Amino acids

College of medicine
Second stage

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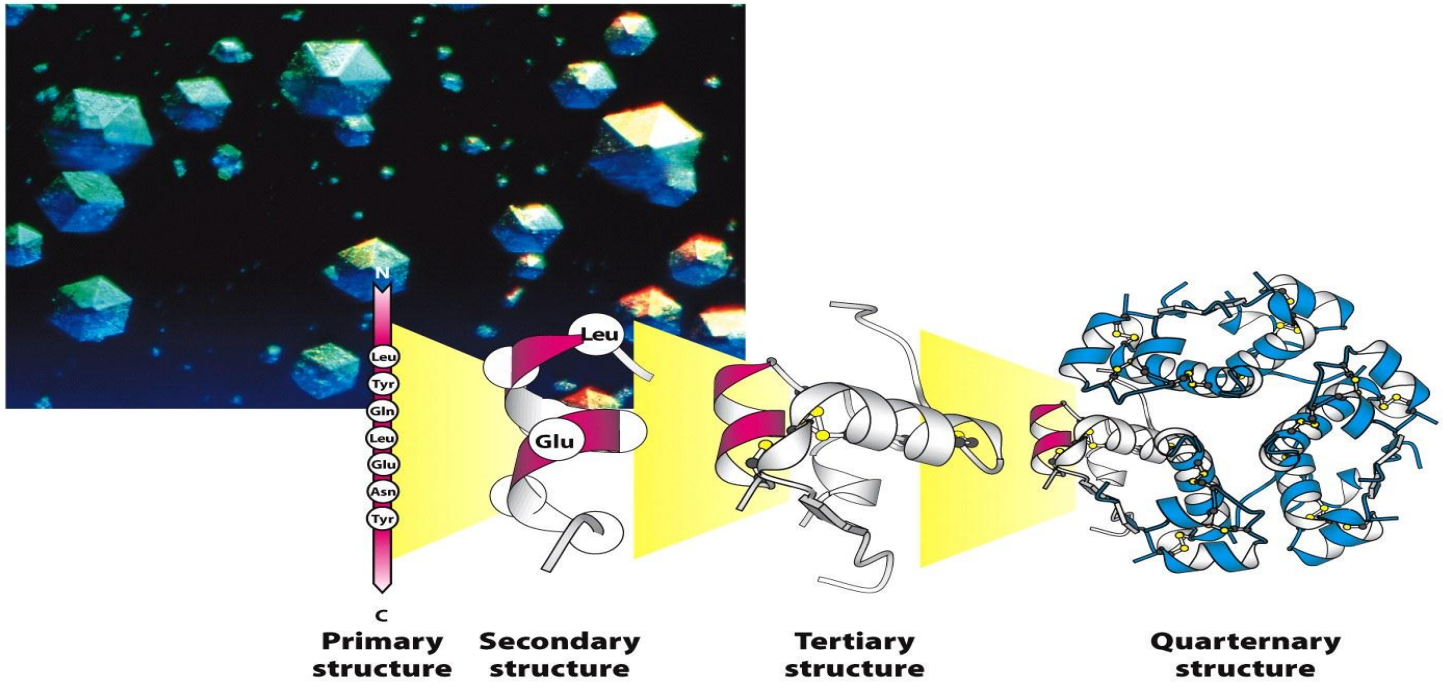
Amino Acids

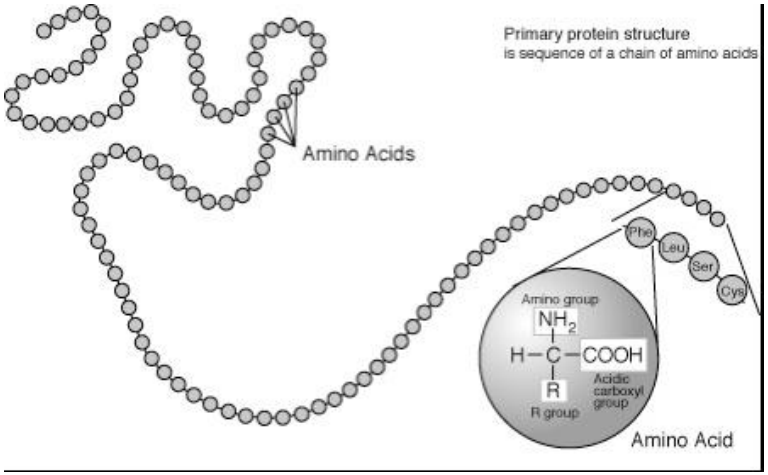
- Proteins are polymers of amino acids.
- A protein's amino acid sequence is know as the protein's primary structure.
- The amino acid sequence (primary structure) determines its three-dimensional structure (conformation).
- In turn, a protein's structure determines the function of that protein.



Protein Structure

1. **Proteins are amino acid polymers. Amino acids join via peptide bonds.**

2. **The functional groups of amino acids account for the large variety in protein function:**
   - **Structure.**
   - **Catalysis (enzymes).**
   - **Regulation: interaction with other proteins and macromolecules (DNA, RNA, carbohydrates).**



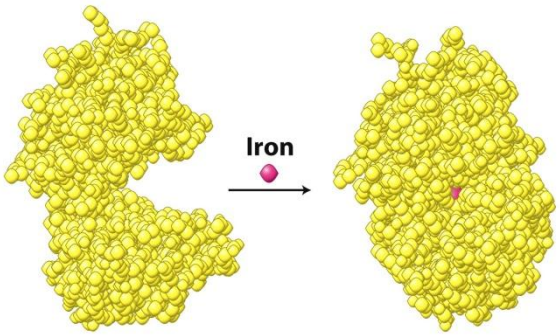


Figure 2.3
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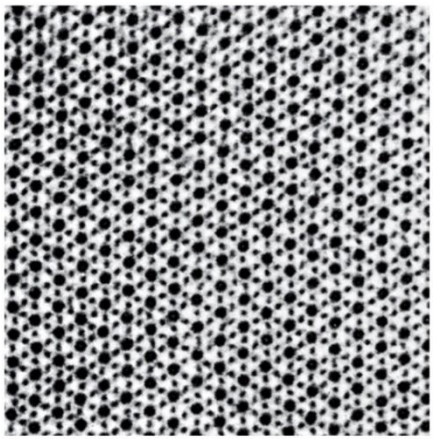

Figure 2.2
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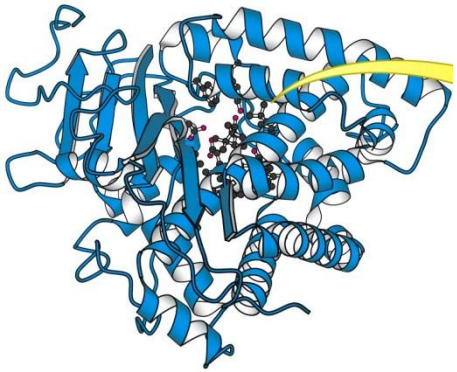

Figure 8.5
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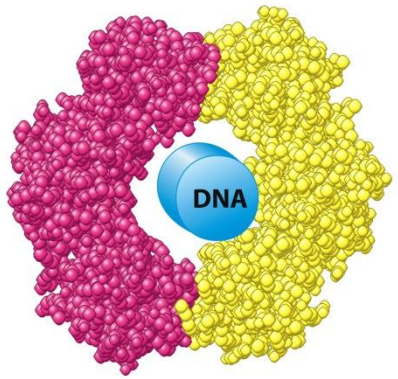

Figure 2.1
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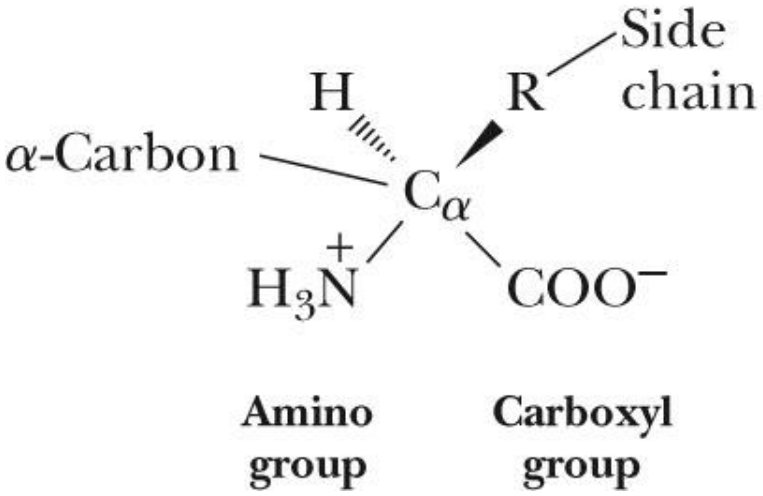
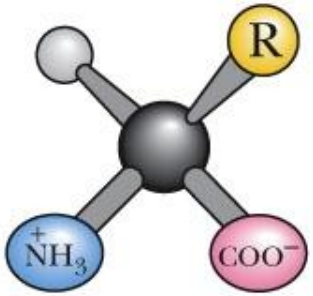
https://sites.google.com/site/mrsebiology97/cell-chemistry-objective-1d-1e

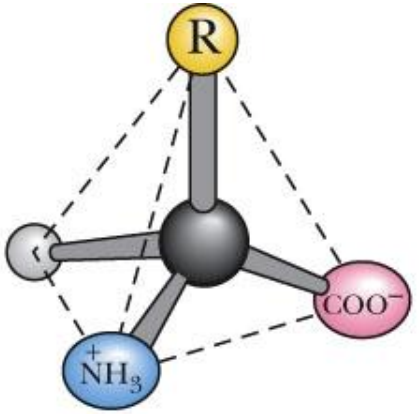
Structures and Properties of Amino Acids

Amino acids contain a central tetrahedral carbon atom.





