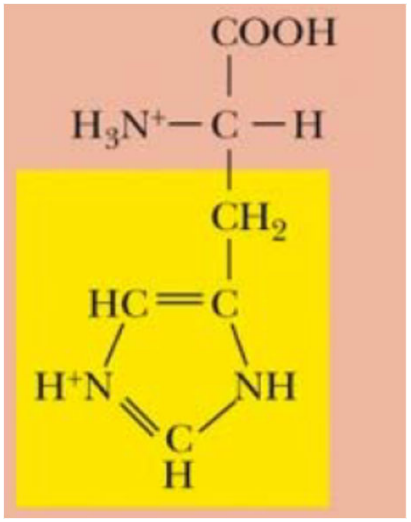
Tyrosine



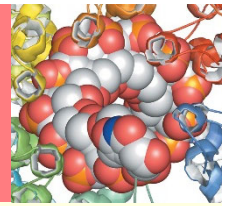
- **Cysteine**
- Deprotonate at pH values greater than 7,
- the most potent **nucleophile**



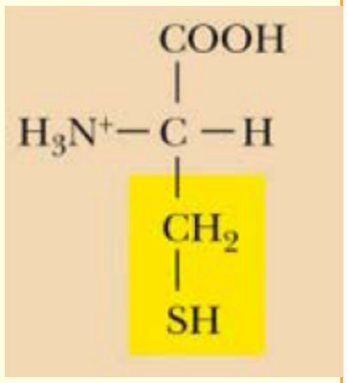
- **Histidine**
- Imidazole ring
- Two nitrogen each with an H,
- Two pKa =6 & 10

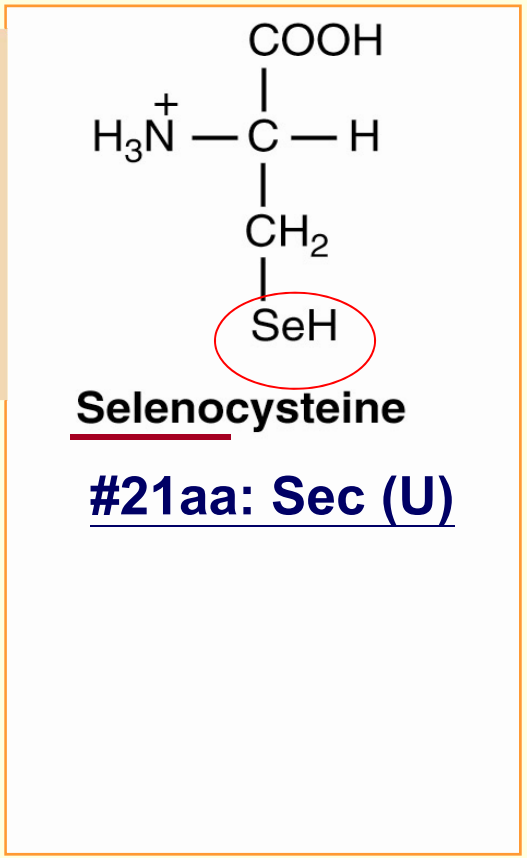


4.1e Amino Acids 21 and 22– and More?

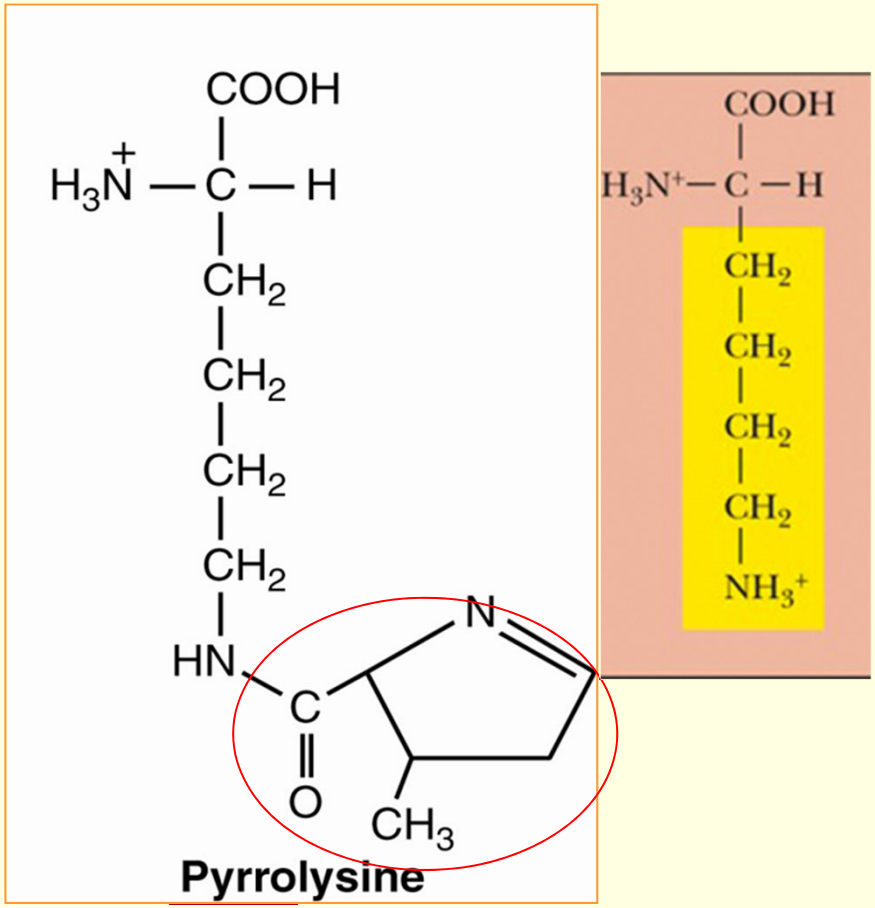


- **Selenocysteine** in many organisms
- **Pyrrolysine** in several archaeal species



