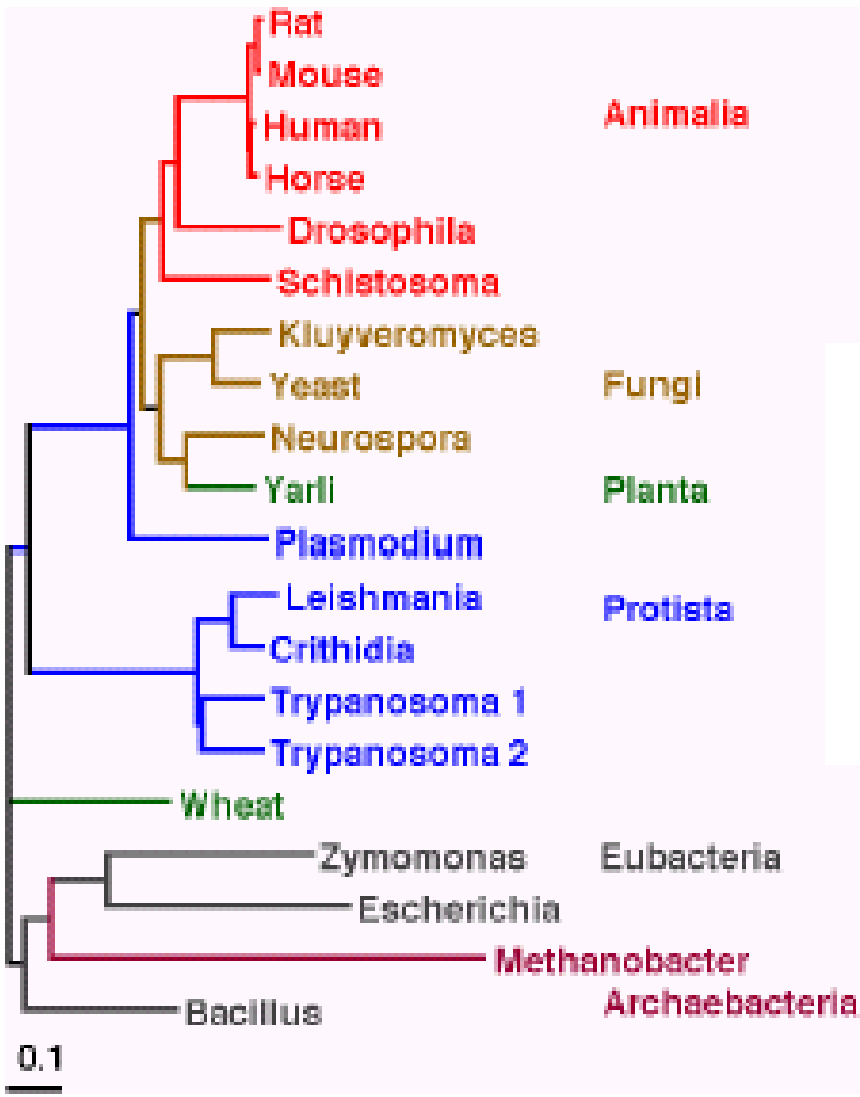
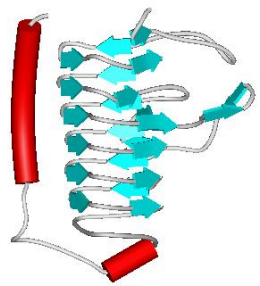
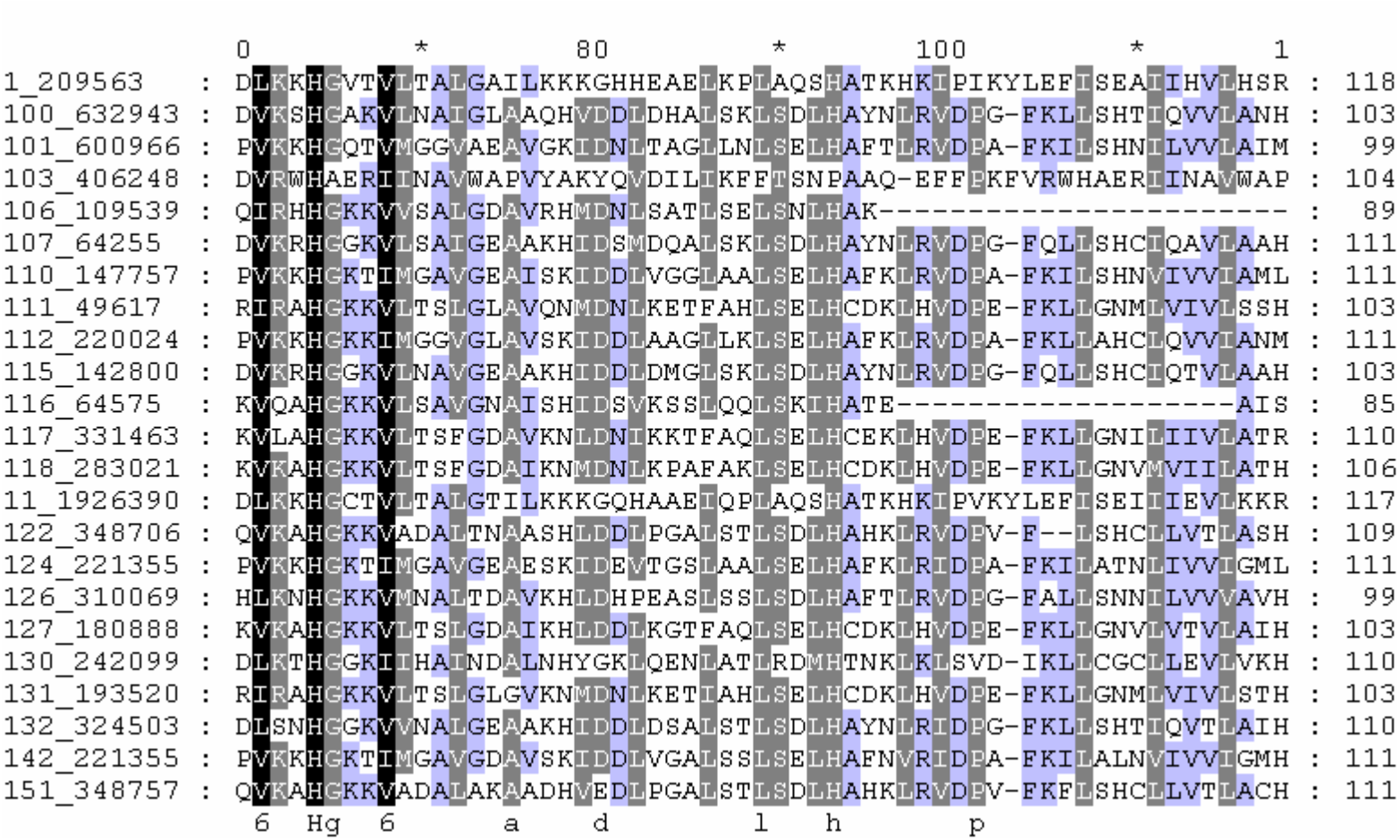
Propiedades Fisicoquímicas de los aminoácidos