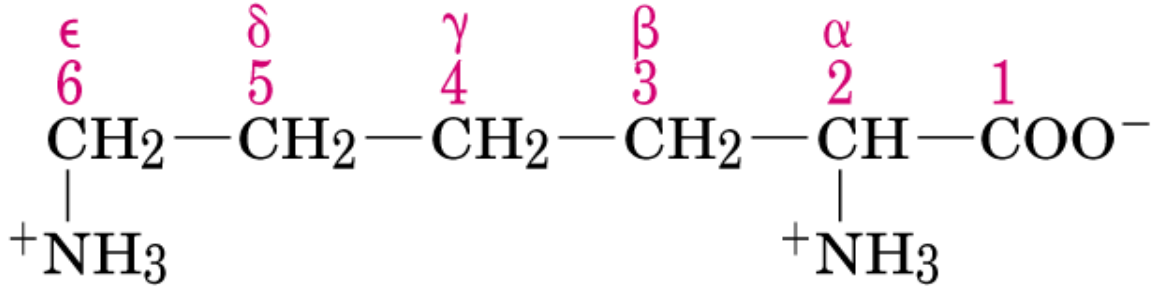
Ball-and-stick model



Amino acids are tetrahedral structures

All of the amino acids commonly found in proteins possess this type of structure except for proline and its derivatives.

How to assign the position of carbon in an amino acid?



Lysine

a) The numerical number,1,2,3, . . . , or Roman symbol, α β,γ, . . . , can be used to assign the position of carbons in a molecule.

b) If numeric number is used, it starts out from the carboxylic functional group being assigned as 1.

c) If Roman symbol is used, the carbon atom that directly covalently linked to the carboxylic acid is assigned as α.

Amino Acids

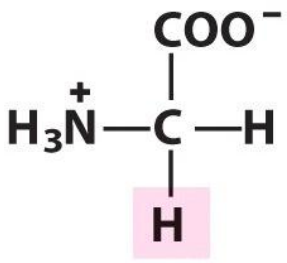
There are 20 common amino acids.

Table 2.2 Abbreviations for amino acids

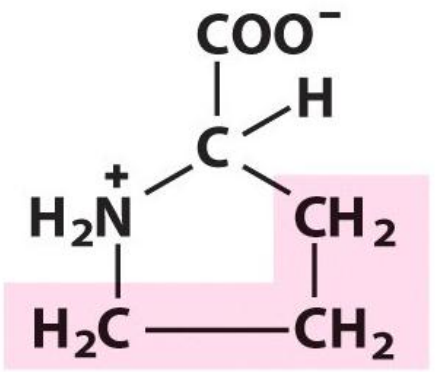
Amino acid	Three-letter abbreviation	One-letter abbreviation	Amino acid	Three-letter abbreviation	One-letter abbreviation
Alanine	Ala	A	Methionine	Met	M
Arginine	Arg	R	Phenylalanine	Phe	F
Asparagine	Asn	N	Proline	Pro	P
Aspartic acid	Asp	D	Serine	Ser	S
Cysteine	Cys	C	Threonine	Thr	T
Glutamine	Gln	Q	Tryptophan	Trp	W
Glutamic acid	Glu	E	Tyrosine	Tyr	Y
Glycine	Gly	G	Valine	Val	V
Histidine	His	H	Asparagine or aspartic acid	Asx	B
Isoleucine	Ile	I	Glutamine or glutamic acid	Glx	Z
Leucine	Leu	L			
Lysine	Lys	K			

The 20 Common Amino Acids

- **You should know names, structures, pKa values, 3-letter and 1-letter codes.**
- **Note these structural features**
  - **All 20 are α-amino acids.**
  - **For 19 of the 20, the α-amino group is primary; for proline it is secondary.**
  - **With the exception of glycine, the α-carbon of each is a stereocenter.**
  - **L-amino acids predominate in nature.**



Glycine



Proline

Amino Acid Classification

Amino acids are classified according to the physical & chemical properties of the side chains.

Five groups:

1) Non-polar aliphatic.

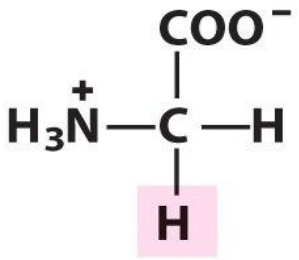
2) Aromatic.

3) Polar uncharged.

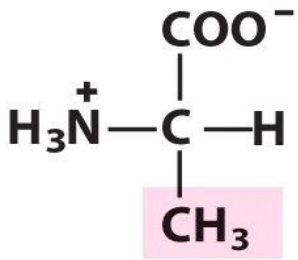
4) Positively charged (basic).

5) Negatively charged (acidic).

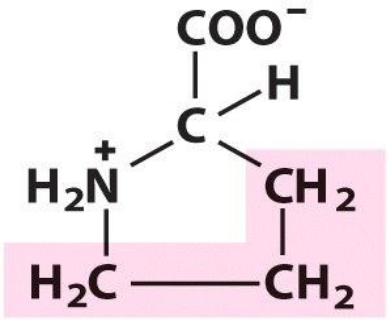
Nonpolar, aliphatic R groups



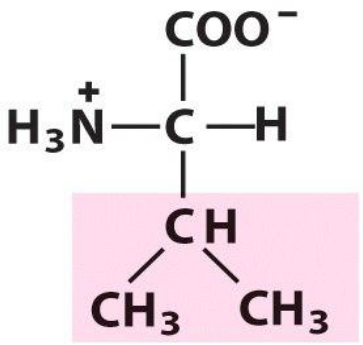
Glycine



Alanine



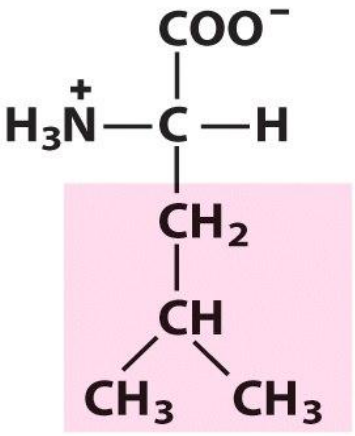
Proline



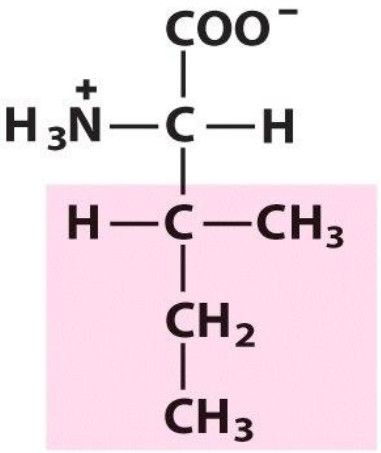
Valine

Ala, Val, Leu, Ile, Pro- contain aliphatic hydrocarbon group. Pro has cyclic structure.

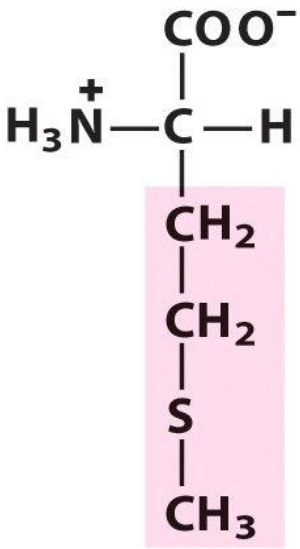
Met- Sulfur atom in side chain.



Leucine



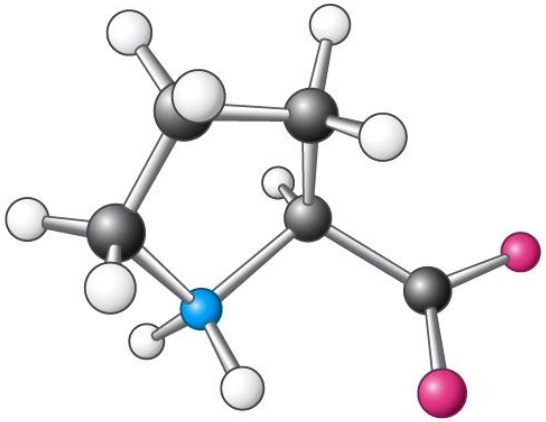
Isoleucine

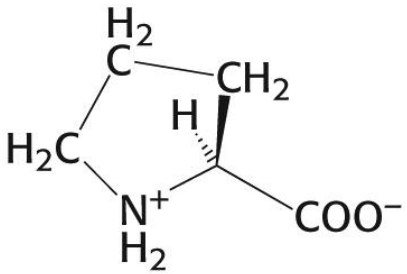


Methionine

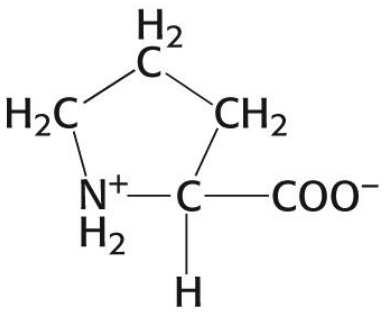
Cyclic structure of proline

- Pro has an aliphatic side chain bonded to both the α-carbon and α-amino group.
- Rigid ring structure.
- Is an "imino acid“ containing secondary amine group.

