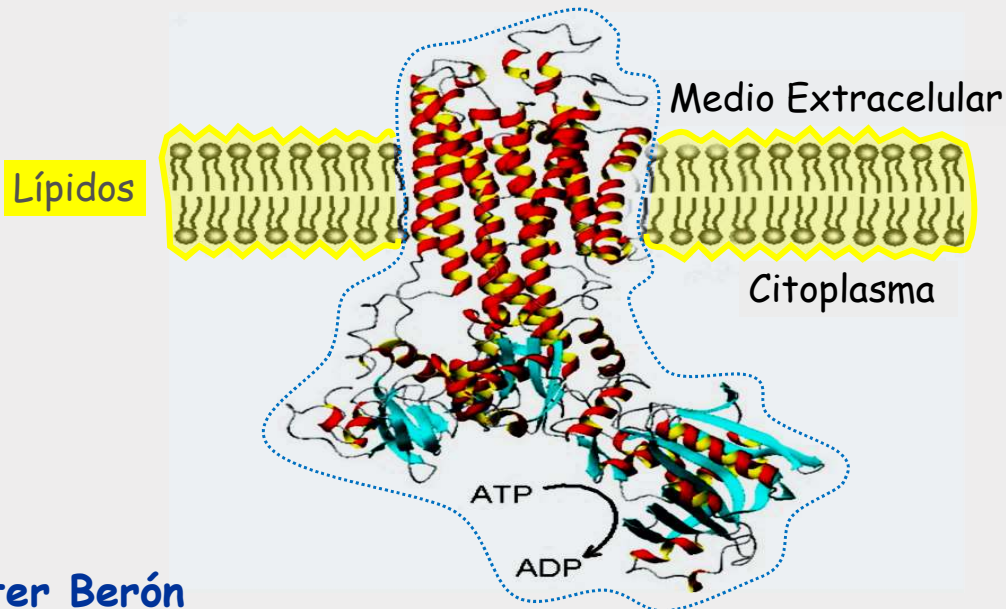


## Aminoácidos ↔ Péptidos ↔ Proteínas



Walter Berón

## Contenido de la clase

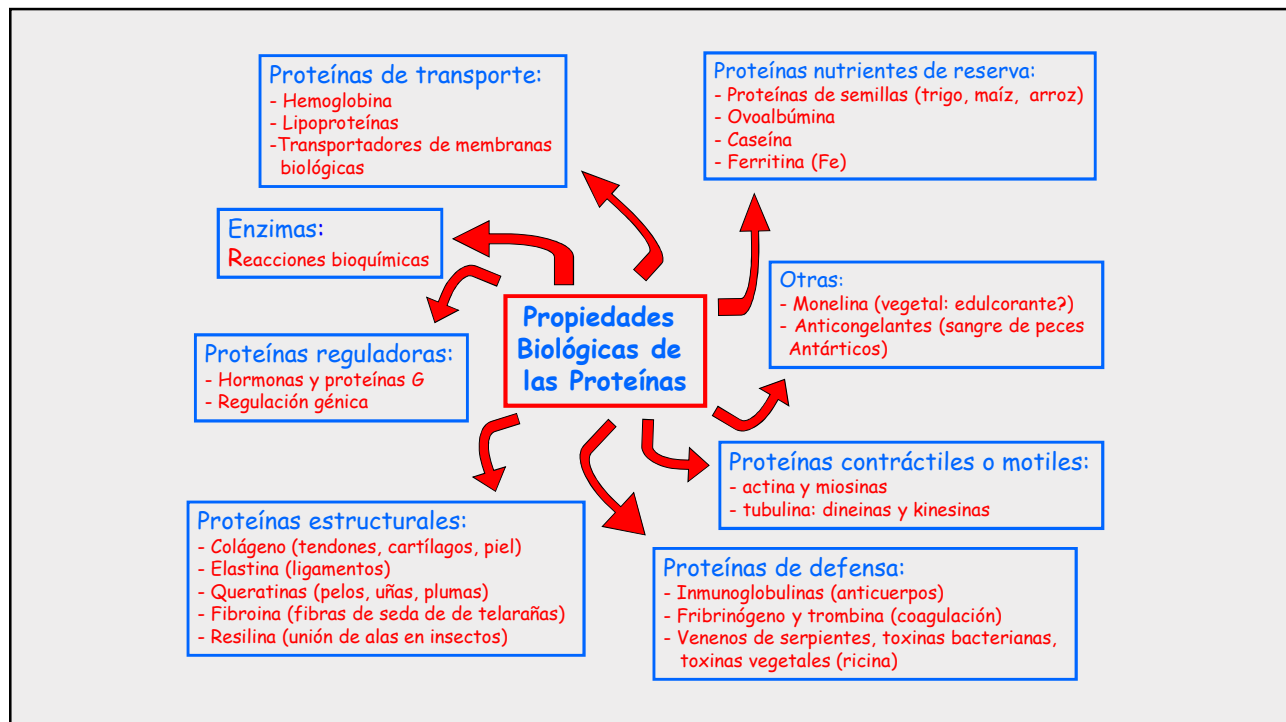
### Proteínas: funciones

#### Aminoácidos:

- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas



## Contenido de la clase

### Proteínas: funciones

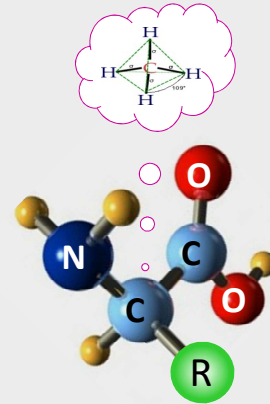
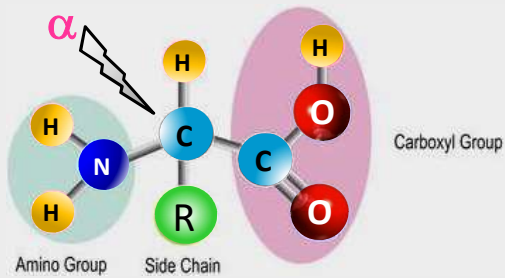
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- Propiedades ácido-base

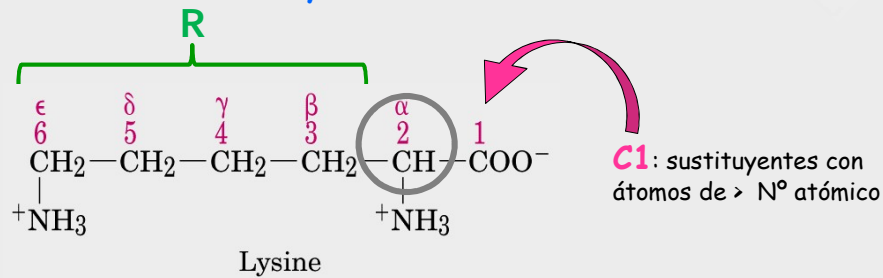
#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

## Estructura general de los Aa



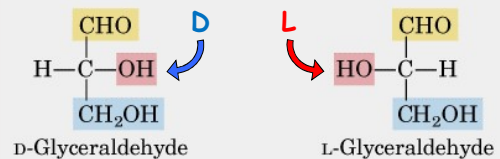
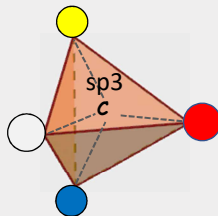
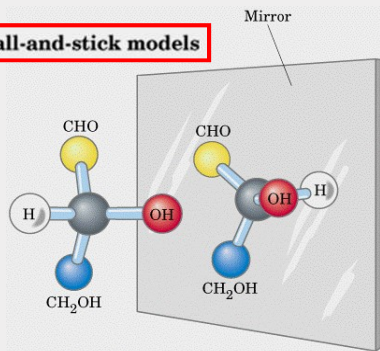
## Identificación y numeración de los C



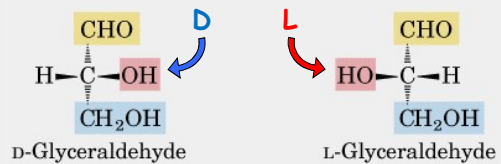
## Los aminoácidos poseen centros asimétricos: Gliceraldehído

- **C<sub>α</sub>**: **asimétrico** (quiral) ⇒ isómeros ópticos “**estereoisómeros**” (enantiómeros): **L** o **D**
- **Gliceraldehído**: molécula de **referencia**.
- imágenes especulares **NO** superponibles

### Ball-and-stick models



### Fischer projection formulas



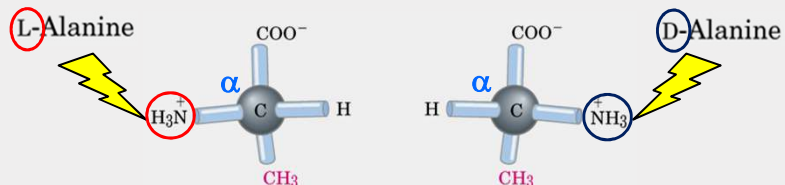
### Perspective formulas

## Estereoisómeros o enantiómeros: aminoácidos

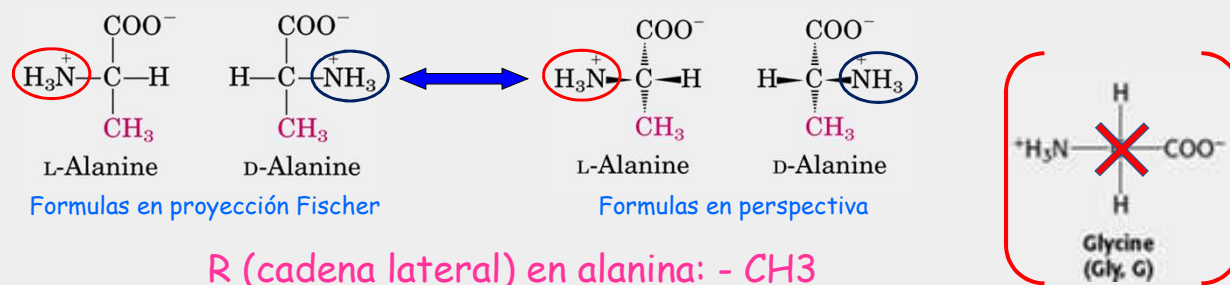
**L** (levógiro): Aa en la mayoría de las proteínas

