Amino Acids and Peptides

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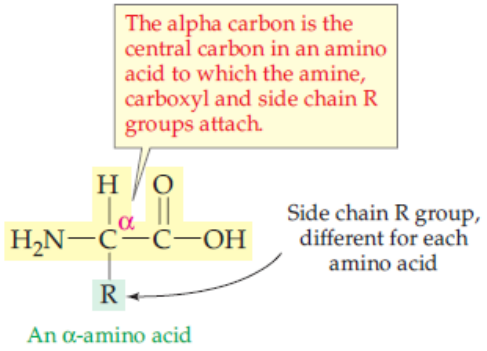
Protein structure and function

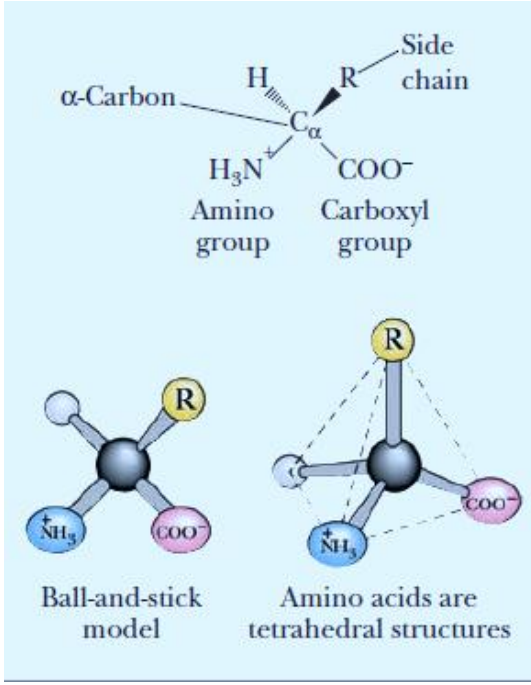
- Greek: proteios, primary (importance)
- 50 % of body's dry weight is protein
- Wide range of different functions
- Polymers of amino acids
- Structure of the amino acids

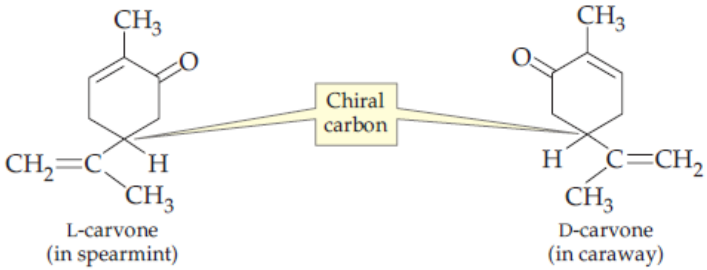
TYPE	FUNCTION	EXAMPLE
Enzymes	Catalysts	*Amylase*—begins digestion of carbohydrates by hydrolysis
Hormones	Regulate body functions by carrying messages to receptors	*Insulin*—facilitates use of glucose for energy generation
Storage proteins	Make essential substances available when needed	*Myoglobin*—stores oxygen in muscles
Transport proteins	Carry substances through body fluids	*Serum albumin*—carries fatty acids in blood
Structural proteins	Provide mechanical shape and support	*Collagen*—provides structure to tendons and cartilage
Protective proteins	Defend the body against foreign matter	*Immunoglobulin*—aids in destruction of invading bacteria
Contractile proteins	Do mechanical work	*Myosin and actin*—govern muscle movement

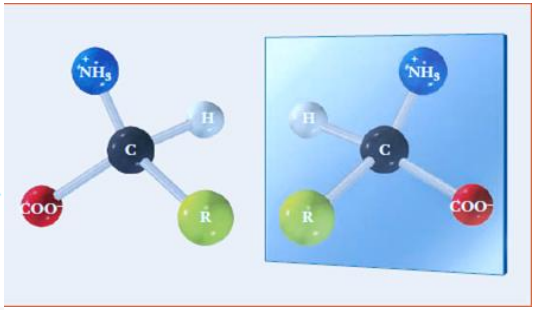


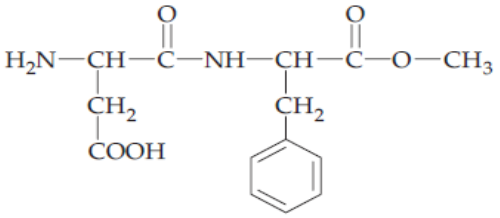
What should not be forgotten for good?

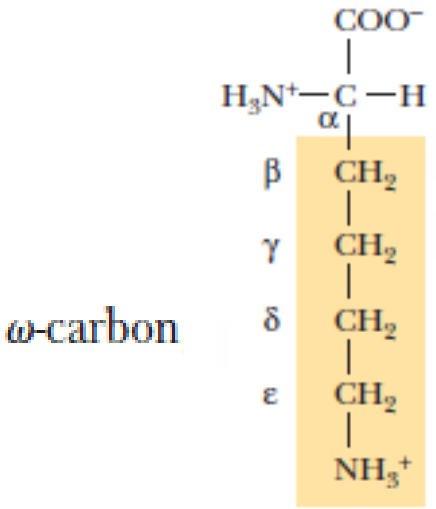
- There are a lot of amino acids in life
- There are 20 encoded by the genetic code
- Their general structure(amino, carboxyl, H, R), the basis of their classification
- Two vs. 3-dimentional (handedness, chirality, chiral vs. achiral, left vs. right, L vs. D)









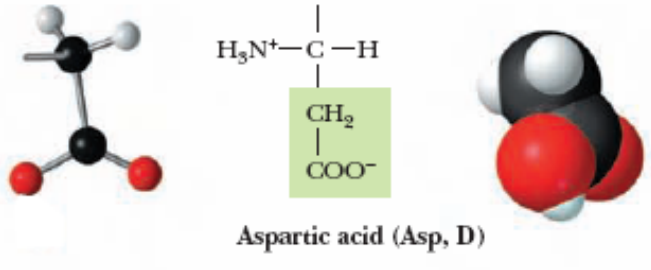


Names and codes

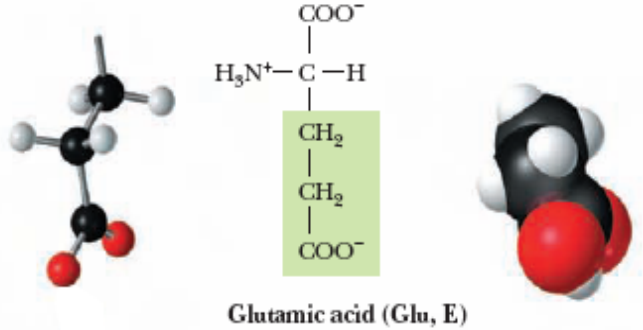
Amino Acid	3-letter code	1-letter code
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamic acid	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I

Amino Acid	3-letter code	1-letter code
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

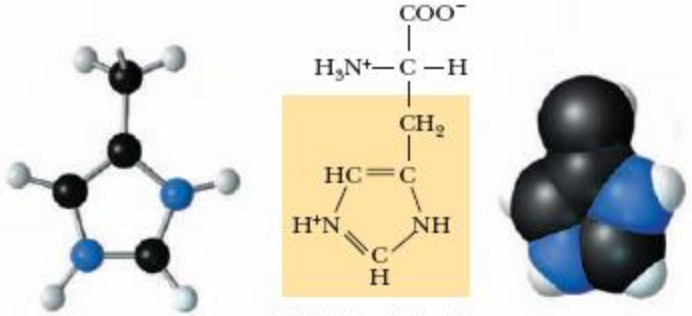
Charged



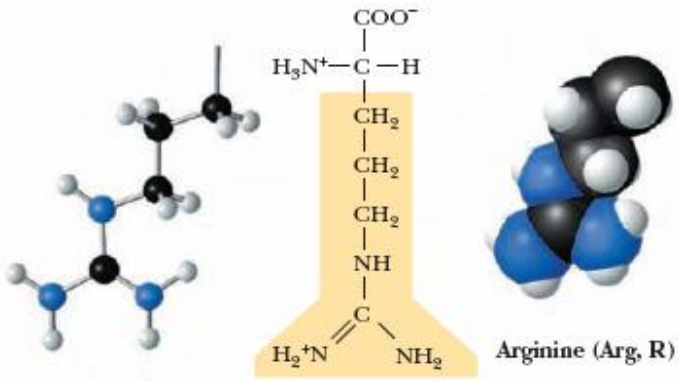
Aspartic acid (Asp, D)



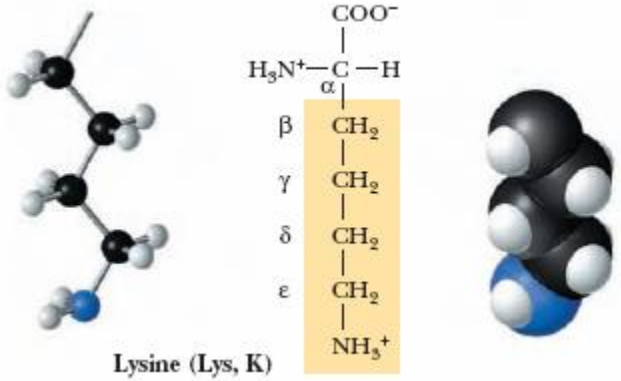
Glutamic acid (Glu, E)



Histidine (His, H)

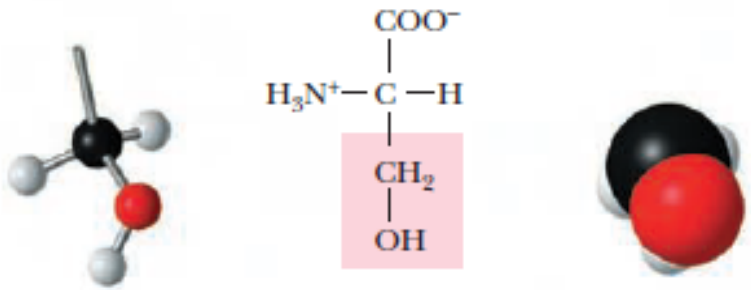


Arginine (Arg, R)