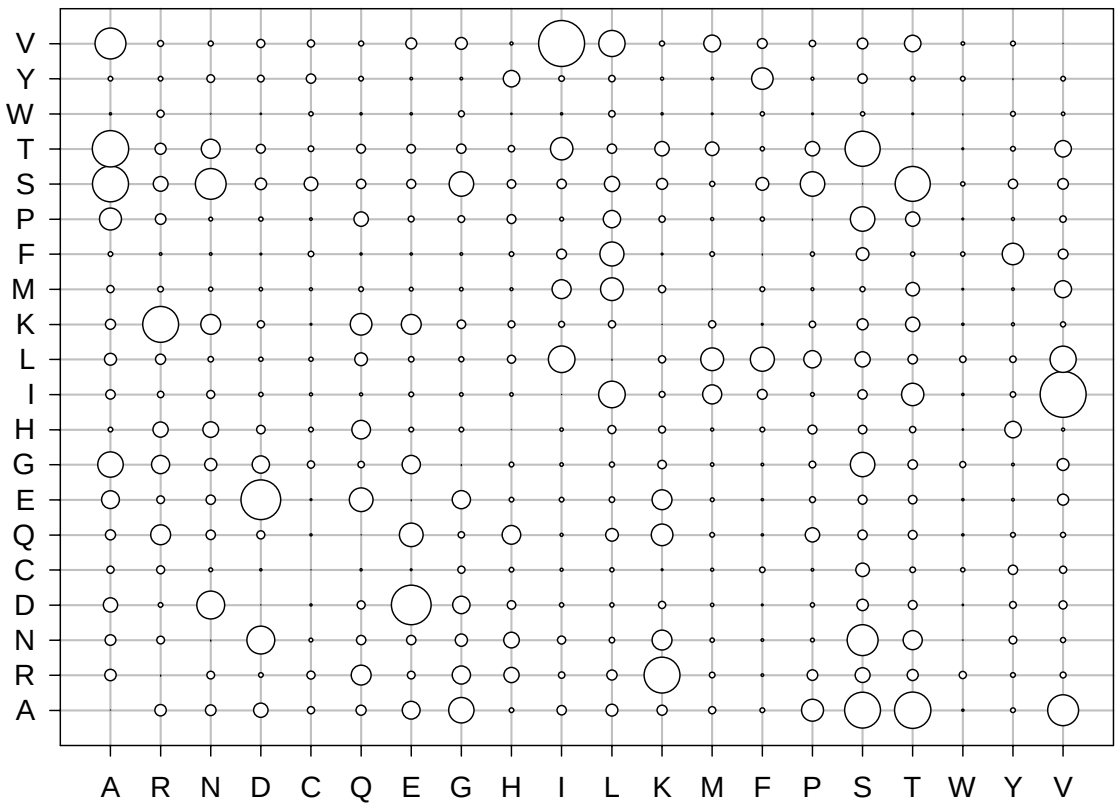
(primera parte)