**D** (dextrógiro): péptidos pequeños  
(pared bacteriana, antibióticos)

### Alanina



Dos convenciones diferentes de la configuración de los estereoisómeros: **L y D**

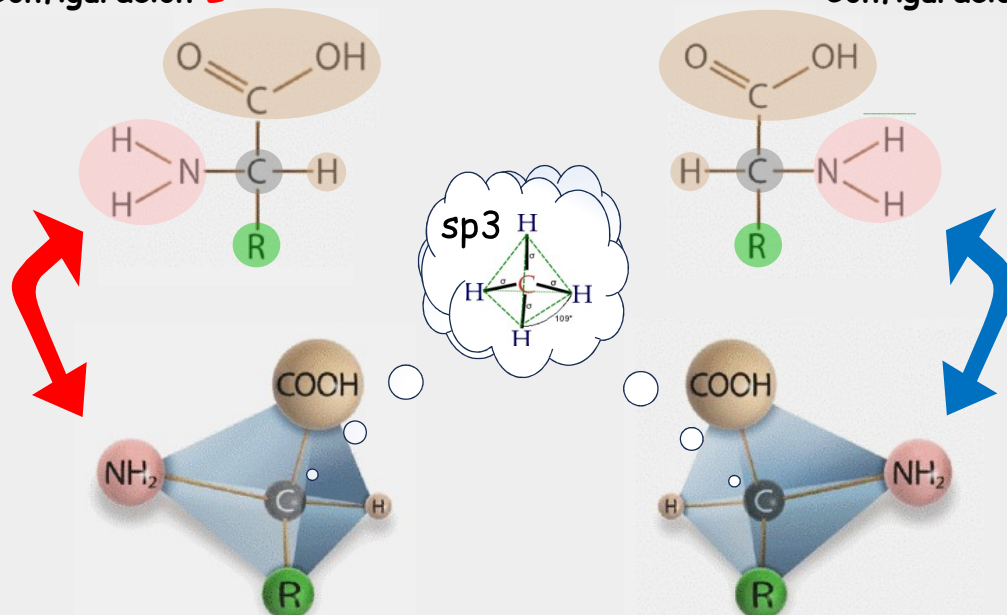


**R** (cadena lateral) en alanina: - CH<sub>3</sub>

## Configuración de Aa: **L y D**

Configuración **L**

Configuración **D**



## Enantiómeros: **R** y **S** (sistema Cahn-Ingold-Prelog)

- Rotación de luz polarizada a la derecha  $\Rightarrow$  **D**, disolución de **D**-gliceraldehído  $\approx$  a varios **D**-aminoácidos

### Desventajas de nomenclatura L-D:

- Correspondencia no siempre cierta ya que la **dirección de la rotación óptica** y **magnitud** son una función complicada de las **estructuras electrónicas** que rodea al centro quiral.
- **No es absoluta** ya que se hace en base a un **compuesto de referencia** (gliceraldehído)

### Convenio absoluto: **R** (*rectus*) y **S** (*sinister*)

**Designación estereoquímica** a cualquier compuesto a partir de la **observación de su estructura tridimensional**

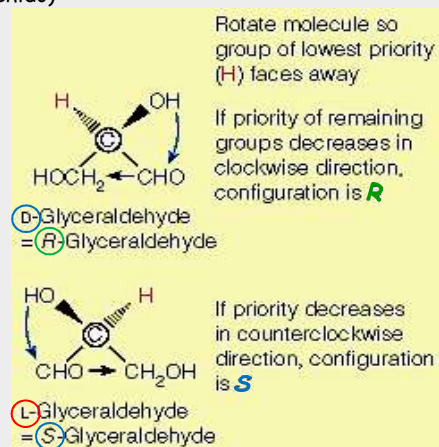
- Prioridad de grupos (átomos de  $\rightarrow$  número atómico):

$OR > OH > NH_2 > COOH > CHO > CH_2OH > CH_3 > H$

**Prioridad**

H: grupo de  $<$  prioridad

- prioridad disminuye en sentido **horario**  $\Rightarrow$  **R** (*rectus: derecha*)
- prioridad disminuye en sentido **antihorario**  $\Rightarrow$  **S** (*sinister: izquierda*) (*sinistrus*)



"Difícil de aplicar en moléculas que contienen más de un C asimétrico  $\Rightarrow$  siguen usando L-D"

Grupos: - se asignan las letras **W, X, Y, Z**

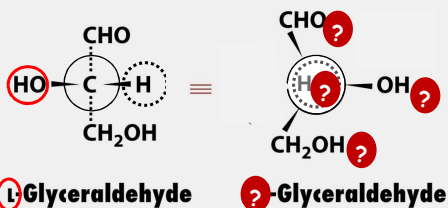
- orden de prioridad: **W > X > Y > Z**

$SH^*, OR > OH > NH_2 > COOH > CHO > CH_2OH > CH_3 > H$

**Prioridad**

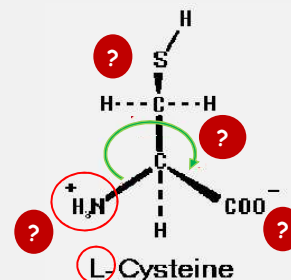
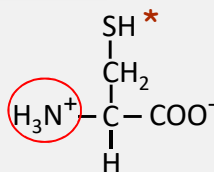
Grupos grandes se ordenan en los puntos de divergencia, por ejemplo:

$-CH_2CH_2SH > -CH_2CH_2OH$



• L-Aa son **?**

Excepción: L-cisteína es **R** cisteína

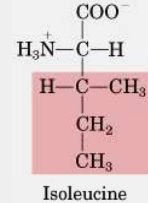
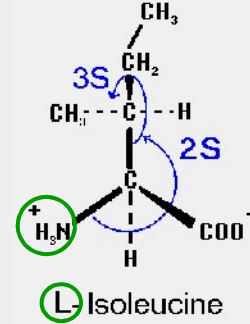
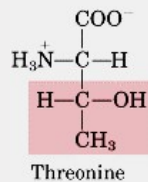
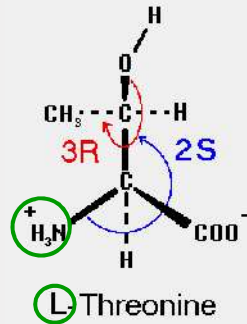


Los invito a que analicen y expliquen este esquema

SH, OR > OH > NH<sub>2</sub> > COOH > CHO > CH<sub>2</sub>OH > CH<sub>3</sub> > H