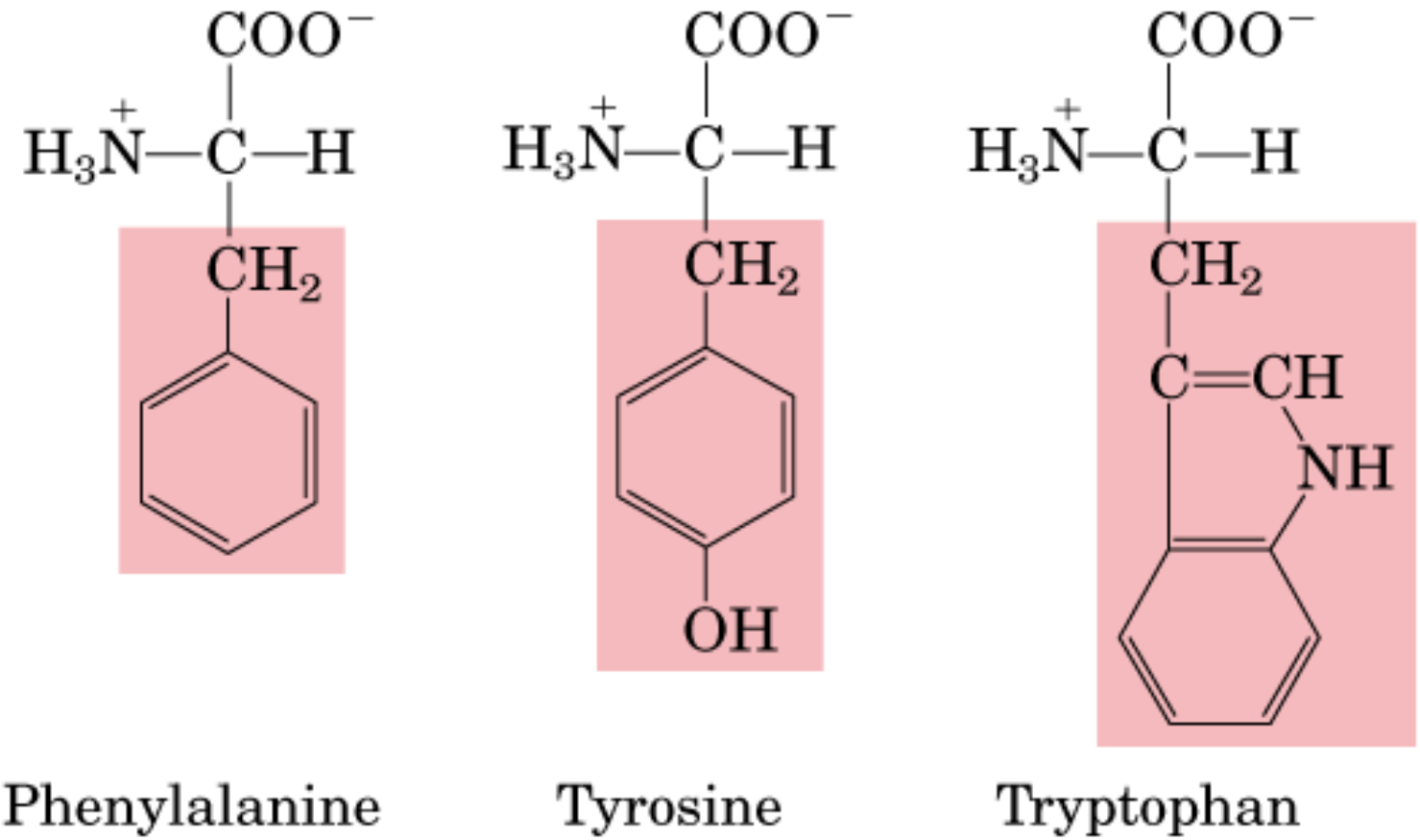




Proline
(Pro, P)



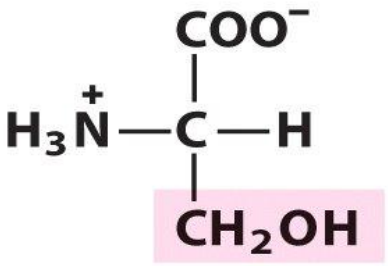
Aromatic R groups



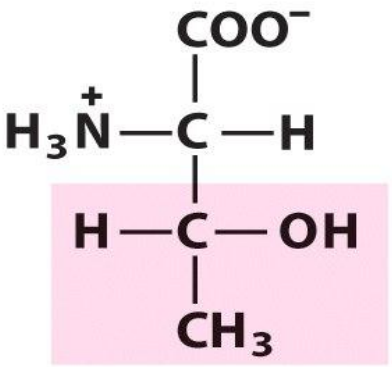
Phenylalanine Tyrosine Tryptophan

- **Phe, Tyr- hydrocarbon aromatic ring.**
- **Trp- Indole ring side chain, aromatic.**

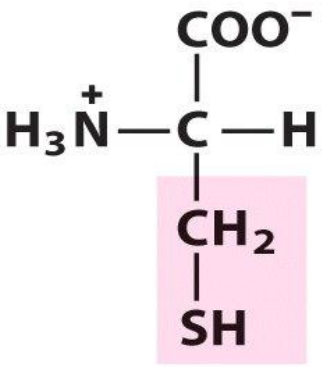
Polar, uncharged R groups



Serine

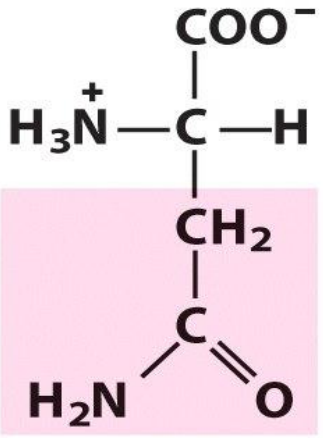


Threonine

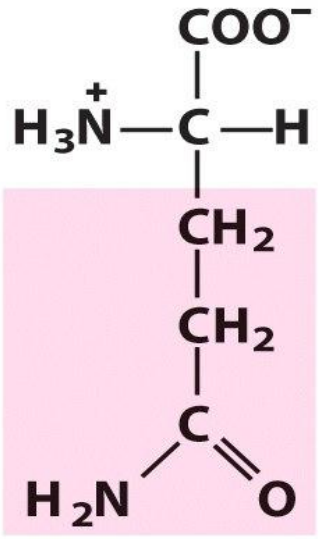


Cysteine

- Ser, Thr- polar hydroxyl group.
- Cys- Side chain contains thiol group (-SH).
- Gln, Asn- contain amide bonds in side chain

