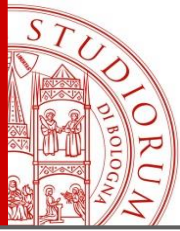




GENERAL BIOCHEMISTRY MODULE 1

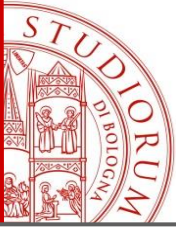
- **Biological macromolecules:**
 - ✓ **Carbohydrates**
 - ✓ **Lipids**
 - ✓ **Amino acids and Peptides**
 - ✓ **Proteins**
 - **myoglobin and hemoglobin**
 - **enzymes and enzymology**



NUCLEIC ACIDS – GENERAL BIOCHEMISTRY

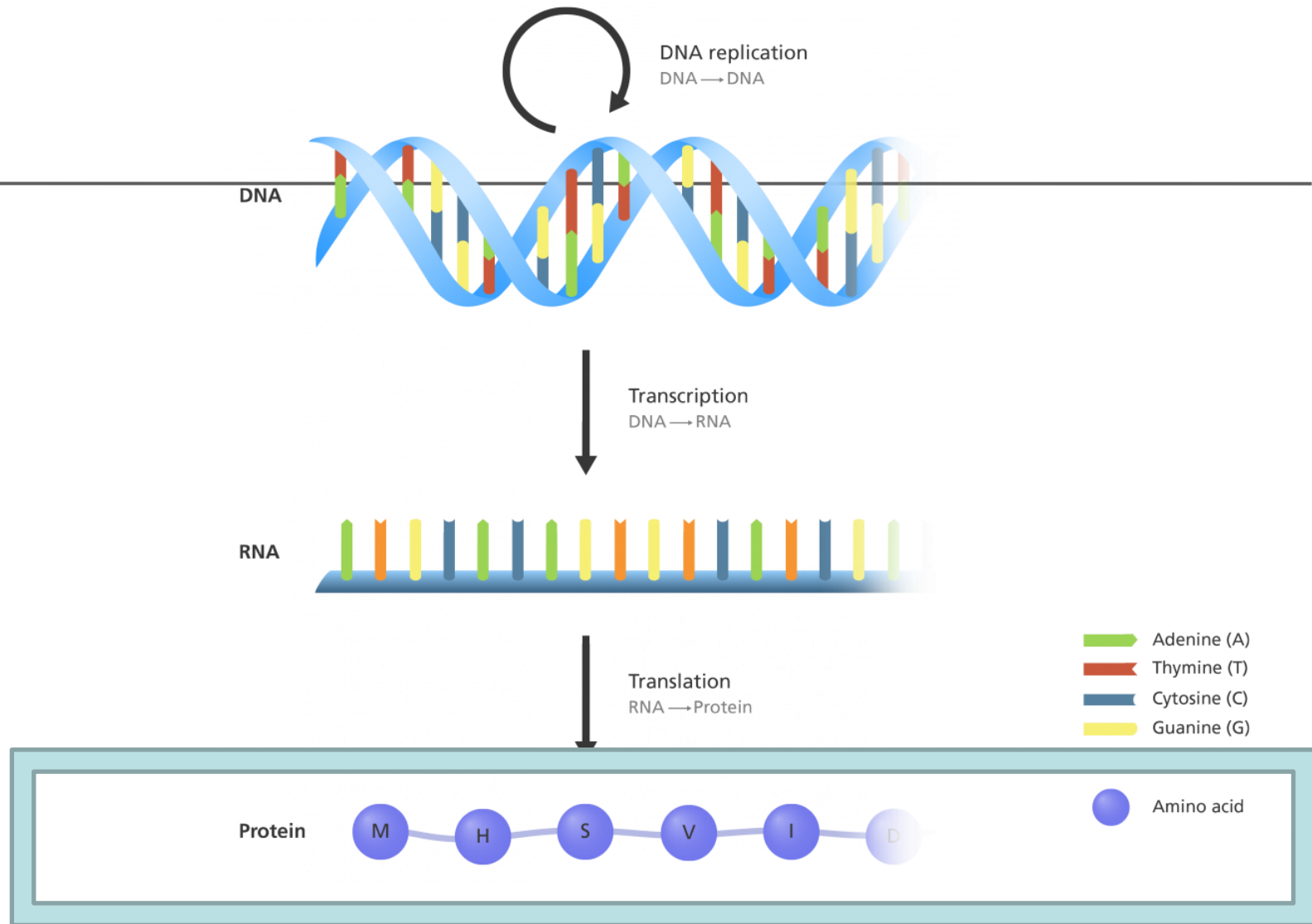
MODULE 2

- **Structure and Function of Nucleic Acids**
- **Genes and Chromosomes (summary)**
- **DNA metabolism (replication)**
- **RNA metabolism (synthesis and transcription)**
- **Protein Synthesis (translation)**

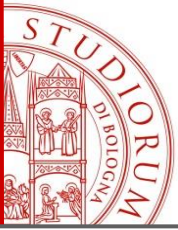


BIOCHEMISTRY LABORATORY

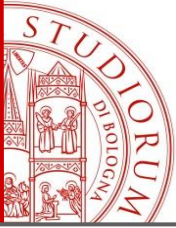
- December 19th 2025, 9-11 AULA MAGNA DERMATOLOGIA -Sant'Orsola
Prof. Vadim Viviani «Bioluminescence color modulating luciferases for cellular biosensing and environmental analysis»
- January 9th 2025, 11-13 AULA MAGNA DERMATOLOGIA -Sant'Orsola
Clinical case presentations (4/5 people per group- G1 and G2)
- January 13th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Clinical case presentations (4/5 people per group- G3 and G4)
- January 15th 2025, 11-13 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Prof. Antonio Pannuti «RNA in diagnostics and therapy»
- January 17th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
«Mock exam – Chemistry and Biochemistry (with results discussion)»
- January 27th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Dr. Akram Ghantous «Epigenomics and Big Data: Linking the Environment with Health and Disease»



The 'Central Dogma' is the process by which the instructions in DNA are converted into a functional product. It was first proposed in 1958 by Francis Crick, discoverer of the structure of DNA.



Classification of Amino Acids

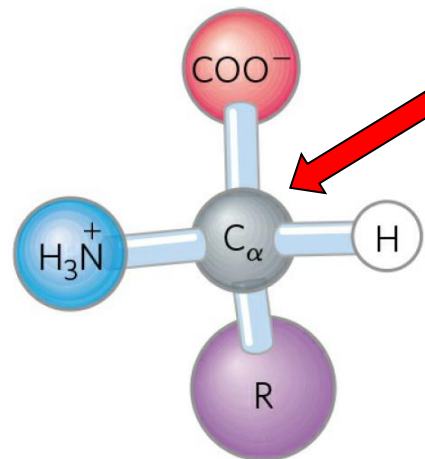


Amino acids

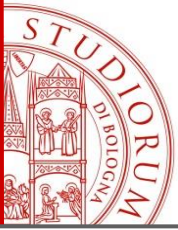
- **Proteins are polymers of amino acids (aa)**, with each amino acid residue joined to its neighbor by a specific type of **covalent bond** (an amide called “**peptide bond**”). Proteins may consist of thousands of aa and can have molecular weights of up to several million Dalton (Da).
- **Twenty** different amino acids are commonly found in human proteins even if more than 500 amino acids have been found in nature. They have a variety of functions, but not all are constituents of proteins.
- All the amino acids have trivial or common names, in some cases derived from the source from which they were first isolated. Asparagine was first found in asparagus, and glutamate in wheat gluten; tyrosine was first isolated from cheese (its name is derived from the Greek tyros “cheese”); and glycine (Greek glykos, “sweet”) was so named because of its sweet taste.
- The sequence of the aa within the molecule is essential for the structure and function of proteins and peptides in biological processes.

Fundamentals

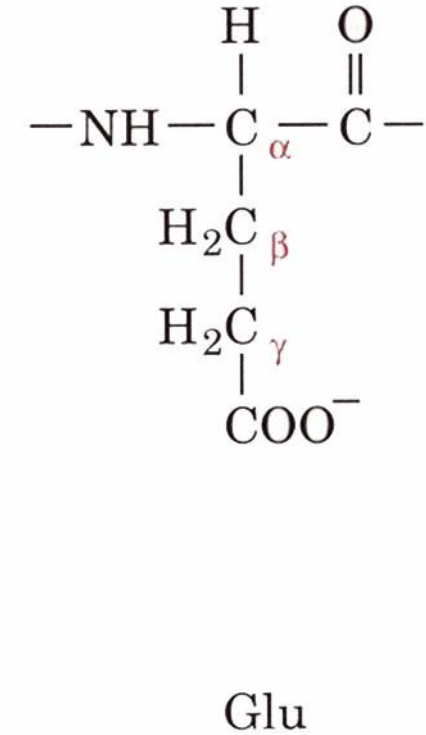
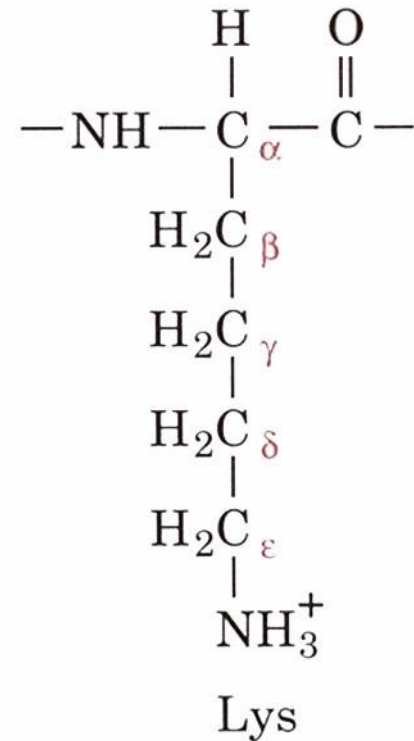
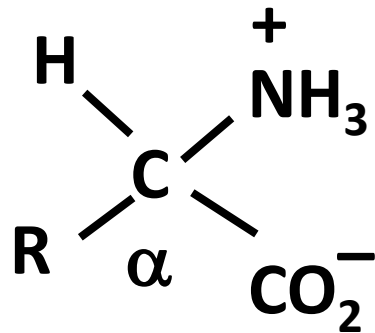
- While their name implies that amino acids are compounds that contain an —NH_2 group and a —COOH group, these groups can be present as —NH_3^+ and —COO^- respectively (at pH 7).
- The additional carbons in an R group are commonly designated β , γ , δ , ϵ , and so forth, proceeding out from the α carbon.

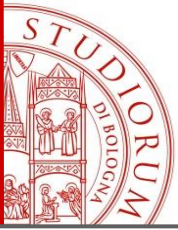


α -amino acids have a carboxyl group and an amino group bonded to the same carbon atom (the α carbon)



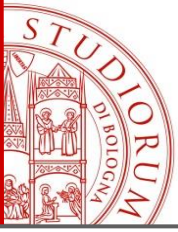
Amino acids





The 20 Key Amino Acids

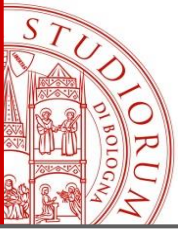
- More than 500 amino acids occur naturally, but 20 of them are important to build proteins.
- These 20 amino acids are the building blocks of proteins. All are α -amino acids.
- They differ in respect to the group attached to the α carbon (-R) which varies in structure, size, and charge, and which influences the solubility of the amino acids in water.



The 20 Key Amino Acids

- The 20 common α -amino acids have been assigned **three-letter abbreviations** and **one-letter symbols**.

Amino acid	Three-letter code	One-letter code
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Asparagine or aspartic acid	Asx	B
Cysteine	Cys	C

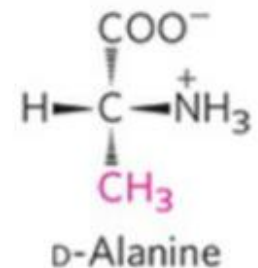
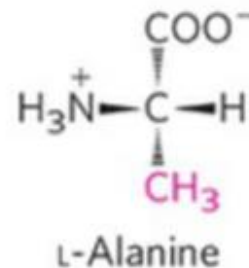


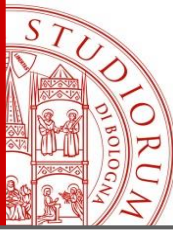
The 20 Key Amino Acids

For all the common amino acids except glycine, the α -carbon is bonded to **four different groups**: thus, the α -carbon atom is a **chiral center**.

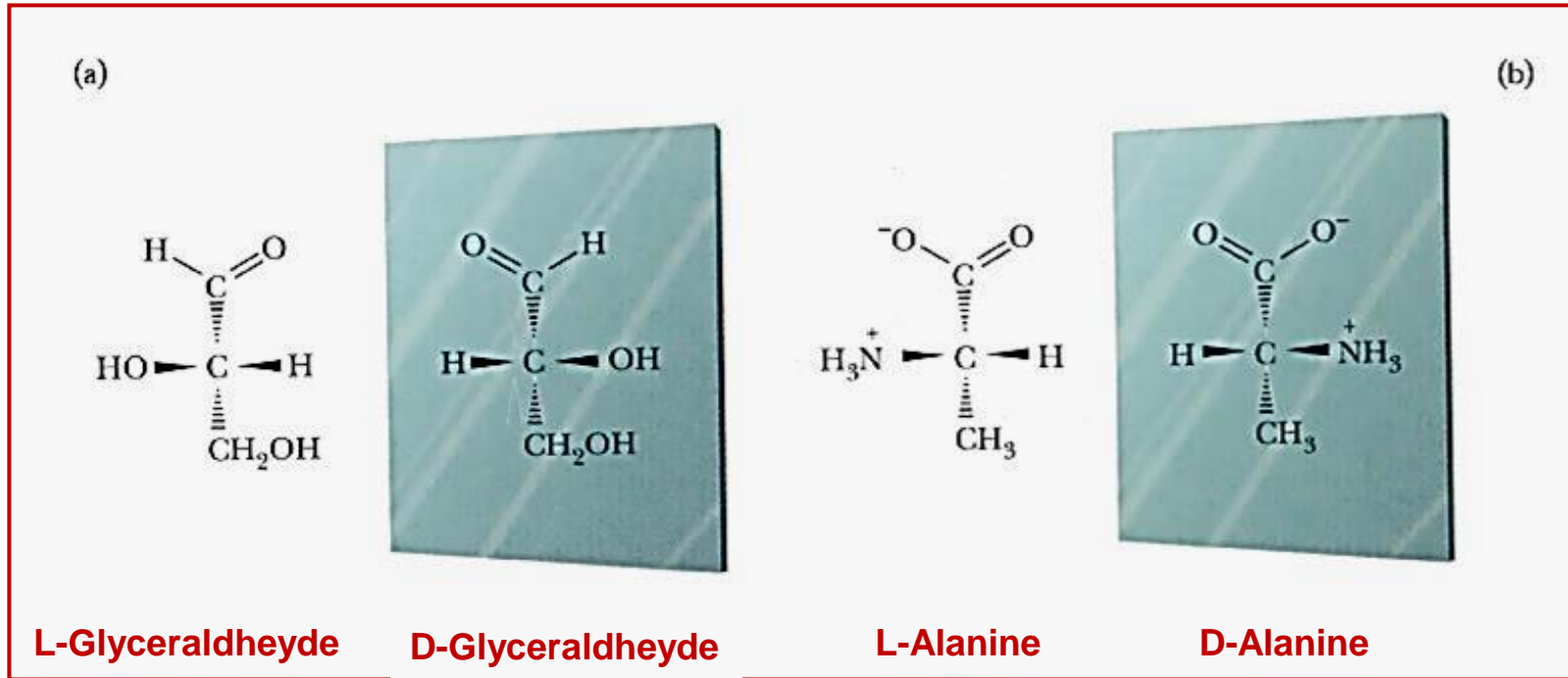
Because of the tetrahedral arrangement of the bonding orbitals around the α -carbon atom, the four different groups can occupy two unique spatial arrangements, and thus amino acids have two possible stereoisomers (**enantiomers**). **The amino acids in proteins are exclusively L-stereoisomers.**

All molecules with a chiral center are optically active—that is, they rotate the plane of plane-polarized light.