L-Treonina: (2S,3R) Treonina

L-Isoleucina: (2S,3S) Isoleucina



## Contenido de la clase

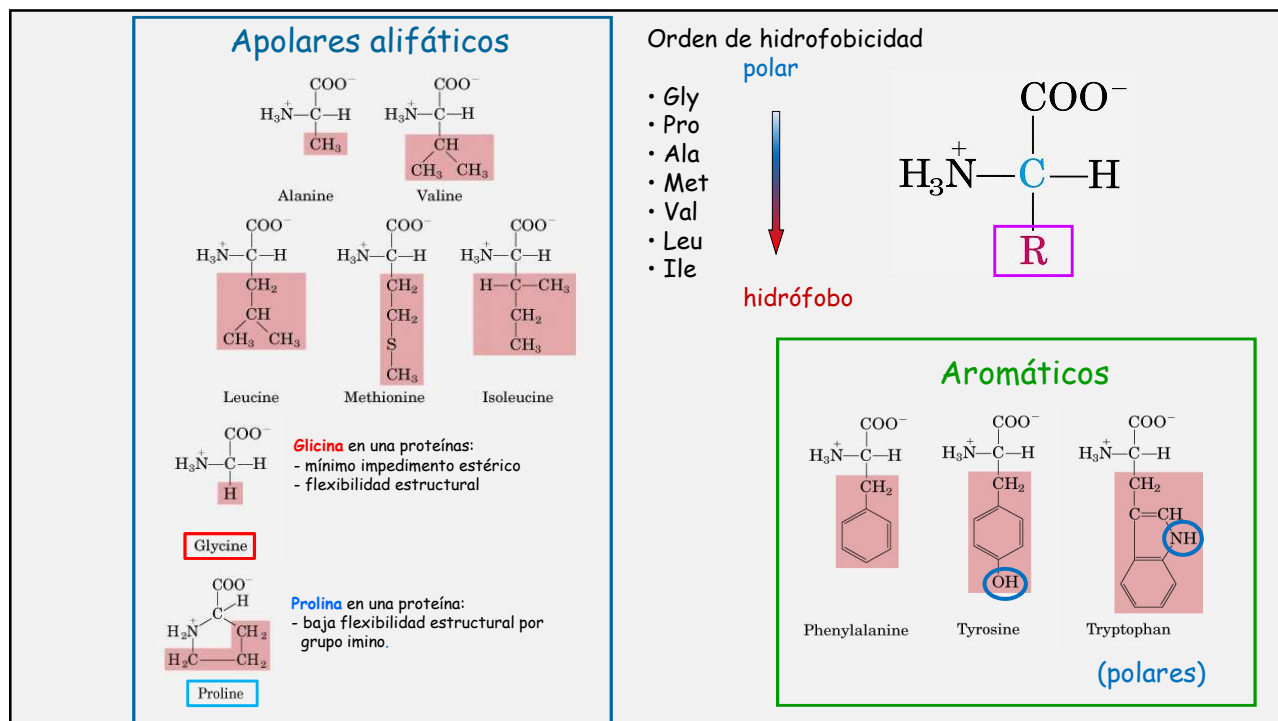
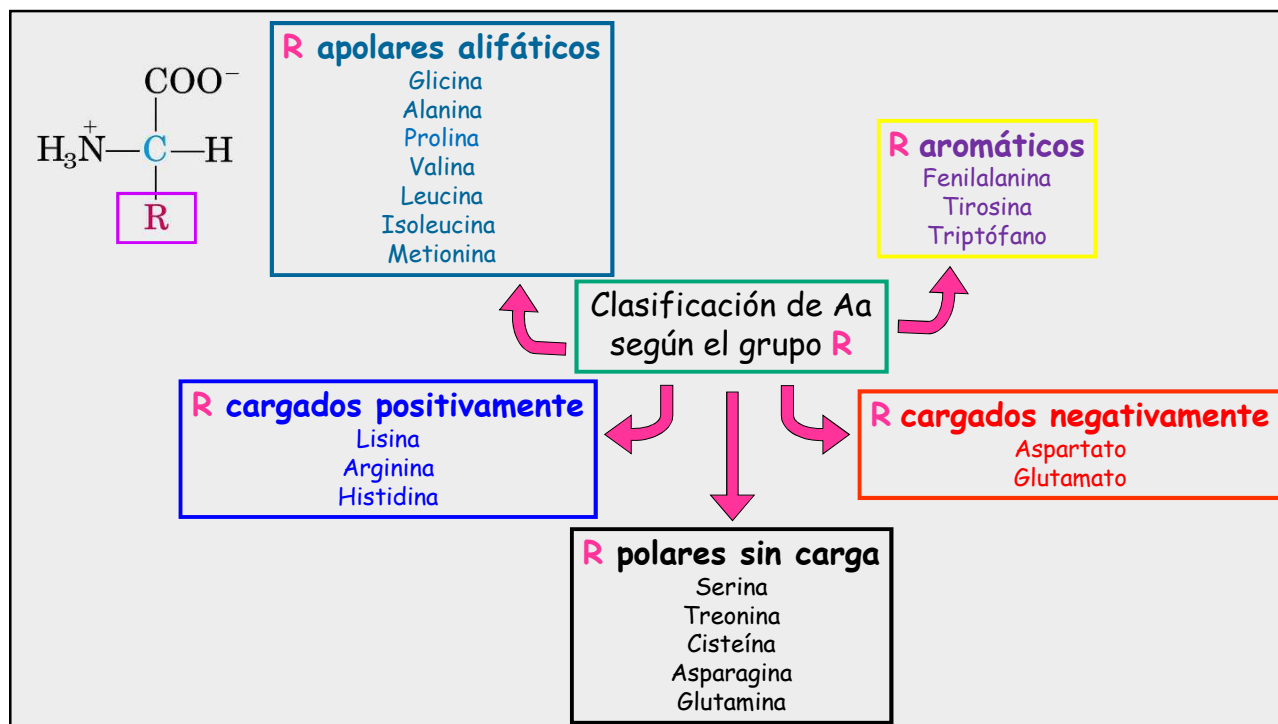
### Proteínas: funciones

#### Aminoácidos:

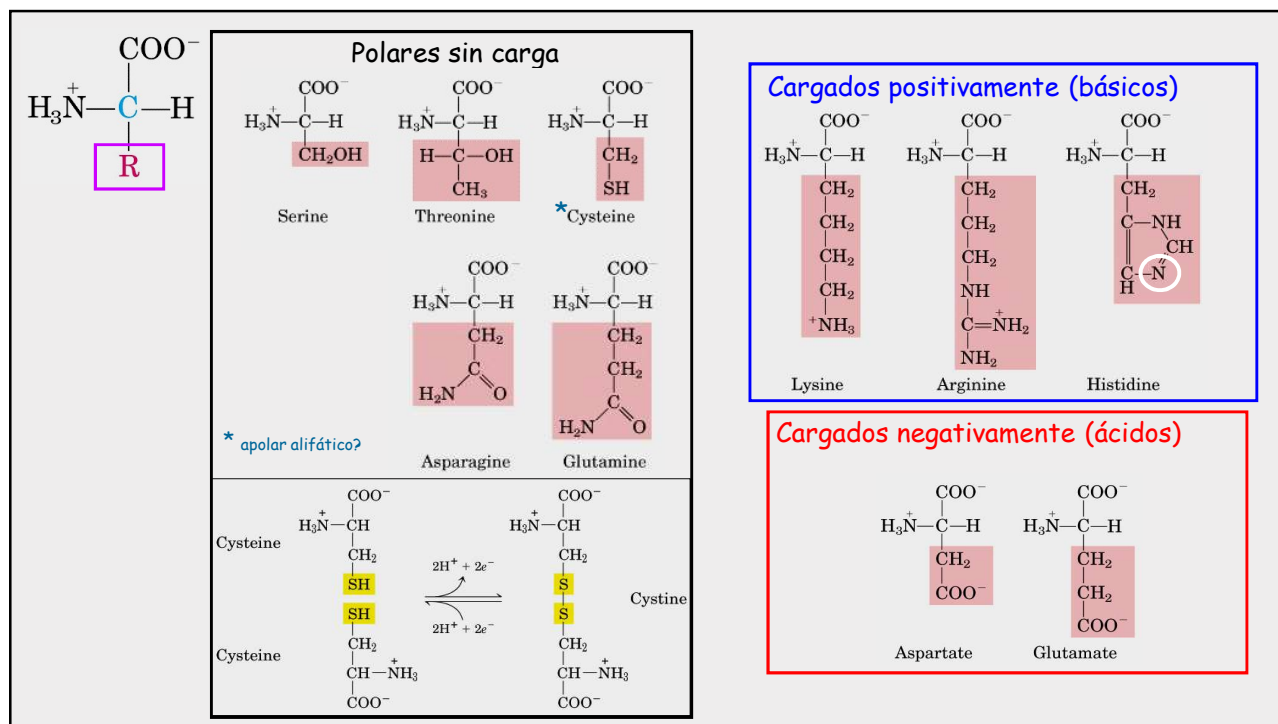
- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas







| Amino acid                              | Abbreviation/<br>symbol | M   | $\Delta G$ (solvente hidrofóbico $\rightarrow$ H <sub>2</sub> O)<br>$\Delta G$ : (-) $\equiv$ cargados o polares<br>$\Delta G$ : (+) $\equiv$ no polares o hidrofóbicos |       |       | Hydropathy<br>index <sup>a</sup> | Occurrence in<br>proteins (%) <sup>b</sup> |     |
|-----------------------------------------|-------------------------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-------|----------------------------------|--------------------------------------------|-----|
| <b>Nonpolar, aliphatic<br/>R groups</b> |                         |     |                                                                                                                                                                         |       |       |                                  |                                            |     |
| Glycine                                 | Gly G                   | 75  | 2.34                                                                                                                                                                    | 9.60  | 5.97  | -0.4                             | 7.2                                        |     |
| Alanine                                 | Ala A                   | 89  | 2.34                                                                                                                                                                    | 9.69  | 6.01  | 1.8                              | 7.8                                        |     |
| Proline                                 | Pro P                   | 115 | 1.99                                                                                                                                                                    | 10.96 | 6.48  | -1.6                             | 5.2                                        |     |
| Valine                                  | Val V                   | 117 | 2.32                                                                                                                                                                    | 9.62  | 5.97  | 4.2                              | 6.6                                        |     |
| Leucine                                 | Leu L                   | 131 | 2.36                                                                                                                                                                    | 9.60  | 5.98  | 3.8                              | 9.1                                        |     |
| Isoleucine                              | Ile I                   | 131 | 2.36                                                                                                                                                                    | 9.68  | 6.02  | 4.5                              | 5.3                                        |     |
| Methionine                              | Met M                   | 149 | 2.28                                                                                                                                                                    | 9.21  | 5.74  | 1.9                              | 2.3                                        |     |
| <b>Aromatic<br/>R groups</b>            |                         |     |                                                                                                                                                                         |       |       |                                  |                                            |     |
| Phenylalanine                           | Phe F                   | 165 | 1.83                                                                                                                                                                    | 9.13  | 5.48  | 2.8                              | 3.9                                        |     |
| Tyrosine                                | Tyr Y                   | 181 | 2.20                                                                                                                                                                    | 9.11  | 10.07 | -1.3                             | 3.2                                        |     |
| Tryptophan                              | Trp W                   | 204 | 2.38                                                                                                                                                                    | 9.39  | 5.89  | -0.9                             | 1.4                                        |     |
| <b>Polar, uncharged<br/>R groups</b>    |                         |     |                                                                                                                                                                         |       |       |                                  |                                            |     |
| Serine                                  | Ser S                   | 105 | 2.21                                                                                                                                                                    | 9.15  | 5.68  | -0.8                             | 6.8                                        |     |
| Threonine                               | Thr T                   | 119 | 2.11                                                                                                                                                                    | 9.62  | 5.87  | -0.7                             | 5.9                                        |     |
| Cysteine <sup>c</sup>                   | Cys C                   | 121 | 1.96                                                                                                                                                                    | 10.28 | 8.18  | 2.5                              | 1.9                                        |     |
| Asparagine                              | Asn N                   | 132 | 2.02                                                                                                                                                                    | 8.80  | 5.41  | -3.5                             | 4.3                                        |     |
| Glutamine                               | Gln Q                   | 146 | 2.17                                                                                                                                                                    | 9.13  | 5.65  | -3.5                             | 4.2                                        |     |
| <b>Positively charged<br/>R groups</b>  |                         |     |                                                                                                                                                                         |       |       |                                  |                                            |     |
| Lysine                                  | Lys K                   | 146 | 2.18                                                                                                                                                                    | 8.95  | 10.53 | 9.74                             | -3.9                                       | 5.9 |
| Histidine                               | His H                   | 155 | 1.82                                                                                                                                                                    | 9.17  | 6.00  | 7.59                             | -3.2                                       | 2.3 |
| Arginine                                | Arg R                   | 174 | 2.17                                                                                                                                                                    | 9.04  | 12.48 | 10.76                            | -4.5                                       | 5.1 |
| <b>Negatively charged<br/>R groups</b>  |                         |     |                                                                                                                                                                         |       |       |                                  |                                            |     |
| Aspartate                               | Asp D                   | 133 | 1.88                                                                                                                                                                    | 9.60  | 3.65  | 2.77                             | -3.5                                       | 5.3 |
| Glutamate                               | Glu E                   | 147 | 2.19                                                                                                                                                                    | 9.67  | 4.25  | 3.22                             | -3.5                                       | 6.3 |