Rat
Mouse
Human
Horse
Drosophila
Schistosoma
Kluyveromyces
Yeast
Neurospora
Yarli
Plasmodium
Leishmania
Crithidia
Trypanosoma 1
Trypanosoma 2
Wheat
Zymomonas
Escherichia
Methanobacter
Bacillus
Animalia
Fungi
Planta
Protista
Eubacteria
Archaebacteria
0.1

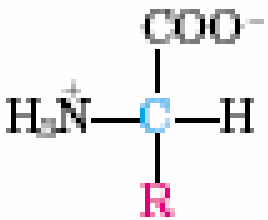



0 * 80 * 100 * 1
1_209563 : DLKKHGVTVLTALGAILKKKGHHEAELKPLAQSHATKHKIPIKYLEFISEAIIHVLHSR : 118
100_632943 : DVKSHGAKVLNAIGLAAQHVDDLDHALSKLSDLHAYNLRVDPG-FKLLSHTIQVVLANH : 103
101_600966 : PVKKHGQTVMGGVAEAVGKIDNLTAGLLNLSELHAFTLRVDPA-FKILSHNILVVLAIM : 99
103_406248 : DVRWHAERIINAVWAPVYAKYQVDILIKFFTSNPAAQ-EFFPKFVRWHAERIINAVWAP : 104
106_109539 : QIRHHGKKVVSALGDAVRHMDNLSATLSELSNLHAK---------- : 89
107_64255 : DVKRHGGKVLSAIGEAAKHIDSMDQALSKLSDLHAYNLRVDPG-FQLLSHCIQAVLAAH : 111
110_147757 : PVKKHGKTIMGAVGEAISKIDDLVGGLAALSELHAFKLRVDPA-FKILSHNVIVVIAML : 111
111_49617 : RIRAHGKKVLTSLGLAVQNMDNLKETFAHLSELHCDKLHVDPE-FKLLGNMLVIVLSSH : 103
112_220024 : PVKKHGKKIMGGVGLAVSKIDDLAAGLLKLSELHAFKLRVDPA-FKLLAHCLQVVIANM : 111
115_142800 : DVKRHGGKVLNAVGEAAKHIDDLDMGLSKLSDLHAYNLRVDPG-FQLLSHCIQTVLAAH : 103
116_64575 : KVQAHGKKVLSAVGNAISHIDSVKSSLQQLSKIHATE----------AIS : 85
117_331463 : KVLAHGKKVLTSFGDAVKNLDNIKKTFAQLSELHCEKLHVDPE-FKLLGNILIIVLATR : 110
118_283021 : KVKAHGKKVLTSFGDAIKNMDNLKPAFAKLSELHCDKLHVDPE-FKLLGNVMVIILATH : 106
11_1926390 : DLKKHGCTVLTALGTILKKKGQHAAEIQPLAQSHATKHKIPVKYLEFISEIIIEVLKKR : 117
122_348706 : QVKAHGKKVADALTNAASHLDDLPGALSTLSDLHAHKLRVDPV-F--LSHCLLVTLASH : 109
124_221355 : PVKKHGKTIMGAVGEAESKIDEVTGSLAALSELHAFKLRIDPA-FKILATNLIVVIGML : 111
126_310069 : HLKNHGKKVMNALTDAVKHLDHPEASLSSLSDLHAFTLRVDPG-FALLSNNILVVVAVH : 99
127_180888 : KVKAHGKKVLTSLGDAIKHLDDLKGTFAQLSELHCDKLHVDPE-FKLLGNVLVTVLAIH : 103
130_242099 : DLKTHGGKIIHAINDALNHYGKLQENLATLRDMHTNKLKLSVD-IKLLCGCLLEVLVKH : 110
131_193520 : RIRAHGKKVLTSLGLGVKNMDNLKETIAHLSELHCDKLHVDPE-FKLLGNMLVIVLSTH : 103
132_324503 : DLSNHGGKVVNALGEAAKHIDDLDSALSTLSDLHAYNLRIDPG-FKLLSHTIQVTLAIH : 110
142_221355 : PVKKHGKTIMGAVGDAVSKIDDLVGALSSLSELHAFNVRIDPA-FKILALNVIVVIGMH : 111
151_348757 : QVKAHGKKVADALAKAADHVEDLPGALSTLSDLHAHKLRVDPV-FKFLSHCLLVTLACH : 111
6 Hg 6 a d l h p