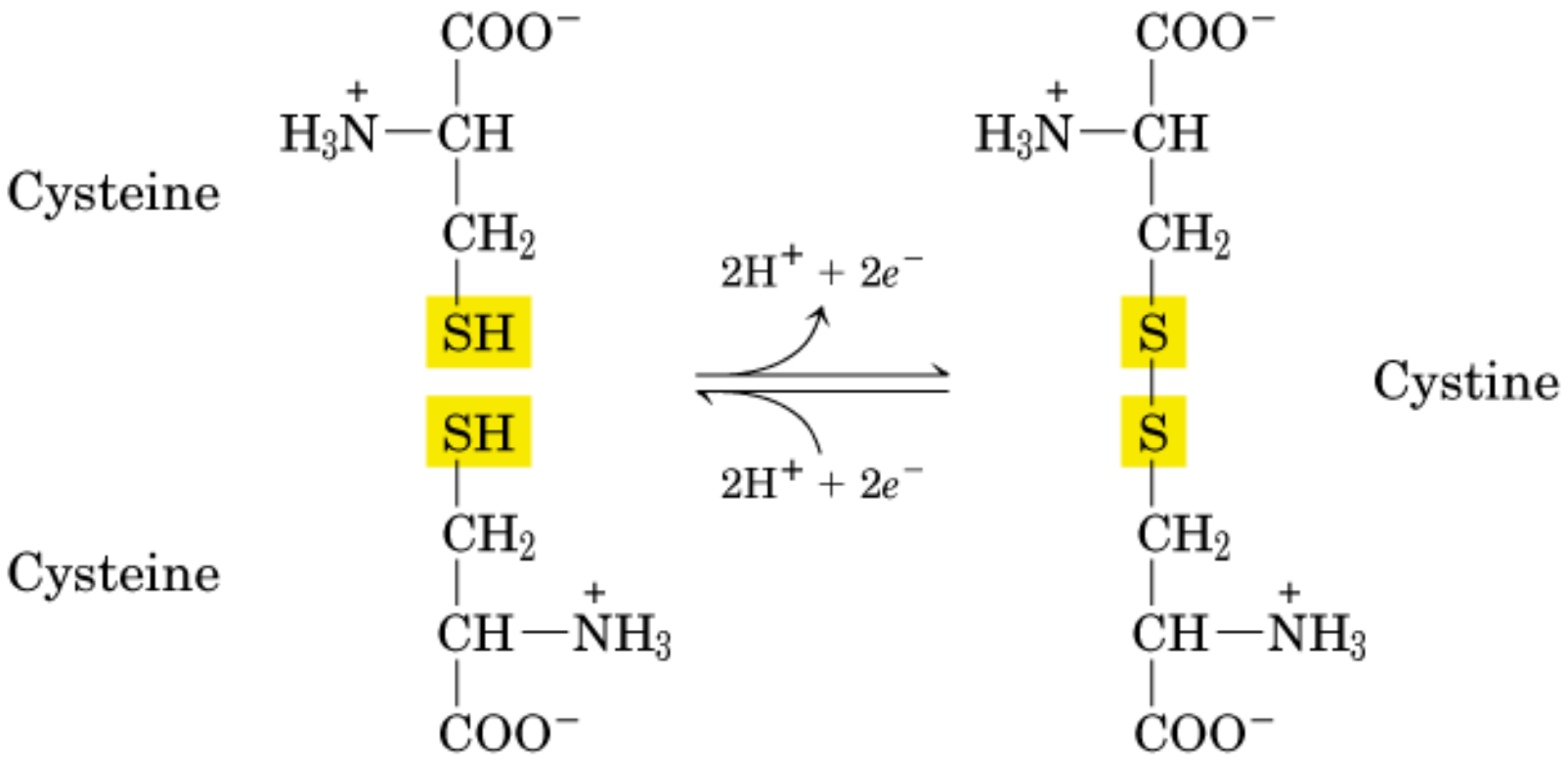


Asparagine

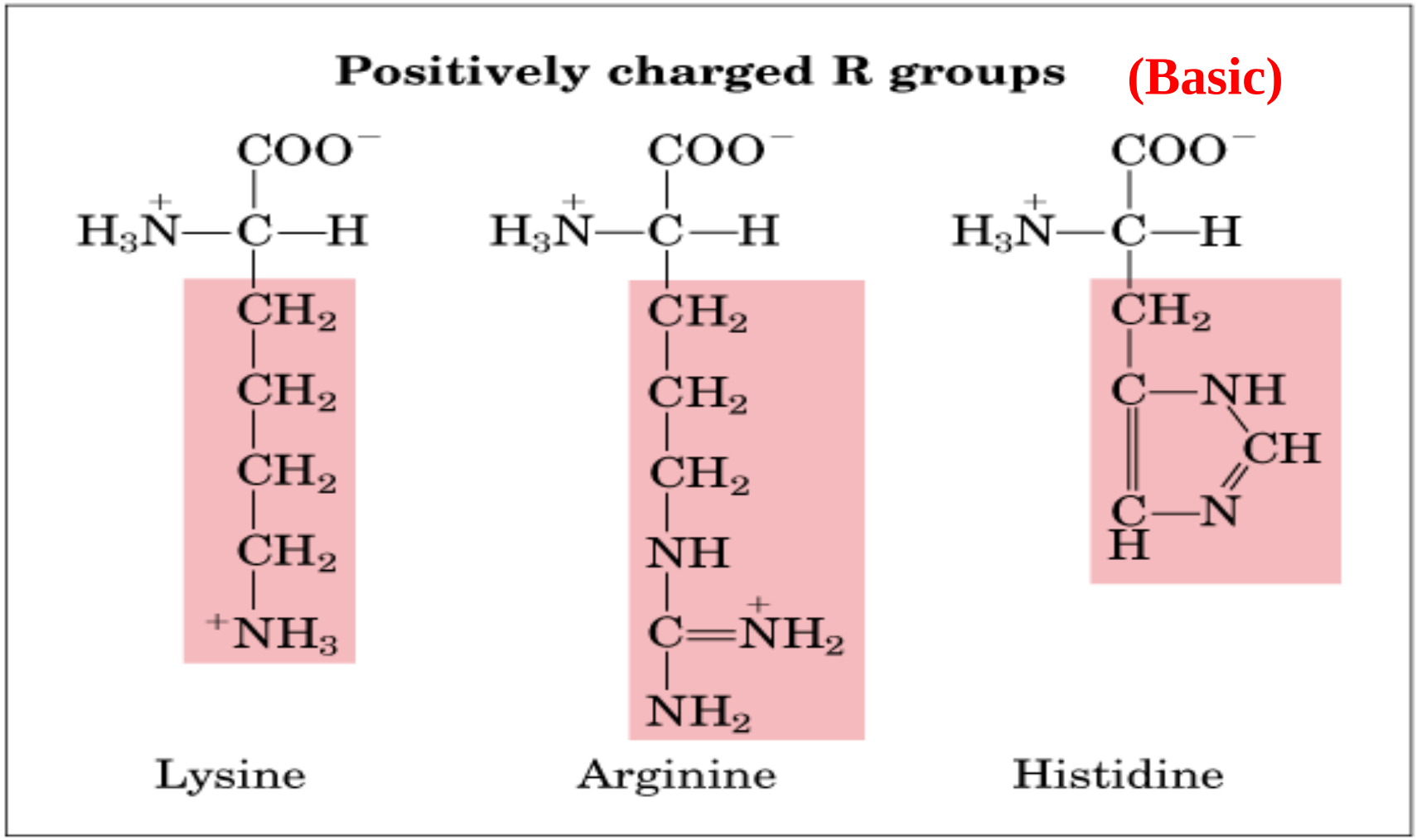


Glutamine

Reactions of Amino Acid Side Chains

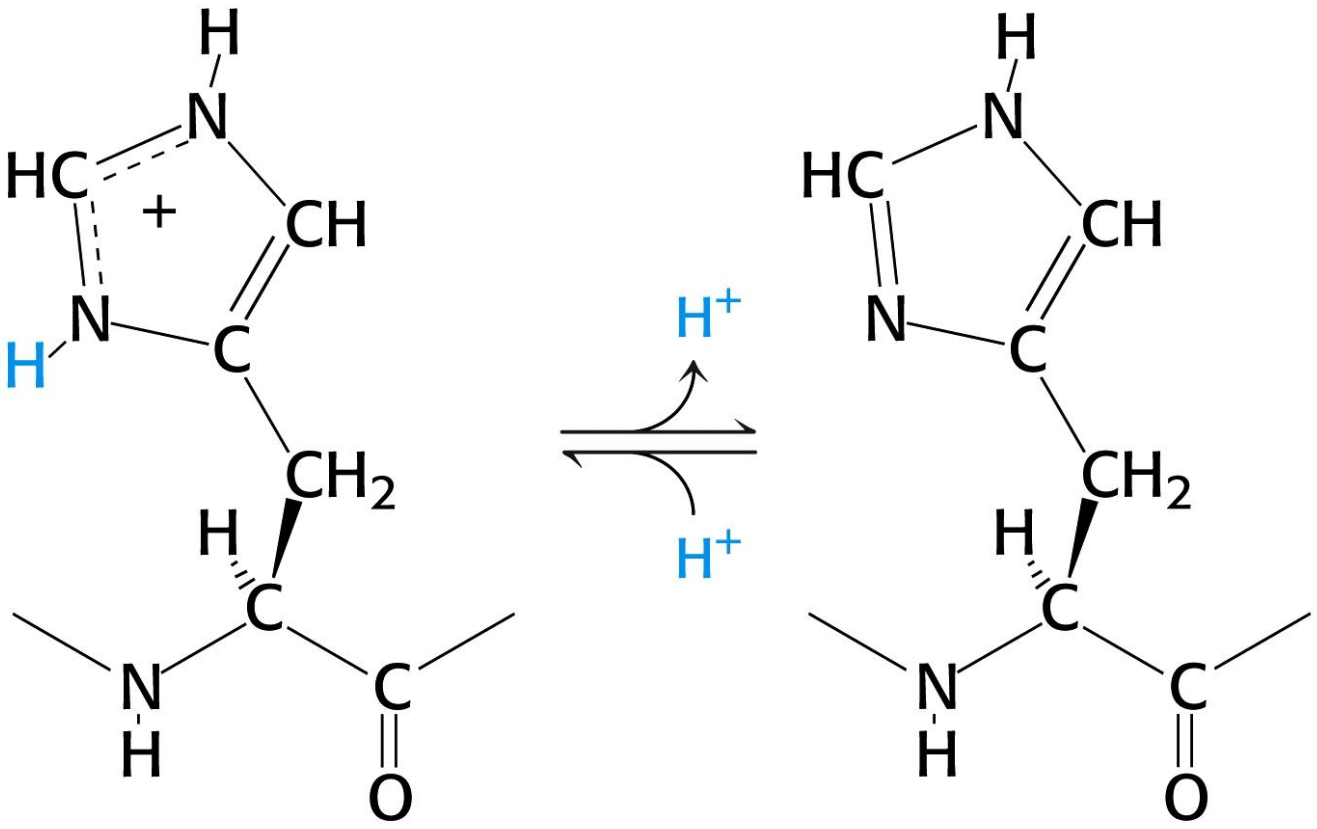


Cysteine residues react with each other to form disulfides. This reaction is an oxidation-reduction reaction.