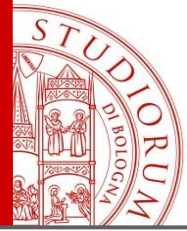


By Fischer's convention, L and D refer to the absolute configuration of the four substituents around the chiral carbon (based on the absolute configuration of the three carbons sugar glyceraldehyde)



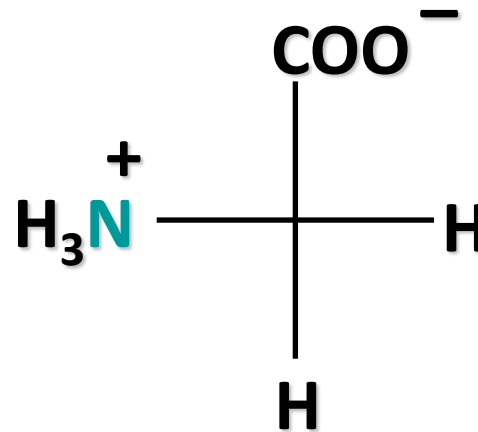
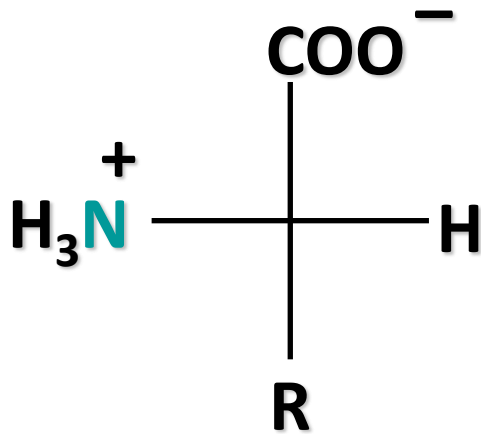
The amino acid residues in protein molecules are exclusively L stereoisomers. D-amino acid residues have been found in only a few, generally small peptides, including some peptides of bacterial cell walls and certain peptide antibiotics.

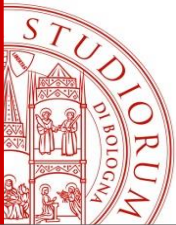
https://www.youtube.com/watch?v=RBtgAz70_JY&feature=youtu.be



Configuration of α -Amino Acids

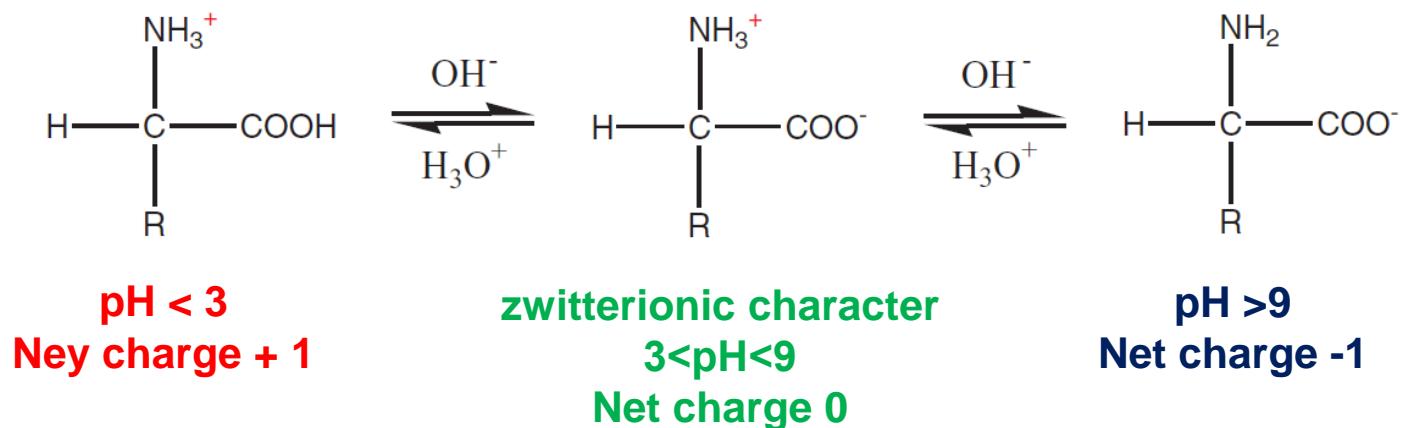
- Glycine is NOT chiral. All of the other amino acids in proteins have the L-configuration.



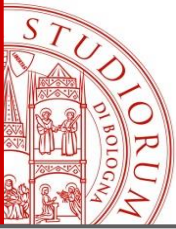


ACID- BASE PROPERTY

Amino acids contain a basic and an acid functional group, they are called **amphoteric**.

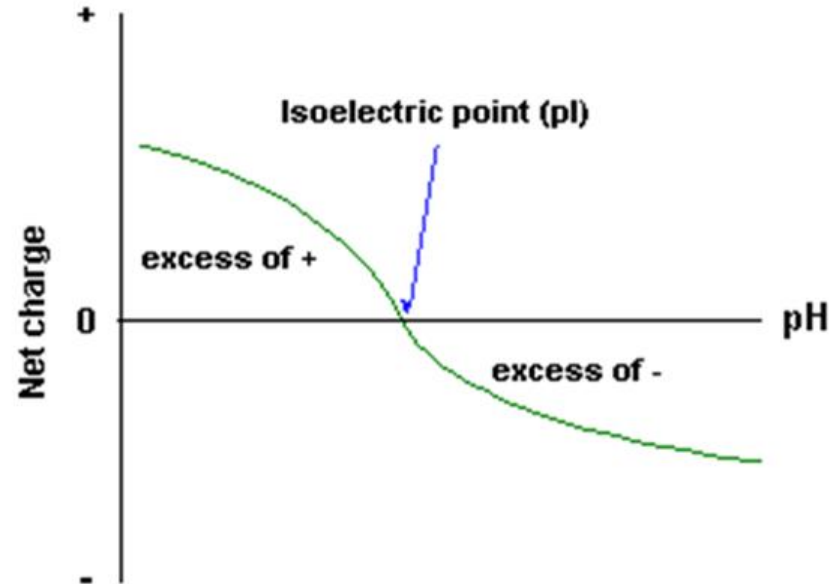


At the pH found close to physiological conditions, the amino group is ionised to $-\text{NH}_3^+$ and the carboxyl group is ionised to $-\text{COO}^-$. **For every amino acid, there is a specific pH value at which it exhibits no net charge, due to the $-\text{R}$ group (zwitterionic form).** This is called the **isoelectric point, pI**.

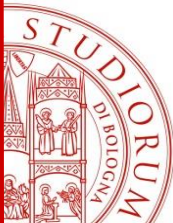


Isoelectric point (pI) – amino acids

Differences in pI can be utilised to separate amino acids or proteins (e.g. in the electrophoresis and chromatographic separation).

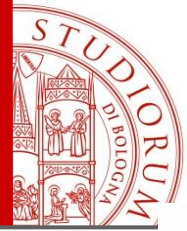


The side chain of several amino acids contain acid (glutamic acid) or basic group (histidine), thus they must be considered triprotic acids instead of diprotic



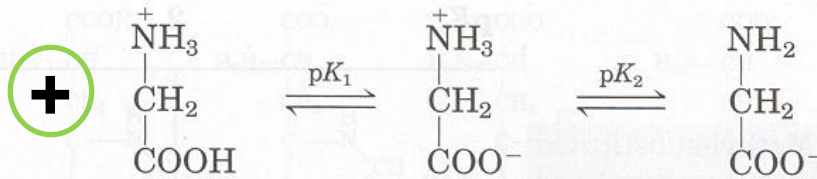
ISOELECTRIC POINT

Amino acids Non-polar chain	pI	Amino acids Polar chain	pI	Amino acids Charged chain	pI
Alanine	6.02	Glycine	5.97	Lysine	9.74
Valine	5.97	Asparagine	5.41	Histidine	7.58
Leucine	5.98	Glutamine	5.65	Arginine	10.76
Isoleucine	6.02	Tyrosine	5.65	Aspartic acid	2.87
Phenylalanine	5.98	Cysteine	5.02	Glutamic acid	3.22
Tryptophan	5.88	Serine	5.68		
Methionine	5.75	Threonine	6.53		
Proline	6.10				



Amino acids have characteristic titration curves

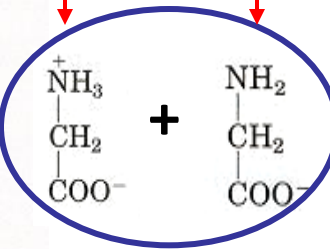
Glycine



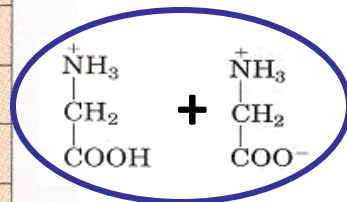
$$pI = \frac{1}{2}(pK_1 + pK_2) = \frac{1}{2}(2.34 + 9.60) = 5.97$$

Proton donor

Proton acceptor

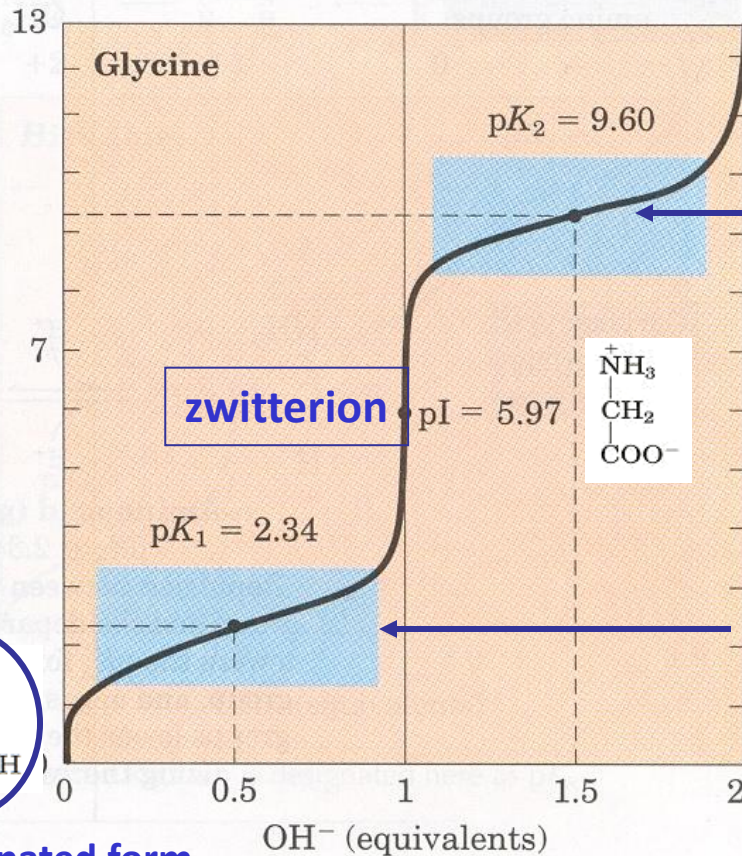


Isoelectric point



Proton donor

Proton acceptor

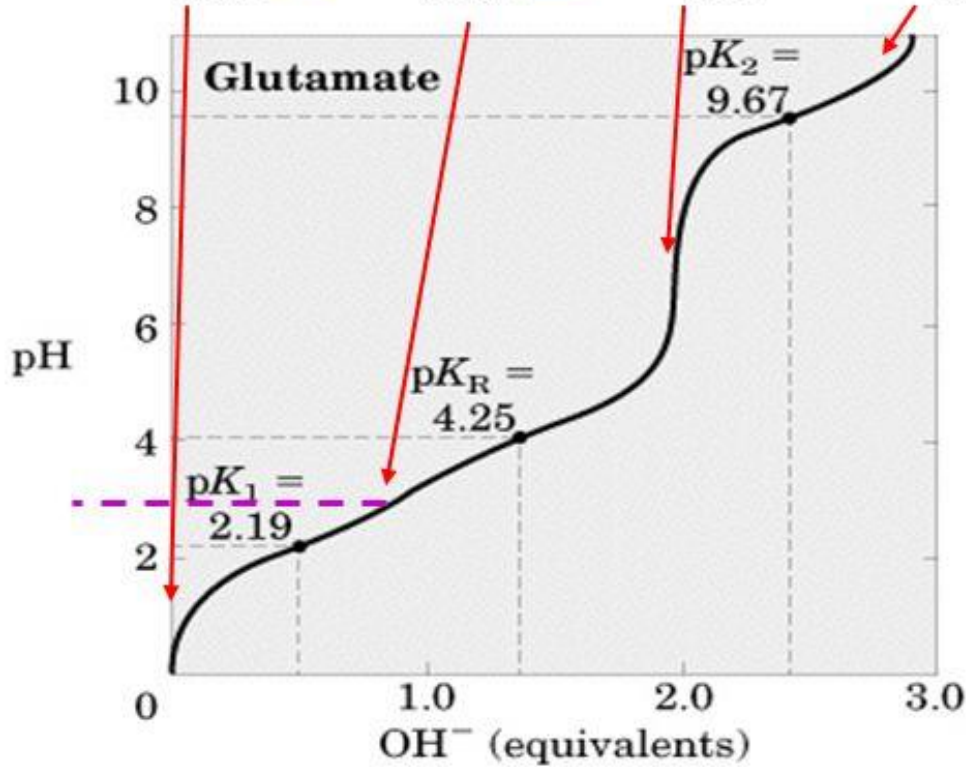
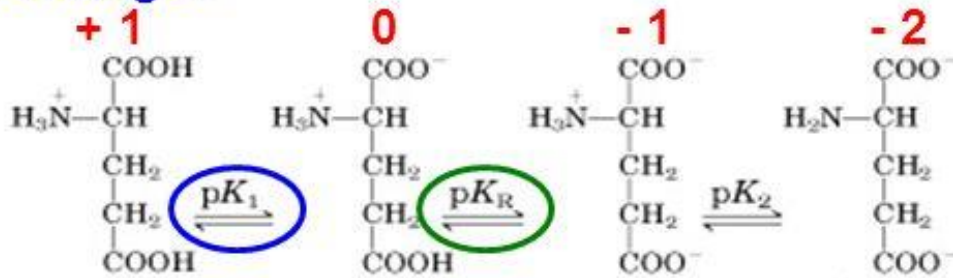


Fully protonated form at a very low pH



Glutamate

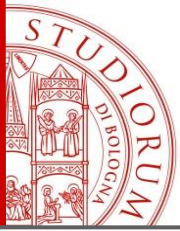
Net Charge?