Matriz de sustitución

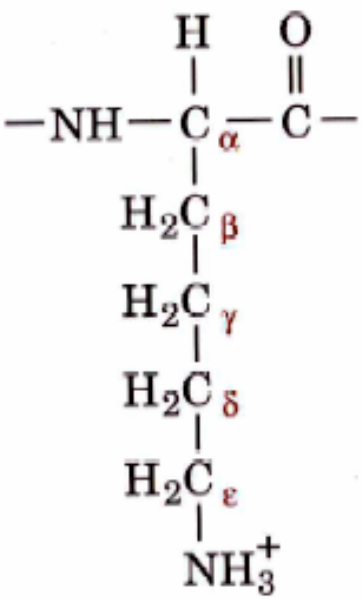


Características generales

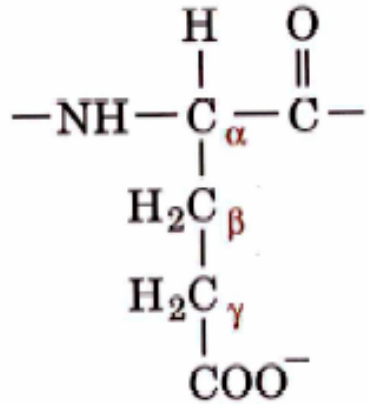


- Todos los AA son alfa aminoácidos
- Las propiedades fisico-químicas de un AA dependen en gran medida de su grupo R
- Existen 20 aminoácidos codificados en el código genético
- Por tener un centro quiral, existen dos estereoisómeros D y L
- Tienen actividad óptica (levógiros o dextrógiros)
- Son anfolítos