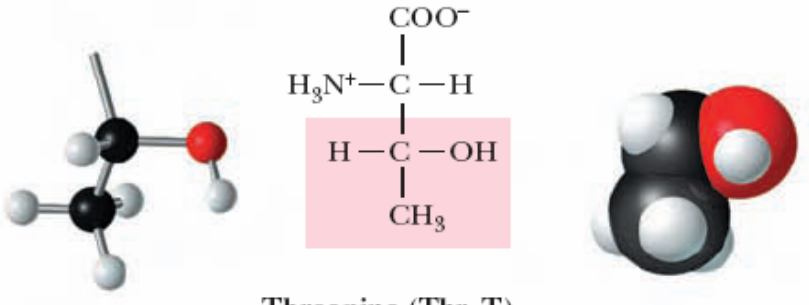


Lysine (Lys, K)

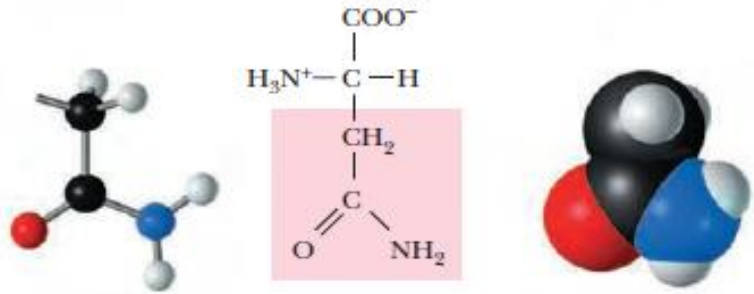
Polar, Uncharged



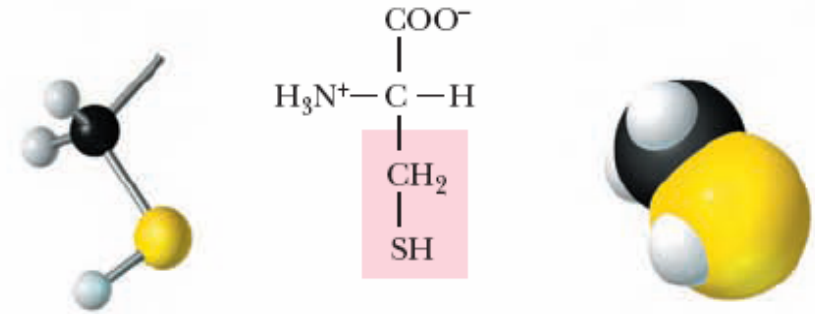
Serine (Ser, S)



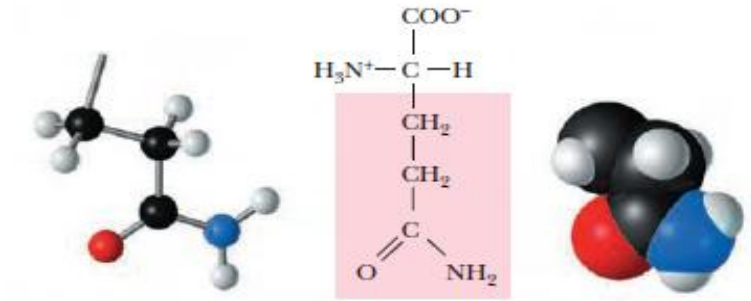
Threonine (Thr, T)



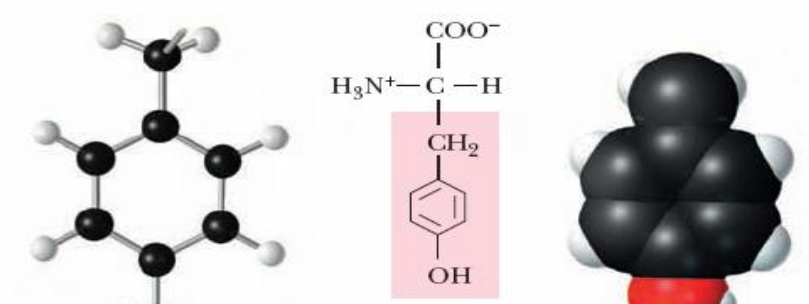
Asparagine (Asn, N)



Cysteine (Cys, C)

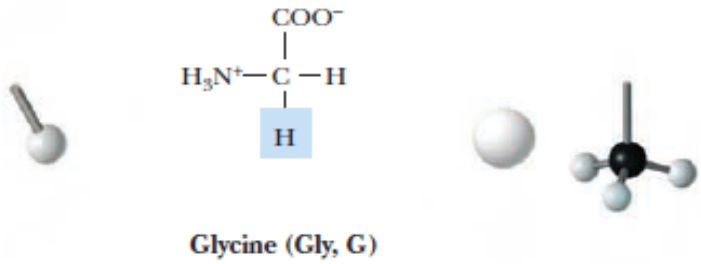


Glutamine (Gln, Q)

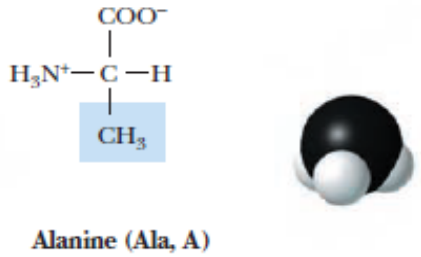


Tyrosine (Tyr, Y)

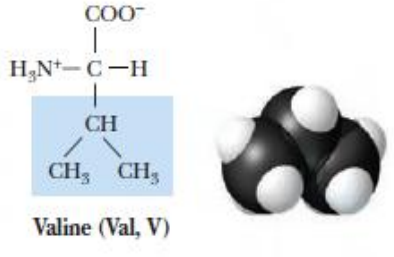
Non-polar, Uncharged



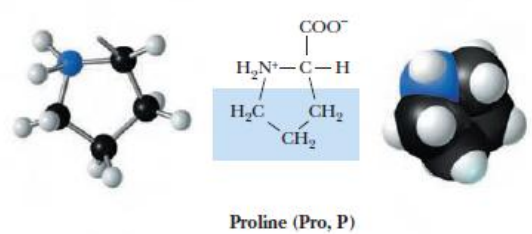
Glycine (Gly, G)



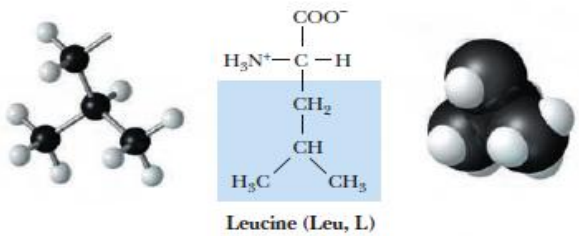
Alanine (Ala, A)



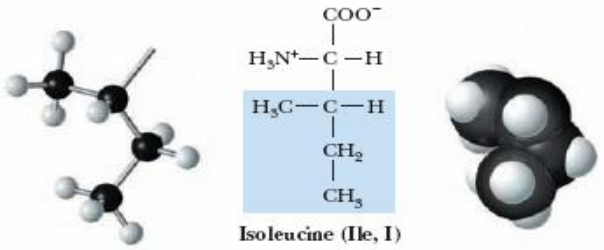
Valine (Val, V)



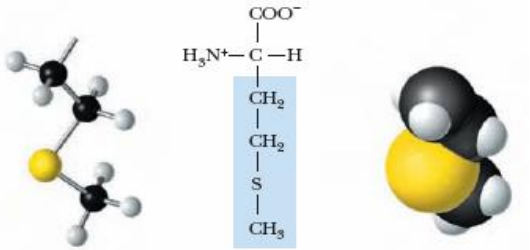
Proline (Pro, P)



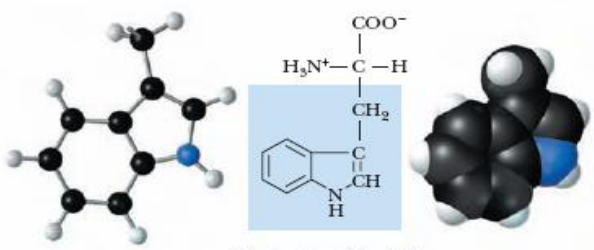
Leucine (Leu, L)



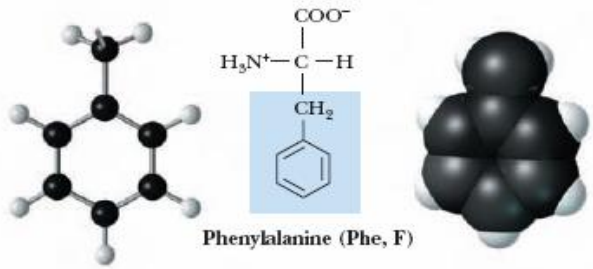
Isoleucine (Ile, I)



Methionine (Met, M)

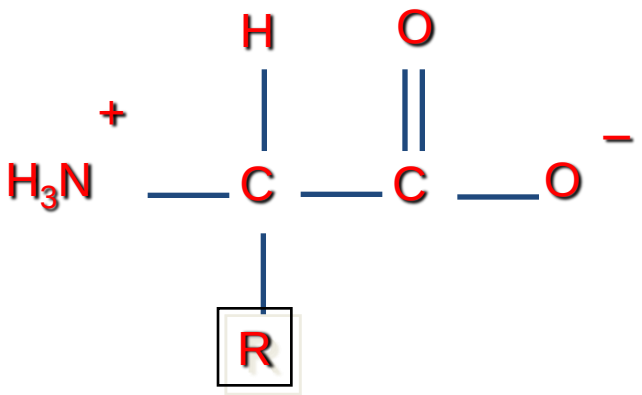


Tryptophan (Trp, W)