Glu: the pI is given by the average of the $\text{p}K_a$ values of the two COOH groups which ionize on **either side of the neutral species**:

$$\text{pI} = (\text{p}K_1 + \text{p}K_R) / 2$$

For amino acids with **polar charged groups** (His, Lys, Arg, Glu and Asp), pI reflects the chemical nature of the side chain R group



Lysine

pK_1 carboxylic acid = 2.2

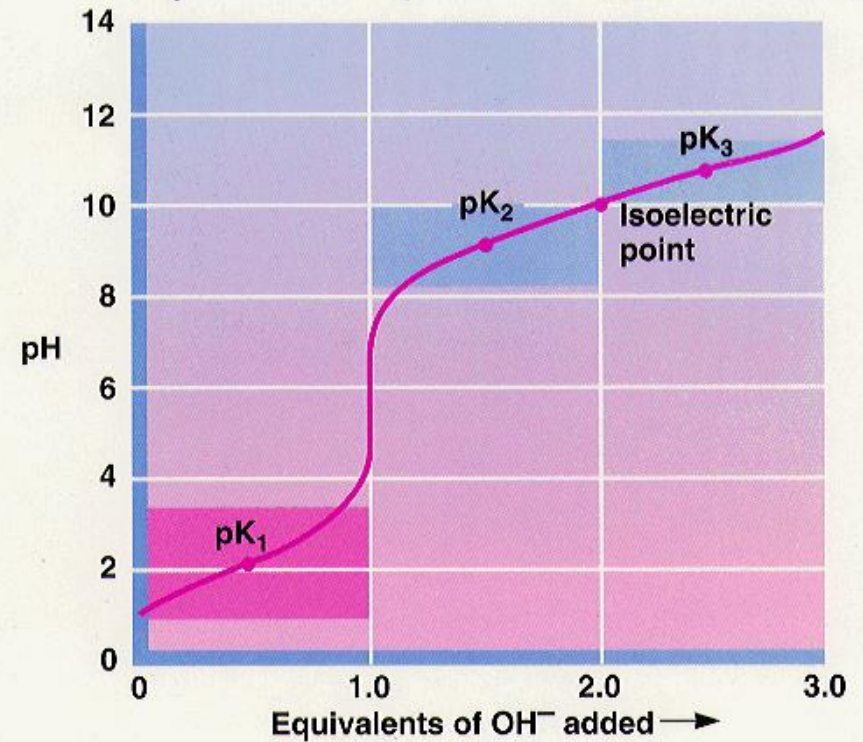
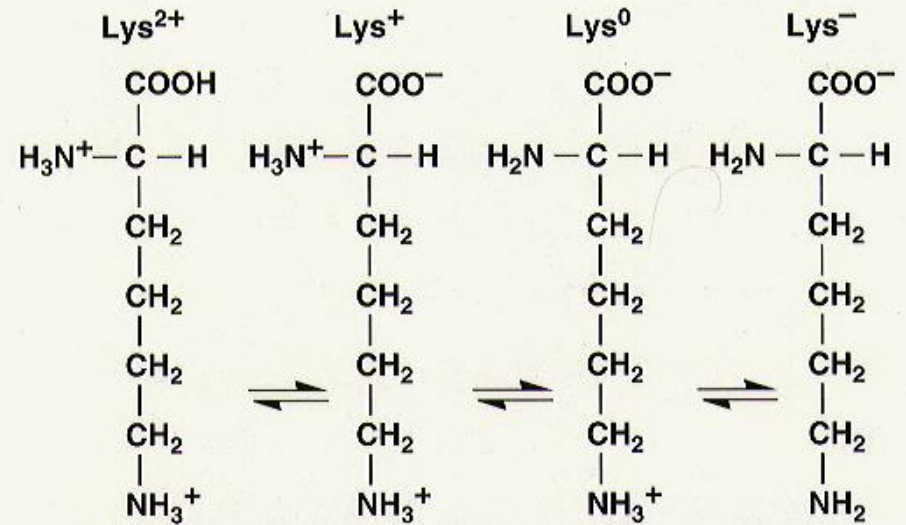
pK_2 amino group = 9.0

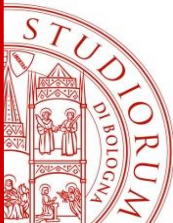
pK_3 R group = 10.5

$pI = (pK_2 + pK_3)/2$

$pI = (9 + 10.5)/2$

$pI = 9.75$





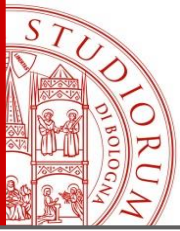
ISOELECTRIC POINT

Amino acids Non-polar chain	pI	Amino acids Polar chain	pI	Amino acids Charged chain	pI
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Methionine	5.75	Threonine	6.53		
Proline	6.10				

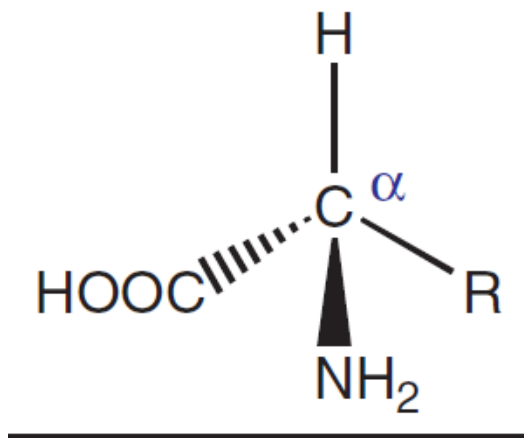
pK_a Values of Common Amino Acids

Acid	α -COOH	α -NH ₃ ⁺	R-Group
Gly	2.34	9.60	
Ala	2.34	9.69	
Val	2.32	9.62	
Leu	2.36	9.68	
Ile	2.36	9.68	
Ser	2.21	9.15	
Thr	2.63	10.43	
Met	2.28	9.21	
Phe	1.83	9.13	
Trp	2.38	9.39	
Asn	2.02	8.80	
Gln	2.17	9.13	
Pro	1.99	10.6	
Asp	2.09	9.82	3.86*
Glu	2.19	9.67	4.25*
His	1.82	9.17	6.0*
Cys	1.71	10.78	8.33*
Tyr	2.20	9.11	10.07
Lys	2.18	8.95	10.53
Arg	2.17	9.04	12.48

* For these amino acids, the R group ionization occurs before the α -NH₃⁺ ionization.



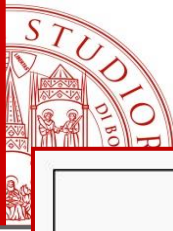
AMINO ACIDS CLASSIFICATION



Amino acids can be classified according to:

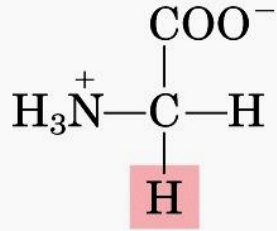
- their substituent R groups;
- their polarity and charge around pH 7 (which corresponds to the pH range found in most biological systems).

The polarity of the R groups varies widely, from nonpolar and hydrophobic (water-insoluble) to highly polar and hydrophilic (water-soluble).

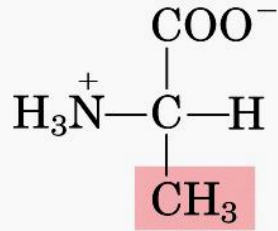


Aliphatic -R, non-polar

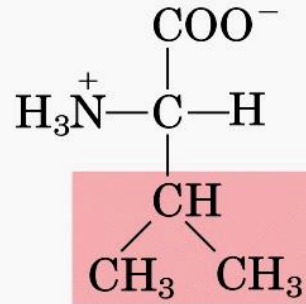
Nonpolar, aliphatic R groups



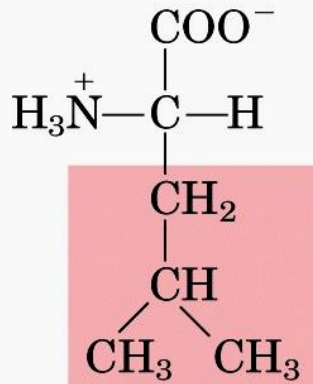
Glycine
2-Aminoethanoic acid



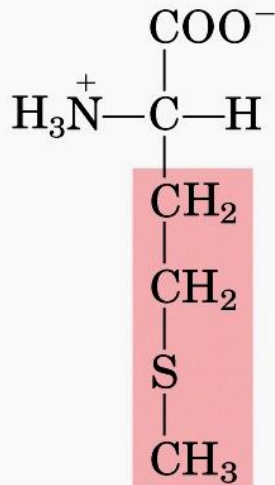
Alanine



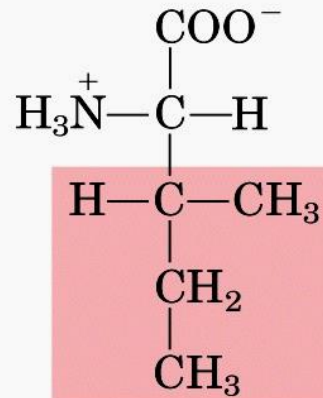
Valine



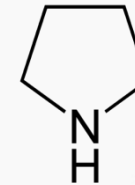
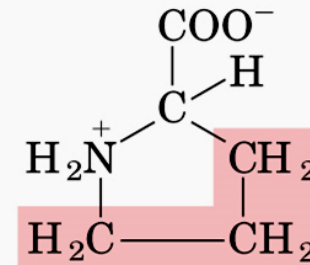
Leucine



Methionine



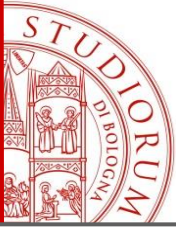
Isoleucine



Pyrrole ring

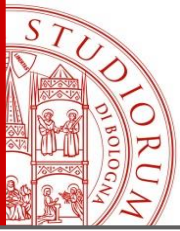
Proline

Pyrrolidine-2-carboxylic acid



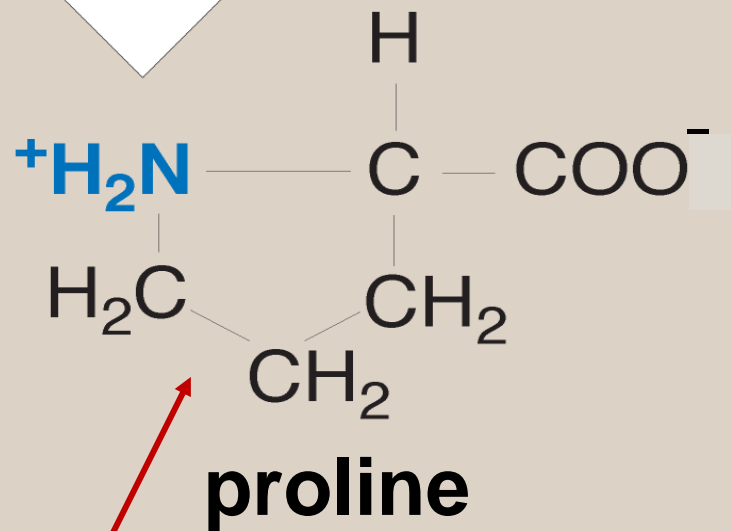
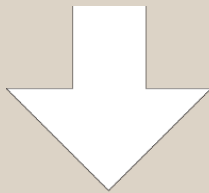
Aliphatic –R, non-polar

- The side chains of **alanine**, **valine**, **leucine**, and **isoleucine** tend to cluster together within proteins, stabilizing protein structure through the hydrophobic effect.
- **Glycine** has the simplest structure (is not chiral) . Although it is most easily grouped with the nonpolar amino acids, its very small side chain makes no real contribution to interactions driven by the hydrophobic effect. It is found on the surface of many proteins because it is flexible and so can fold.
- **Methionine**, one of the two sulfur-containing amino acids, has a slightly nonpolar thioether group in its side chain.
- **Proline** has an aliphatic side chain with a rigid cyclic structure. The secondary amino (imino) group of proline residues is held in a rigid conformation that reduces the structural flexibility of polypeptide regions containing proline.



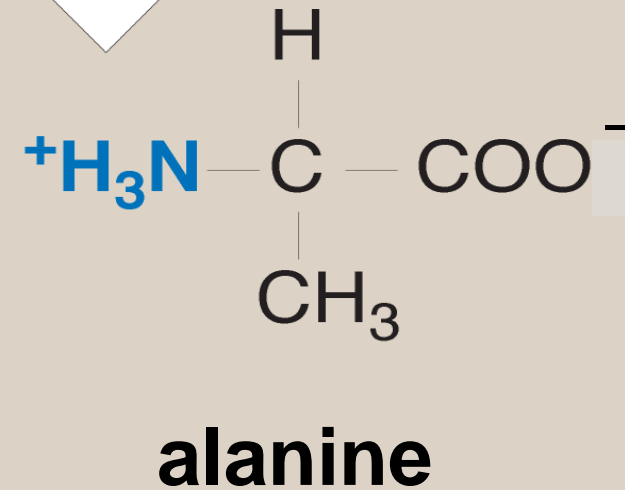
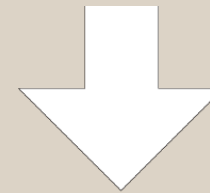
PROLINE STRUCTURE