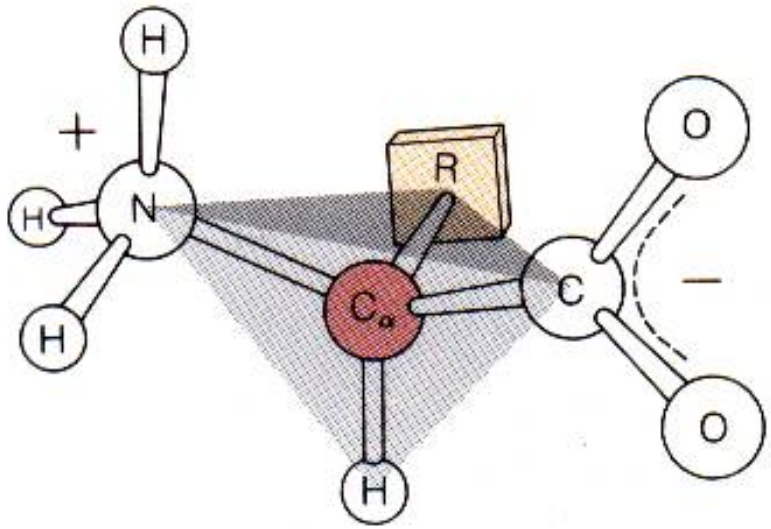
Nomenclatura



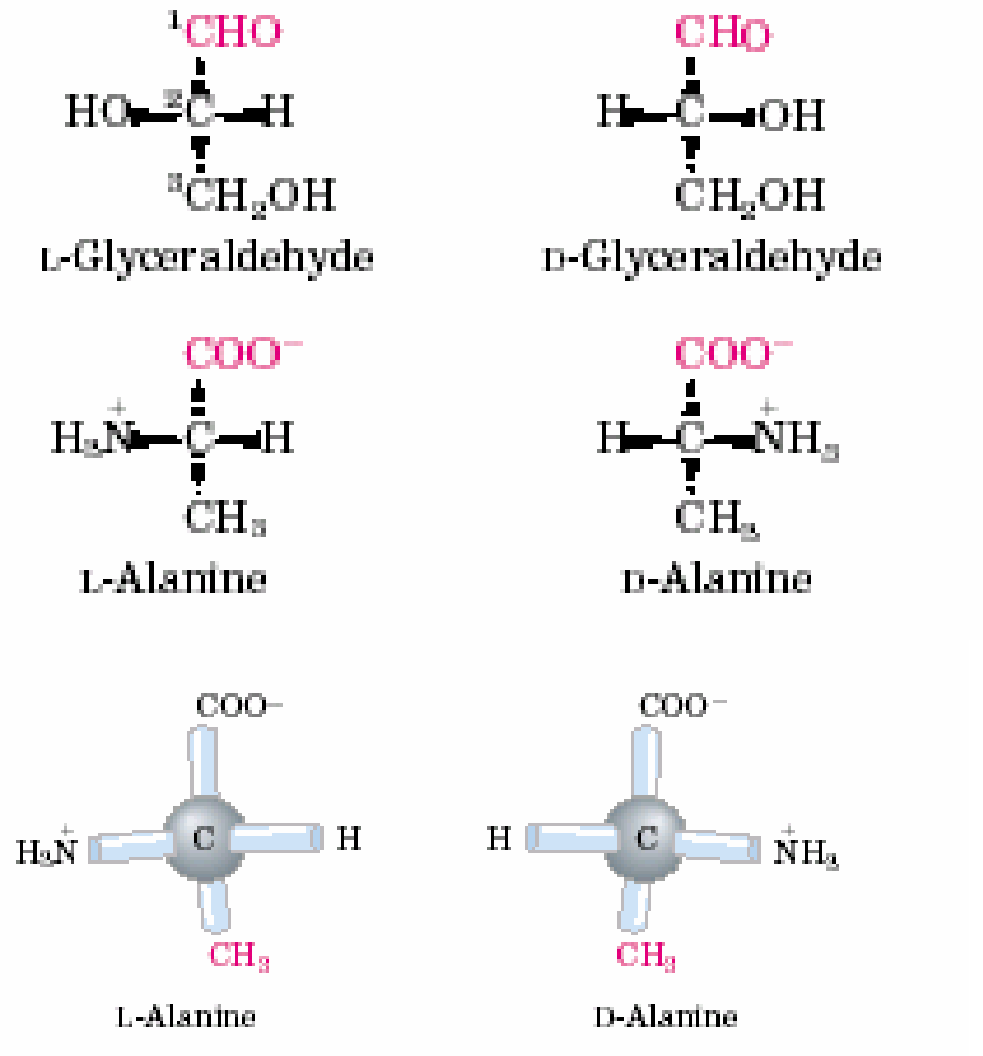
Lys



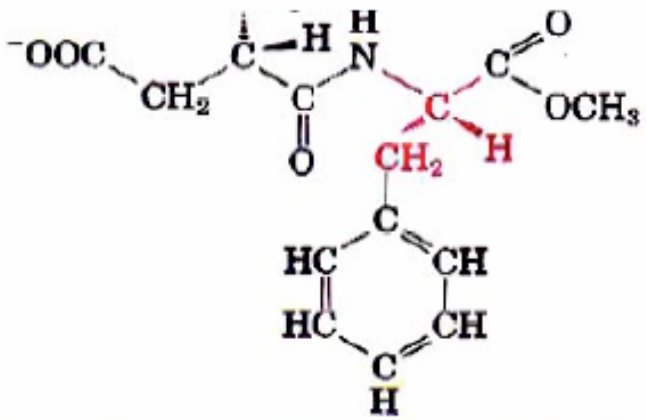
Glu


H
+
H
N
R
O
H
C_α
C
−
H
O

Isómeros ópticos

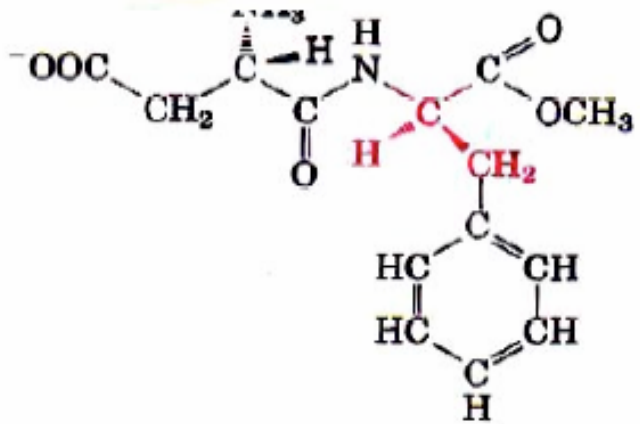


Quiralidad y función

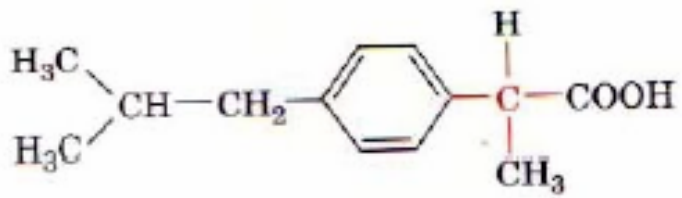


D-Aspartyl-L-phenylalanine methyl ester
(aspartame) (sweet)