Phenylalanine (Phe, F)

Amino acids – general structure

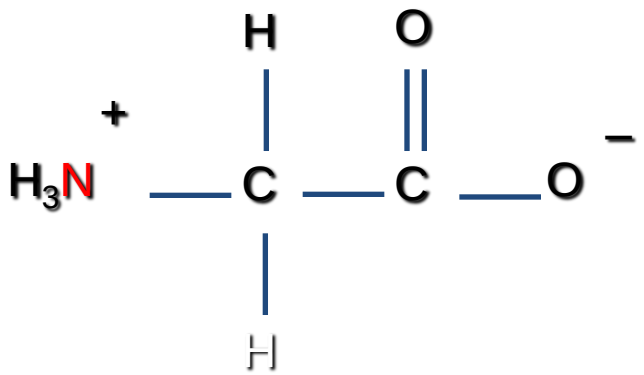


- The amino acids obtained by hydrolysis of proteins differ in respect to R (the side chain)
- The properties of the amino acid vary as the structure of R varies

Glycine

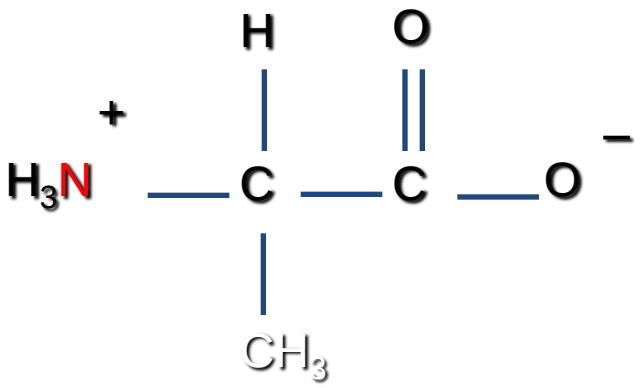
Glycine

(Gly or G)



- Glycine is the simplest amino acid. It is the only one that is achiral
- In all of the other amino acids the α-carbon is a stereogenic center

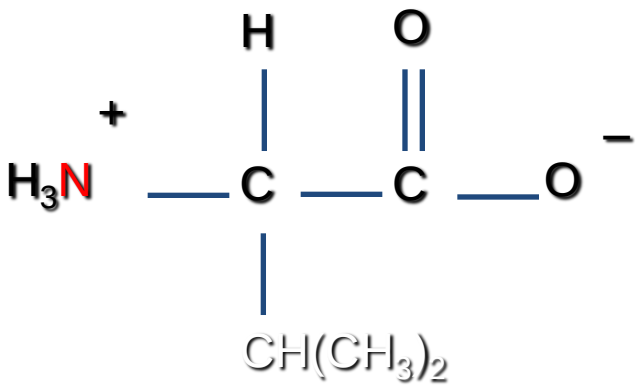
Alanine



Alanine

(Ala or A)

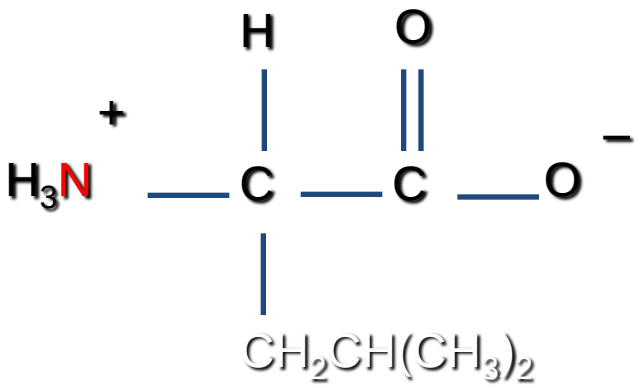
Valine



Valine

(Val or V)

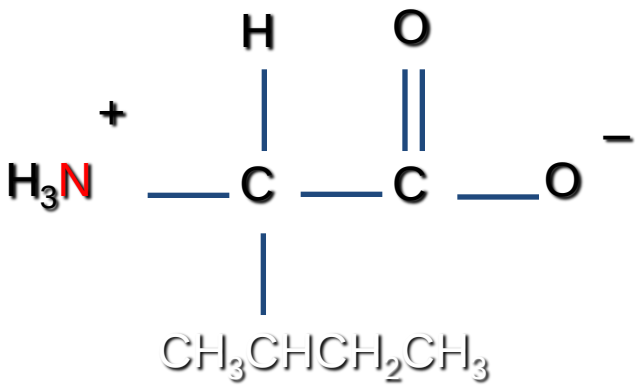
Leucine



Leucine

(Leu or L)

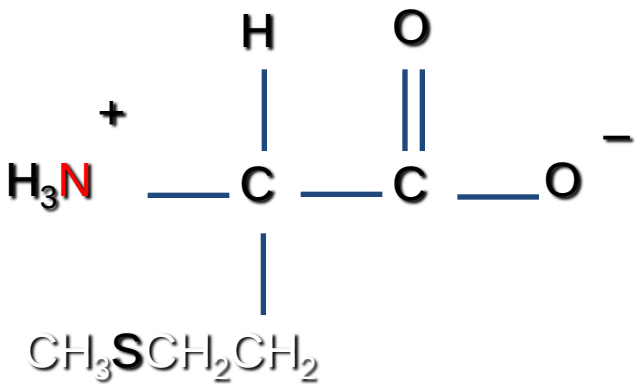
Isoleucine



Isoleucine

(Ile or I)

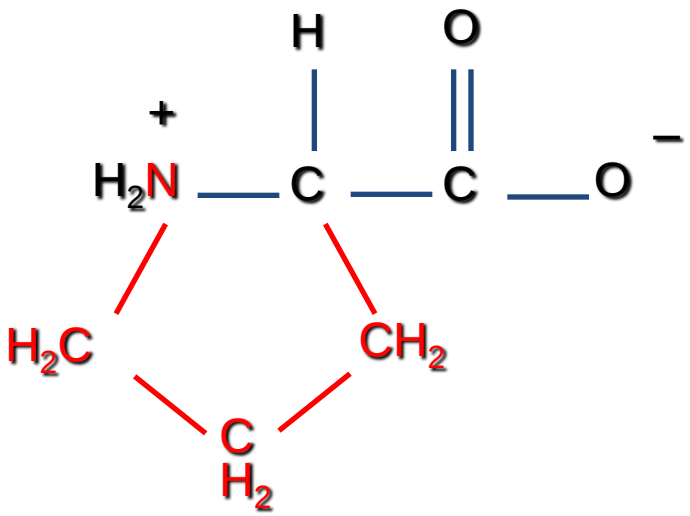
Methionine



Methionine

(Met or M)

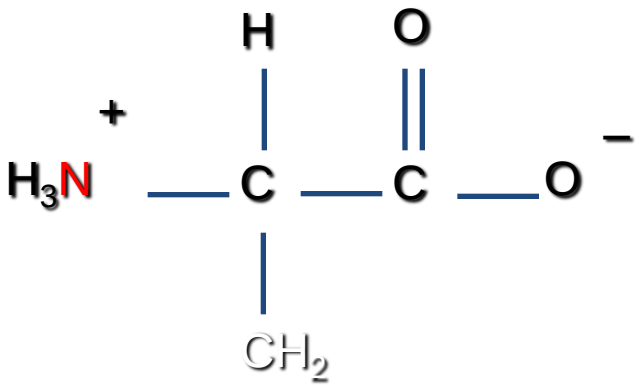
Proline



Proline

(Pro or P)

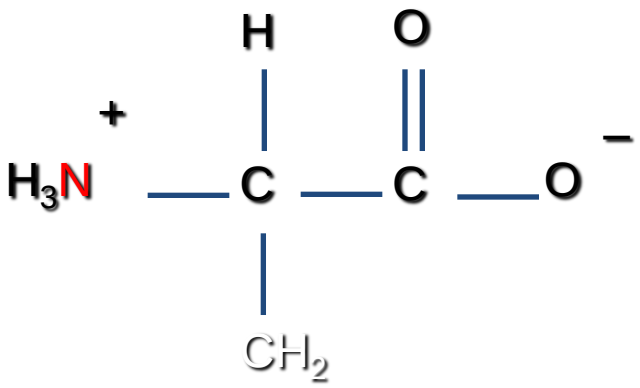
Phenylalanine



Phenylalanine

(Phe or F)

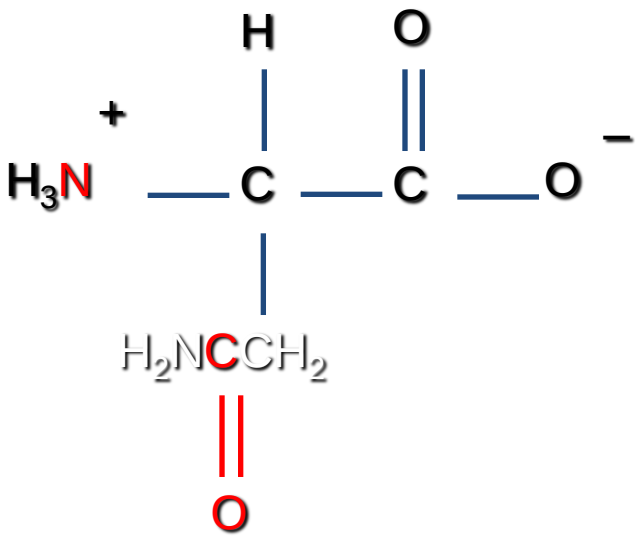
Tryptophan



Tryptophan

(Trp or W)