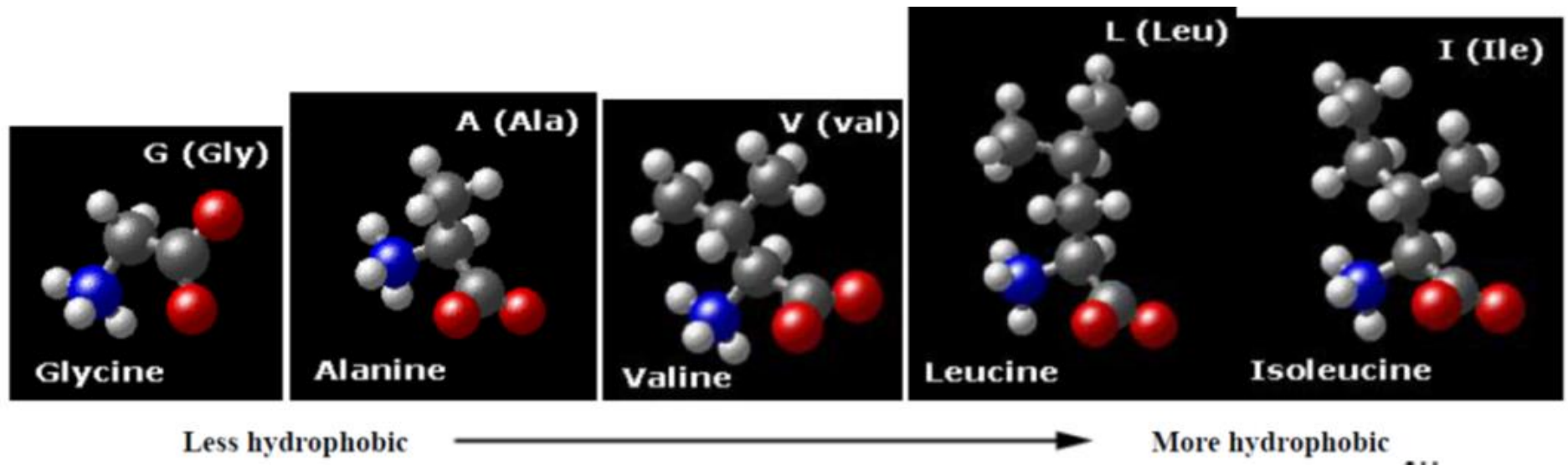
**imino
group**



Pyrrole ring

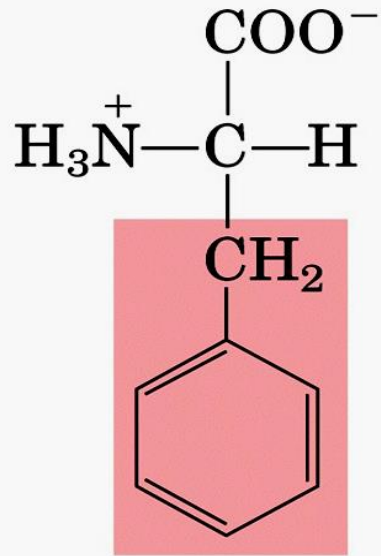
**amino
group**



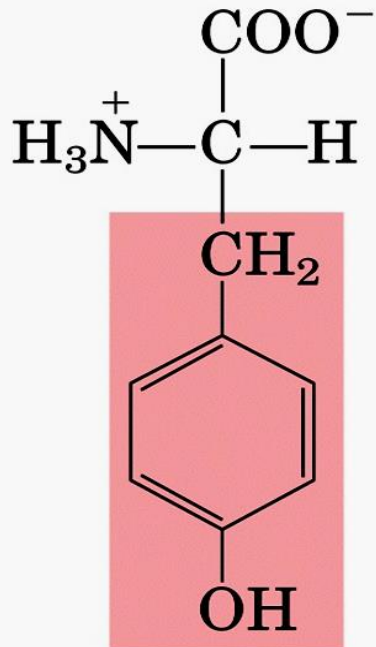


Aromatic -R

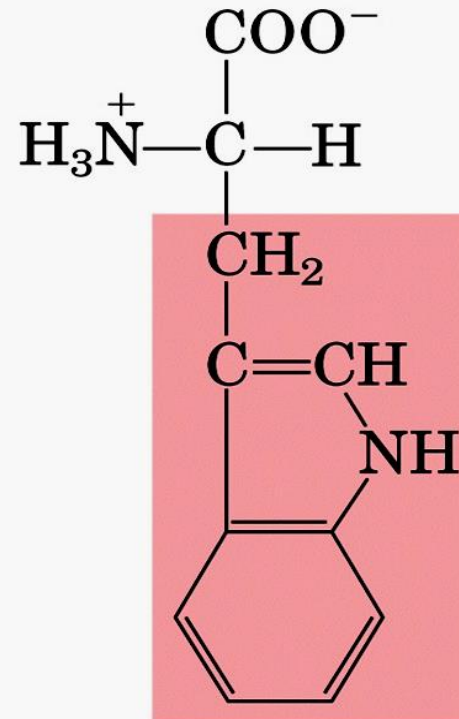
Aromatic R groups



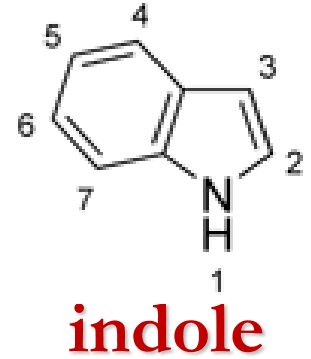
Phenylalanine



Tyrosine



Tryptophan



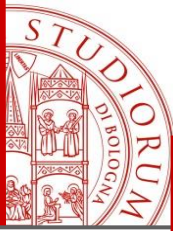


Aromatic –R

Phenylalanine, and tryptophan, with their aromatic side chains, are relatively nonpolar. All can contribute to the hydrophobic effect.

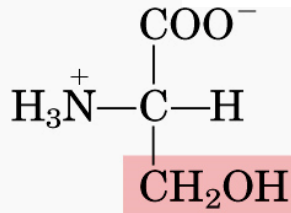
The hydroxyl group of tyrosine can form hydrogen bonds, and it is an important functional group in some enzymes.

Tyrosine and tryptophan are significantly more polar than phenylalanine because of the tyrosine hydroxyl group and the nitrogen of the tryptophan indole ring.

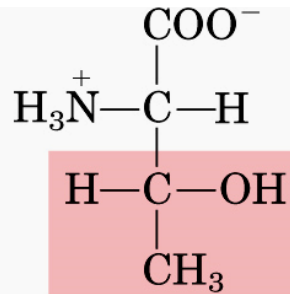


Polar, but not-charged –R

alcohols

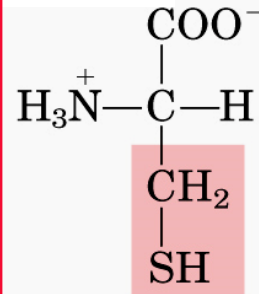


Serine



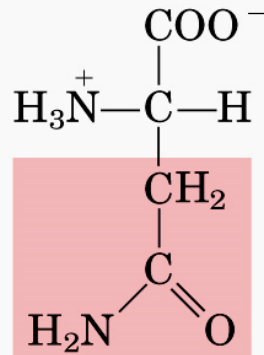
Threonine

thiol

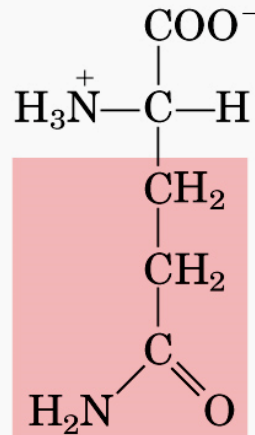


Cysteine

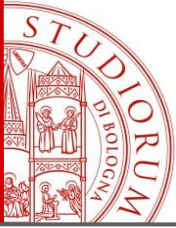
amide



Asparagine



Glutamine



Polar, but not-charged –R

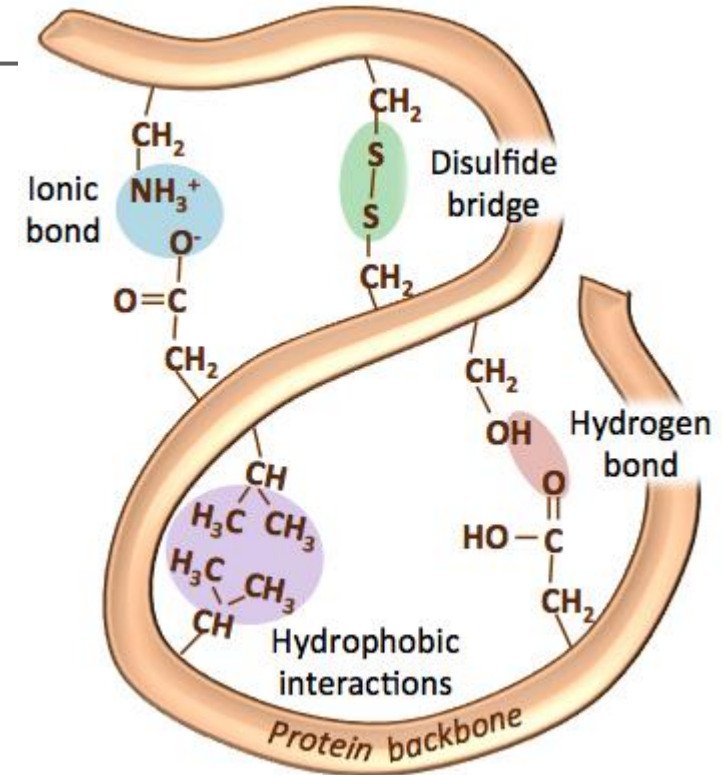
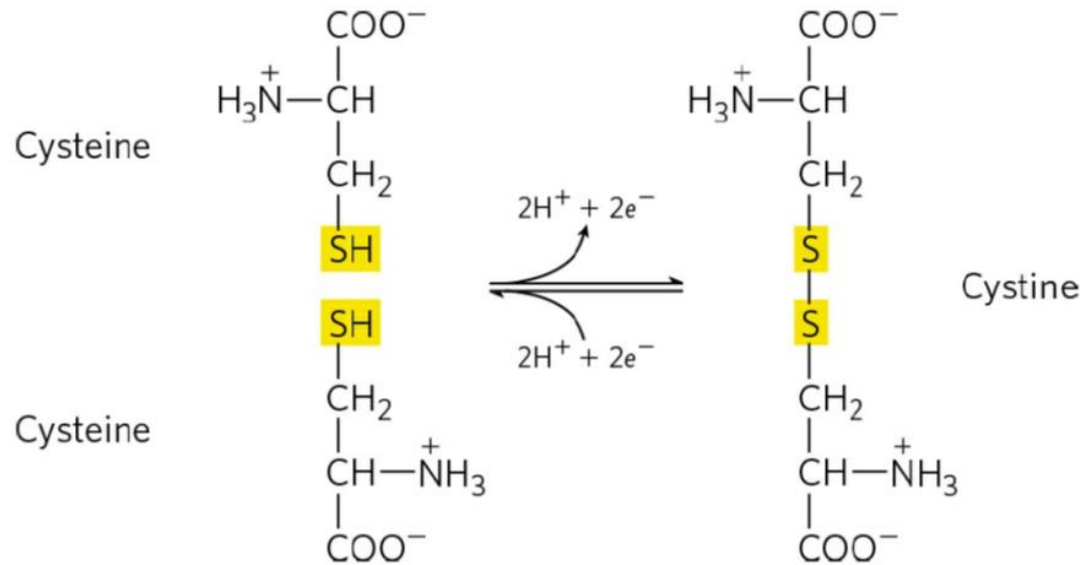
This class of amino acids includes **serine, threonine, cysteine, asparagine, and glutamine.**

The R groups of these amino acids are more soluble in water, or more hydrophilic, than those of the nonpolar amino acids, because they contain functional groups that form hydrogen bonds with water.

The polarity of **serine and threonine** is contributed by their hydroxyl groups, and that of **asparagine and glutamine** by their amide groups. **Asparagine and glutamine** are the amides of two other amino acids, aspartate and glutamate.

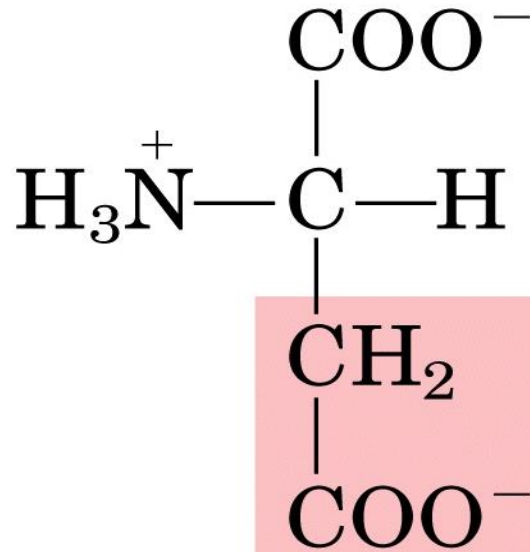
Cysteine with its thiol group is a weak acid and can make weak hydrogen bonds with oxygen or nitrogen.

Oxidation of the sulfide functional group of cysteine

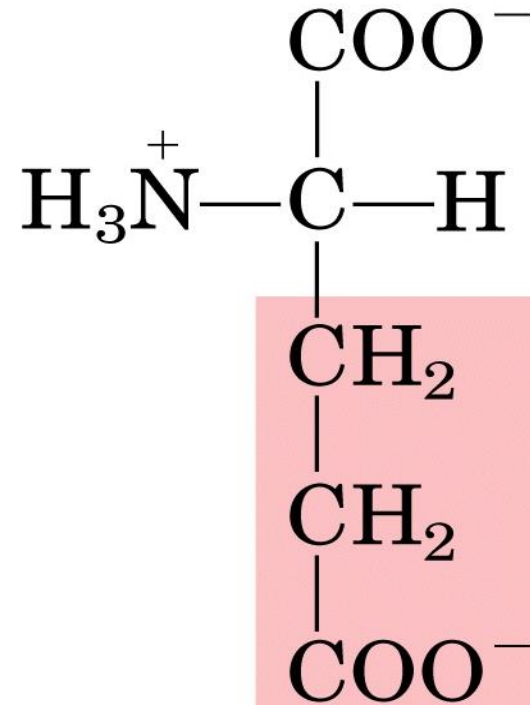


- Two molecules of cysteine may undergo an oxidation reaction resulting in the formation of a **disulfide bridge**.
- In disulfide bridges, the bond is covalent, but weak and easily formed/breakable.
- In a protein the disulfide bridge can be formed even between cysteines very far from each other, bringing together portions of polypeptide chain (ex. Insulin).

Negatively Charged (Acid) R Groups



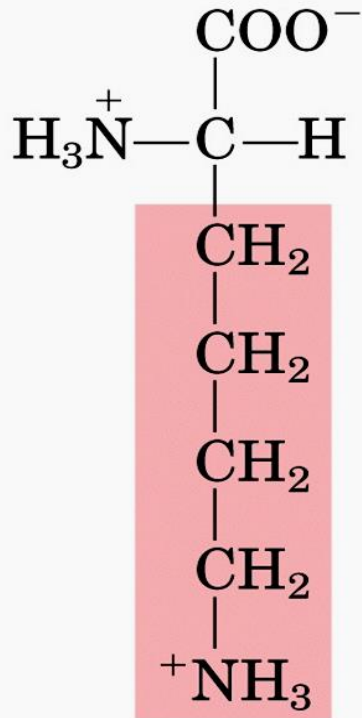
Aspartate



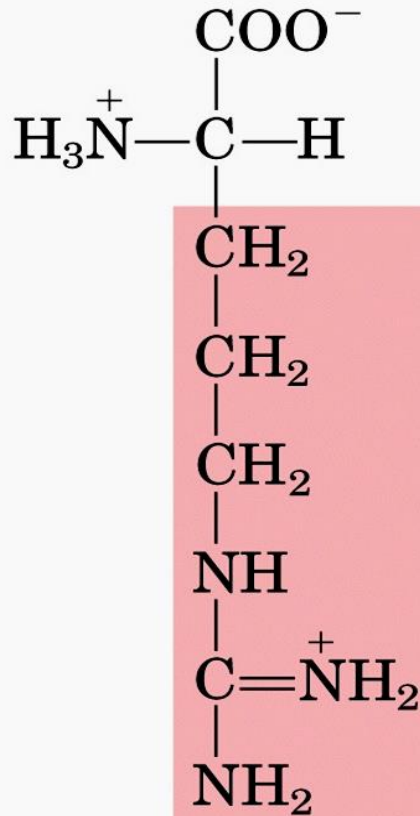
Glutamate

R groups (with a second carboxyl group) with a net negative charge at pH 7.0.