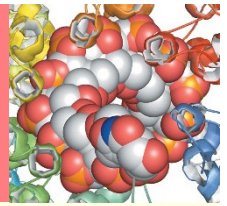


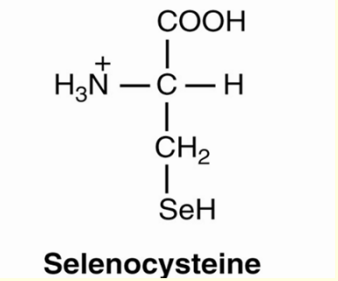
#21aa: Sec (U)



#22aa: Pyl (O)

Selenocysteine and Selenoproteins



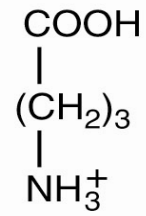


Selenocysteine

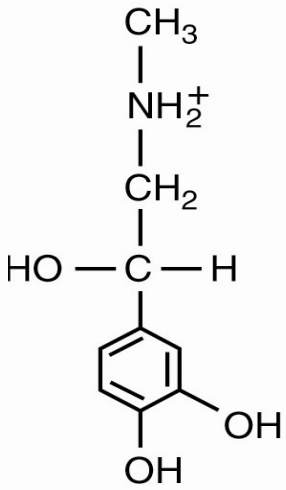
- **Seleno**cysteine ("**Sec**") has been found in many organisms
- Half of eukaryotes and most bacteria contain selenoproteins
- **Selenocysteine** is the only common amino acid that humans can make but higher plants cannot
- The pK_a of the Sec R group is 5.2; thus, Sec is an even better nucleophile than Cys (pK_a = 8.3)
- Human **seleno**enzymes are involved in
  peroxide removal,
  reduction of thioredoxins,
  selenophosphate synthesis,
  activation and inactivation of thyroid hormones, and
  repair of oxidized Met in proteins.

Several amino acids act as neurotransmitters & hormones

(c)

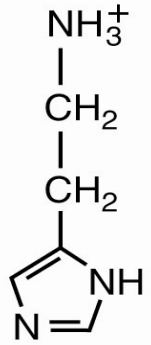


γ-Aminobutyric acid (GABA)



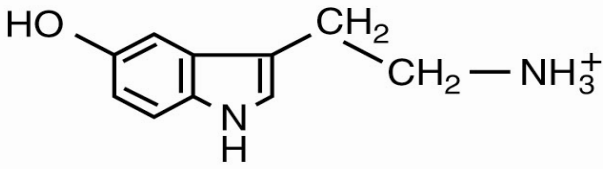
Epinephrine

腎上腺素



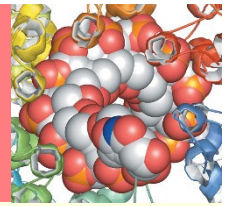
Histamine

組織胺

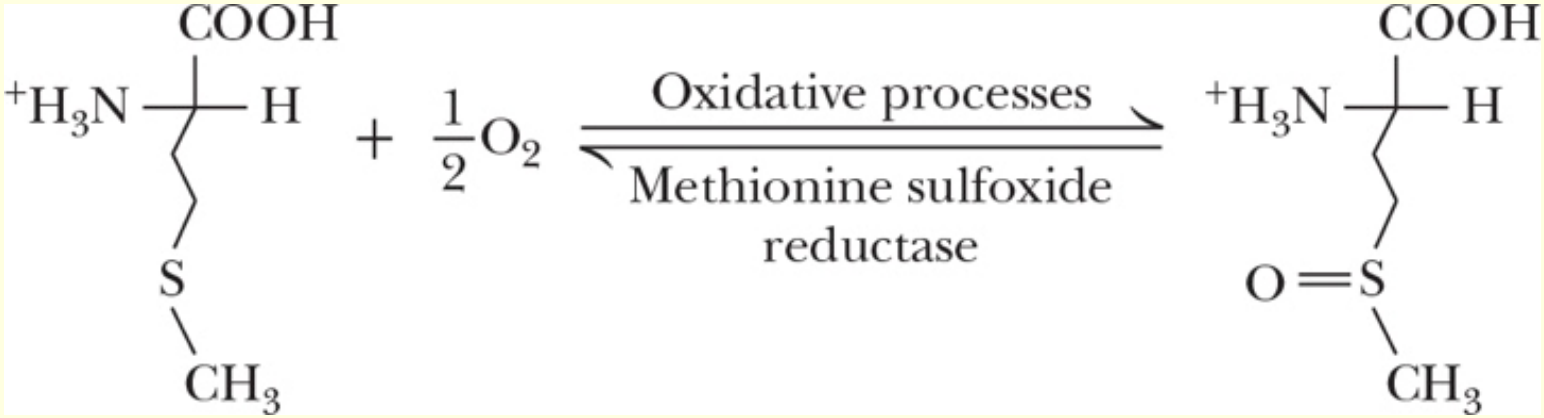


Serotonin

Methionine sulfoxide reductases



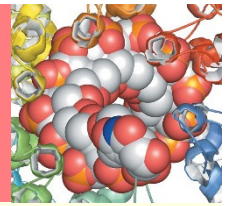
- One critical role of **Sec** lies in the function of **methionine sulfoxide reductases**
- **Methionine sulfoxide** accumulated in protein and tissues over time, contributing to many aspects of **aging**
- In smokers, oxidation of a crucial **Met** inactivates α_1-Antitrypsin, leading to emphysema.