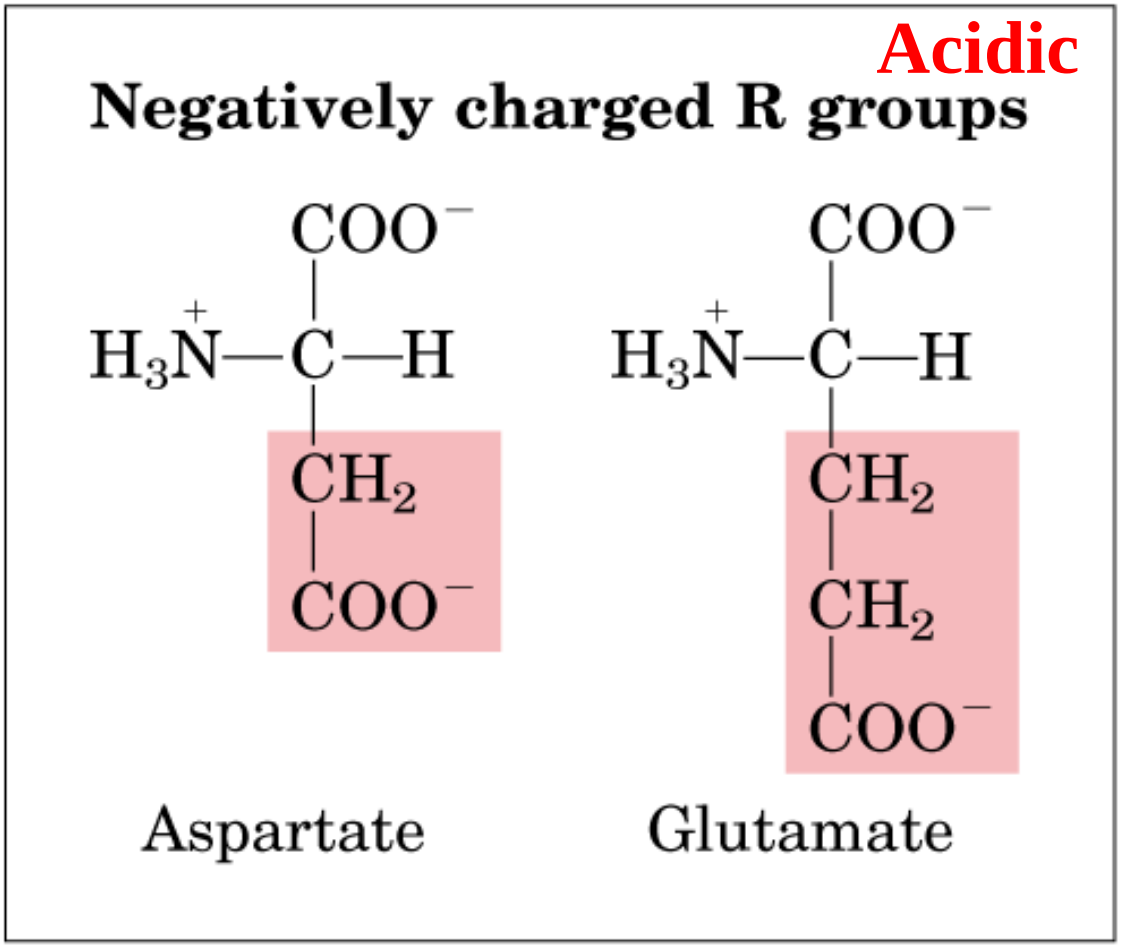


- Side chains are positively charged at pH 7.
- Arg-side chain is a guanidino group.
- His-side chain is an imidazole group.
- Lys-side chain NH_3 group is attached to an aliphatic hydrocarbon chain.

Histidine ionization



His can bind and release protons near physiological pH.



- Carboxyl group in side chain.
- Can lose a proton, forming a carboxylate ion.
- These amino acids are negatively charged at neutral pH.

Acidic Side Chains

- **Acidic Side Chains: Glu (E), Asp (D)**
- **Both have a carboxyl group in side chain**
- **Can lose a proton, forming a carboxylate ion**
- **These amino acids are negatively charged at neutral pH**

Three-letter and one letter codes - shorthand representation of the common amino acids

Table 2.2 Abbreviations for amino acids

Amino acid	Three-letter abbreviation	One-letter abbreviation	Amino acid	Three-letter abbreviation	One-letter abbreviation
Alanine	Ala	A	Methionine	Met	M
Arginine	Arg	R	Phenylalanine	Phe	F
Asparagine	Asn	N	Proline	Pro	P
Aspartic acid	Asp	D	Serine	Ser	S
Cysteine	Cys	C	Threonine	Thr	T
Glutamine	Gln	Q	Tryptophan	Trp	W
Glutamic acid	Glu	E	Tyrosine	Tyr	Y
Glycine	Gly	G	Valine	Val	V
Histidine	His	H	Asparagine or aspartic acid	Asx	B
Isoleucine	Ile	I	Glutamine or glutamic acid	Glx	Z
Leucine	Leu	L			
Lysine	Lys	K			

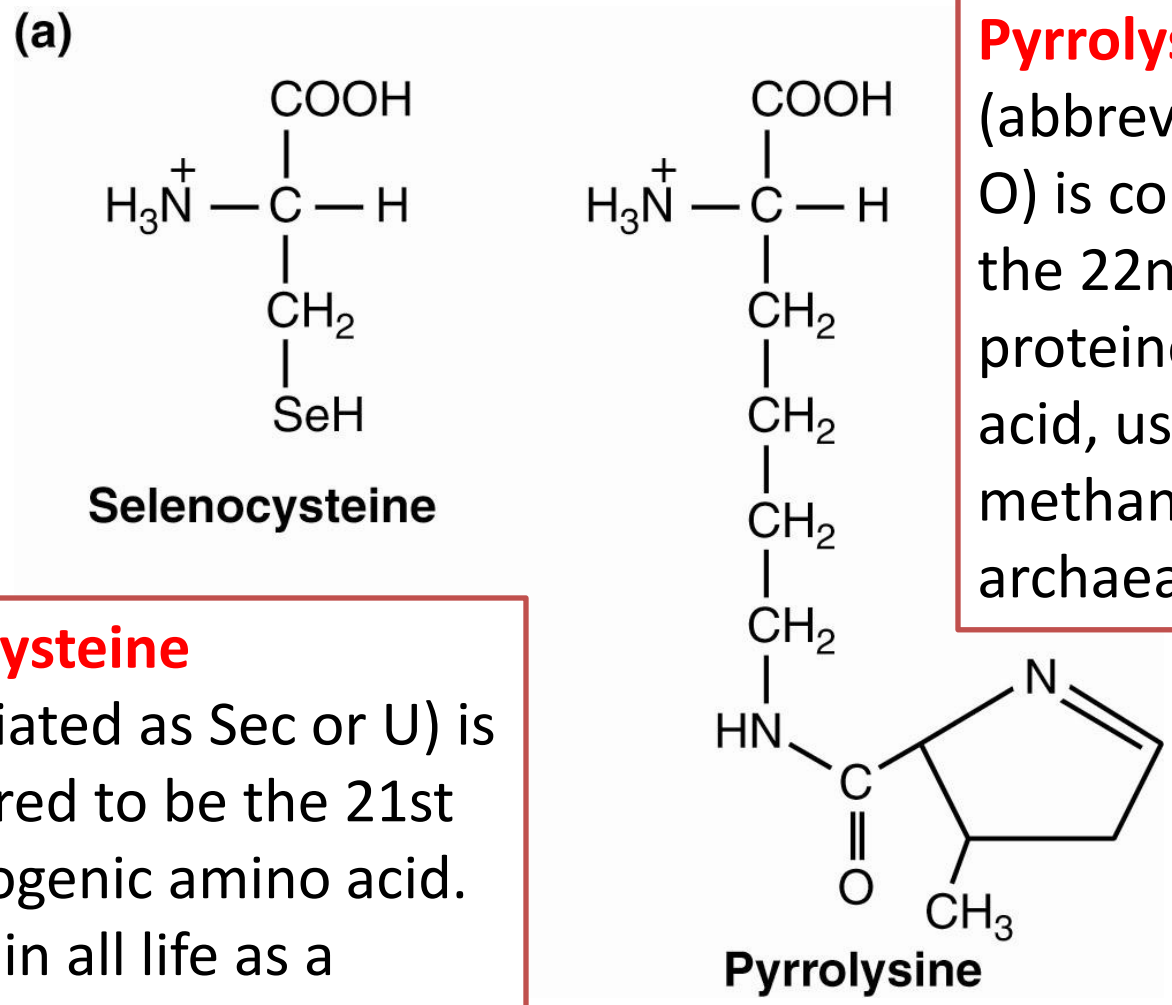
Table 2.2
Biochemistry, Seventh Edition

Several Amino Acids are Rare in Proteins

Modified amino acids:

- **Selenocysteine** in many organisms.
- **Pyrrolysine** in several archaeal species.
- **Hydroxylysine**, **hydroxyproline** – collagen.
- **Carboxyglutamate** - blood-clotting proteins.
- **Pyroglutamate** – in bacteriorhodopsin.
- **GABA**, **epinephrine**, **histamine**, **serotonin** act as neurotransmitters and hormones.
- **Phosphorylated** amino acids – a signaling device.