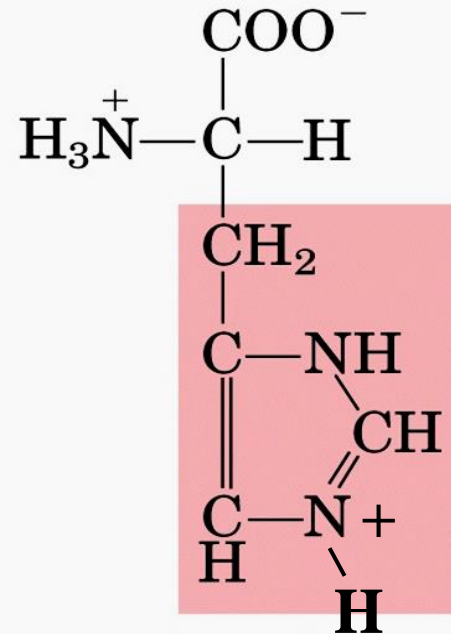
Positively Charged (Basic) R Groups



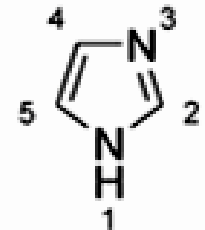
Lysine



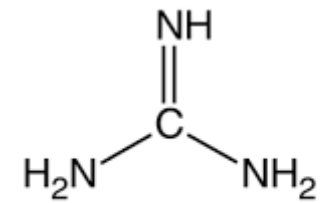
Arginine



Histidine



imidazole



guanidine



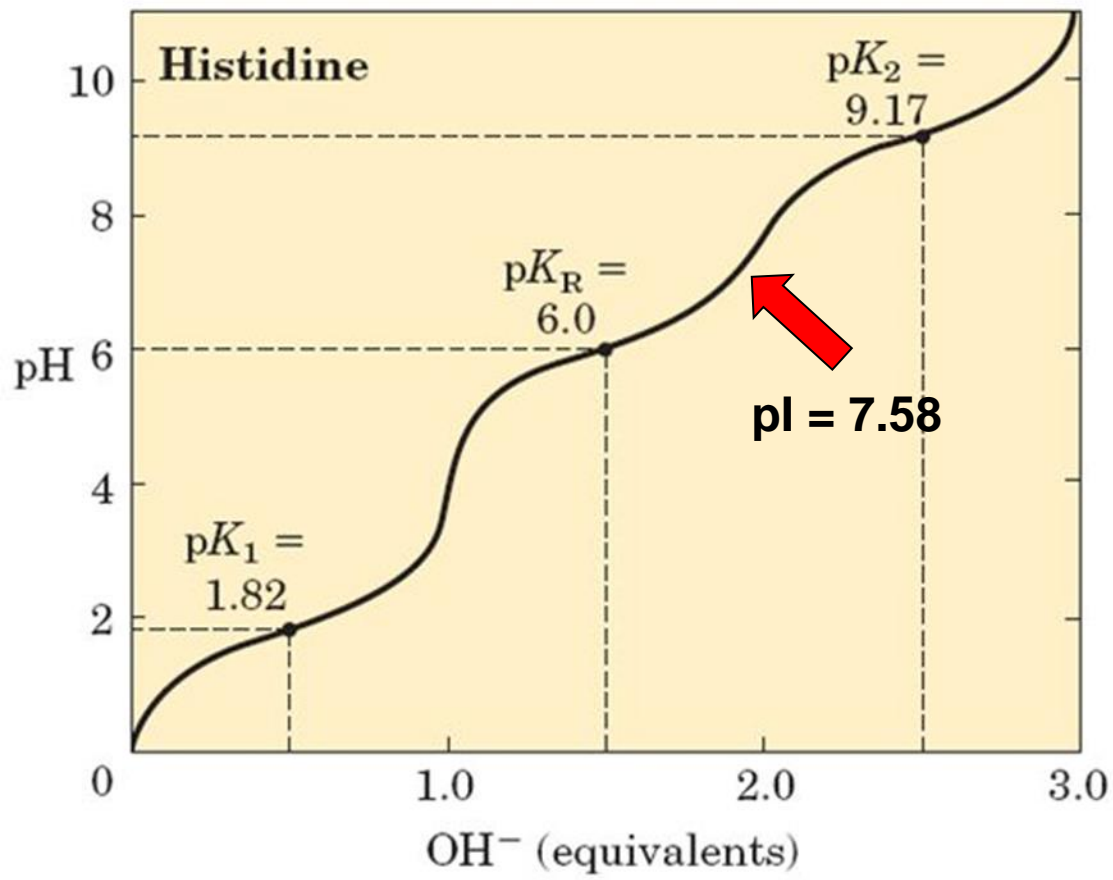
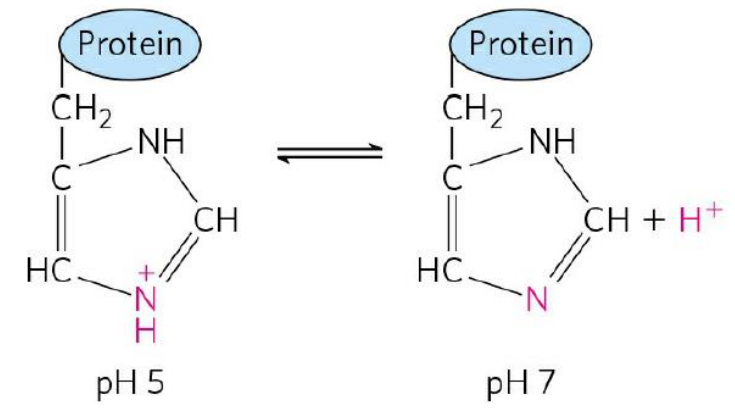
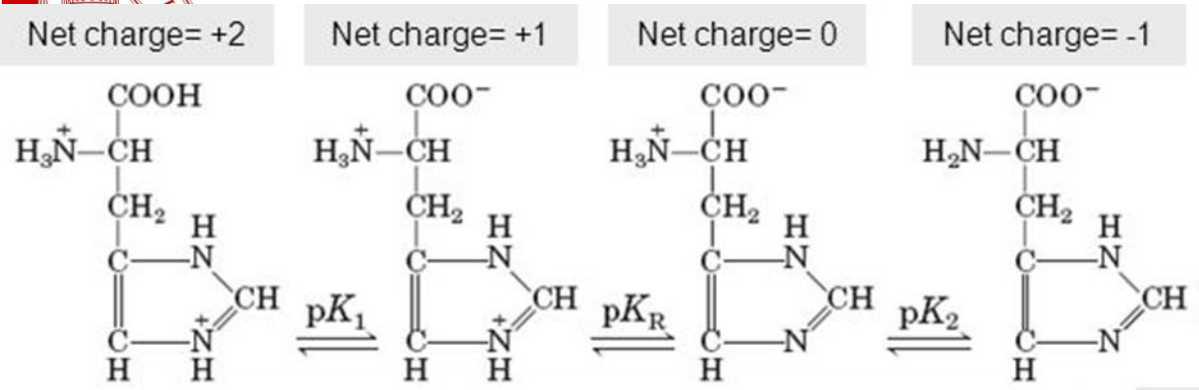
Positively Charged (Basic) R Groups

the R groups have significant positive charge at pH 7.0:

- **lysine** has a primary amino group on its aliphatic chain;
- **arginine** has a positively charged guanidinium group;
- **histidine** has an aromatic imidazole group.

Histidine is the only common amino acid having a pI near 7.4. His residues facilitate many enzyme-catalyzed reactions by serving as proton donors/acceptors.

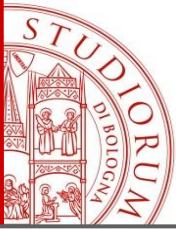
Histidine



$$pI = \frac{pKa_2 + pKa_R}{2}$$

There are three ionizable groups and, therefore, three transitions in the titration.

The pI corresponds to the midpoint between the two transitions that involve the species with no net charge.



Functional Classification of Amino Acids

Amino acids are generally divided into groups on the basis of their side chains (R groups).

The most helpful start-point is to separate amino acids into:

Nonpolar

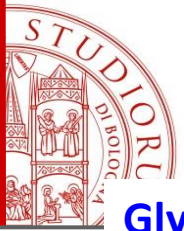
Neutral polar

Charged polar

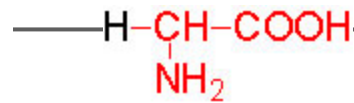
1. Nonpolar amino acids

- ➡ Only carbon and hydrogen in their side chains
- ➡ Generally *unreactive* but *hydrophobic*
- ➡ Determine the 3-D structure of proteins (they tend to cluster on the inside of the molecule)

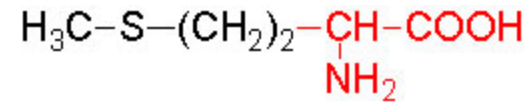
Nonpolar (Hydrophobic) R Groups



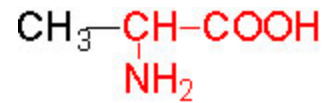
Glycine (Gly)



Methionine (Met)



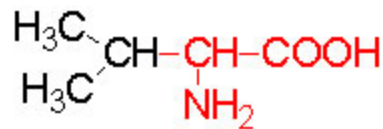
Alanine (Ala)



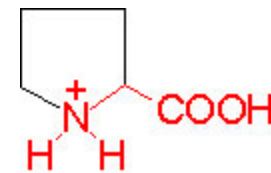
Phenylalanine (Phe)



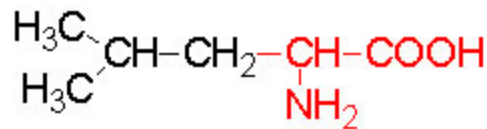
Valine (Val)



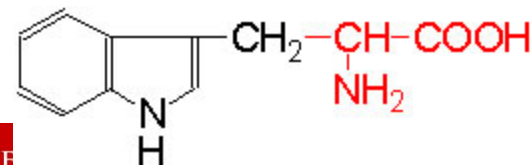
Proline (Pro)



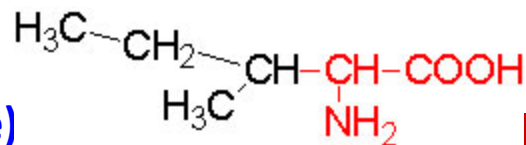
Leucine (Leu)

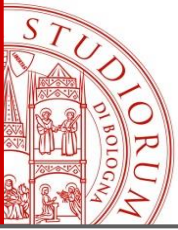


Tryptophan (Trp)



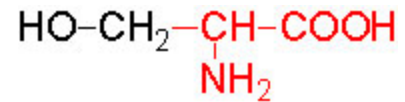
Isoleucine (Ile)



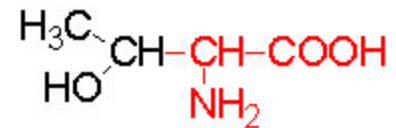


Polar (Hydrophilic) R Groups

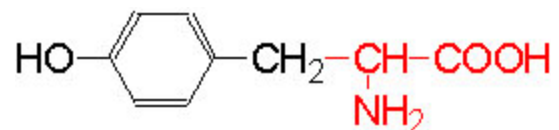
Serine (Ser)



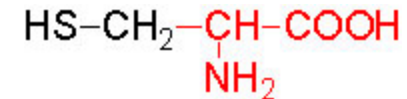
Threonine (Thr)



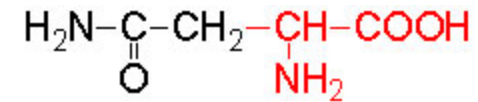
Tyrosine (Tyr)



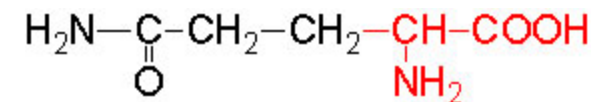
Cysteine (cys)

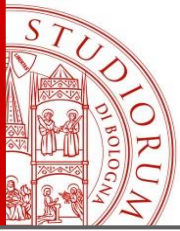


Asparagine (Asn)



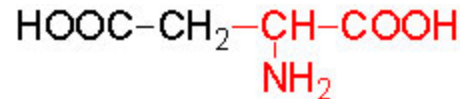
Glutamine (Gln)



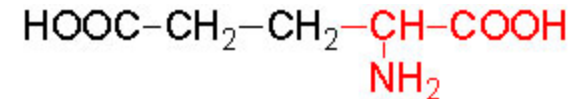


Negatively Charged R Groups

Aspartic acid (Asp)



Glutamic acid (Glu)

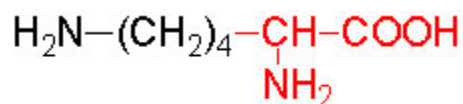


Two amino acids with negatively charged (i.e. acid) side chains - Aspartate (Aspartic acid) and Glutamate (Glutamic acid).

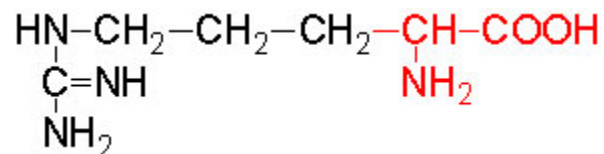
These amino acids confer a negative charge on the proteins.

Positively Charged R Groups

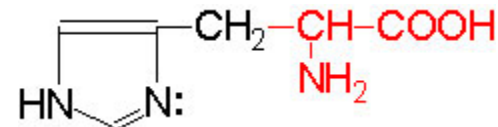
Lysine (Lys)



Arginine (Arg)



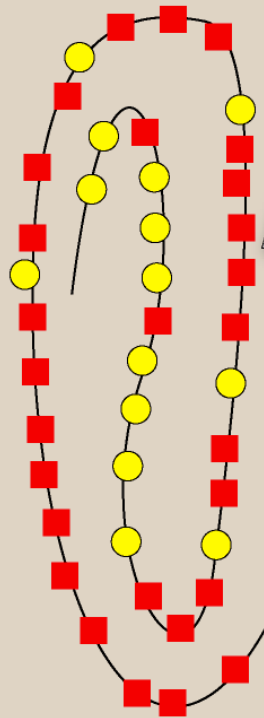
Histidine (His)



- Lysine and Arginine both have pKaR around 10.0 and are therefore always positively charged at neutral pH.
- With a pKaR around 7, Histidine can be uncharged or positively charged depending upon its local environment.
- Histidine has an important role in the catalytic mechanism of enzymes and explains why it is often found in the active site.