<sup>a</sup>M values reflect the structures as shown in Figure 3-5. The elements of water (M, 18) are deleted when the amino acid is incorporated into a polypeptide.

<sup>b</sup>Ascale combining hydrophobicity and hydrophilicity of R groups. The values reflect the free energy ( $\Delta G$ ) of transfer of the amino acid side chain from a hydrophobic solvent to water. This transfer is favorable ( $\Delta G$ , 0; negative value in the index) for charged or polar amino acid side chains, and unfavorable ( $\Delta G$ , 0; positive value in the index) for amino acids with nonpolar or more hydrophobic side chains. See Chapter 11. From Kyte, J., & Doolittle, R.F. (1982) A simple method for displaying the hydropathic character of a protein. *J. Mol. Biol.* **157**, 105-132.

<sup>c</sup>Average occurrence in more than 1,150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In: *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed.), pp. 599-623, Plenum Press, New York.

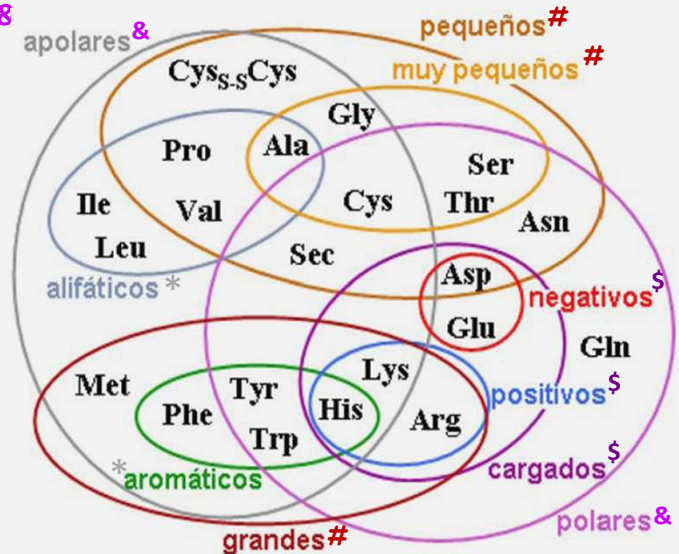
<sup>d</sup>Cysteine is generally classified as apolar despite having a positive hydropathy index. This reflects the ability of the sulfhydryl group to act as a weak acid and to form a weak hydrogen bond with oxygen or nitrogen.



| Aminoacid                               | Abbreviation/<br>symbol |
|-----------------------------------------|-------------------------|
| <b>Nonpolar, aliphatic<br/>R groups</b> |                         |
| Glycine                                 | Gly G                   |
| Alanine                                 | Ala A                   |
| Proline                                 | Pro P                   |
| Valine                                  | Val V                   |
| Leucine                                 | Leu L                   |
| Isoleucine                              | Ile I                   |
| Methionine                              | Met M                   |
| <b>Aromatic<br/>R groups</b>            |                         |
| Phenylalanine                           | Phe F                   |
| Tyrosine                                | Tyr Y                   |
| Tryptophan                              | Trp W                   |
| <b>Polar, uncharged<br/>R groups</b>    |                         |
| Serine                                  | Ser S                   |
| Threonine                               | Thr T                   |
| Cysteine <sup>†</sup>                   | Cys C                   |
| Asparagine                              | Asn N                   |
| Glutamine                               | Gln Q                   |
| <b>Positively charged<br/>R groups</b>  |                         |
| Lysine                                  | Lys K                   |
| Histidine                               | His H                   |
| Arginine                                | Arg R                   |
| <b>Negatively charged<br/>R groups</b>  |                         |
| Aspartate                               | Asp D                   |
| Glutamate                               | Glu E                   |

### Relación:

- estructura (alifáticos-aromáticos) \*
- tamaño #
- polaridad &
- carga \$



## Contenido de la clase

### Proteínas: funciones

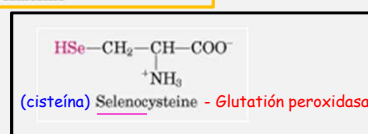
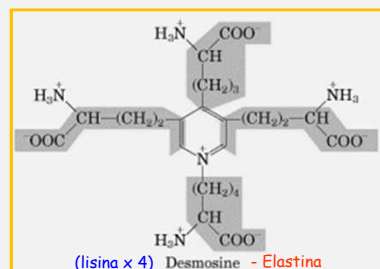
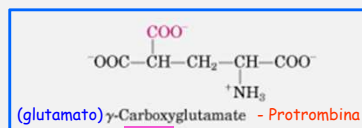
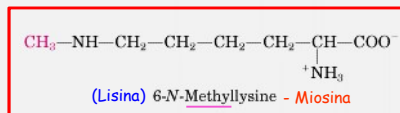
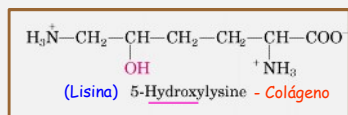
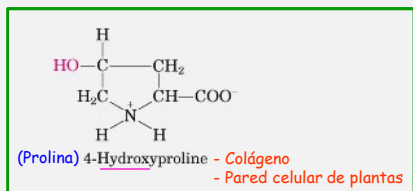
#### Aminoácidos:

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- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

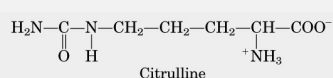
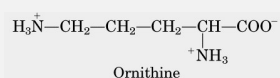
#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

**Aa NO convencionales:** modificados luego de incorporarse a la proteína (modificaciones postraduccionales)



**Aa que NO forman parte de proteínas**



Biosíntesis de arginina  
y en el ciclo de la urea

### Aa que NO forman parte de proteínas

| Name                        | Formula                                                                                                                                                                                         | Biochemical Source, Function                                                 |
|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| $\beta$ -Alanine            | $\text{H}_3\text{N}^+-\text{CH}_2-\text{CH}_2-\text{COO}^-$                                                                                                                                     | Found in the vitamin pantothenic acid and in some important natural peptides |
| $\gamma$ -Aminobutyric acid | $\text{H}_3\text{N}^+-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{COO}^-$                                                                                                                         | Brain, other animal tissues; functions as neurotransmitter                   |
| D-Alanine                   | $\begin{array}{c} \text{COO}^- \\   \\ \text{H}-\text{C}-\text{NH}_3^+ \\   \\ \text{CH}_3 \end{array}$                                                                                         | In polypeptides in some bacterial cell walls                                 |
| D-Glutamic acid             | $\begin{array}{c} \text{COO}^- \\   \\ \text{H}-\text{C}-\text{NH}_3^+ \\   \\ \text{CH}_2 \\   \\ \text{CH}_2-\text{COO}^- \end{array}$                                                        | In polypeptides in some bacterial cell walls                                 |
| L-Homoserine                | $\begin{array}{c} \text{COO}^- \\   \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\   \\ \text{CH}_2-\text{CH}_2\text{OH} \end{array}$                                                             | Many tissues; an intermediate in amino acid metabolism                       |
| Sarcosine                   | $\begin{array}{c} \text{CH}_3-\text{N}-\text{CH}_2-\text{COO}^- \\   \\ \text{H} \end{array}$                                                                                                   | Many tissues; intermediate in amino acid synthesis                           |
| L-Thyroxine                 | $\begin{array}{c} \text{COO}^- \\   \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\   \\ \text{CH}_2-\text{C}_6\text{H}_3\text{I}_2-\text{O}-\text{C}_6\text{H}_3\text{I}_2-\text{OH} \end{array}$ | Thyroid gland; is thyroid hormone (I = iodine)                               |

## Contenido de la clase

### Proteínas: funciones

#### Aminoácidos:

- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

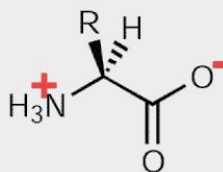
### Propiedades ácido-base

Ionización de Aa en solución acuosa

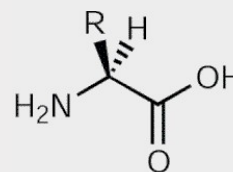
**Zwitterion** (iones dipolares, iones híbridos)