Thalidomide

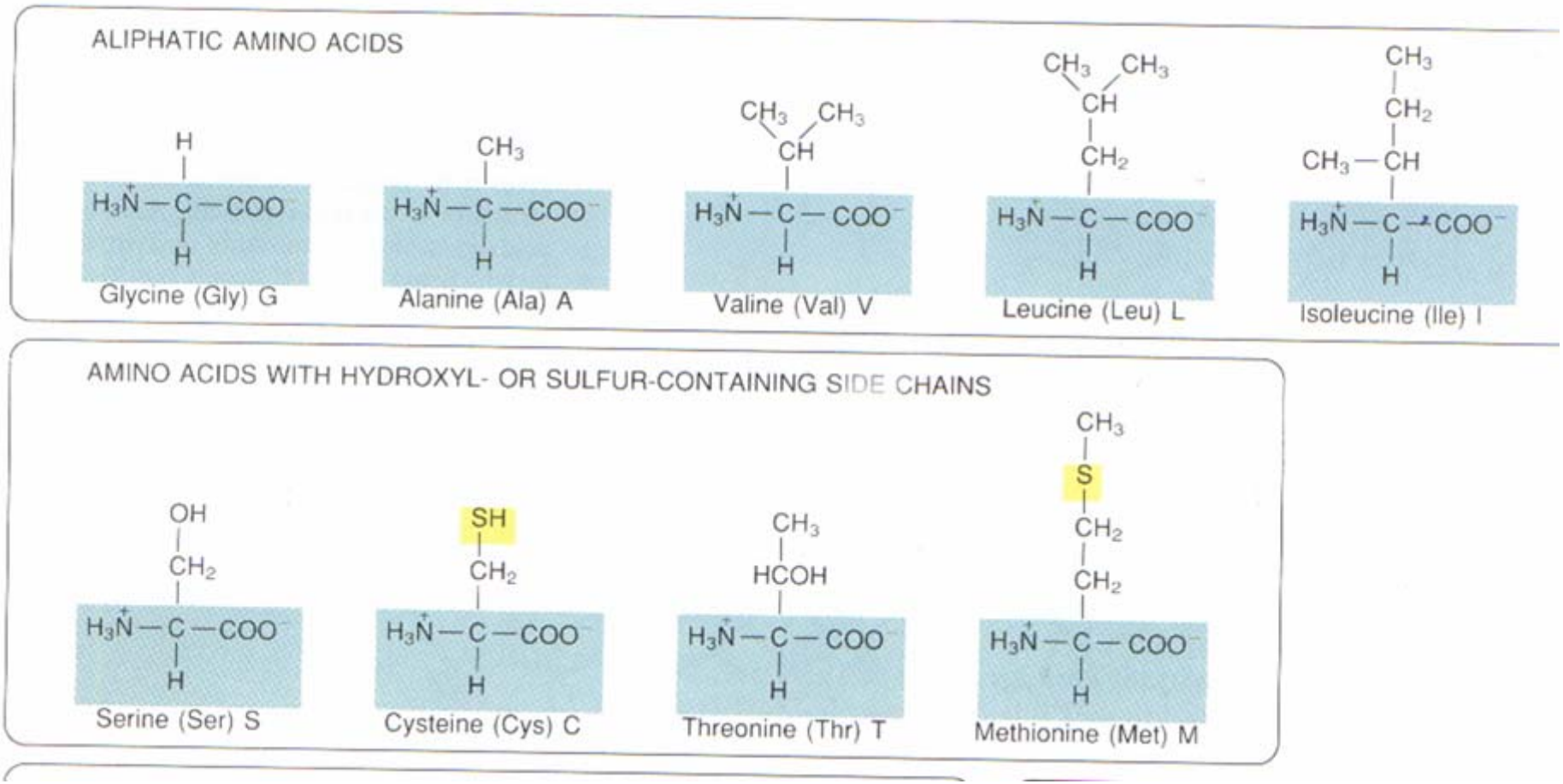


L-Aspartyl-D-phenylalanine methyl ester
(bitter)