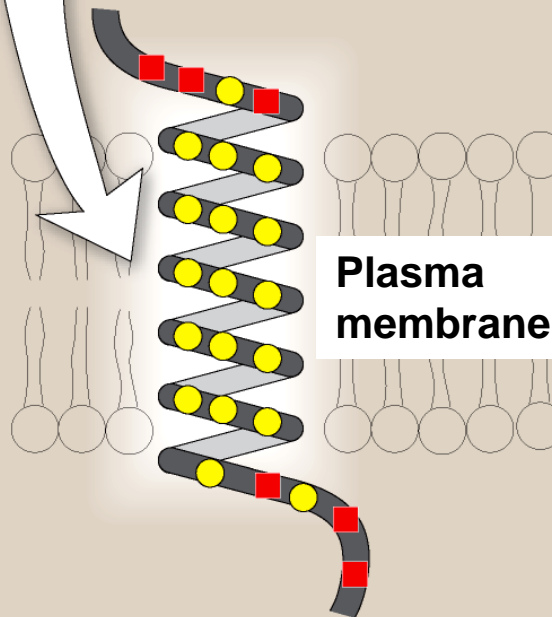
POLARITY OF AMINO ACIDS

Polar amino acids are present on the surface of soluble proteins



Soluble protein

Non-polar amino acids are present into the double layer of plasma membranes

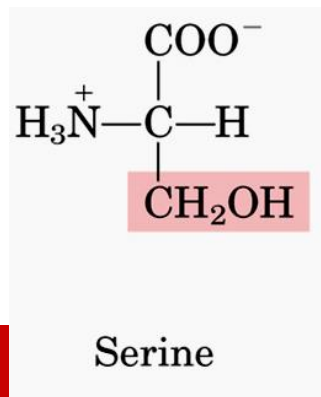
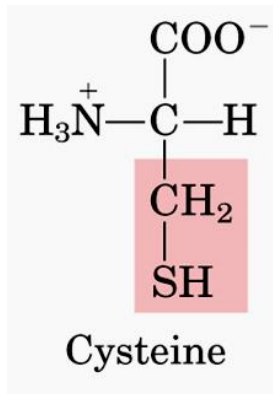
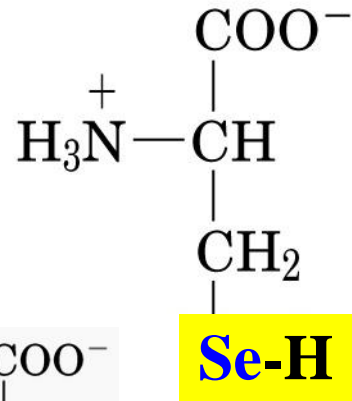


Plasma membrane

Membrane protein



Selenocysteine: amino acid 21



- Selenocysteine contains selenium rather than the sulfur of cysteine.
- Derived from serine, selenocysteine is located in the active sites of enzymes that participate in oxidation–reduction reactions (glutathione peroxidase, thioredoxin reductase, and iodothyronine deiodinase).

Types of Amino Acids



NONESSENTIAL

Nonessential amino acids are produced by our body.



ESSENTIAL

Essential amino acids have to be provided by our diet.



CONDITIONAL

Conditional amino acids may become essential in times of stress or illness.

- | | | | |
|-----------------|-----------------|---------------|---|
| ■ alanine | ■ ■ histidine | ■ ■ arginine | ■ |
| ■ asparagine | ■ ■ isoleucine | ■ ■ cysteine | ■ |
| ■ aspartic acid | ■ ■ leucine | ■ ■ glutamine | ■ |
| ■ glutamic acid | ■ ■ lysine | ■ ■ tyrosine | ■ |
| | ■ methionine | ■ ■ glycine | ■ |
| | ■ phenylalanine | ■ ■ ornithine | ■ |
| | ■ threonine | ■ ■ proline | ■ |
| | ■ tryptophan | ■ ■ serine | ■ |
| | ■ valine | ■ | ■ |

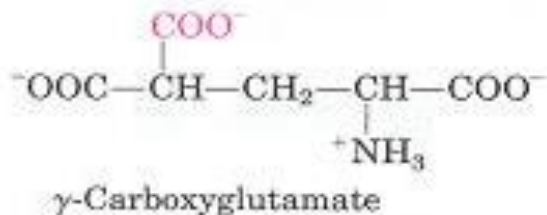
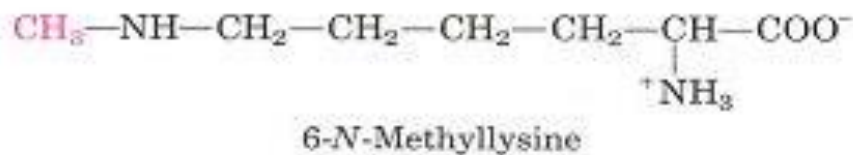
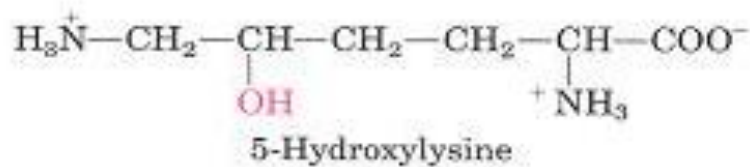
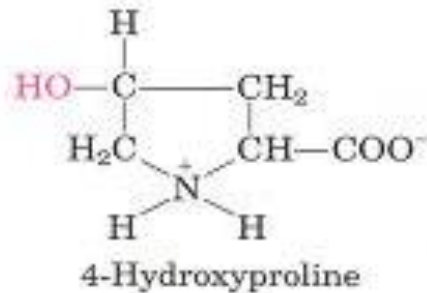
- **9 essential amino acids cannot be physiologically synthesized. As a result, they must come from food.**
- **Conditional amino acids: are usually not essential, except in times of illness and stress.**
- **Nonessential amino acids: our bodies produce these amino acids, so we do not get them from the food.**



Uncommon Amino Acids

- In addition to the 20 common amino acids, proteins may contain residues created by modification of common residues already incorporated into a polypeptide—that is, through post-translational modification.
- They have several functions:
 - taurine, used for the synthesis of bile salts
 - histamine, mediator of allergic reactions
 - dopamine, an important neurotransmitter

Uncommon amino acids found in proteins

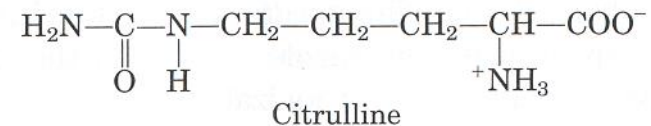
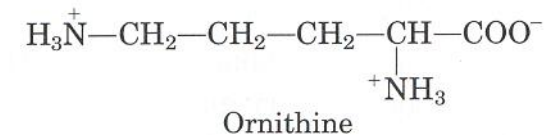


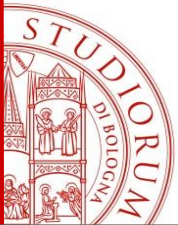
4-hydroxyproline, a derivative of proline, and **5-hydroxylysine**, derived from lysine; both are found in collagen, a fibrous protein of connective tissues.

6-N-Methyllysine is a constituent of myosin, a contractile protein of muscle.

γ -carboxyglutamate, found in the blood-clotting protein prothrombin and in certain other proteins that bind Ca^{2+} as part of their biological function.

Intermediates of biosynthesis of arginine and in urea cycle

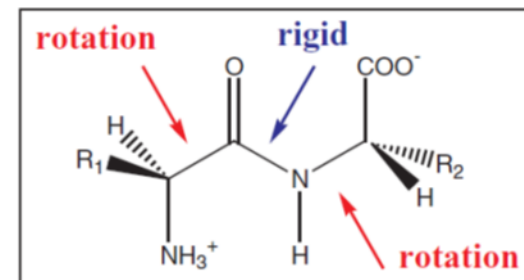
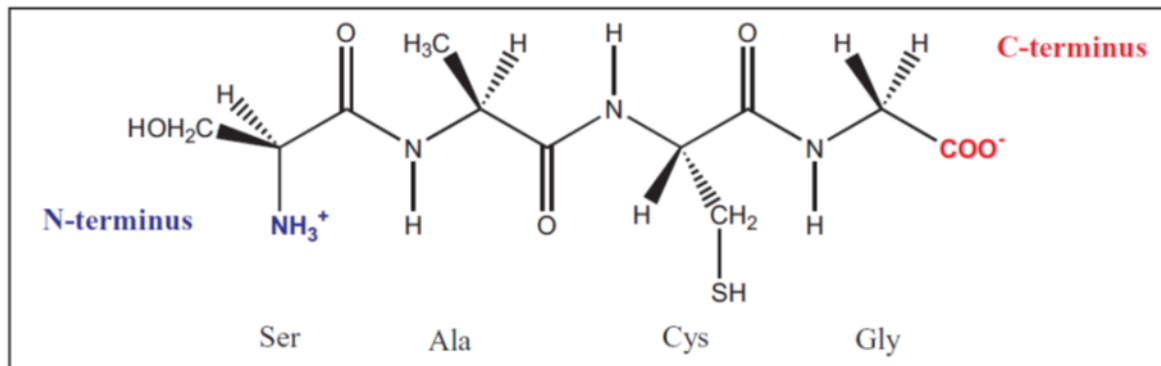




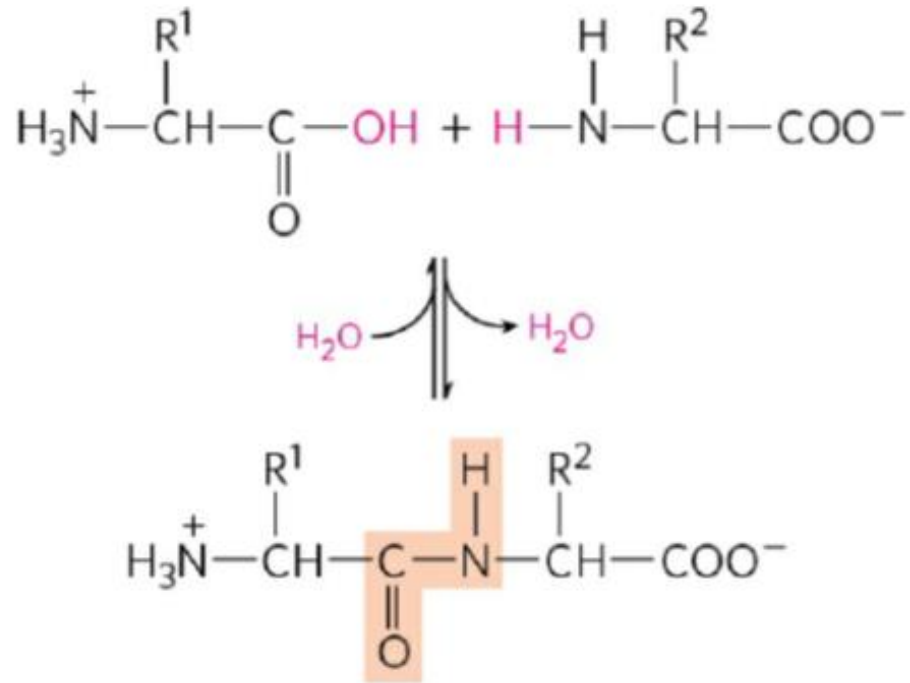
Peptides

Peptides

- Peptides are compounds in which an amide bond links the amino group of one α -amino acid and the carboxyl group of another.
- An amide bond of this type is often referred to as a **peptide bond**.



Peptide bond formation: a condensation reaction



- Two amino acids can be covalently joined through a substituted **amide bond**, termed a **peptide bond**, to yield a dipeptide.
- Such a linkage is formed by removal of water (**dehydration**) from the α -carboxyl group of one amino acid and the α -amino group of another.

- Although hydrolysis of a peptide bond is an exergonic reaction, it occurs only slowly because it has a high activation energy. As a result, the peptide bonds in proteins are quite stable, with an average half-life ($t_{1/2}$) of about 7 years under most intracellular conditions.

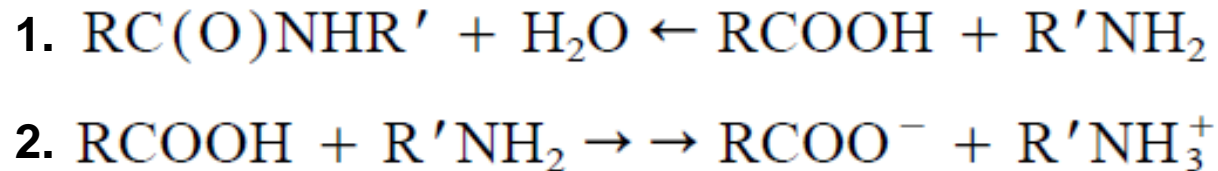


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Received 3 June 1997;
accepted 5 November 1997

Free Energies and Equilibria of Peptide Bond Hydrolysis and Formation

Peptide bond hydrolysis may be advantageously resolved into two contributions:



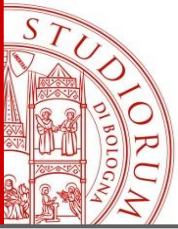
1. amide bond hydrolysis to unionized carboxylic acid and amino groups (free energy change is positive)
2. ionization of the carboxylic and the amino groups at physiological pH (free energy change is negative).