- neutro a pH 7: (+)  $\text{H}_3\text{N}^+$   
(-)  $\text{COO}^-$
- dipolo eléctrico

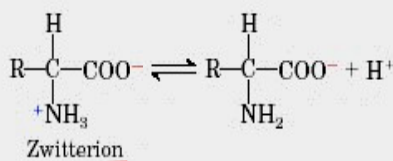
**Zwitterionic**



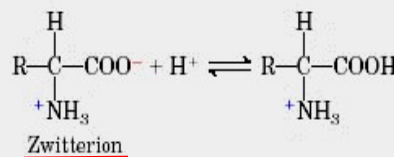
**Nonzwitterionic**



**Ácido:** dador de  $\text{H}^+$

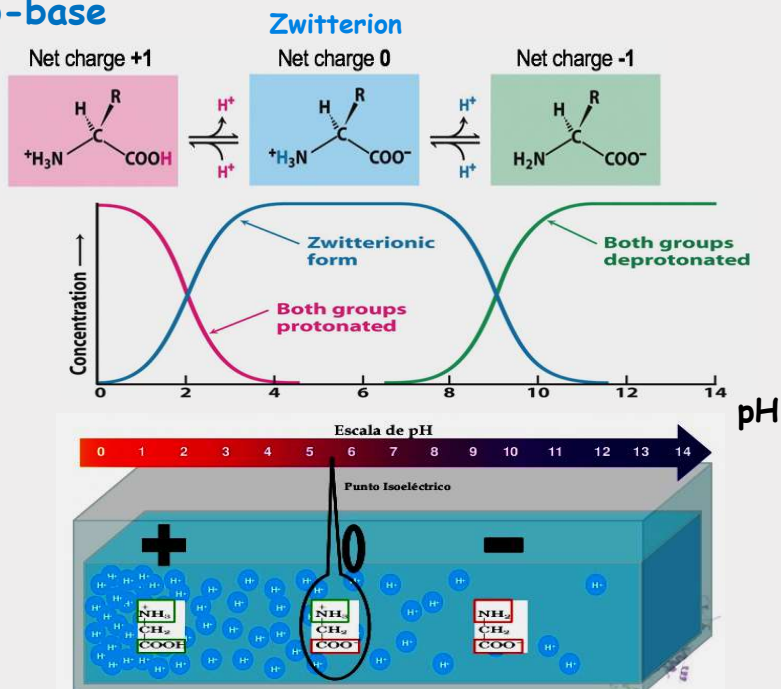


**Base:** aceptor de  $\text{H}^+$

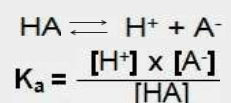


- Naturaleza dual: anfóteros = anfólitos (anfóteros **electrolitos**)
- Par ácido-base conjugados

## Propiedades ácido-base



## Curvas de titulación de Aa: $K_a$ , $pK_a$ y $pI$



$K_a$ : constante de disociación de ácido

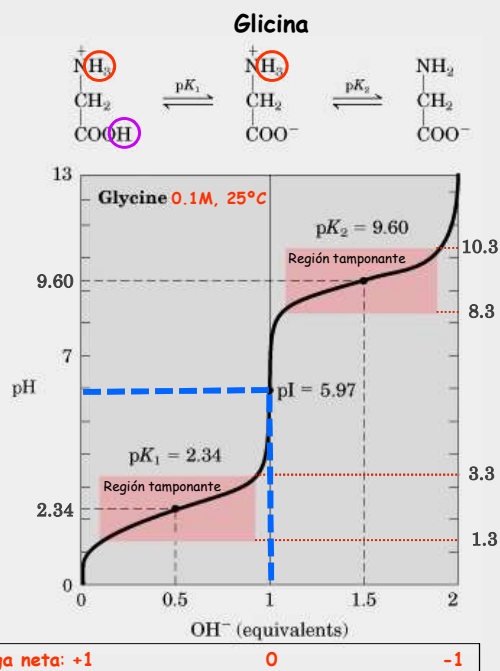
$$pK_a = \log 1/K_a = -\log K_a$$

$pK_a$ : medida de la tendencia de un grupo a ceder un  $H^+$

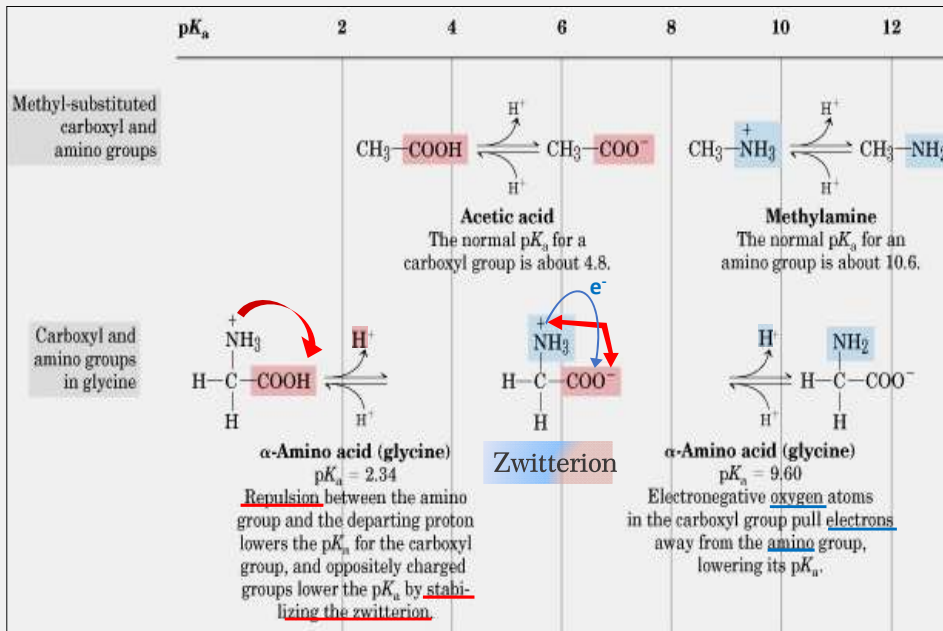
$K_a \uparrow \equiv pK_a \downarrow \equiv$  ácido fuerte

**pI**: punto isoelectrico (pH isoelectrico)

- Aa en forma dipolar.
- Sin carga eléctrica neta.
- $pH < pI$ : carga neta (+)
- $pH > pI$ : carga neta (-)

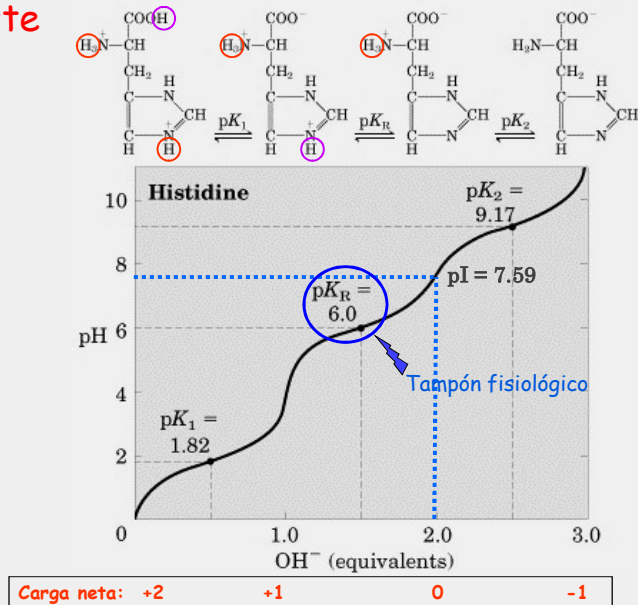


## Interacción entre los grupos $\alpha$ -amino y $\alpha$ -carboxilo de un $\alpha$ -Aa



## Curva de titulación de histidina (aa básico)

Los invito a que analicen este esquema en sus casas.