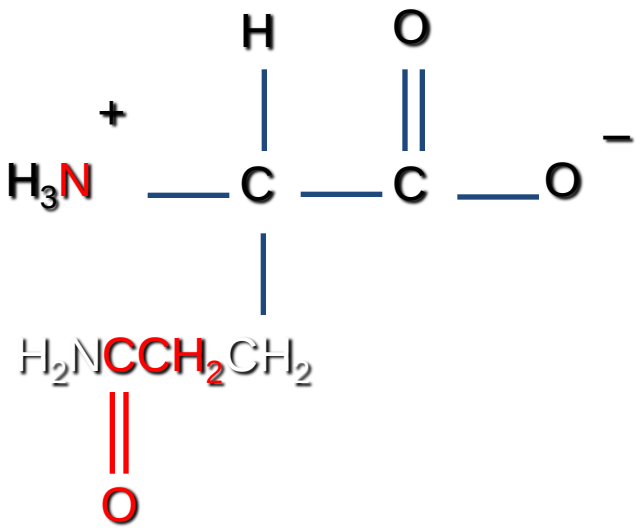
Asparagine



Asparagine

(Asn or N)

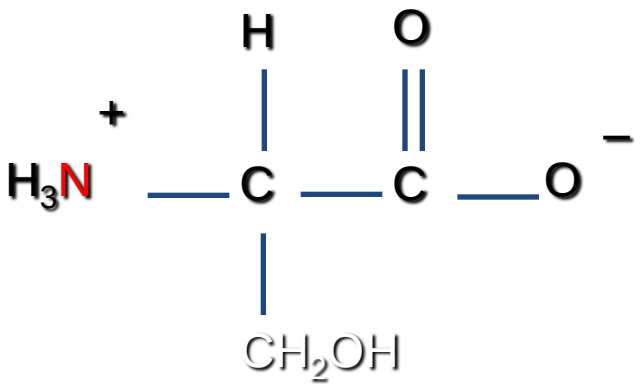
Glutamine



Glutamine

(Gln or Q)

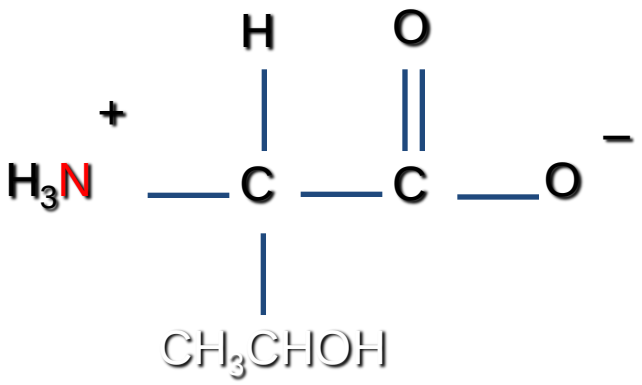
Serine



Serine

(Ser or S)

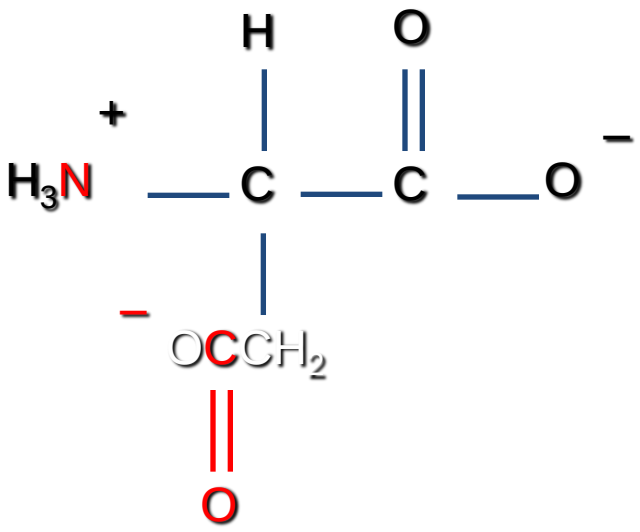
Threonine



Threonine

(Thr or T)

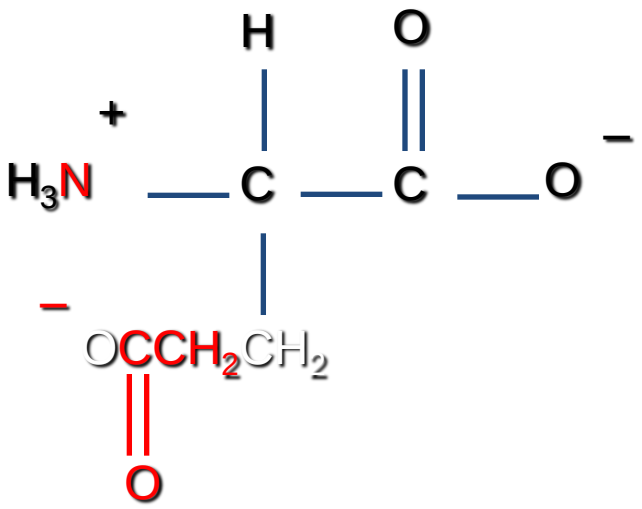
Aspartic Acid



Aspartic Acid

(Asp or D)

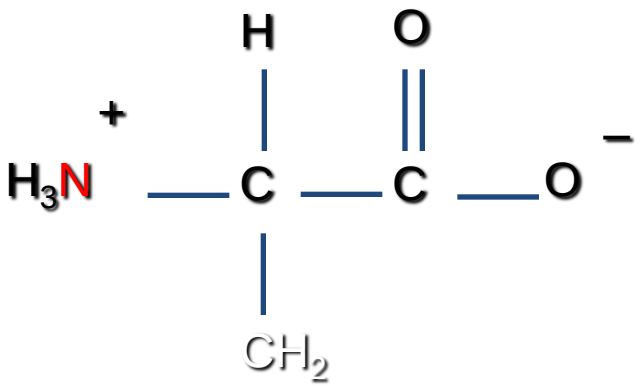
Glutamic Acid



Glutamic Acid

(Glu or E)

Tyrosine

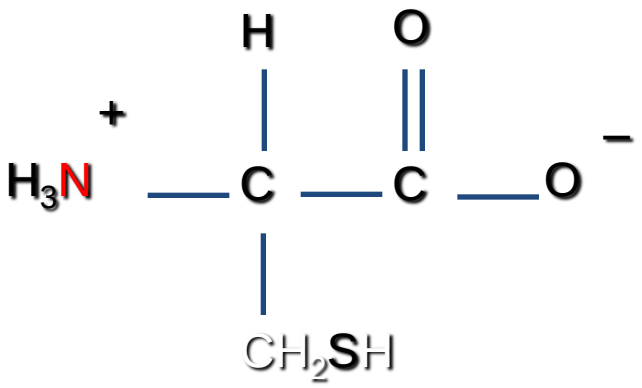


Tyrosine

(Tyr or Y)

OH

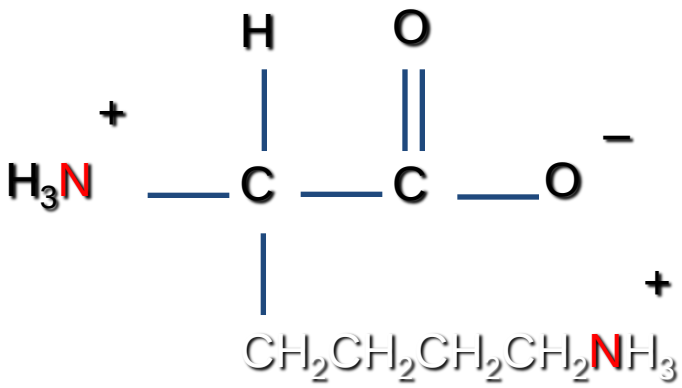
Cysteine



Cysteine

(Cys or C)

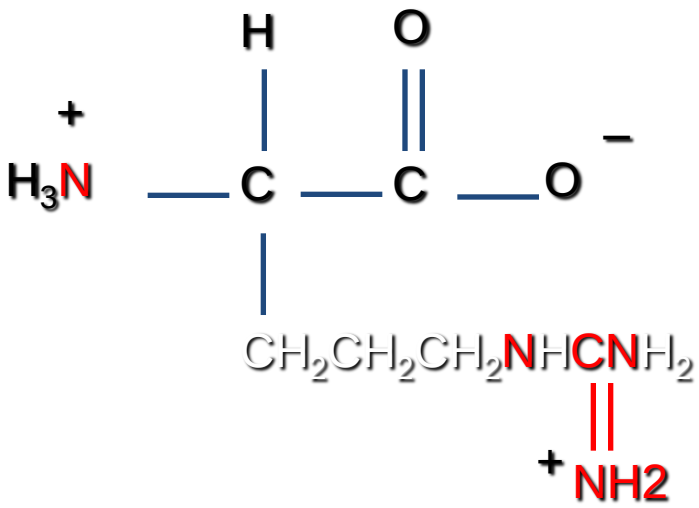
Lysine



Lysine

(Lys or K)

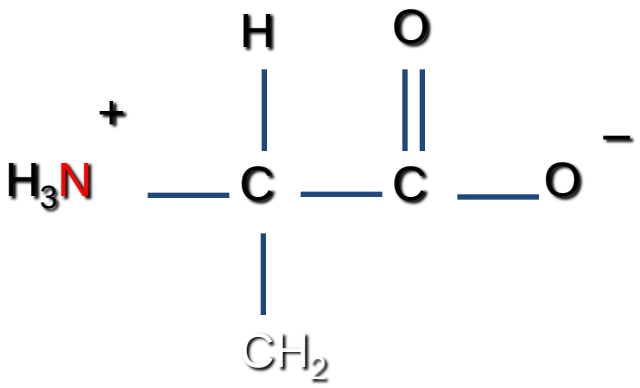
Arginine



Arginine

(Arg or R)