The overall free energy change is:

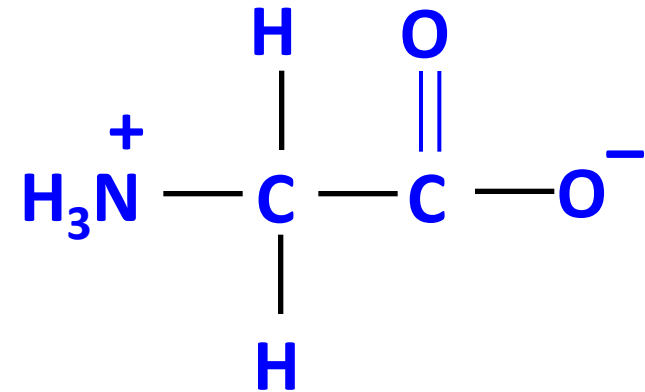
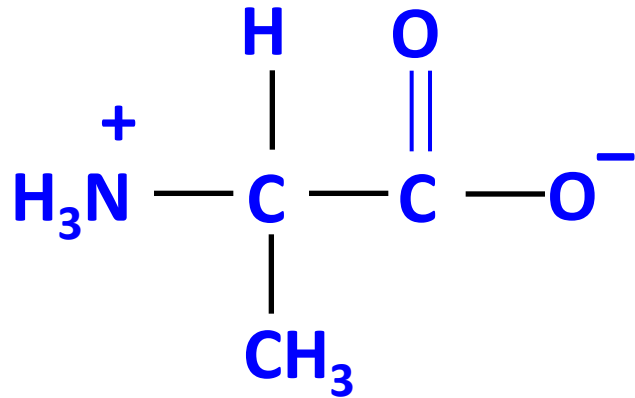
$$\Delta G_h = \Delta G_m + \Delta G_i \quad \longrightarrow \quad \text{The sum is negative}$$

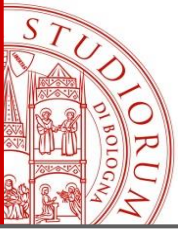
ΔG_m is the free energy of hydrolysis of the amide bond to uncharged products (+)

ΔG_i is the free energy of ionization (-)

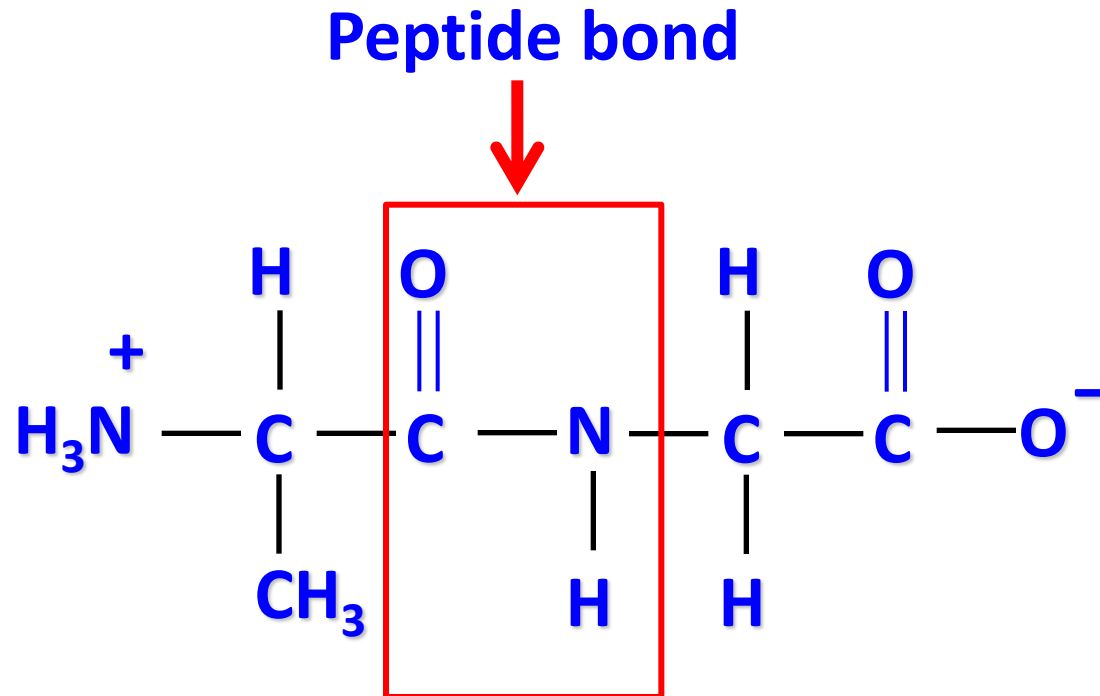


Alanine and Glycine



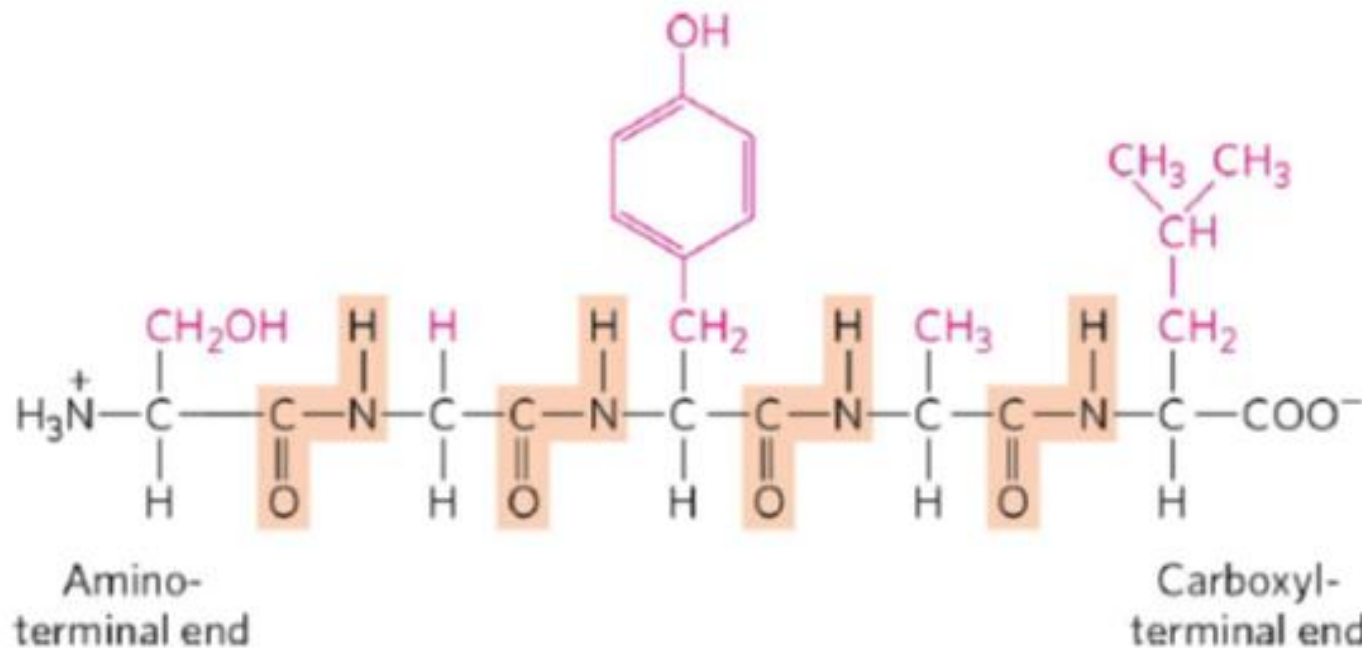


Alanylglycine, a dipeptide

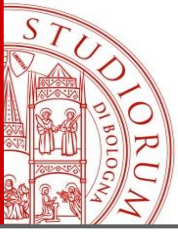


- Two α -amino acids are joined by a peptide bond in alanylglycine. It is a *dipeptide*.

Ser-Gly-Tyr-Ala-Leu, a pentapeptide

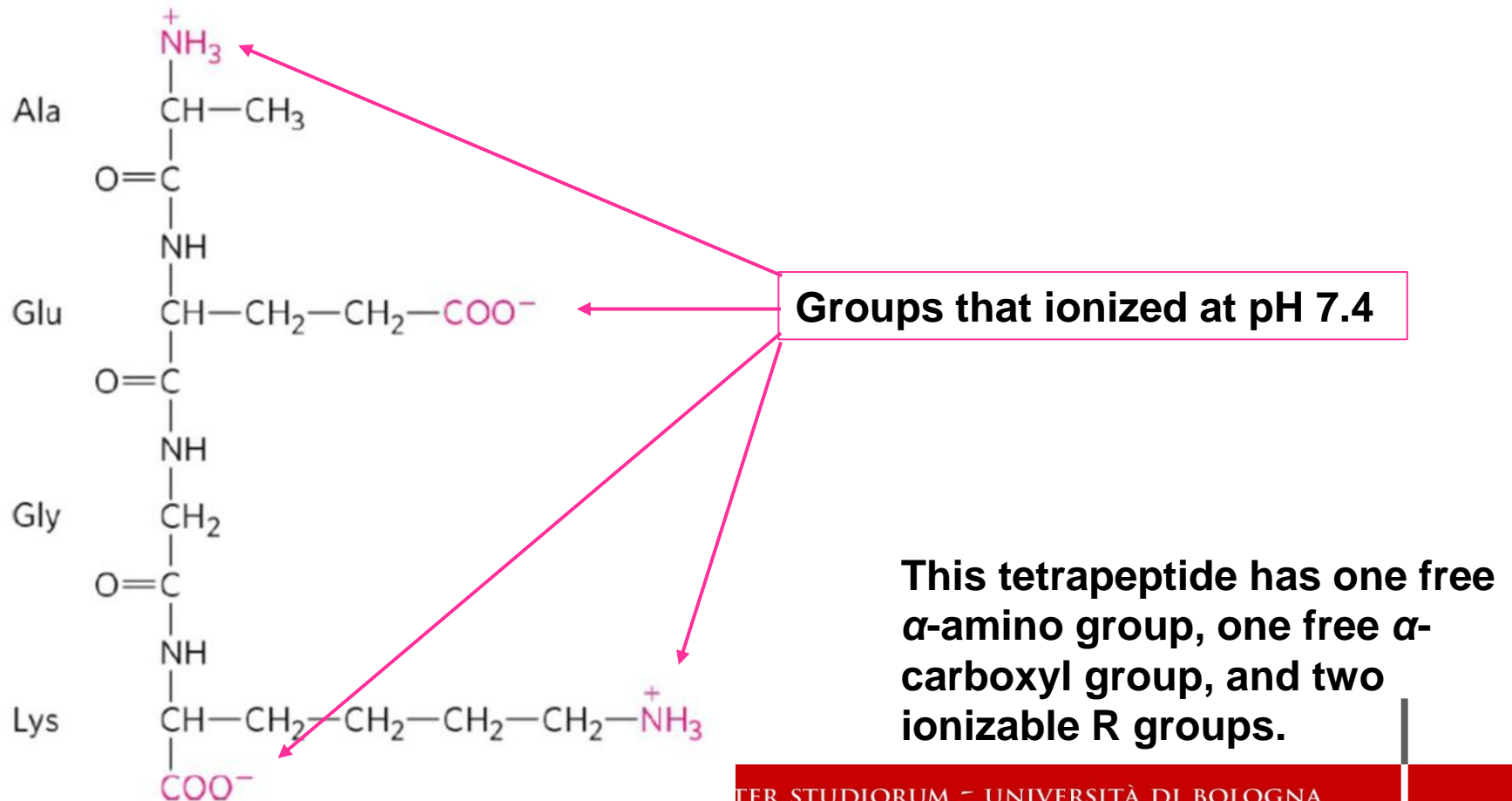


- ✓ In a peptide, the amino acid residue at the end with a free α -amino group is the amino-terminal (or N-terminal) residue; the residue at the other end, which has a free carboxyl group, is the carboxyl-terminal (C-terminal) residue.
- ✓ When an amino acid sequence of a peptide, polypeptide, or protein is displayed, the amino-terminal end is placed on the left, the carboxyl-terminal end on the right. The sequence is read left to right, beginning with the amino-terminal end.

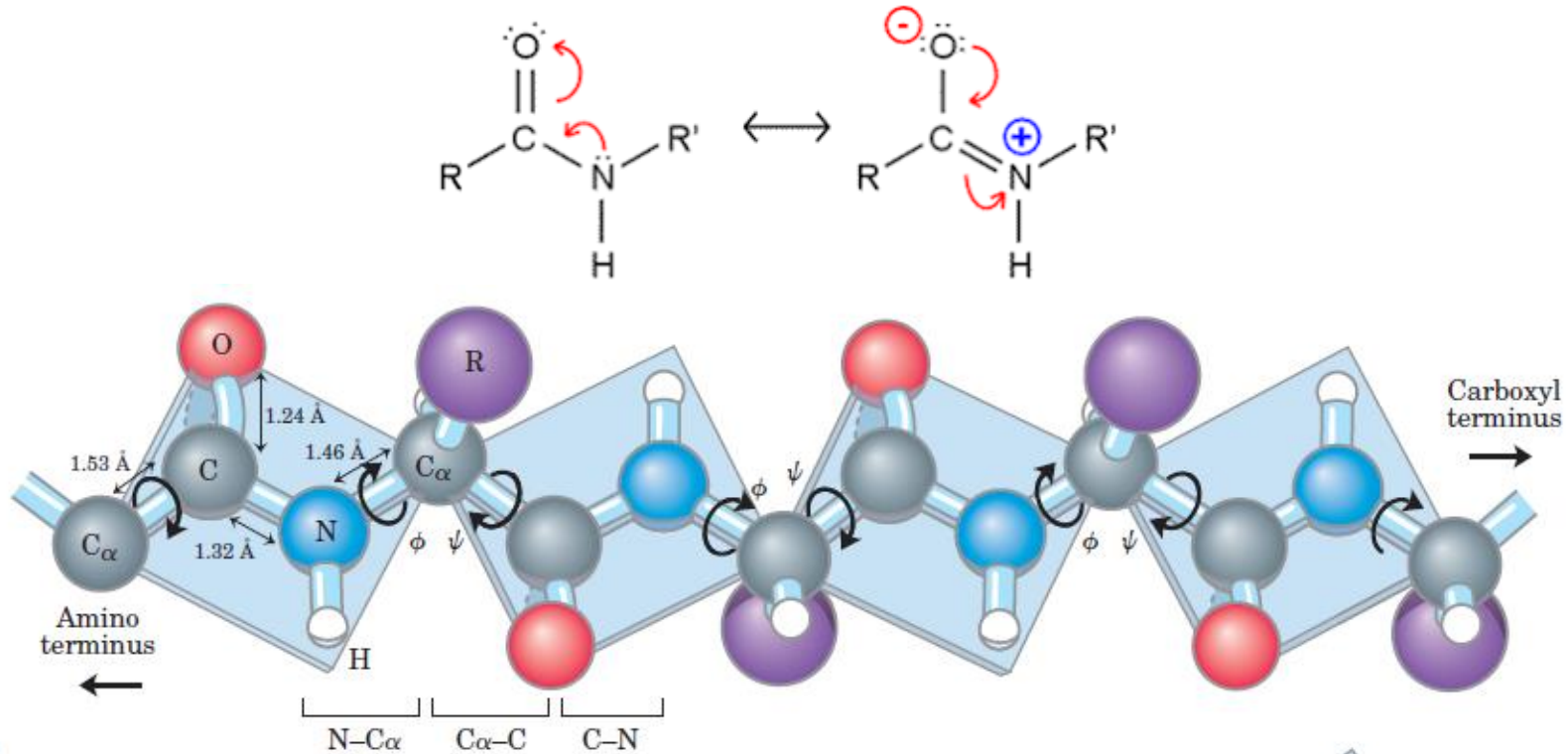


Acid - base properties of peptides

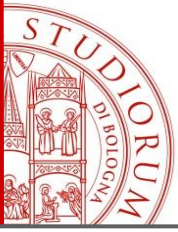
- ✓ The acid-base behavior of a peptide can be predicted from its free α -amino and α -carboxyl groups combined with the nature and number of its ionizable R groups.