**TABLE 3-1** Properties and Conventions Associated with the Common Amino Acids Found in Proteins

| Properties and Resonance Structures of the Common Amino Acids Found in Proteins |                         |         |                   |                                            |                     |       |                                  |                                            |
|---------------------------------------------------------------------------------|-------------------------|---------|-------------------|--------------------------------------------|---------------------|-------|----------------------------------|--------------------------------------------|
| Amino acid                                                                      | Abbreviation/<br>symbol | $M_r^*$ | $pK_a$ values     |                                            |                     | $pI$  | Hydropathy<br>index <sup>†</sup> | Occurrence in<br>proteins (%) <sup>‡</sup> |
|                                                                                 |                         |         | $pK_1$<br>(-COOH) | $pK_2$<br>(-NH <sub>3</sub> <sup>+</sup> ) | $pK_R$<br>(R group) |       |                                  |                                            |
| <b>Nonpolar, aliphatic<br/>R groups</b>                                         |                         |         |                   |                                            |                     |       |                                  |                                            |
| Glycine                                                                         | Gly G                   | 75      | 2.34              | 9.60                                       |                     | 5.97  | -0.4                             | 7.2                                        |
| Alanine                                                                         | Ala A                   | 89      | 2.34              | 9.69                                       |                     | 6.01  | 1.8                              | 7.8                                        |
| Proline                                                                         | Pro P                   | 115     | 1.99              | 10.96                                      |                     | 6.48  | -1.6                             | 5.2                                        |
| Valine                                                                          | Val V                   | 117     | 2.32              | 9.62                                       |                     | 5.97  | 4.2                              | 6.6                                        |
| Leucine                                                                         | Leu L                   | 131     | 2.36              | 9.60                                       |                     | 5.98  | 3.8                              | 9.1                                        |
| Isoleucine                                                                      | Ile I                   | 131     | 2.36              | 9.68                                       |                     | 6.02  | 4.5                              | 5.3                                        |
| Methionine                                                                      | Met M                   | 149     | 2.28              | 9.21                                       |                     | 5.74  | 1.9                              | 2.3                                        |
| <b>Aromatic<br/>R groups</b>                                                    |                         |         |                   |                                            |                     |       |                                  |                                            |
| Phenylalanine                                                                   | Phe F                   | 165     | 1.83              | 9.13                                       |                     | 5.48  | 2.8                              | 3.9                                        |
| Tyrosine                                                                        | Tyr Y                   | 181     | 2.20              | 9.11                                       | 10.07               | 5.66  | -1.3                             | 3.2                                        |
| Tryptophan                                                                      | Trp W                   | 204     | 2.38              | 9.39                                       |                     | 5.89  | -0.9                             | 1.4                                        |
| <b>Polar, uncharged<br/>R groups</b>                                            |                         |         |                   |                                            |                     |       |                                  |                                            |
| Serine                                                                          | Ser S                   | 105     | 2.21              | 9.15                                       |                     | 5.68  | -0.8                             | 6.8                                        |
| Threonine                                                                       | Thr T                   | 119     | 2.11              | 9.62                                       |                     | 5.87  | -0.7                             | 5.9                                        |
| Cysteine <sup>§</sup>                                                           | Cys C                   | 121     | 1.96              | 10.28                                      | 8.18                | 5.07  | 2.5                              | 1.9                                        |
| Asparagine                                                                      | Asn N                   | 132     | 2.02              | 8.80                                       |                     | 5.41  | -3.5                             | 4.3                                        |
| Glutamine                                                                       | Gln Q                   | 146     | 2.17              | 9.13                                       |                     | 5.65  | -3.5                             | 4.2                                        |
| <b>Positively charged<br/>R groups</b>                                          |                         |         |                   |                                            |                     |       |                                  |                                            |
| Lysine                                                                          | Lys K                   | 146     | 2.18              | 8.95                                       | 10.53               | 9.74  | -3.9                             | 5.9                                        |
| Histidine                                                                       | His H                   | 155     | 1.82              | 9.17                                       | 6.00                | 7.59  | -3.2                             | 2.3                                        |
| Arginine                                                                        | Arg R                   | 174     | 2.17              | 9.04                                       | 12.48               | 10.76 | -4.5                             | 5.1                                        |
| <b>Negatively charged<br/>R groups</b>                                          |                         |         |                   |                                            |                     |       |                                  |                                            |
| Aspartate                                                                       | Asp D                   | 133     | 1.88              | 9.60                                       | 3.65                | 2.77  | -3.5                             | 5.3                                        |
| Glutamate                                                                       | Glu E                   | 147     | 2.19              | 9.67                                       | 4.25                | 3.22  | -3.5                             | 6.3                                        |

\* $M_r$  values reflect the structures as shown in Figure 3-5. The elements of water ( $M_r 18$ ) are deleted when the amino acid is incorporated into a polypeptide.  
<sup>†</sup>Ascale combining hydrophobicity and hydrophilicity of R groups. The values reflect the free energy (DG) of transfer of the amino acid side chain from a hydrophobic solvent to water. The transfer is favorable (DG, 0; negative value in the index) for charged or polar amino acid side chains, and unfavorable (DG, 0; positive value in the index) for amino acids with nonpolar or more hydrophobic side chains. See Chapter 11. From Kyte, J. & Doolittle, R.F. (1982) A simple method for displaying the hydropathic character of a protein. *J. Mol. Biol.* **157**, 105-132.  
<sup>‡</sup>Average occurrence in more than 1,150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed.), pp. 599-623. Plenum Press, New York.  
<sup>§</sup>Cysteine is generally classified as polar despite having a positive hydropathy index. This reflects the ability of the sulfhydryl group to act as a weak acid and to form a weak hydrogen bond with oxygen or nitrogen.

**TABLE 3-1** Properties and Conventions Associated with the Common Amino Acids Found in Proteins

| Aminoacid                               | Abbreviation/<br>symbol | M <sub>r</sub> <sup>*</sup> | pK <sub>a</sub> values     |                                                     |                              | pI    | Hydropathy<br>index <sup>†</sup> | Occurrence in<br>proteins (%) <sup>‡</sup> |
|-----------------------------------------|-------------------------|-----------------------------|----------------------------|-----------------------------------------------------|------------------------------|-------|----------------------------------|--------------------------------------------|
|                                         |                         |                             | pK <sub>1</sub><br>(-COOH) | pK <sub>2</sub><br>(-NH <sub>3</sub> <sup>+</sup> ) | pK <sub>R</sub><br>(R group) |       |                                  |                                            |
| <b>Nonpolar, aliphatic<br/>R groups</b> |                         |                             |                            |                                                     |                              |       |                                  |                                            |
| Glycine                                 | Gly G                   | 75                          | 2.34                       | 9.60                                                |                              | 5.97  | -0.4                             | 7.2                                        |
| Alanine                                 | Ala A                   | 89                          | 2.34                       | 9.69                                                |                              | 6.01  | 1.8                              | 7.8                                        |
| Proline                                 | Pro P                   | 115                         | 1.99                       | 10.96                                               |                              | 6.48  |                                  | 5.2                                        |
| Valine                                  | Val V                   | 117                         | 2.32                       | 9.62                                                |                              | 5.97  |                                  | 6.6                                        |
| Leucine                                 | Leu L                   | 131                         | 2.36                       | 9.60                                                |                              | 5.98  |                                  | 9.1                                        |
| Isoleucine                              | Ile I                   | 131                         | 2.36                       | 9.68                                                |                              | 6.02  |                                  | 5.3                                        |
| Methionine                              | Met M                   | 149                         | 2.28                       | 9.21                                                |                              | 5.74  |                                  | 2.3                                        |
| <b>Aromatic<br/>R groups</b>            |                         |                             |                            |                                                     |                              |       |                                  |                                            |
| Phenylalanine                           | Phe F                   | 165                         | 1.83                       | 9.13                                                |                              | 5.48  |                                  | 3.9                                        |
| Tyrosine                                | Tyr Y                   | 181                         | 2.20                       | 9.11                                                | 10.07                        | 5.66  |                                  | 3.2                                        |
| Tryptophan                              | Trp W                   | 204                         | 2.38                       | 9.39                                                |                              | 5.89  |                                  | 1.4                                        |
| <b>Polar, uncharged<br/>R groups</b>    |                         |                             |                            |                                                     |                              |       |                                  |                                            |
| Serine                                  | Ser S                   | 105                         | 2.21                       | 9.15                                                |                              | 5.68  |                                  | 6.8                                        |
| Threonine                               | Thr T                   | 119                         | 2.11                       | 9.62                                                |                              | 5.87  |                                  | 5.9                                        |
| Cysteine <sup>§</sup>                   | Cys C                   | 121                         | 1.96                       | 10.28                                               | 8.18                         | 5.07  |                                  | 1.9                                        |
| Asparagine                              | Asn N                   | 132                         | 2.02                       | 8.80                                                |                              | 5.41  |                                  | 4.3                                        |
| Glutamine                               | Gln Q                   | 146                         | 2.17                       | 9.13                                                |                              | 5.65  |                                  | 4.2                                        |
| <b>Positively charged<br/>R groups</b>  |                         |                             |                            |                                                     |                              |       |                                  |                                            |
| Lysine                                  | Lys K                   | 146                         | 2.18                       | 8.95                                                | 10.53                        | 9.74  | -3.9                             | 5.9                                        |
| Histidine                               | His H                   | 155                         | 1.82                       | 9.17                                                | 6.00                         | 7.59  | -3.2                             | 2.3                                        |
| Arginine                                | Arg R                   | 174                         | 2.17                       | 9.04                                                | 12.48                        | 10.76 | -4.5                             | 5.1                                        |
| <b>Negatively charged<br/>R groups</b>  |                         |                             |                            |                                                     |                              |       |                                  |                                            |
| Aspartate                               | Asp D                   | 133                         | 1.88                       | 9.60                                                | 3.65                         | 2.77  |                                  | 5.3                                        |
| Glutamate                               | Glu E                   | 147                         | 2.19                       | 9.67                                                | 4.25                         | 3.22  |                                  | 6.3                                        |

\* $M_r$  values reflect the structures as shown in Figure 3-5. The elements of water ( $M_r 18$ ) are deleted when the amino acid is incorporated into a polypeptide.  
<sup>†</sup>Ascale combining hydrophobicity and hydrophilicity of R groups. The values reflect the free energy (DG) of transfer of the amino acid side chain from a hydrophobic solvent to water. The transfer is favorable (DG, 0; negative value in the index) for charged or polar amino acid side chains, and unfavorable (DG, 0; positive value in the index) for amino acids with nonpolar or more hydrophobic side chains. See Chapter 11. From Kyte, J. & Doolittle, R.F. (1982) A simple method for displaying the hydropathic character of a protein. *J. Mol. Biol.* **157**, 105-132.  
<sup>‡</sup>Average occurrence in more than 1,150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed.), pp. 599-623. Plenum Press, New York.  
<sup>§</sup>Cysteine is generally classified as polar despite having a positive hydropathy index. This reflects the ability of the sulfhydryl group to act as a weak acid and to form a weak hydrogen bond with oxygen or nitrogen.