Met

methionine sulfoxide

4.1f Several Amino Acids Occur Only Rarely in Proteins



- **Selenocysteine** in many organisms
- **Pyrrolysine** in several archaeal species
- **Hydroxylysine**, **hydroxyproline** - collagen
- **Carboxyglutamate** - blood-clotting proteins
- **Pyroglutamate** – in bacteriorhodopsin
- **GABA** (γ-Aminobutyric acid),
- **Epinephrine,**
- **Histamine,**
- **Serotonin** act as neurotransmitters and hormones
- **Phosphorylated** amino acids – a signaling device

Several Amino Acids Occur Rarely in Proteins

(b)

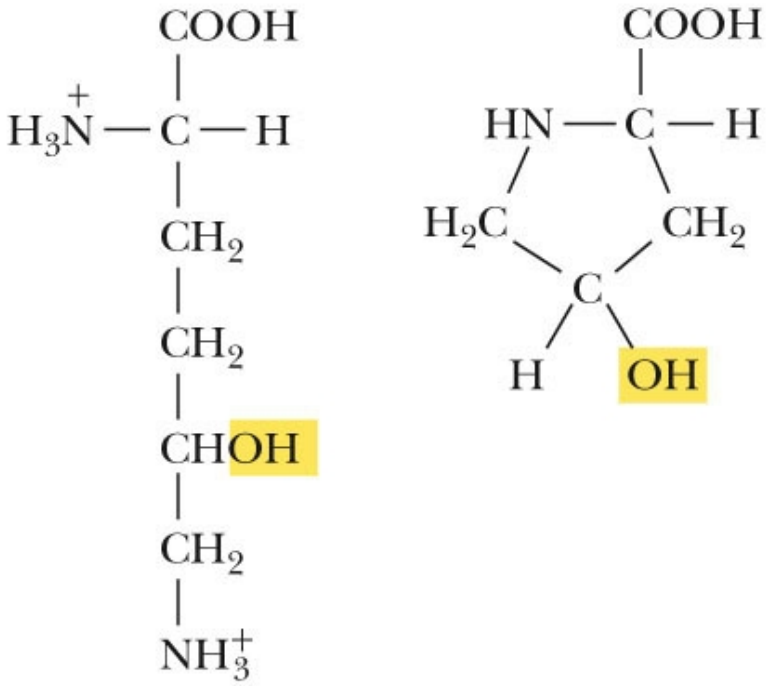


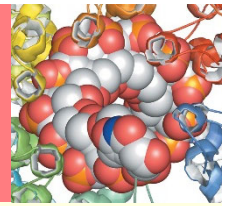
Figure 4.4 (b) Some amino acids are less common, but nevertheless found in certain proteins.

Hydroxylysine and hydroxyproline are found in connective-tissue proteins;

Carboxy-glutamate is found in blood-clotting proteins;

Pyroglutamate is found in bacteriorhodopsin

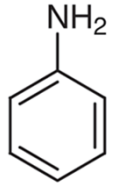
Adding New Chemistry to Proteins with **Unnatural Amino Acids (UAA)**



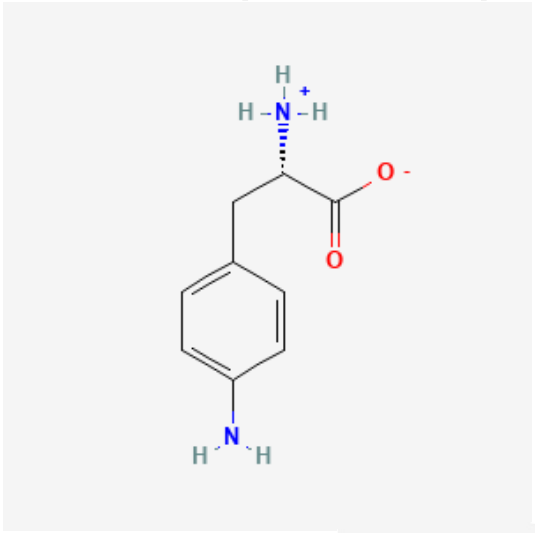
- Peter Schultz and co-workers have developed methods to incorporate **160** novel and **unnatural amino acids** (**UAAs**) in proteins in *E. coli*, yeast, and mammalian cells.
- Incorporation of **UAAs** at unique sites in proteins enables an array of new methods for study of structure and function in these proteins.
- Also, **UAA** methodology has **therapeutic potential** for development of **novel** antibodies, immunotoxins, and vaccines.

p-Aminophenylalanine

a)