Several Amino Acids are Rare in Proteins

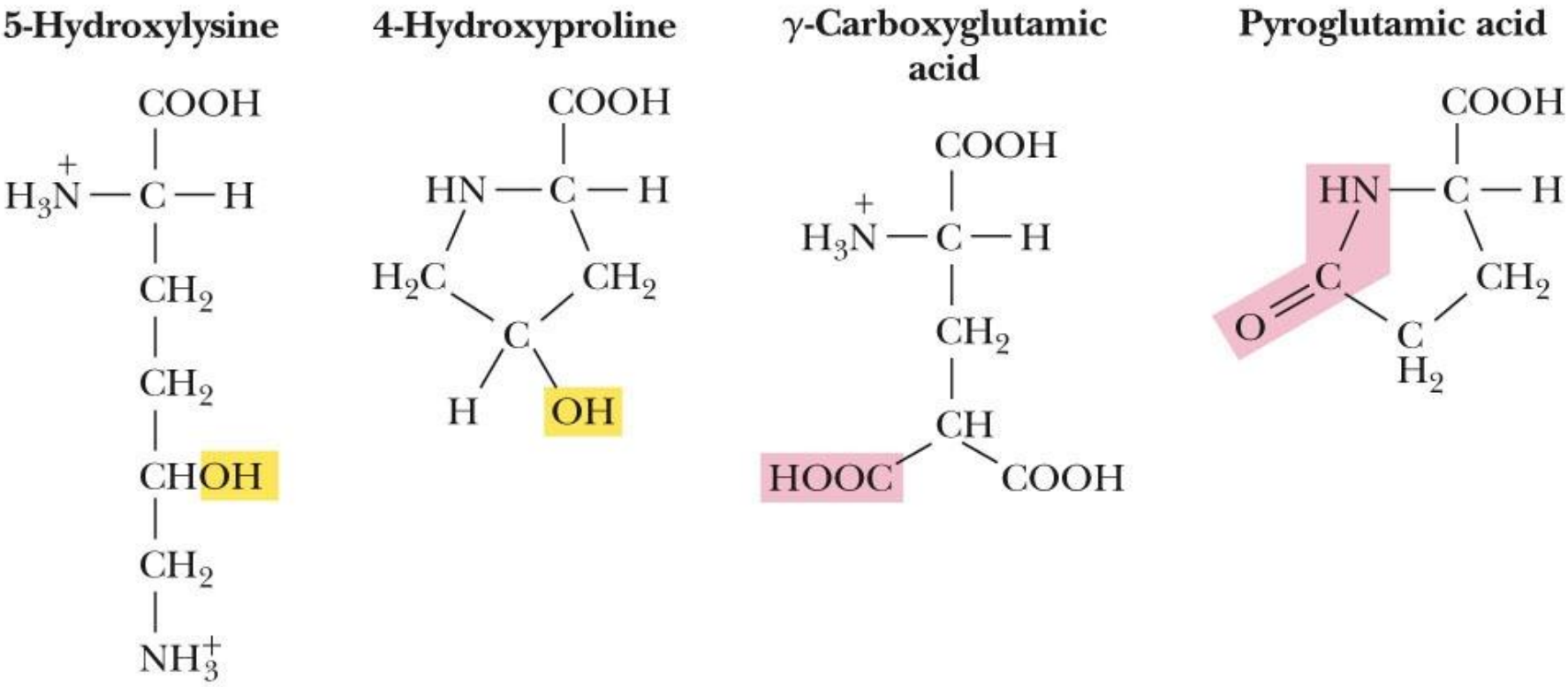


Selenocysteine
(abbreviated as Sec or U) is considered to be the 21st proteinogenic amino acid. It exists in all life as a building block of selenoproteins.

Pyrrolysine
(abbreviated as Pyl or O) is considered to be the 22nd proteinogenic amino acid, used by some methanogenic archaea.

Several Amino Acids are Rare in Proteins

(b)



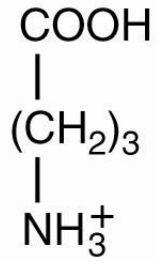
Hydroxylysine and hydroxyproline are found in connective-tissue proteins.

Carboxy-glutamate is found in blood-clotting proteins.

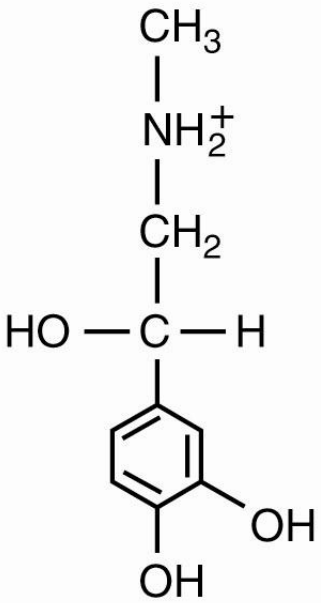
Pyroglutamate is found in bacteriorhodopsin.

Several amino acid derivatives act as neurotransmitters and hormones.

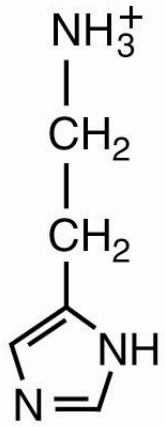
(c)



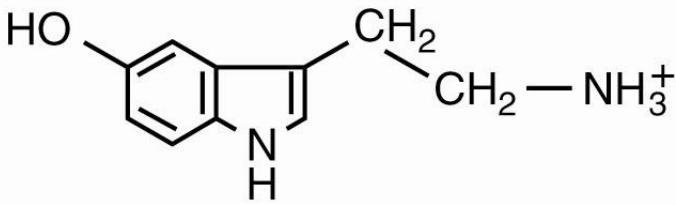
γ-Aminobutyric acid (GABA)



Epinephrine



Histamine



Serotonin

GABA, an integral part of the mammalian central nervous system, is derived from Glu.

Epinephrine (aka adrenaline) is a hormone and a neurotransmitter It is derived from Tyr.

Histamine is derived from decarboxylation of His. It involved in local immune responses and acting as a neurotransmitter

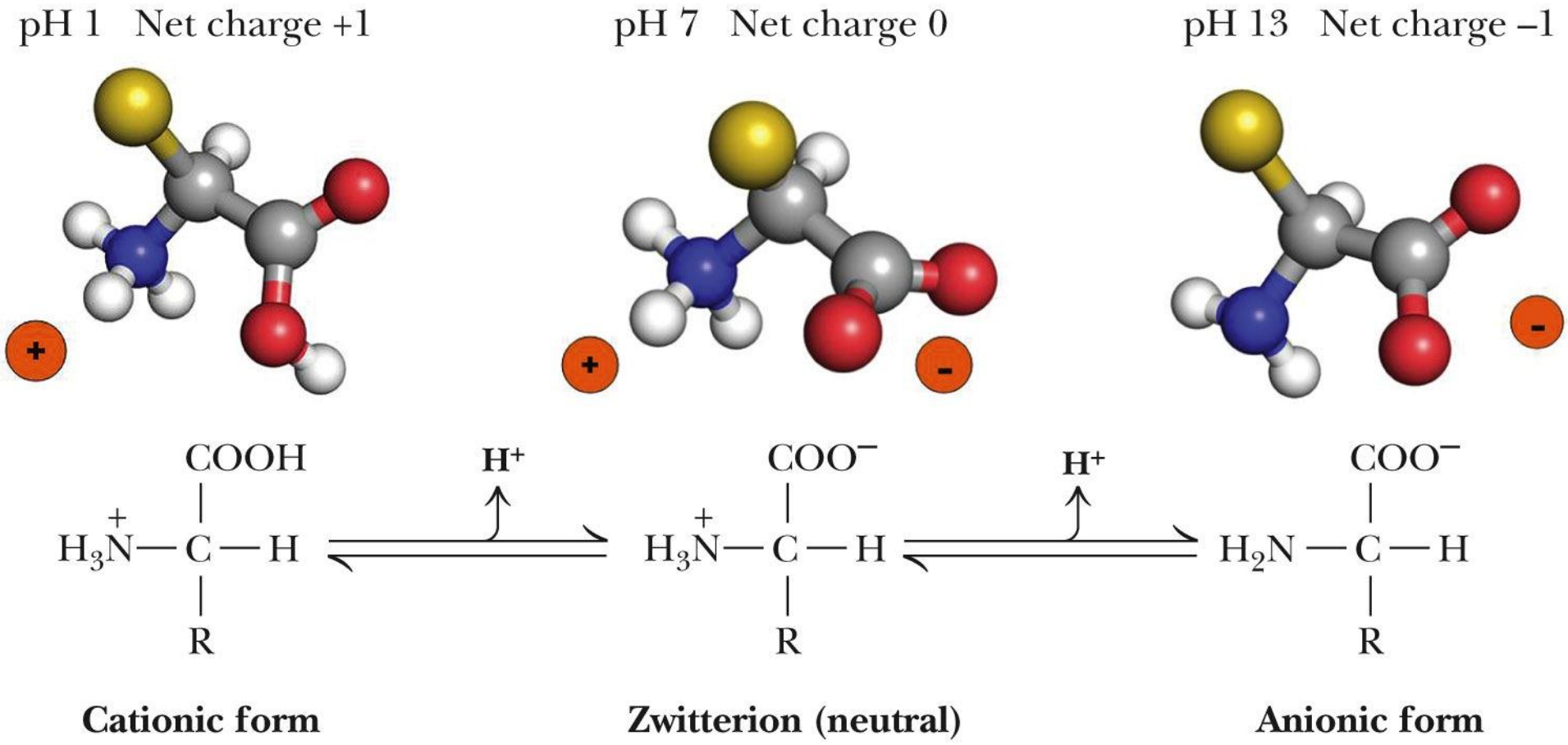
5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter. It is derived from tryptophan.