## PI de algunas proteínas

The Isoelectric Points of Some Proteins

| Protein                | pI   |
|------------------------|------|
| Pepsin                 | ~1.0 |
| Egg albumin            | 4.6  |
| Serum albumin          | 4.9  |
| Urease                 | 5.0  |
| $\beta$ -Lactoglobulin | 5.2  |
| Hemoglobin             | 6.8  |
| Myoglobin              | 7.0  |
| Chymotrypsinogen       | 9.5  |
| Cytochrome c           | 10.7 |
| Lysozyme               | 11.0 |

## Contenido de la clase

### Proteínas: funciones

#### Aminoácidos:

- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

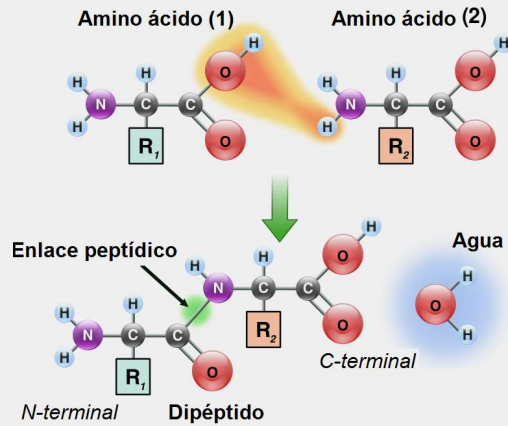
#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

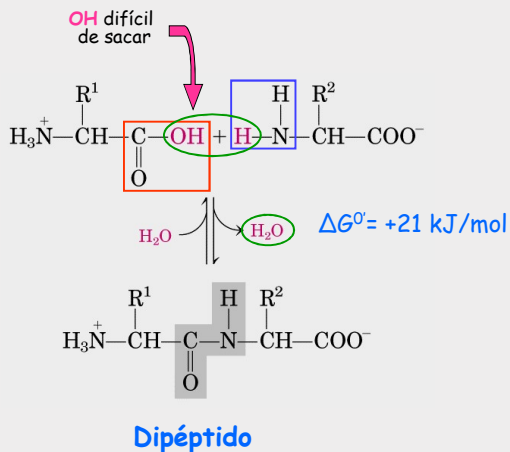
## Péptidos - Proteínas

- Polímero de Aa
  - Péptidos: 2-3 Aa
  - Oligopéptidos: menos de 10-20 Aa (sin estructura 2ª)
- pocas docenas a miles Aa: **Polipéptido**  $\longleftrightarrow$  **Proteína**: uno o más polipéptidos

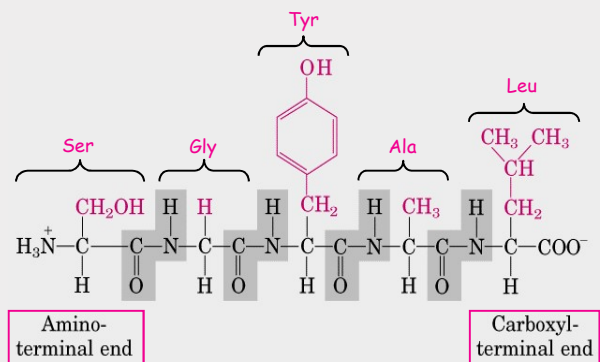
### Enlace peptídico: unión covalente



## Enlace peptídico



### Cadenas laterales: residuos R

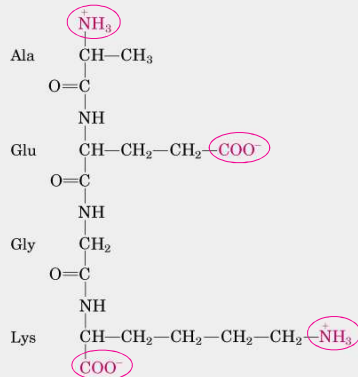


**Penta péptido: Ser-Gly-Tyr-Ala-Leu**

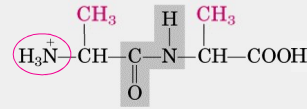
## Los péptidos se ionizan

**Grupos ionizables** = propiedades ácido-base de un péptido

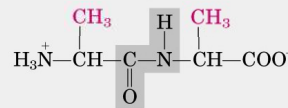
### Alanilglutamilglicilisina



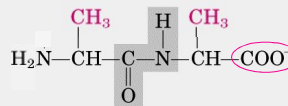
### Alanilalanina



Forma catiónica < pH 3



Forma isoelectrica

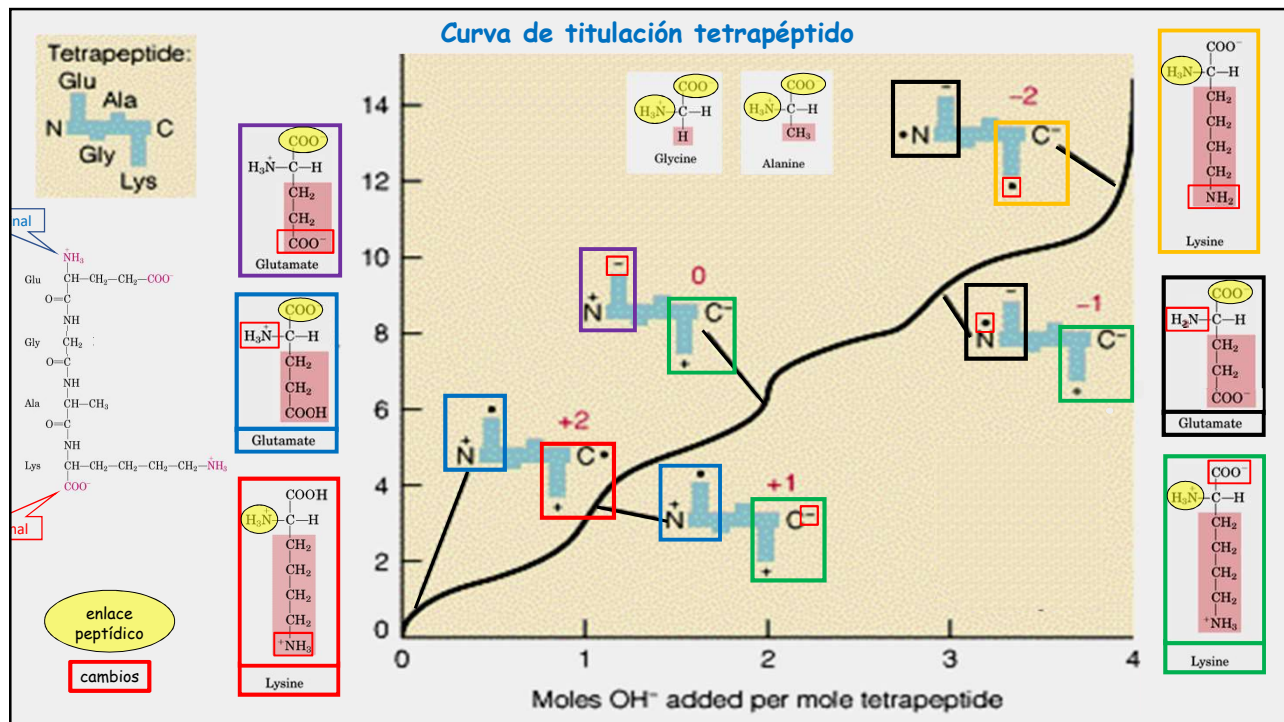


Forma aniónica > pH 10

Los invito a que razonen y expliquen el próximo esquema

Les solicito que en sus casas, escriban la fórmula del tetrapéptido y los cambios secuenciales que se van registrando en los aminoácidos durante la titulación.

Les sugiero que compartan y discutan la resolución de este ejercicio entre ustedes.



## Contenido de la clase

### Proteínas: funciones

#### Aminoácidos:

- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

## Obtención y Síntesis de péptidos y proteínas

### Purificación a partir de un tejido

- trabajoso
- bajas concentraciones

### Síntesis química directa

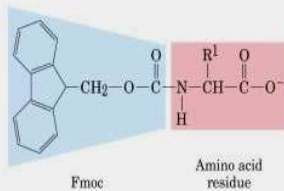
- automatizada, 100Aa en 4 días  
(5 seg. en una bacteria)

### Ingeniería genética

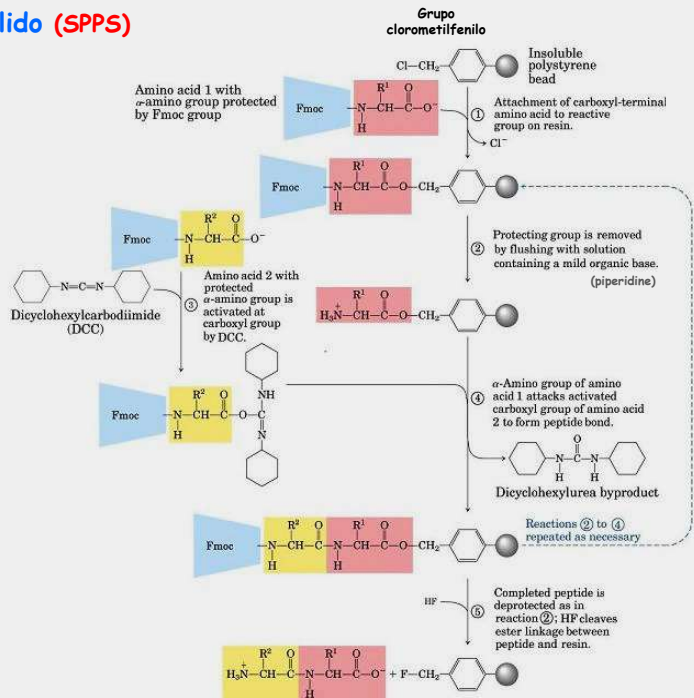
- metodología del DNA recombinante

### Síntesis química de un Péptido en Fase Sólido (SPPS)

- Fmoc: Fluorenyl methoxy carbonyl



- t-Boc (or Boc): tert Butyl oxy carbonyl



## Contenido de la clase

### Proteínas: funciones

#### Aminoácidos:

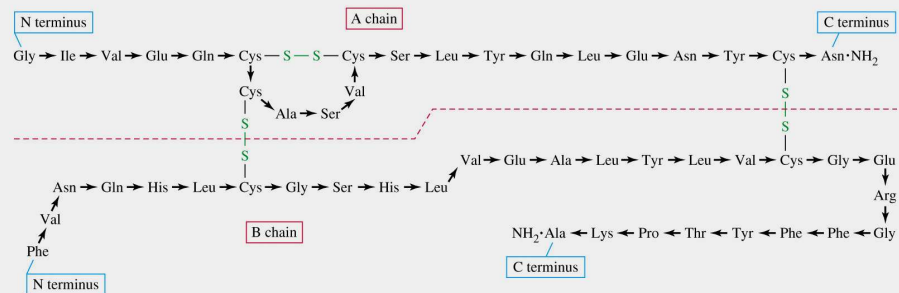
- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