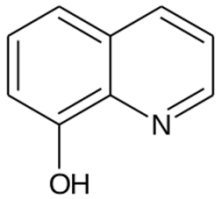
aniline



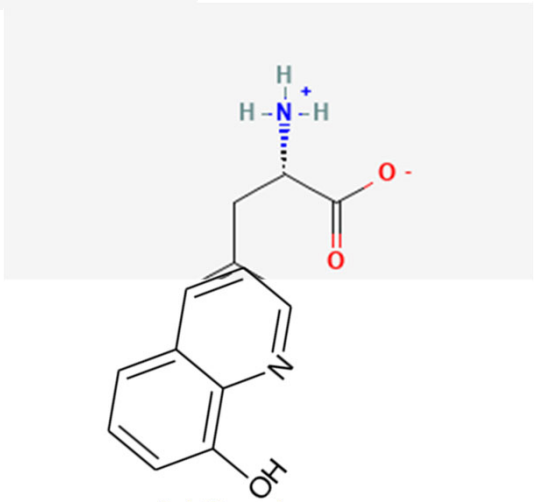
Aniline is the simplest aromatic amine. It is an industrially significant commodity chemical, as well as a versatile starting material for fine chemical

Designer enzyme

b)



8-hydroxyquinoline

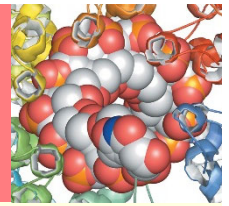


HQ-ala

Metalloenzyme

used as chelating ligand (Cu^{+2}, Zn^{+2})

4.2 What Are **Acid-Base** Properties of Amino Acids?



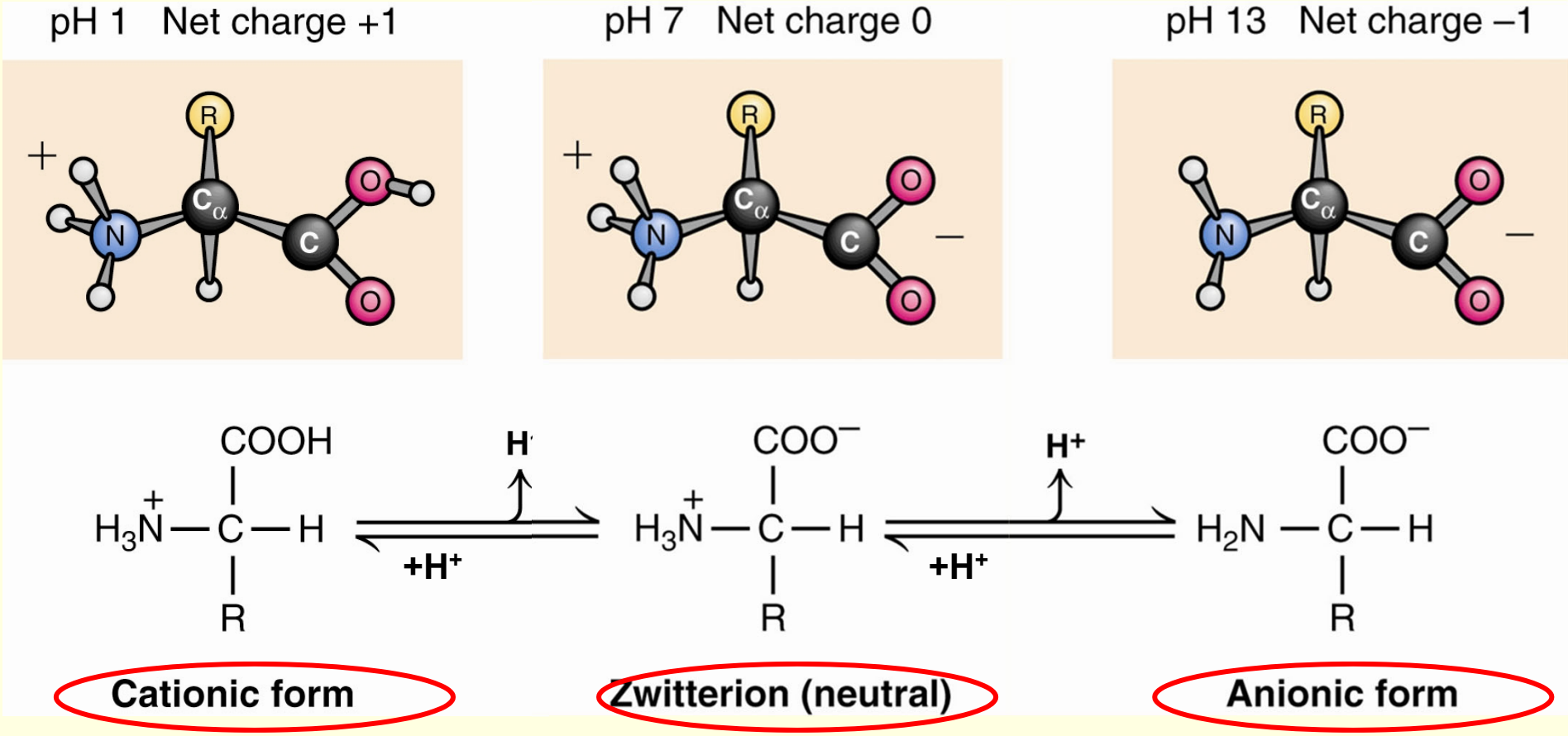
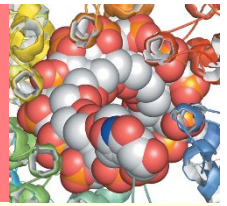


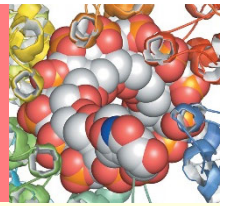
Figure 4.5 The ionic forms of the amino acids, shown without consideration of any ionizations on the side chain.