Biochemistry by Garret and Grisham, 5th ed.

Acid-Base Properties of Amino Acids

- **Amino acids are weak polyprotic acids.**
- **The degree of dissociation depends on the pH of the medium.**
- **All the amino acids contain at least two dissociable hydrogens.**
  - **-COOH**
  - **-NH_3^+**

Acid-Base Properties of Amino Acids



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

How to memorize the amino acids?

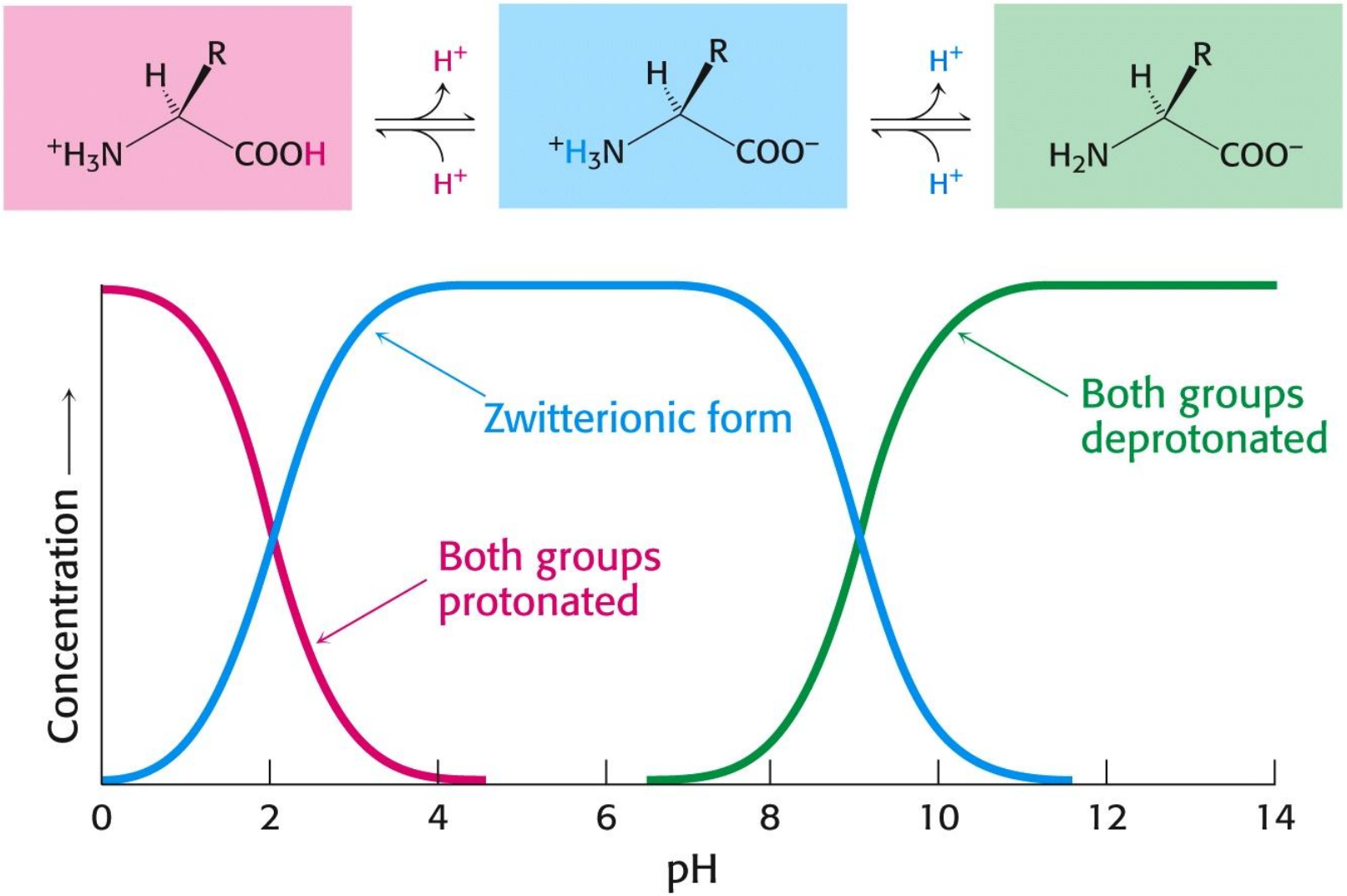
Video

pK_a Values of the Amino Acids

You should know these numbers and know what they mean.

- **Alpha carboxyl group: pK_a = 2.**
- **Alpha amino group: pK_a = 9.**
- **These numbers are approximate, but entirely suitable for our purposes.**

Ionization State of Amino Acids as a Function of pH



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	
Threonine	2.6	10.4	
Tryptophan	2.4	9.4	
Tyrosine	2.2	9.1	10.1
Valine	2.3	9.6	

Biochemistry by Garret and Grisham, 5th ed.

pK_a Values of the Amino Acids

You should know the pKa values for these R groups and what they mean.

- Arginine, Arg, R: pK_a(guanidino group) = 12.5
- Aspartic Acid, Asp, D: pK_a (β–carboxyl) = 3.9
- Cysteine, Cys, C: pK_a (sulfhydryl) = 8.3
- Glutamic Acid, Glu, E: pK_a (γ–carboxyl) = 4.3
- Histidine, His, H: pK_a (imidazole) = 6.0
- Lysine, Lys, K: pKa (e-amino) = 10.5
- Tyrosine, Tyr, Y: pKa (phenolic OH) = 10.1

The Isoelectric Point

- **The isoelectric point, pI, is the pH of an amino acid (or peptide) at which the molecules on average have no net charge.**
- **For simple amino acids such as alanine, the pI is an average of the pK_a's of the carboxyl (2.34) and ammonium (9.69) groups. Thus, the pI for alanine is calculated to be: (2.4 + 9.7)/2 = 6.05.**
- **If additional acidic or basic groups are present as side-chain functions, the pI is the average of the pK_a's of the two most similar acids.**
- **In the case of glutamic acid, the similar acids are the α-carboxyl group (pK_a = 2.2) and the side-chain carboxyl group (pK_a = 4.3), so pI = (2.2 + 4.3)/2 = 3.25.**
- **For arginine, the similar acids are the guanidinium species on the side-chain (pK_a = 12.5) and the α-NH_3^+ function (pK_a = 9.0), so the calculated pI = (12.5 + 9.0)/2 = 10.75.**