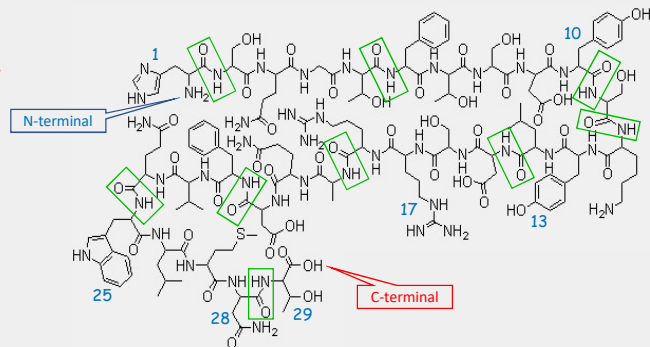
### Polipéptidos pequeños con actividad biológica

**Insulina:** polipéptidos A (21 Aa)  
B (30 Aa):  
Páncreas. Absorción de glucosa:  
hipoglucemiante



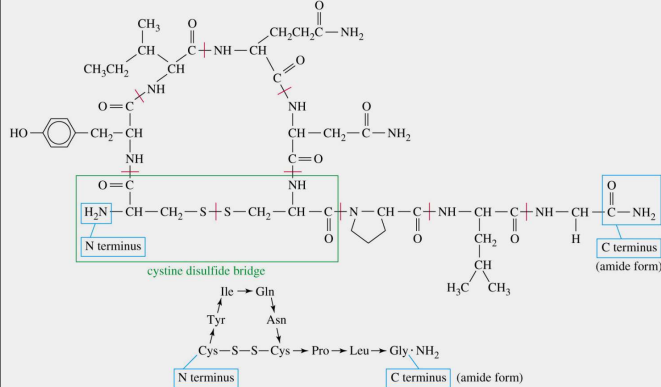
**Glucagón:** polipéptido de 29 Aa  
Páncreas. Gluconeogénesis-glucogenólisis: hiperglucemiante

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-  
1 2 3 4 5 6 7 8 9 10 11  
Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-  
12 13 14 15 16 17 18 19 20 21 22  
Val-Gln-Trp-Leu-Met-Asn-Thr  
23 24 25 26 27 28 29



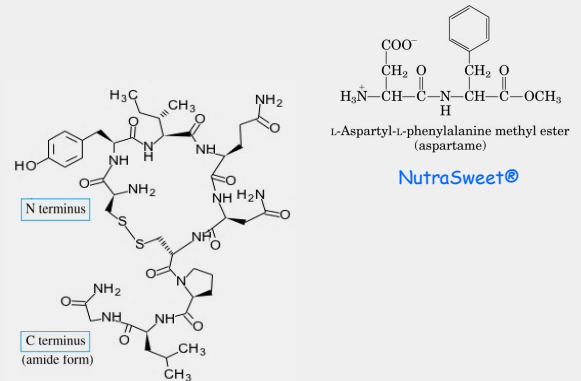


**Oxitocina: (9 Aa): hipotálamo.**  
**Contracción uterina, lactancia**

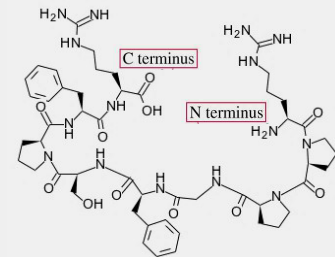
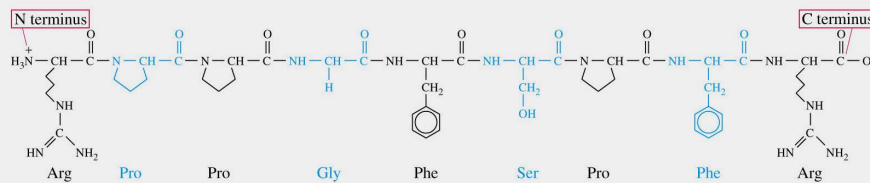


## Péptidos pequeño naturales

## Péptido pequeño sintético



**Bradiquinina (9 Aa): Hígado. Precursor de BQ: coagulación, inflamación, presión sanguínea**



| Aminoacid                           | Abbreviation/<br>symbol |
|-------------------------------------|-------------------------|
| <b>Nonpolar, aliphatic R groups</b> |                         |
| Glycine                             | Gly G                   |
| Alanine                             | Ala A                   |
| Proline                             | Pro P                   |
| Valine                              | Val V                   |
| Leucine                             | Leu L                   |
| Isoleucine                          | Ile I                   |
| Methionine                          | Met M                   |
| <b>Aromatic R groups</b>            |                         |
| Phenylalanine                       | Phe F                   |
| Tyrosine                            | Tyr Y                   |
| Tryptophan                          | Trp W                   |
| <b>Polar, uncharged R groups</b>    |                         |
| Serine                              | Ser S                   |
| Threonine                           | Thr T                   |
| Cysteine <sup>T</sup>               | Cys C                   |
| Asparagine                          | Asn N                   |
| Glutamine                           | Gln Q                   |
| <b>Positively charged R groups</b>  |                         |
| Lysine                              | Lys K                   |
| Histidine                           | His H                   |
| Arginine                            | Arg R                   |
| <b>Negatively charged R groups</b>  |                         |
| Aspartate                           | Asp D                   |
| Glutamate                           | Glu E                   |

## Glándula pituitaria e hipotálamo.

### "Analgésicos endógenos": inhibición del dolor

**Leucina encefalina**

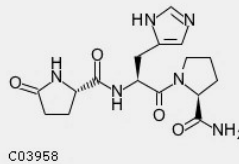
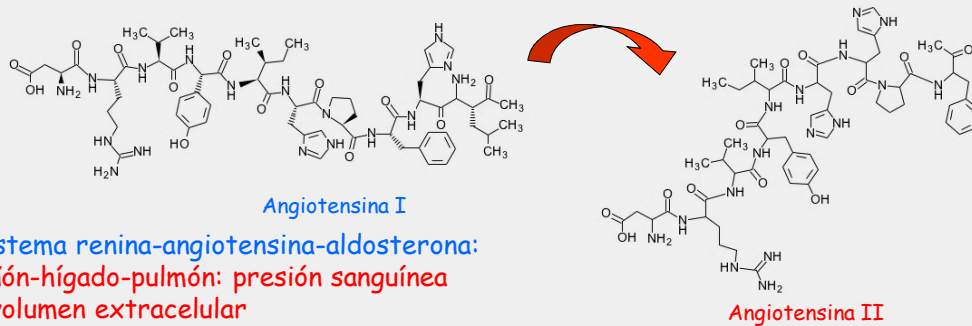
Try-Gly-Gly-Phe-Leu-OH

**Metionina encefalina**

Try-Gly-Gly-Phe-Met-OH

**β-Endorfina**

Try-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Val-Lys-Asn-Ala-His-Lys-Gly-Gln-OH



TRH (hipotálamo): H. liberadora de  
 Tirotropina (TSH). En hipófisis: estimula  
 liberación de TSH (producción de H.  
 tiroideas) y PRL (producción de leche)

## Contenido de la clase

### Proteínas: funciones

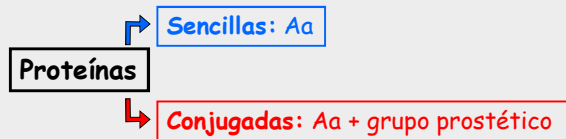
#### Aminoácidos:

- Estructura y clasificación según la estructura
- Clasificación según los grupos R
- No convencionales
- Propiedades ácido-base

#### Péptidos - Proteínas

- Enlace peptídico
- Síntesis
- Propiedades biológicas
- Proteínas conjugadas

## Proteínas compuestas por grupos químicos diferentes a Aa



**TABLE 3-4 Conjugated Proteins**

| Class           | Prosthetic group                                | Example                                                                          |
|-----------------|-------------------------------------------------|----------------------------------------------------------------------------------|
| Lipoproteins    | Lipids                                          | $\beta_1$ -Lipoprotein of blood                                                  |
| Glycoproteins   | Carbohydrates                                   | Immunoglobulin G                                                                 |
| Phosphoproteins | Phosphate groups                                | Casein of milk                                                                   |
| Hemoproteins    | Heme (iron porphyrin)                           | Hemoglobin                                                                       |
| Flavoproteins   | Flavin nucleotides                              | Succinate dehydrogenase                                                          |
| Metalloproteins | Iron<br>Zinc<br>Calcium<br>Molybdenum<br>Copper | Ferritin<br>Alcohol dehydrogenase<br>Calmodulin<br>Dinitrogenase<br>Plastocyanin |

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