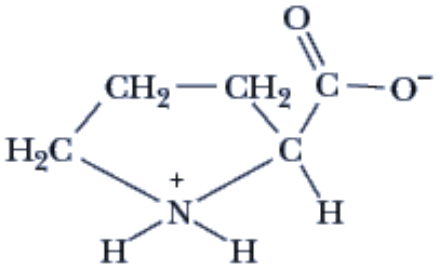
Histidine



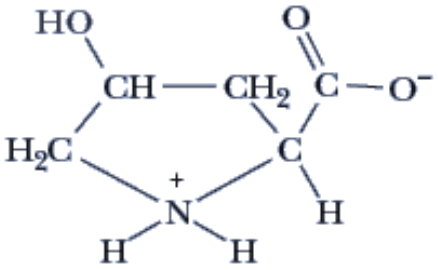
Histidine

(His or H)

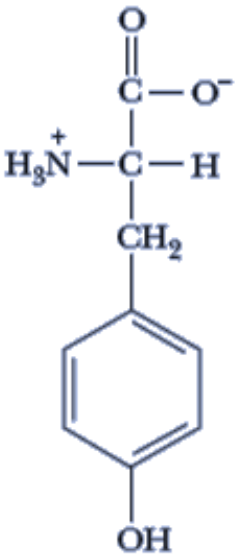
Posttranslational modification of Amino Acids



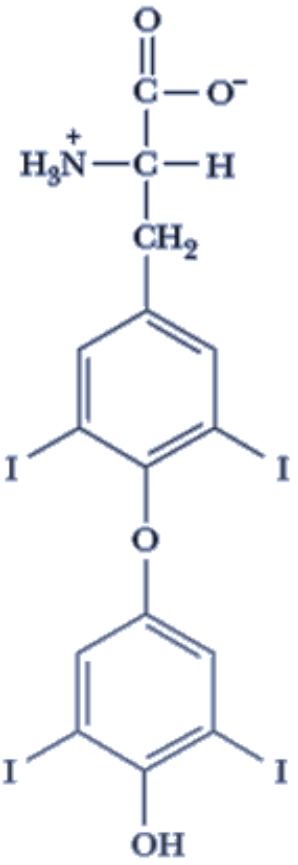
Proline



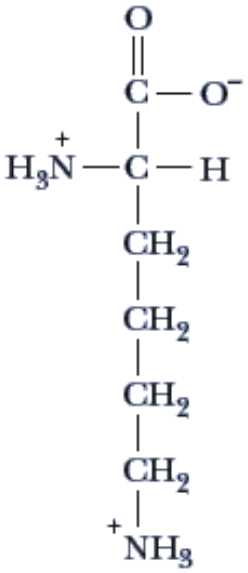
Hydroxyproline



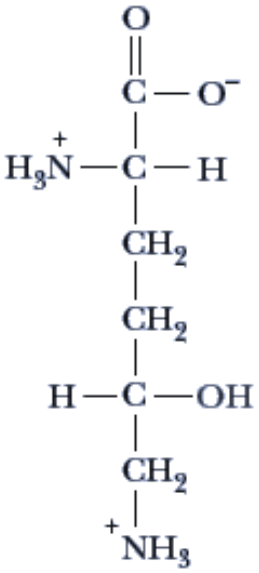
Tyrosine



Thyroxine

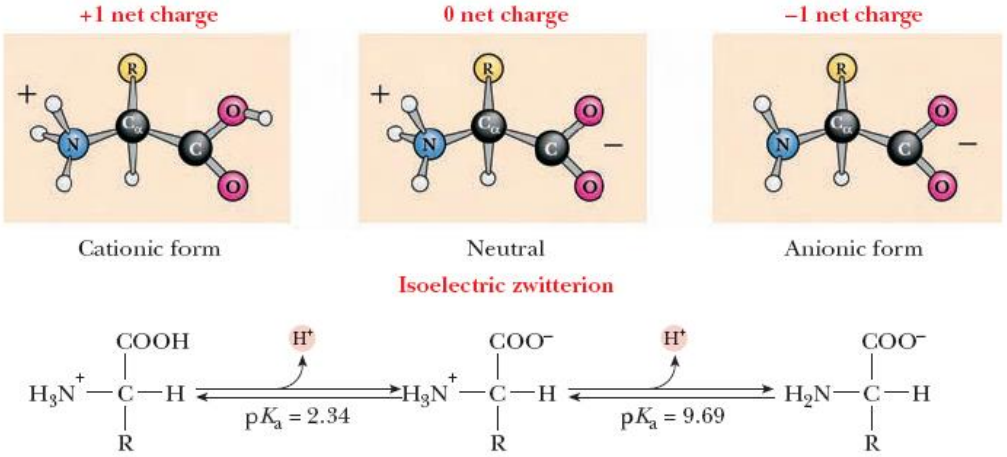


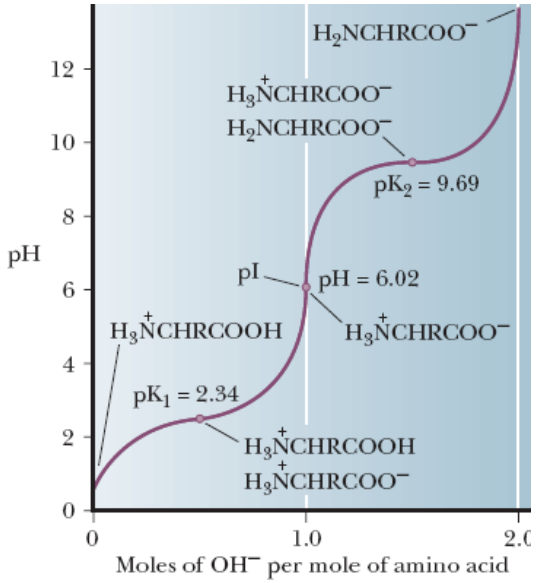
Lysine



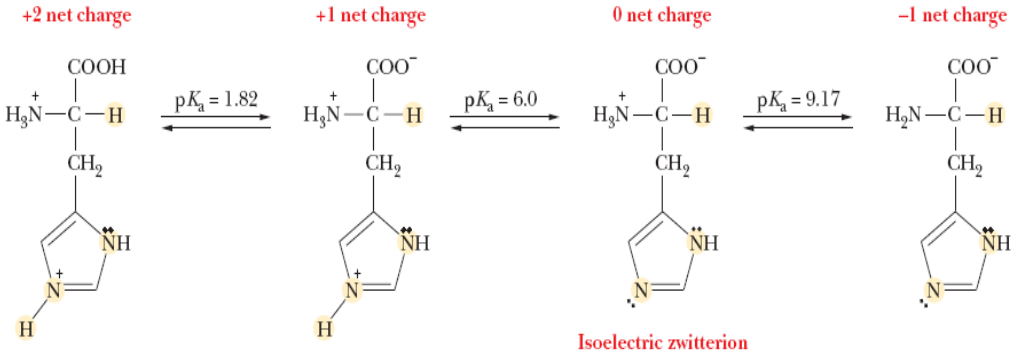
Hydroxylysine

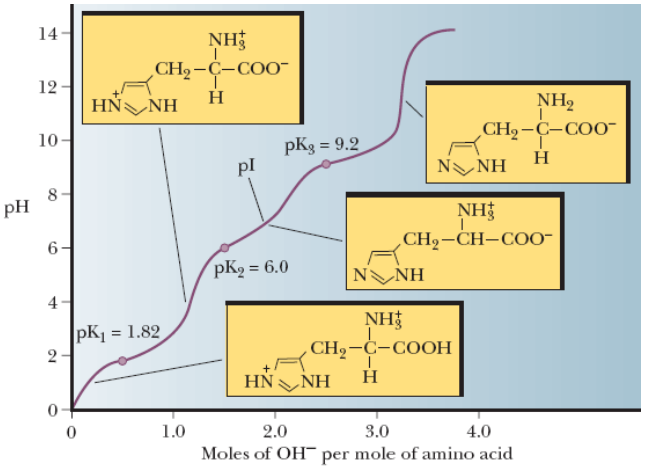
Titration of amino acids: what happens? And what is an isoelecrtic point (pI)?