Ionization *vs.* pH

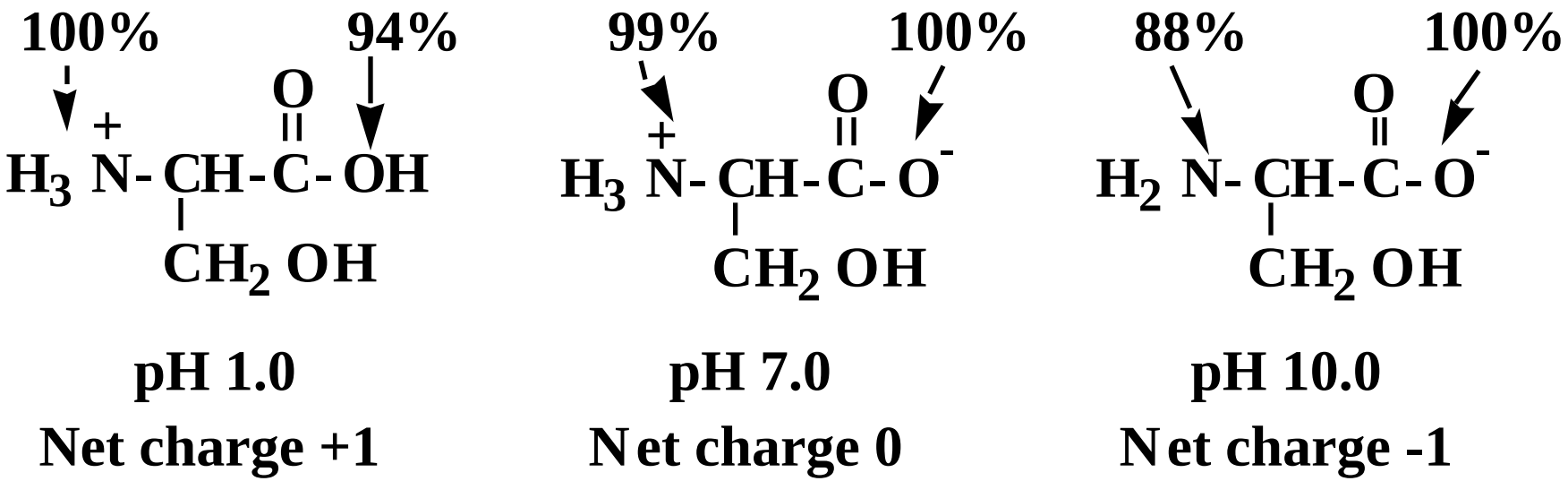
Given the value of pK_a of each functional group, we can calculate the ratio of each acid to its conjugate base as a function of pH using the Henderson-Hasselbalch equation.

$$pH = pK_a + \log \frac{[\text{conjugate base}]}{[\text{weak acid}]}$$

pKa tells us how acidic (or not) a given hydrogen atom in a molecule is.
pH tells us how acidic a solution is.

Henderson-Hasselbalch

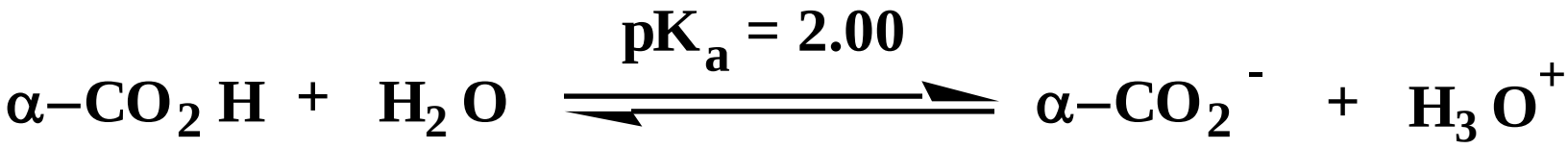
Using the Henderson-Hasselbalch equation, we can calculate the percent of acidic or conjugate base form present and the net charge of serine at pH 1.0, 7.0, and 10.0 (pka_1=2.21, pka_2=9.15).



At physiological pH, the α-carboxyl group of a simple amino acid (with no ionizable side chains) is completely dissociated, whereas the α -amino group has not really begun its dissociation.

Ionization vs. pH

- Consider the ionization of an α -COOH



- substituting the value of pK_a (2.00) and pH at 7.0 gives

  $7 = 2 + \log[COO^-]/[COOH]$

  $[COO^-]/[COOH] = 1 \times 10^5$

  – at pH 7.0, the α-carboxyl group is virtually 100% in the ionized or conjugate base form and has a charge of -1

$$pH = pK_a + \log \frac{[\text{conjugate base}]}{[\text{weak acid}]}$$

Ionization *vs.* pH

- We can repeat this calculation at any pH and determine the ratio of [α-COO^-] to [α-COOH] and the net charge on the α-carboxyl at that pH.
- We can also calculate the ratio of acid to conjugate base for an α-NH_3^+ group; for this calculation, assume a value 10.0 for pK_a

$$\alpha\text{–}NH_3^+ + H_2O \underset{}{\overset{pK_a = 10.00}{\rightleftharpoons}} \alpha\text{–}NH_2 + H_3O^+$$

Ionization *vs.* pH

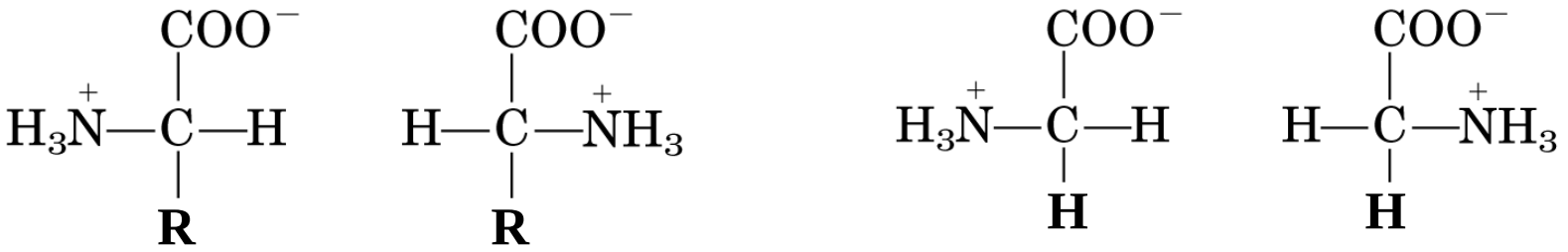
$7 = 10 + \log [NH_2] / [NH_3^+]$

- $[NH_2] / [NH_3^+] = 0.001$
- at pH 7.0, the ratio of α-NH_3^+ to α-NH_2 is approximately 1 to 1000
- at this pH, an α-amino group is 99.9% in the acid or protonated form and has a charge of +1

Stereochemistry of Amino Acids

- **All but glycine are chiral.**
- **L-amino acids predominate in nature.**
- **D, L-nomenclature is based on D- and L-glyceraldehyde.**
- **Isoleucine and threonine have two chiral centers.**

Stereochemistry of Amino Acids



19 amino acids are chiral molecules

Glycine is not a chiral molecule

Amino Acids

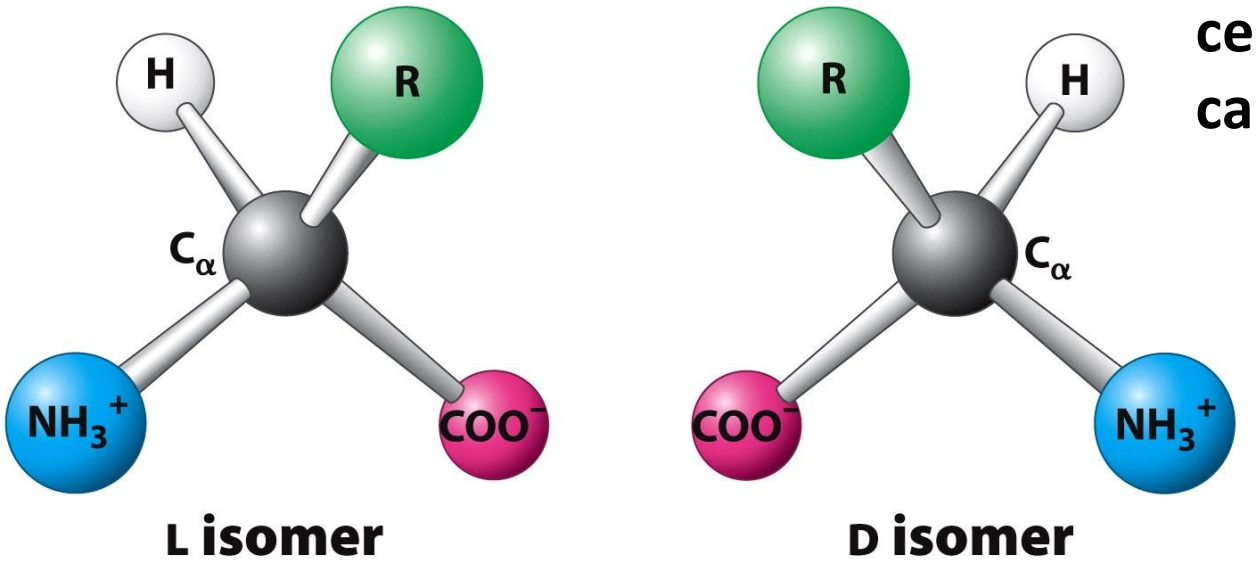


Figure 2.4
***Biochemistry*, Seventh Edition**

Amino acids contain a central tetrahedral carbon atom.

Only L-isomers are found naturally.

Remember: L=life.

Spectroscopic Properties

- All amino acids absorb at infrared wavelengths.
- Tyr, and Trp absorb UV at 280 nm.
- Absorbance at 280 nm is a good diagnostic test for proteins. It can be used to estimate the concentration of a protein in solution ($A=\varepsilon lc$), which is a nondestructive method for protein detection.
- The peptide bonds between amino acids absorb at 190 nm. Oxygen also absorb at this wavelength, so instead measurements can made at 205-210 nm.

Spectroscopic Properties

The UV spectra of the aromatic amino acids at pH 6. These strong absorptions can be used for spectroscopic determinations of protein concentration.