4.2a *Amino Acids are* ***Weak Polyprotic Acids***



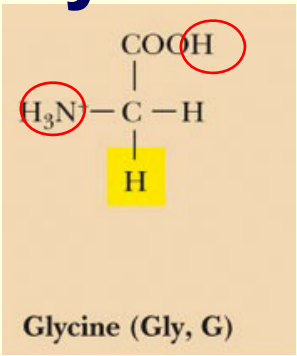
- ***Amino Acids are Weak Polyprotic Acids***
- *The degree of dissociation depends on the pH of the medium*

4.2a *Amino Acids are* ***Weak Polyprotic Acids***



- *The 1st dissociation*

Glycine



$$Gly^{+} + H_2O \rightarrow Gly^{0} + H_3O^{+}$$

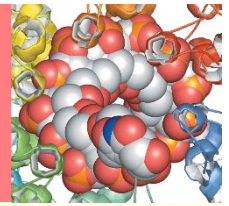
$$K_1 = \frac{[Gly^{0}]\,[H_3O^{+}]}{[Gly^{+}]}$$

The 2nd dissociation :

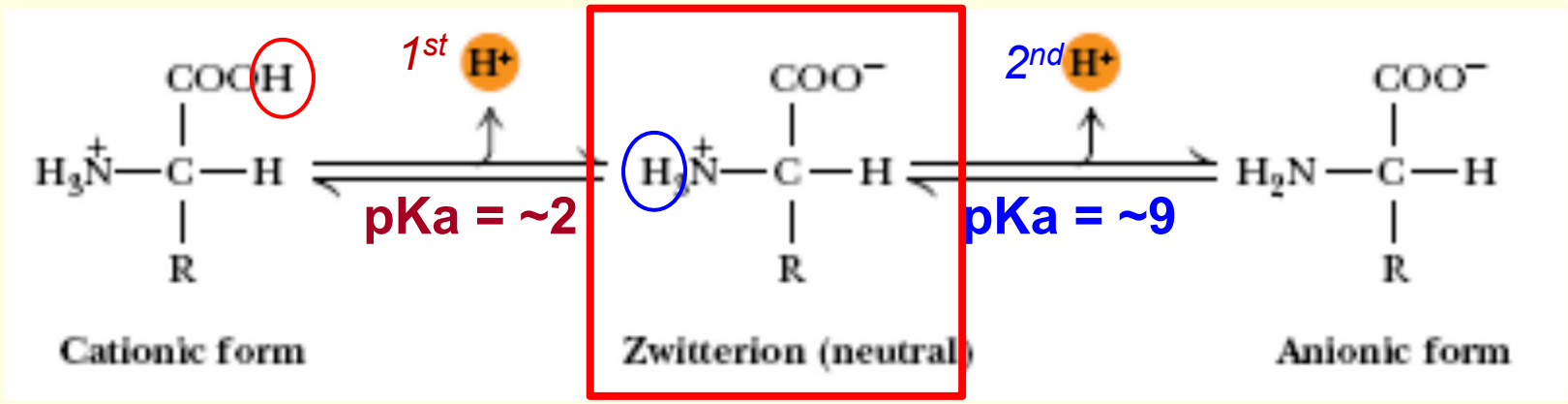
$$Gly^{0} + H_2O \rightarrow Gly^{-} + H_3O^{+}$$