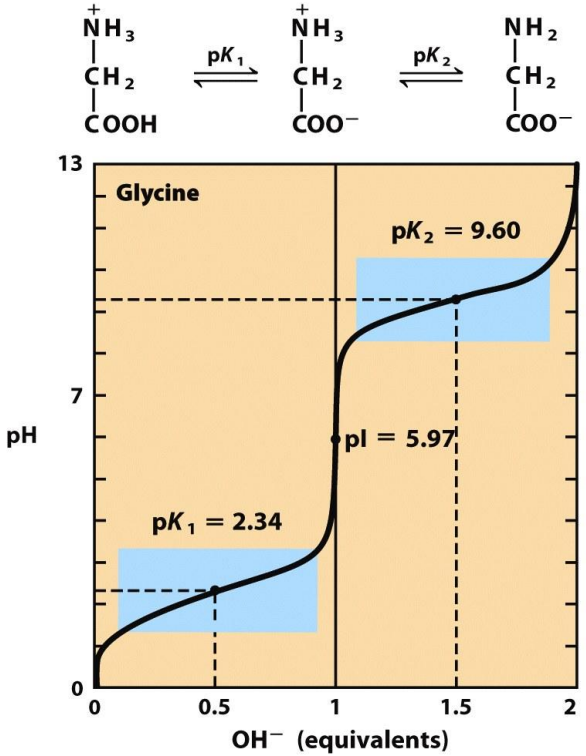
pI =(p*Ka*$_1$ + *pKa*$_2$*)/2





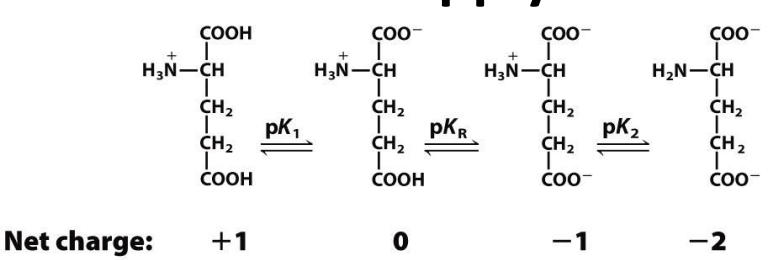
General rules for amino acid ionization

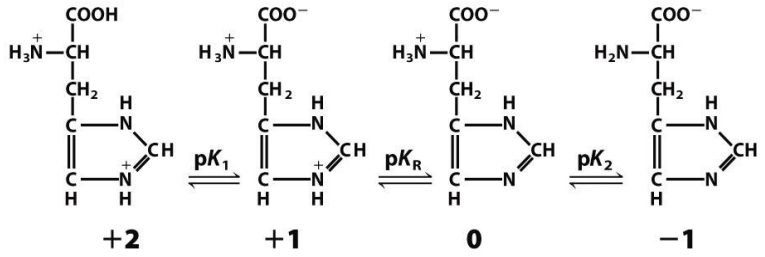
- Alpha carboxylic acids ionize at acidic pH & have pKs < 6; So in titration, alpha carboxylic acids lose the proton first
- Alpha amino groups ionize at basic pH & have pKs > 8; So after acids lose their protons, amino groups lose their proton
- Most of the 20 amino acids are similar to Gly
- There are 5 exceptions (Glu, Asp, Lys, Arg, His)
- Each has 3 ionizible groups and thus, 3 pKs
- Carboxylic acid groups near an amino group in a molecule have a more acidic pK than isolated carboxylic groups
- Amino groups near a carboxylic acid group also have a more acidic pK than isolated amines

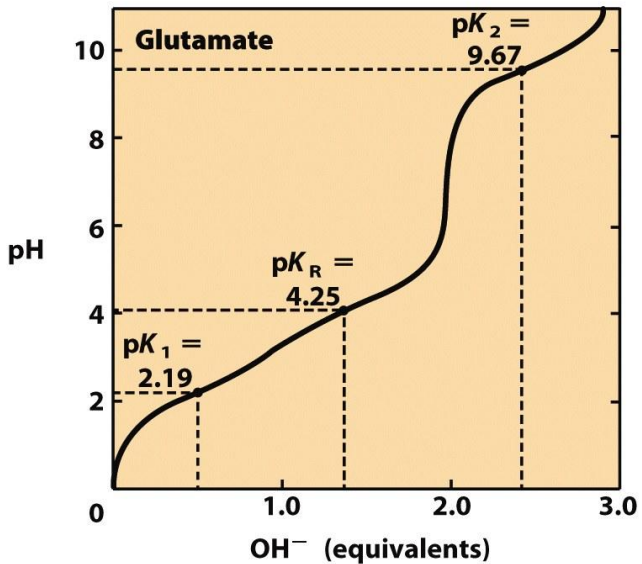


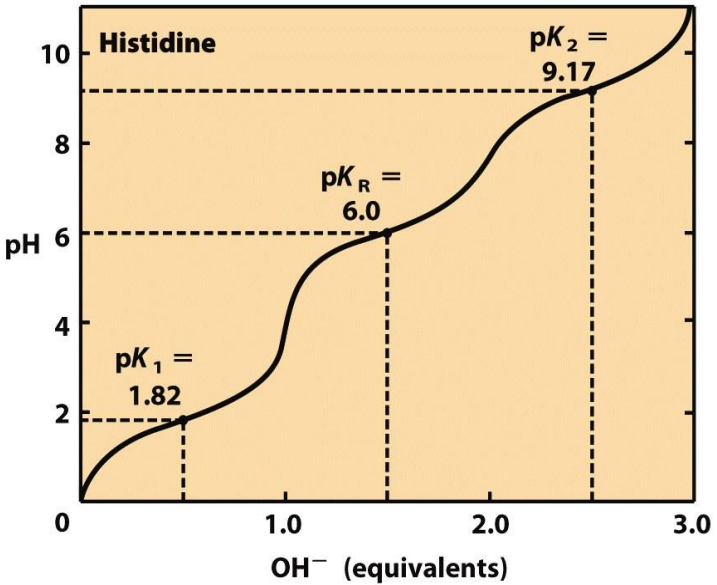
General rules for amino acid ionization

- **Aromatic amines like His have a pK about pH 6**
- **On titration: alpha carboxylic acids lose their proton first, then side chain carboxylic acids, then aromatic amine side chains (His), then alpha amino groups, then side chain amino groups**
- **These rules apply to small peptides too**

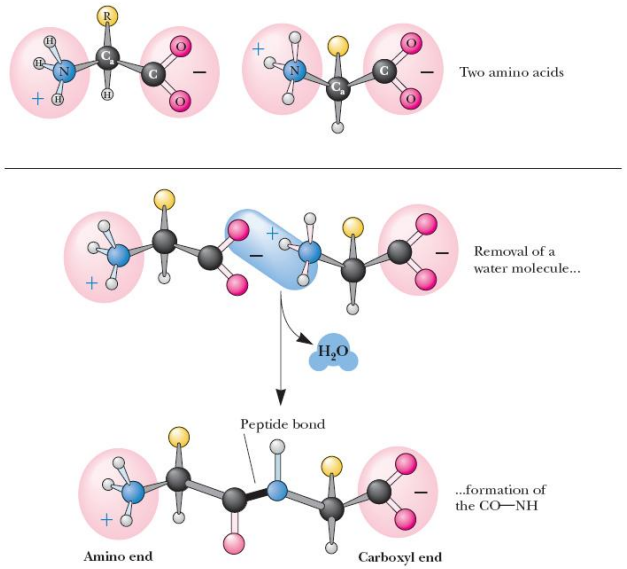


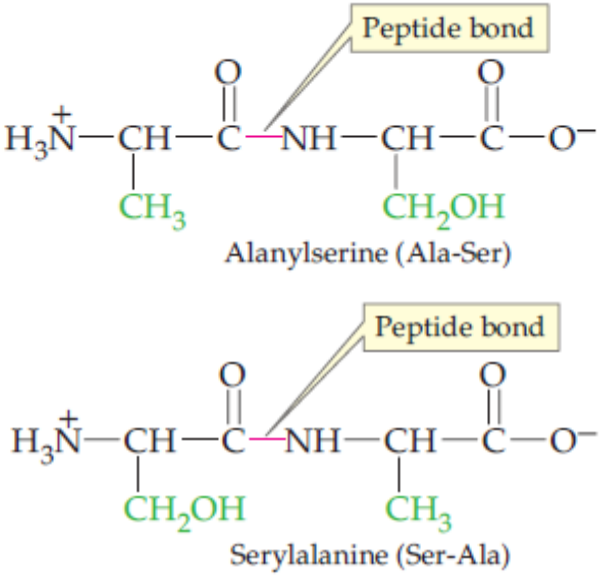


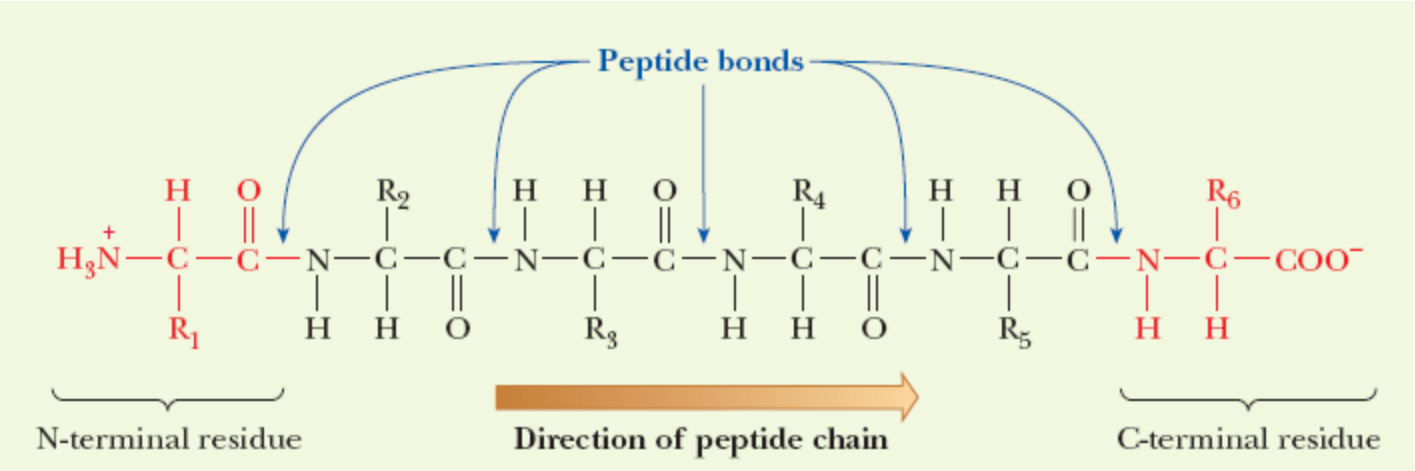




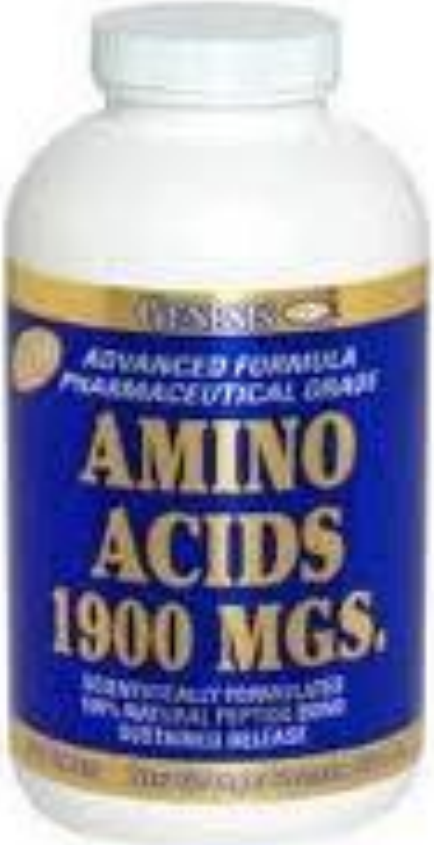
The peptide bond, peptides, and proteins