Peptide bond

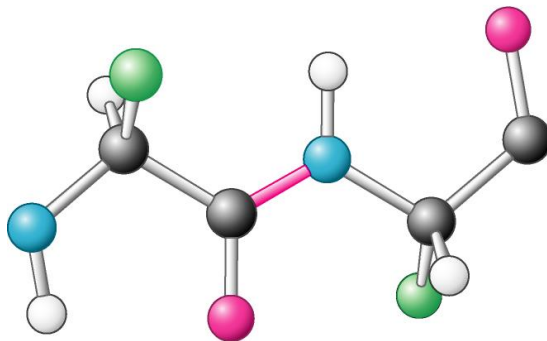
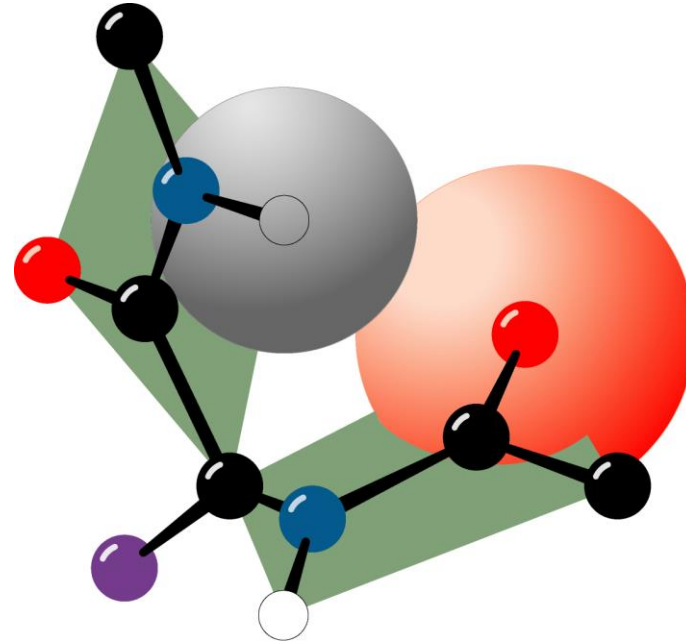


- Although rotation around C α is allowed, the stiffness of C-N strongly reduces the number of possible conformations.
- The bonds between the carboxylic C and C α (Ψ psi) and the one between N and C α (Φ fi) can rotate freely, depending on the steric size of R-residue (R groups)

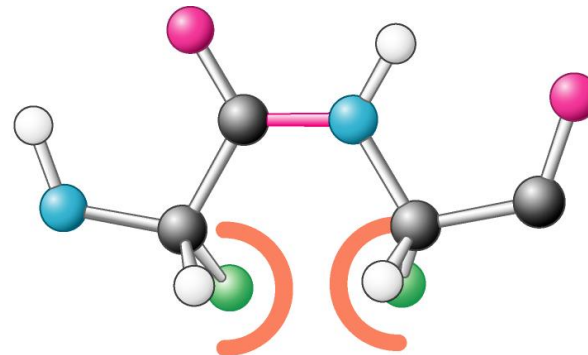


The rotation around $C\alpha-C$ bonds is free, therefore the proteins take on three-dimensional arrangements in space called **CONFORMATIONS**

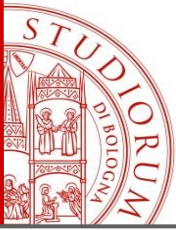
■ These two bonds can rotate, in theory freely, in practice their rotation is conditioned by the steric encumbrance (R groups)



Trans

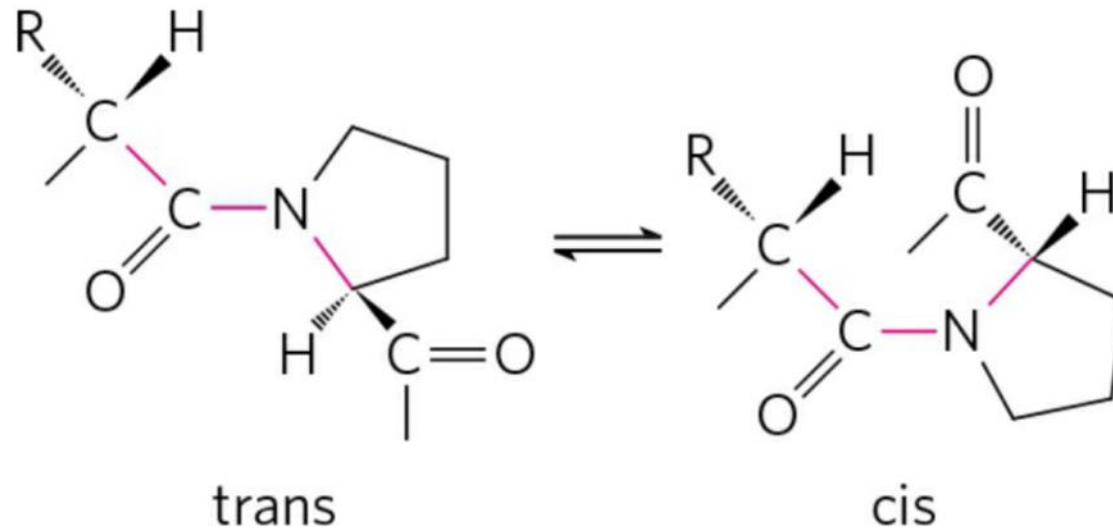


Cis



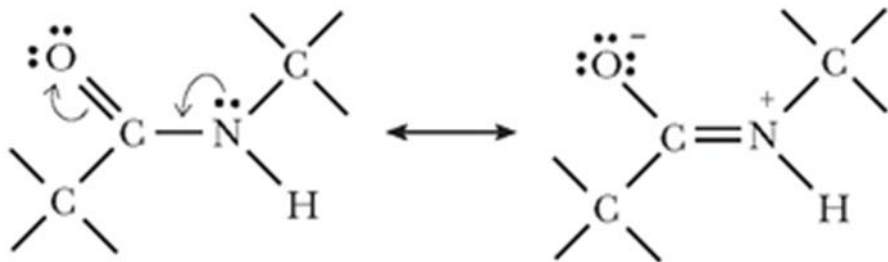
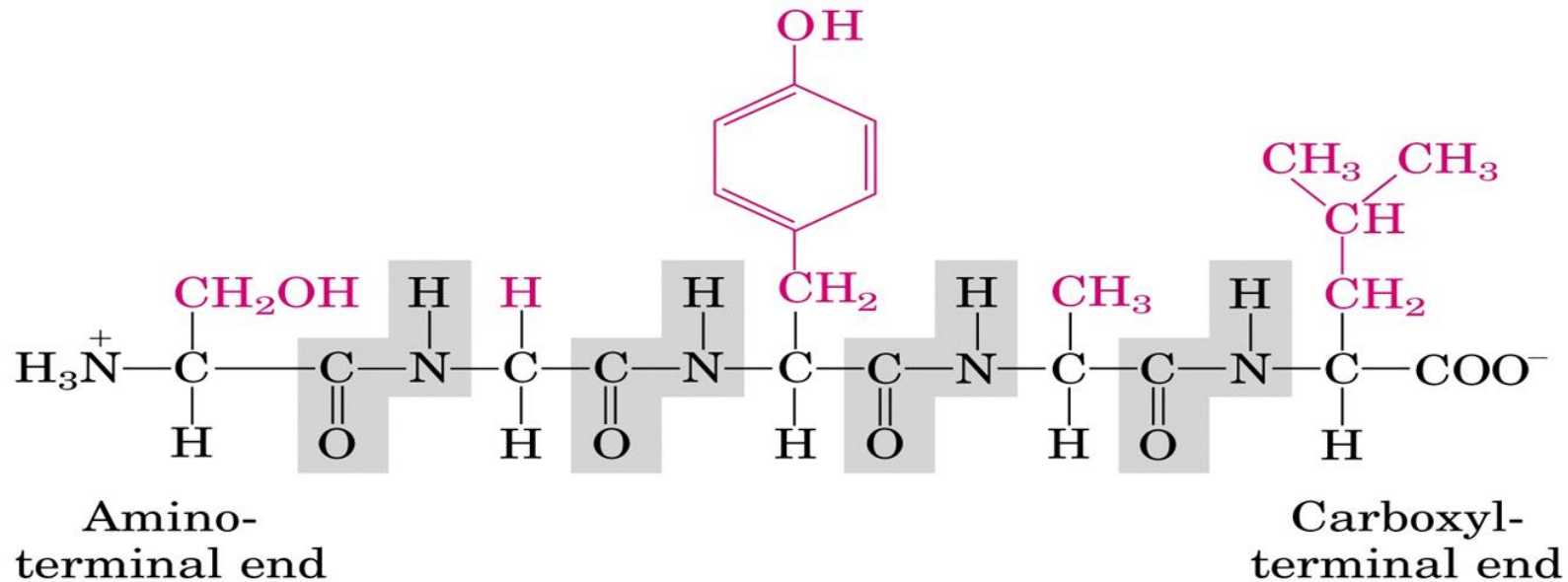
Trans and cis isomers of a peptide bond involving the imino nitrogen of proline

- Of the peptide bonds between amino acid residues, more than 99.95% are in the trans configuration.
- For peptide bonds involving the imino nitrogen of proline, however, about 6% are in the cis configuration (in β turns).

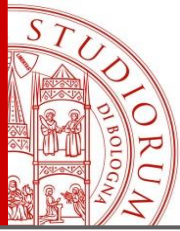


Proline isomers

From the protein skeleton (the part of the molecule that contains the peptide groups) protrude the R groups of the various amino acids



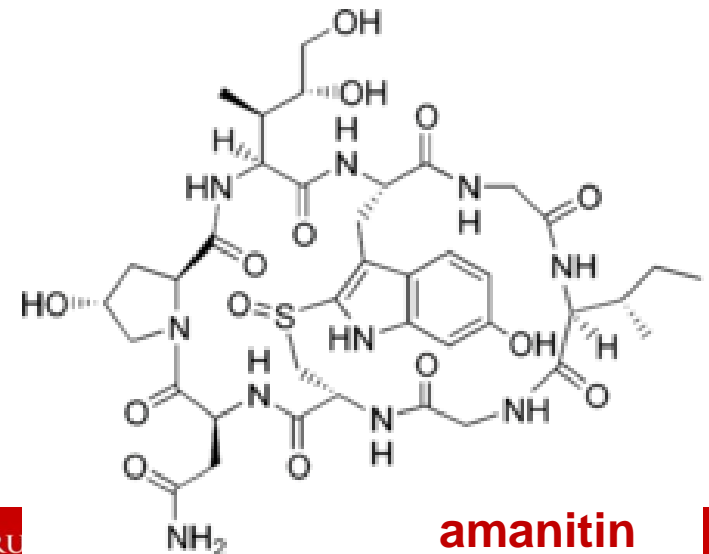
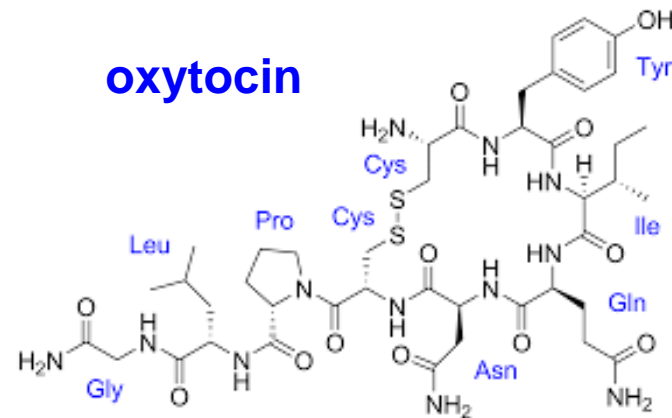
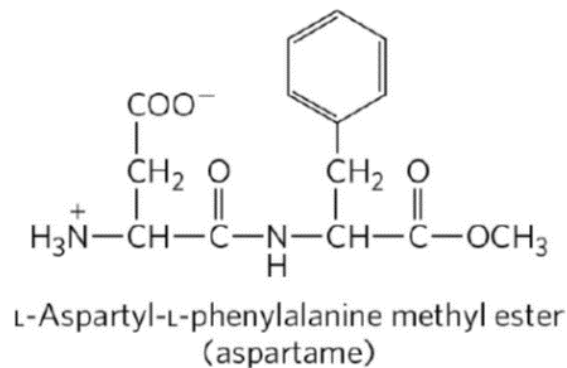
The peptide bond can be represented by two resonance structures, which contribute to its stability. Therefore, both the link C-O and the link C-N are partially double-linked.



Biologically important peptides

Naturally occurring peptides range in length from two to several amino acid residues. Even the smallest peptides can have biologically important effects.

- the commercially synthesized dipeptide L-aspartyl-L-phenylalanine methyl ester, the artificial sweetener aspartame;
- oxytocin (nine amino acids), which is secreted by the posterior pituitary gland and stimulates uterine contractions;
- the toxic amanitin contained in mushrooms, a cyclic peptide of 9 amino acids;

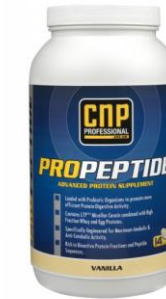


Bioactive peptides commercially available

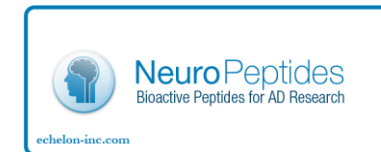
Supplements

Table 2. Products containing bioactive hydrolysates and peptides currently available.

Bioactive peptide	Activity	Product name	Manufacturer	Product type	Source
LKPNM	Antihypertensive	PeptACE	Natural Factors Nutritional Products Ltd., Canada	Capsules	Bonito
LKPNM	Antihypertensive	Vasotensin	Metagenics, USA	Tablet	Bonito
LKPNM	Antihypertensive	Levenorm	Ocean Nutrition Canada Ltd., Canada	N/A	Bonito
LKPNM	Antihypertensive	Peptide ACE 3000	Nippon Supplement Inc., Japan	Capsules	Bonito
LKPNM	Antihypertensive	Peptide Tea	Nippon Supplement Inc., Japan	Powder	Bonito
VY	Antihypertensive	Lapis Support	Tokiwa Yakuin Co., Ltd., Japan	Beverage	Sardine
VY	Antihypertensive	Valtyron	Senmi Ekisu Co., Ltd., Japan	Ingredient	Sardine
FY, VY and IY	Antihypertensive	Wakame Jelly	Riken Vitamin, Japan	Jelly	<i>Undaria pinnatifida</i> (seaweed)
AKYSY	Antihypertensive	Peptide Nori S	Riken Vitamin, Japan	Beverage	<i>Porphyra yezoensis</i> (seaweed)
AKYSY	Antihypertensive	Mainichi Kaisai Nori	Shirako Co., Ltd., Japan	Powder	<i>Porphyra yezoensis</i> (seaweed)
IPP and VPP	Antihypertensive	Ameal S 120	Calpis Co., Ltd., Japan	Beverage	Milk
IPP and VPP	Antihypertensive	Ameal S	Calpis Co., Ltd., Japan	Tablet	Milk
IPP and VPP	Antihypertensive	Evolus	Valio Ltd., Finland	Beverage	Milk



Drugs



Antibiotics

Lafarga & Hayes (2017) Food Rev. Int.,33:3, 217-246,

CLASSIFICATION ACCORDING TO THE SIZE

- **OLIGOPEPTIDES**: a short polymer of amino acids joined by peptide bonds (3 amino acids can be joined to form a tripeptide; 4 amino acids a tetrapeptide, five a pentapeptide, and so forth).
- **POLYPEPTIDES** generally have molecular weights **<10.000 Da**.
- **PROTEINS** have higher molecular weights (**> 10.000 Da**).

We can calculate the approximate number of amino acid present in peptides and proteins by dividing their molecular weight for 110 because the average molecular weight of amino acids is nearer to 128 and a molecule of water (*Molecular mass 18*) is removed to create each peptide bond, so the average molecular weight of an amino acid residue in a protein is about $128 - 18 = 110$.