$$K_2 = \frac{[Gly^{-}]\,[H_3O^{+}]}{[Gly^{o}]}$$

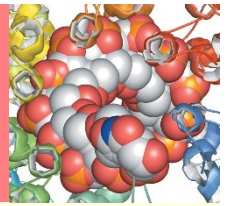
pK_a Values of the Amino Acids

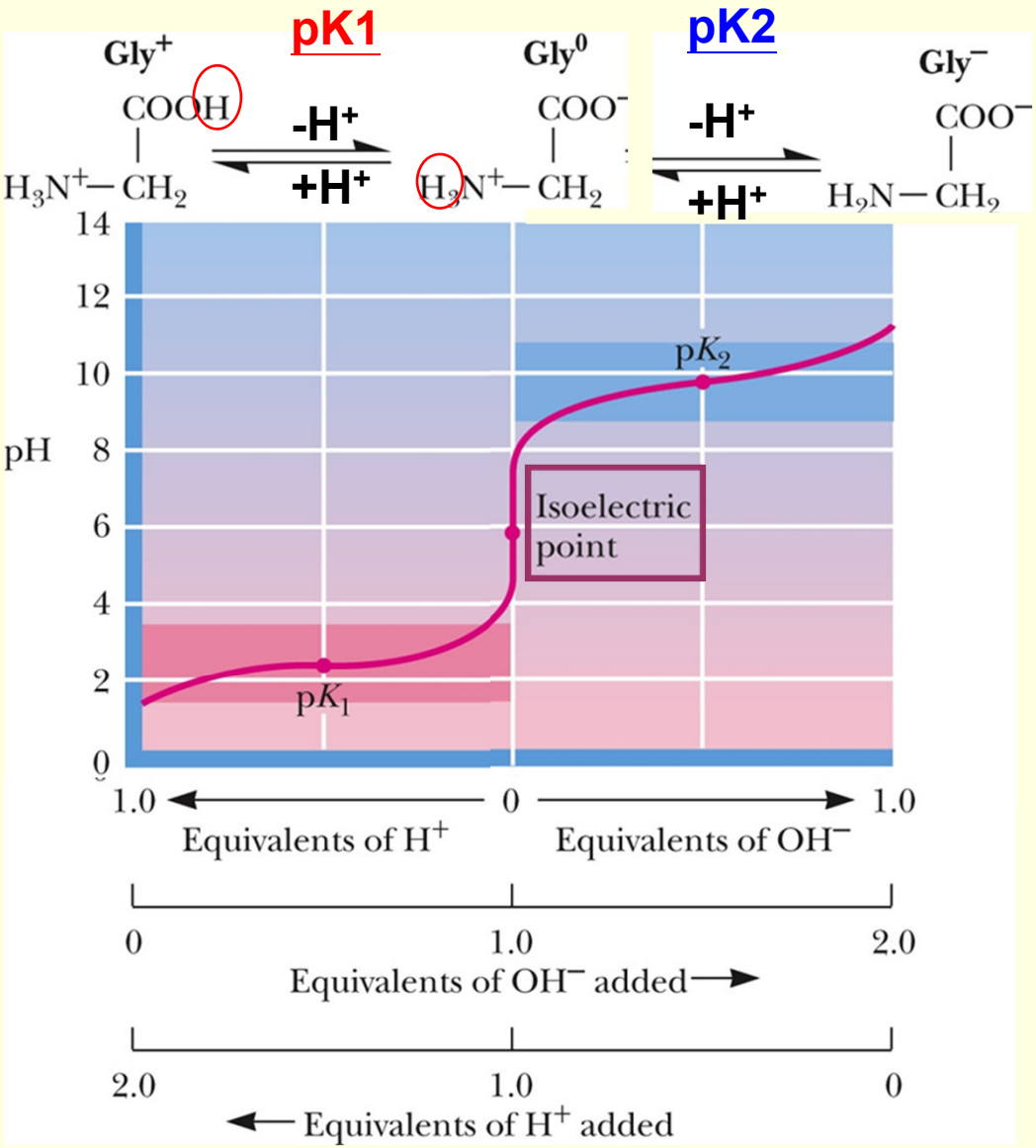


- Alpha carboxyl group pK_a = 2-2.4
- Alpha amino group - pK_a = 9-9.8



4.2 What Are Acid-Base Properties of Amino Acids?





Titration of glycine

Isoelectric point (pI) the pH where the molecule has a net charge of **0**, is defined as **(p*K*1+ p*K*2)/2**.

4.2 What Are Acid-Base Properties of Amino Acids?

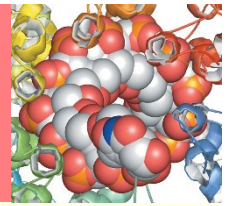
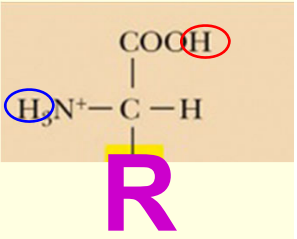


TABLE 4.1 pK_a Values of Common Amino Acids

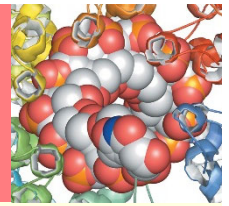
Amino Acid	α-COOH pK_a	α-NH_3^+ pK_a	R group pK_a
Alanine	2.4	9.7	
Arginine	2.2	9.0	12.5
Asparagine	2.0	8.8	
Aspartic acid	2.1	9.8	3.9
Cysteine	1.7	10.8	8.3
Glutamic acid	2.2	9.7	4.3
Glutamine	2.2	9.1	
Glycine	2.3	9.6	
Histidine	1.8	9.2	6.0
Isoleucine	2.4	9.7	
Leucine	2.4	9.6	
Lysine	2.2	9.0	10.5
Methionine	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	

pKa ~ 2

pKa ~ 9



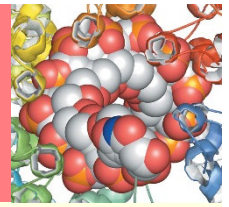
pK_a Values of the Amino Acids



- **Acidic Residues**
- Aspartic Acid, Asp, D: $pK_a = 3.9$
- Glutamic Acid, Glu, E: $pK_a = 4.3$

- **Basic Residues**
- Arginine, Arg, R: pK_a(guanidino group) = 12.5
- Lysine, Lys, K: $pK_a = 10.5$