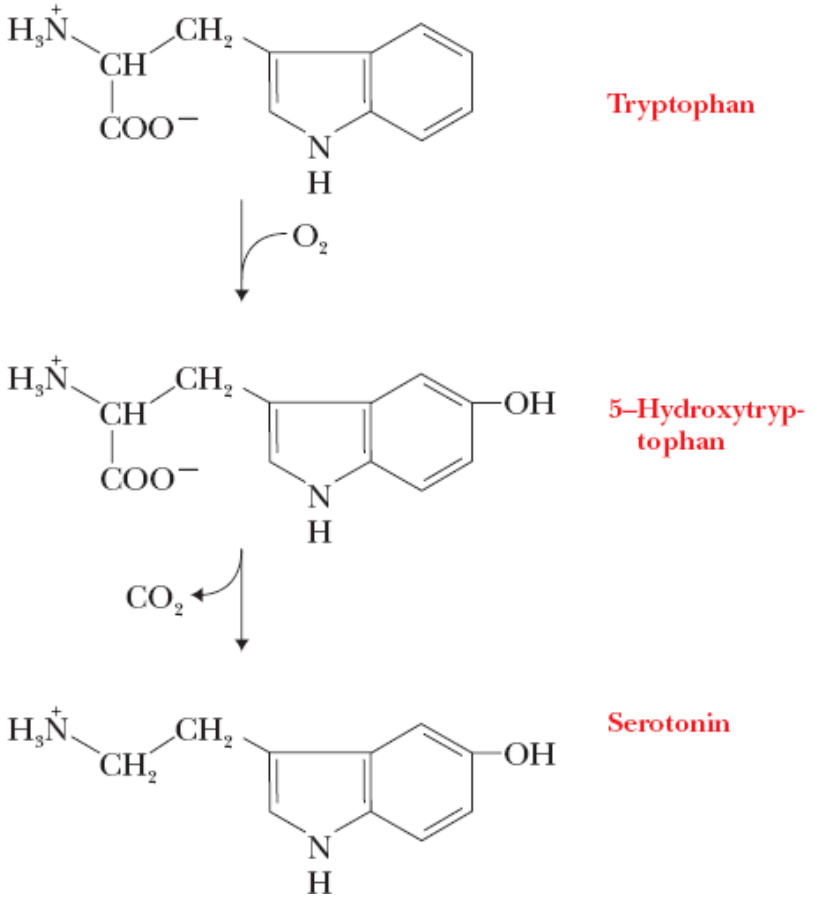


Amino Acids & life



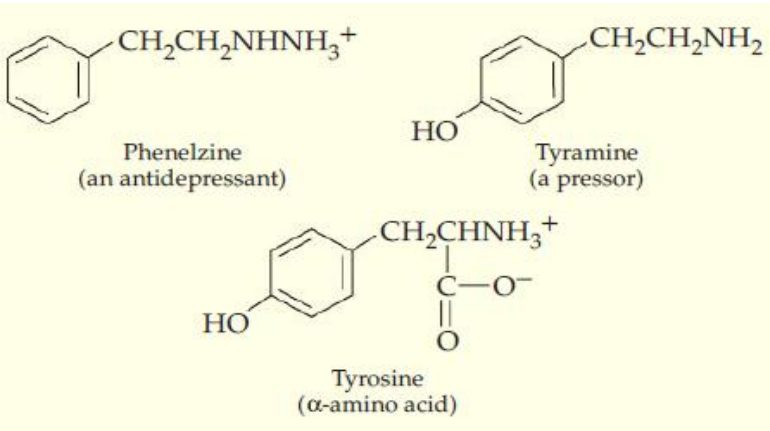
Amino acids & life

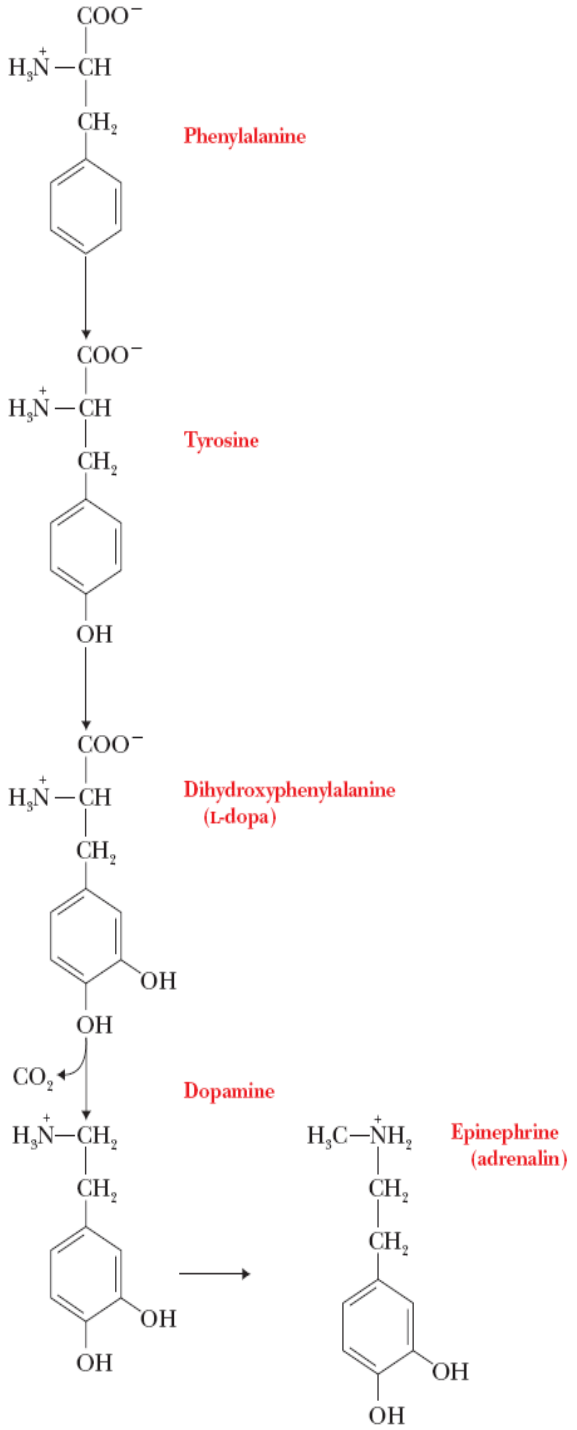
- Two amino acids deserve special attention (**Tyr & Trp**) with respect to neurotransmission
- Tryptophan converted to 5-hydroxytryptamine (**serotonin**, sedative effect)
- Very low levels are associated with depression, while extremely high levels produce manic state
- Tryptophan, milk & sleep



Amino acids & life

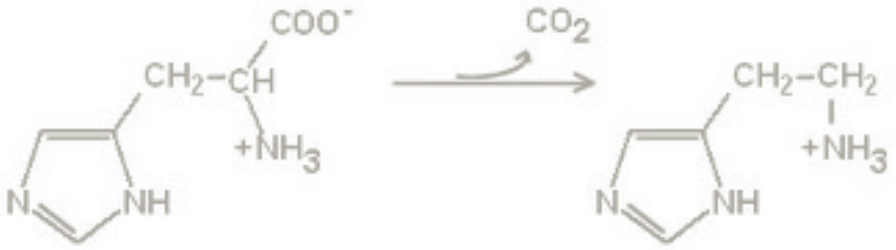
- **The active products of Tyr metabolism are monoamine derivatives (MA). MAOs**
- **Headaches and Phe in aspartame**
- **Phe, Tyr, catecholamines; epinephrine (adrenalin). MAO_i makes metabolism slow**
- ***A Beautiful Mind, focused on Dopamine***
- **Tyrosine supplements & morning lift**
- **Cheese and red wines (tyramine; mimics epinephrine); a cheese omelet is a favorite way to start the day**





Other amino acids

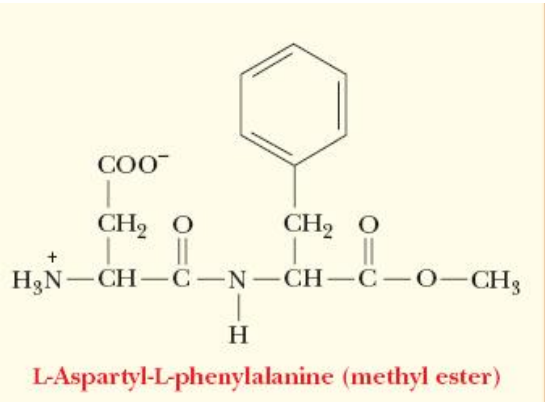
- **Glutamic Acid:** Monosodium glutamate, or MSG, a flavor enhancer. MSG causes a physiological reaction in some people, with chills, headaches, and dizziness resulting in (*Chinese restaurant syndrome)*
- **Histidine:** converted to histamine, a potent vasodilator, part of the immune response, results in swelling and stuffiness that are associated with cold. Most cold medications contain antihistamines to overcome this stuffiness.