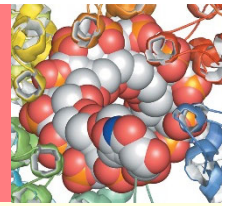
pK_a Values of the Amino Acids



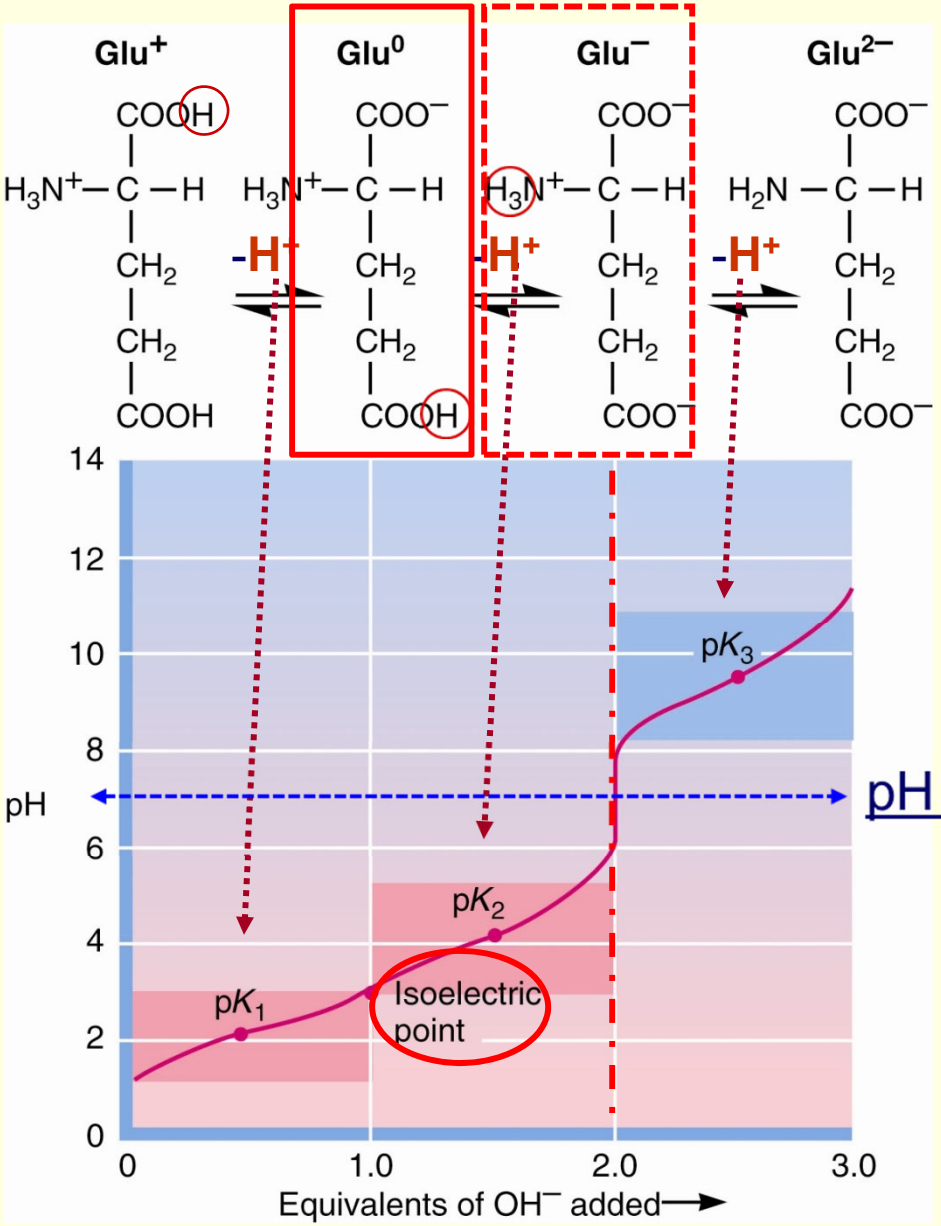
Polar, uncharged amino acids

- Histidine, His, H: pK_a = 6.0
- Cysteine, Cys, C: pK_a = 8.3
- Serine, Ser, S: pK_a = ~13
- Threonine, Thr, T: pK_a = ~13
- Tyrosine, Tyr, Y: pK_a = 10.1

4.2b Side Chains of Amino Acids Undergo Characteristic Ionizations

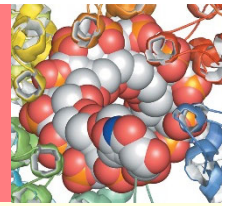


Titration of glutamic acid

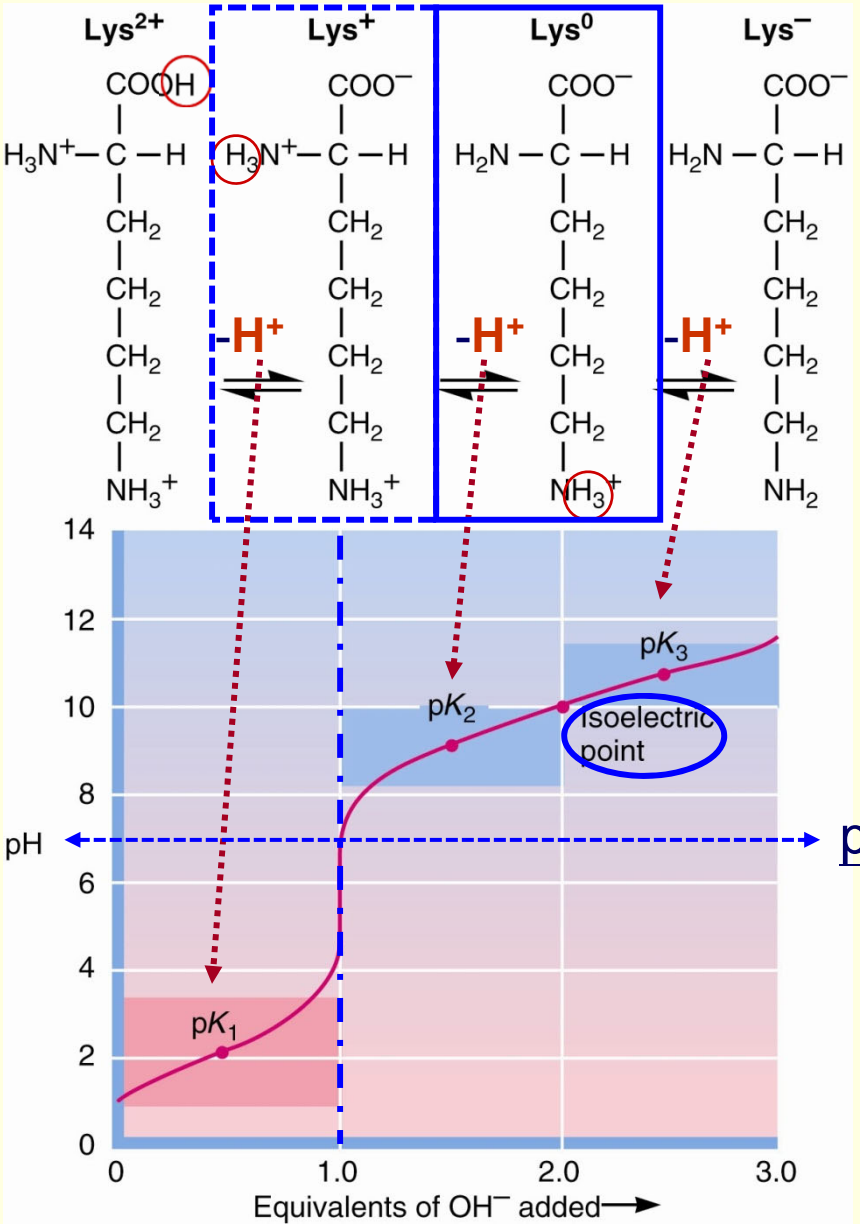


PI=(p*K*1+ p*K*2)/2

Titrations of polyprotic amino acids



Titration of lysine



pH ~7.0 “+”

Basic aa

PI=(p*K*2+ p*K*3)/2

Amino Acids are Weak Polyprotic Acids

Acid → Base

$$H_2A^+ + H_2O \rightarrow HA^0 + H_3O^+ \quad (\sim H_2O + H^+)$$

$$K_a = \frac{[HA^0][H_3O^+]}{[H_2A^+]}$$

$$-\log [H_3O^+] = pH = pK_a + \log \frac{[\text{Base}]}{[\text{Acid}]}$$

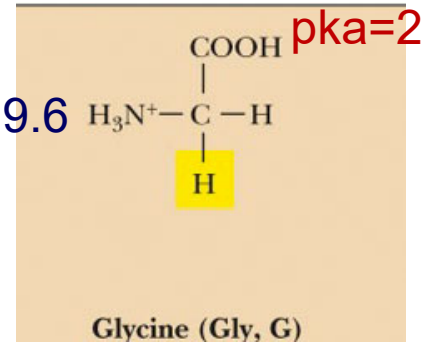
Henderson-Hasselbalch Equation

Example

What is the pH of a **glycine** solution if αNH_3^+ is **1/3** dissociated?

Glycine: $Gly^+ + H_2O \rightarrow Gly^0 + H_3O^+$ 1st

$Gly^0 + H_2O \rightarrow Gly^- + H_3O^+$ 2nd



- $pH = pK_{a1} + \log \frac{[Base]}{[Acid]}$

$pH = pKa + \log([Gly^-]/[Gly^o])$

$= 9.6 + \log(1/2)$

$= 9.3$

Example

a) What is the pH of a 0.3M solution of Leucine hydrochloride solution ?
b) What is the pH of a 0.3M solution of Leucinate?
c) What is the pH of a 0.3M solution of isoelectric Leucine?

a) pKa=2.4, (pKa of αCOOH)
$Ka=10^{-pka}=10^{-2.4}=3.98\times10^{-3}$

Assume only a small amount of H_2A^+ discoiated

$$H_2A^+ + H_2O \rightarrow HA^0 + H_3O^+$$

$$0.3-x \qquad x \qquad x$$

$$K_a = \frac{[HA^0][H_3O^+]}{[H_2A^+]}$$

$=x^2/0.3-x$
$X=3.45\times10^{-2}$
$pH=-\log(X=3.45\times10^{-2})$
$pH=1.46$

b) $HA^o + H_2O \rightarrow A^- + H_3O^+$

$A^- + H_2O \rightarrow HA^0 + OH^-$

Assume only a small amount of A^- protonated

pKa=9.6(pKa of αNH3⁺), Kb=14-9.6=4.4
$Kb=10^{-pkb}=10^{-4.4}=3.98\times10^{-5}$

$$K_b = \frac{[HA^0][OH^-]}{[A^-]}$$

$=x^2/0.3-x$
$X=3.46\times10^{-3}=[OH^-]$
$pOH=2.46$

Then pH=14-2.46=11.54

c)

isoelectric Leucine= 2.4+9.6/2=6.0