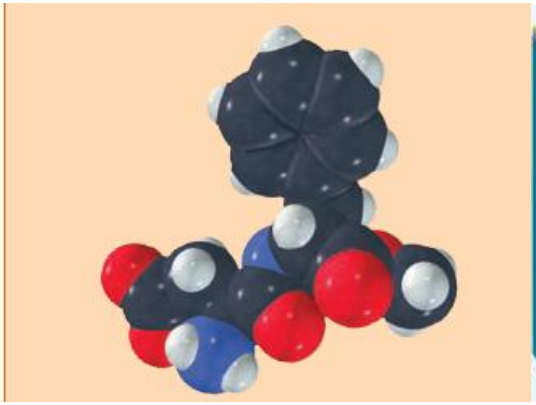


Histidine *Histamine*

Aspartame, the Sweet Peptide

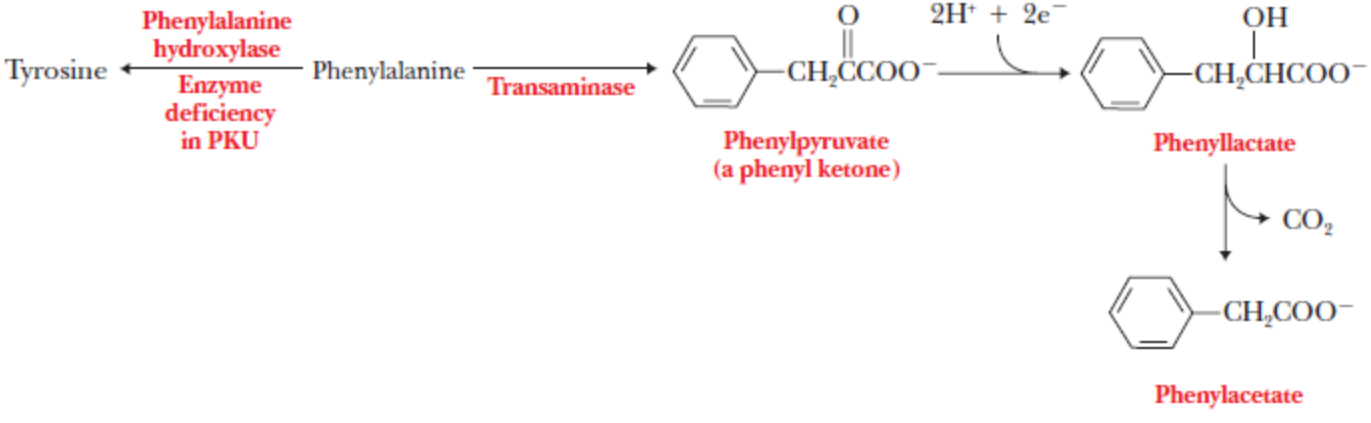
- L-aspartyl-L-phenylalanine, commercial importance
- The methyl ester derivative is called *aspartame*
- 200 times sweeter than sugar





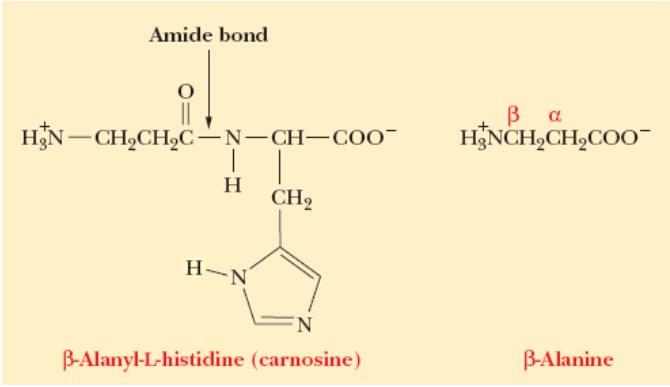
Phenylketonuria

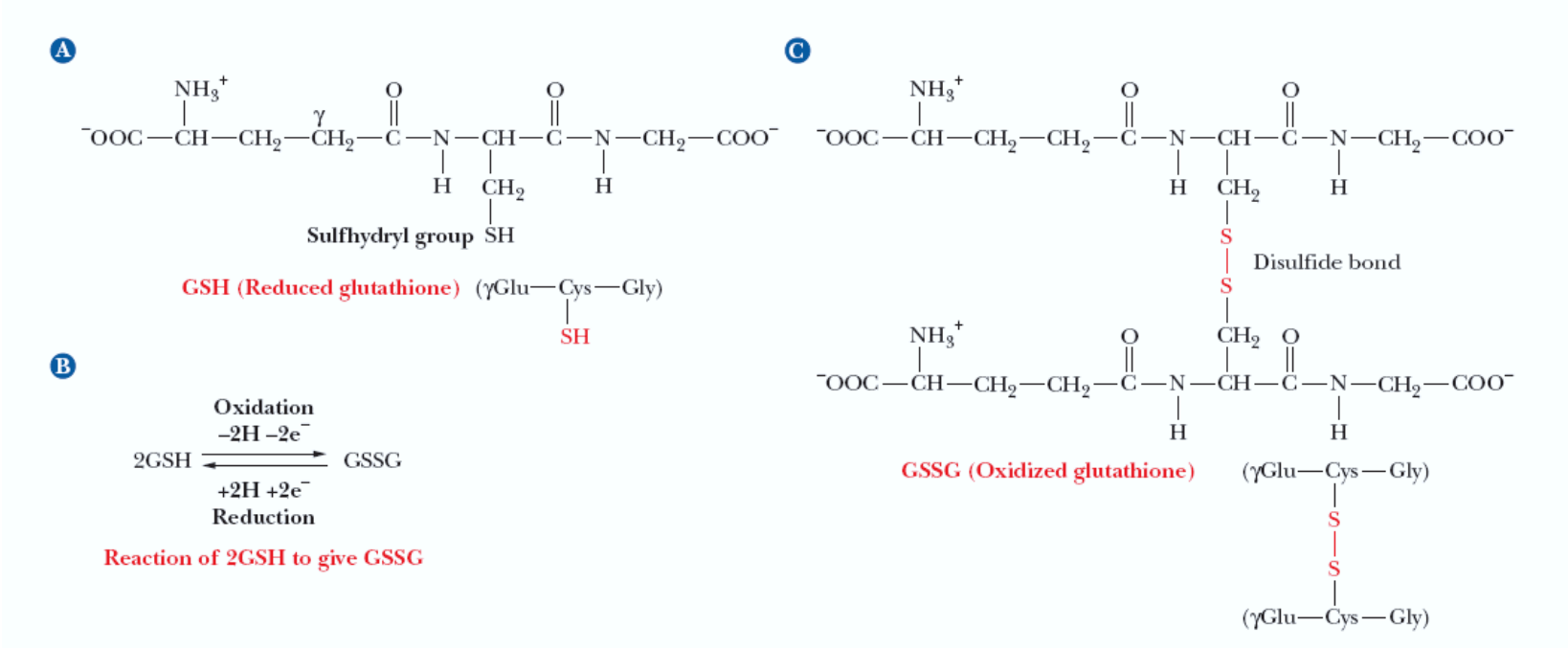
- Inborn errors of metabolism; errors in enzymes of amino acids metabolism
- May have disastrous consequences (mental retardation)
- Phenylketonuria (PKU) is a well-known example
- PKU can be easily detected and managed in newborns
- Aspartame carry a warning
- Alatame (Ala instead of Phe) is a substituent



Small Peptides with Physiological Activity

- Carnosine (dipeptide), found in muscle tissue, (β-alanyl-L-histidine), anti-oxidant
- Glutathione (tripeptide; g-glutamyl-L-cysteinylglycine); a scavenger for oxidizing agents



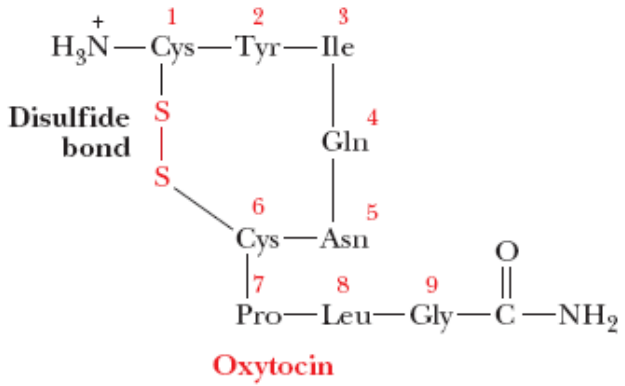


Small Peptides with Physiological Activity

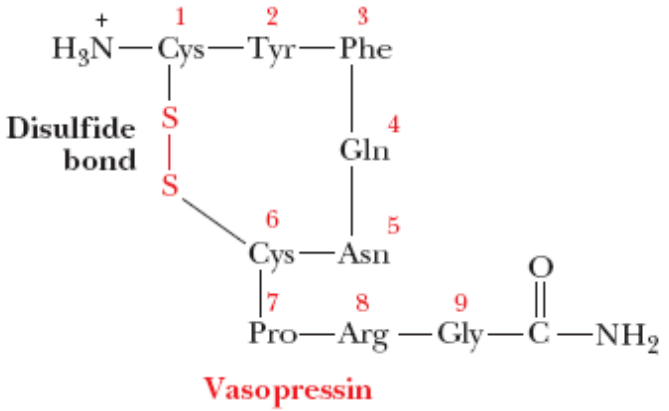
- Enkephalins (pentapeptides), naturally occurring analgesics

  Tyr—Gly—Gly—Phe—Leu (Leucine enkephalin)

  Tyr—Gly—Gly—Phe—Met (Methionine enkephalin)
- Similarities of three-dimensional structures to opiates (e.x, morphine)
- Some important peptides have cyclic structures. Two well-known examples, oxytocin and vasopressin



Oxytocin



Vasopressin

Peptide Hormones-Small Molecules with Big Effects