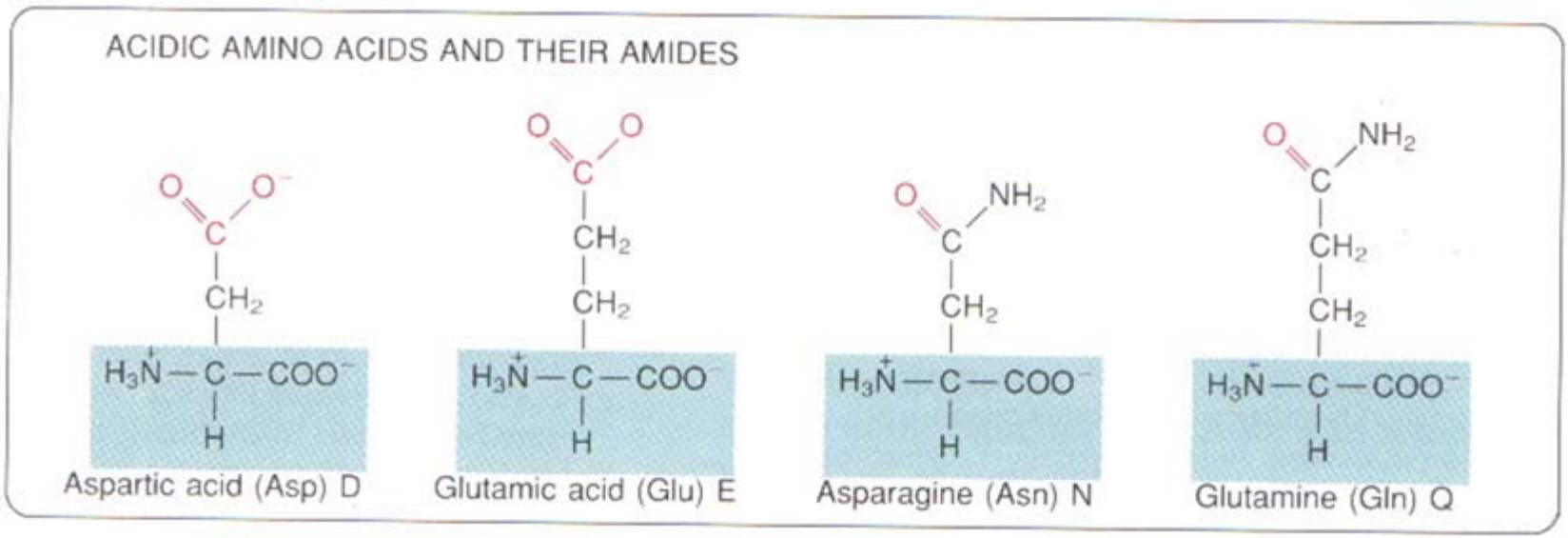


Ibuprofen

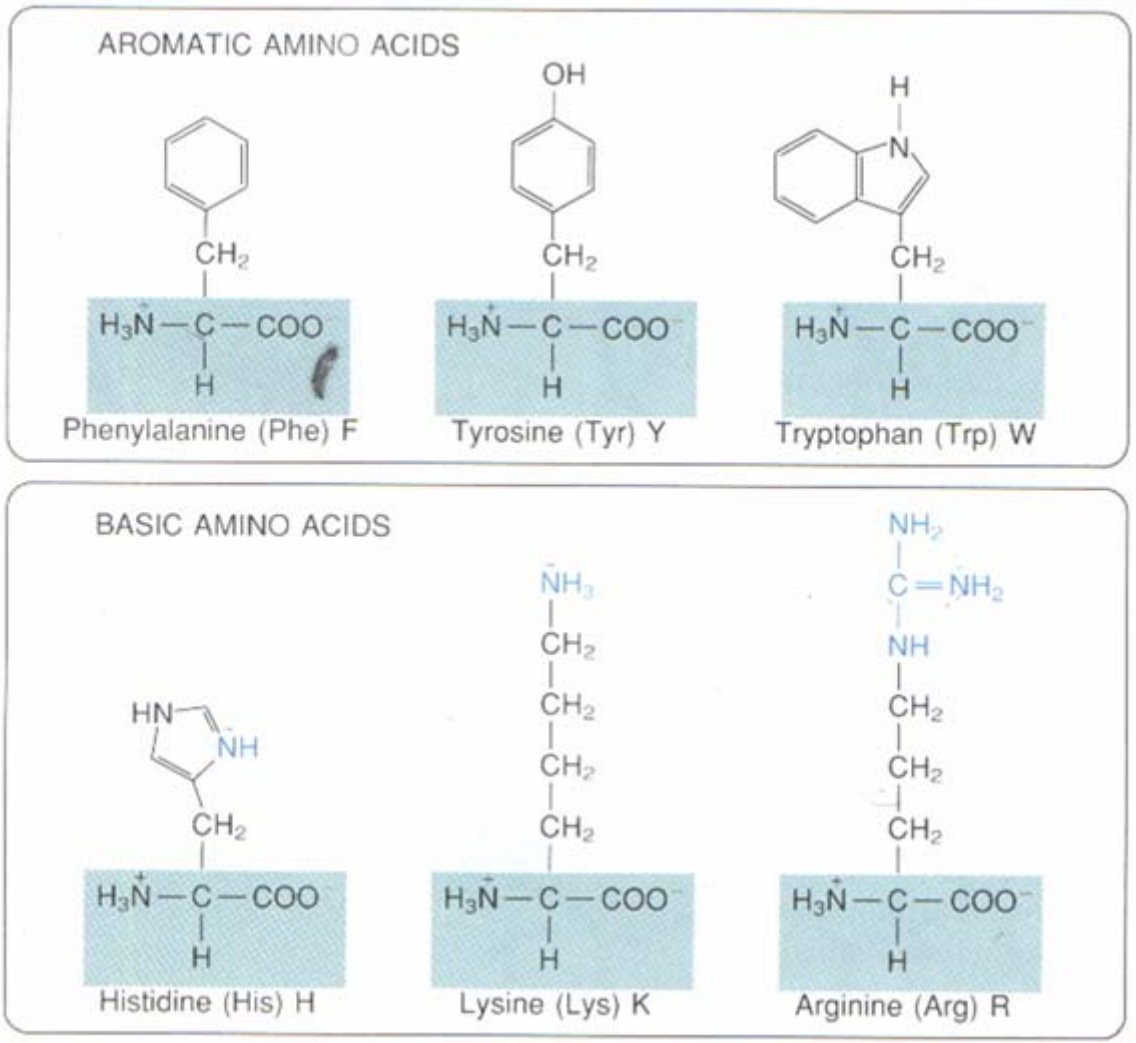
Tipos de aminoácidos



Tipos de aminoácidos



Tipos de aminoácidos



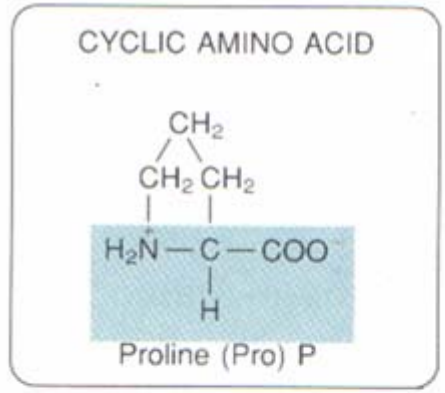
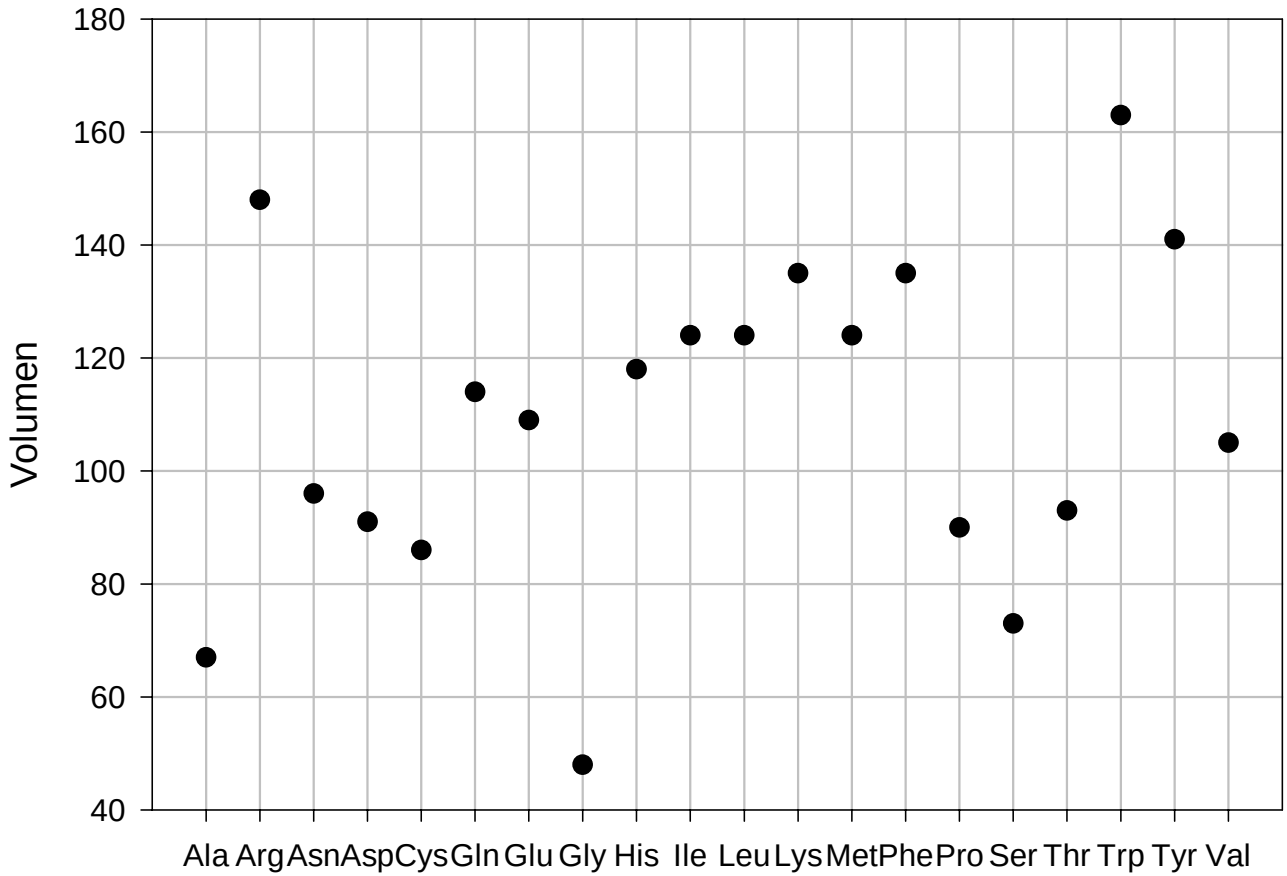


Figure 5.3
The 20 amino acids that are incorporated into proteins. These are arranged in the order discussed in the text. Below each, along with its name, is given a three-letter abbreviation (e.g., Gly) and a one-letter abbreviation (G) often used in describing amino acid sequences in proteins.

Algunas propiedades fisicoquímicas del R



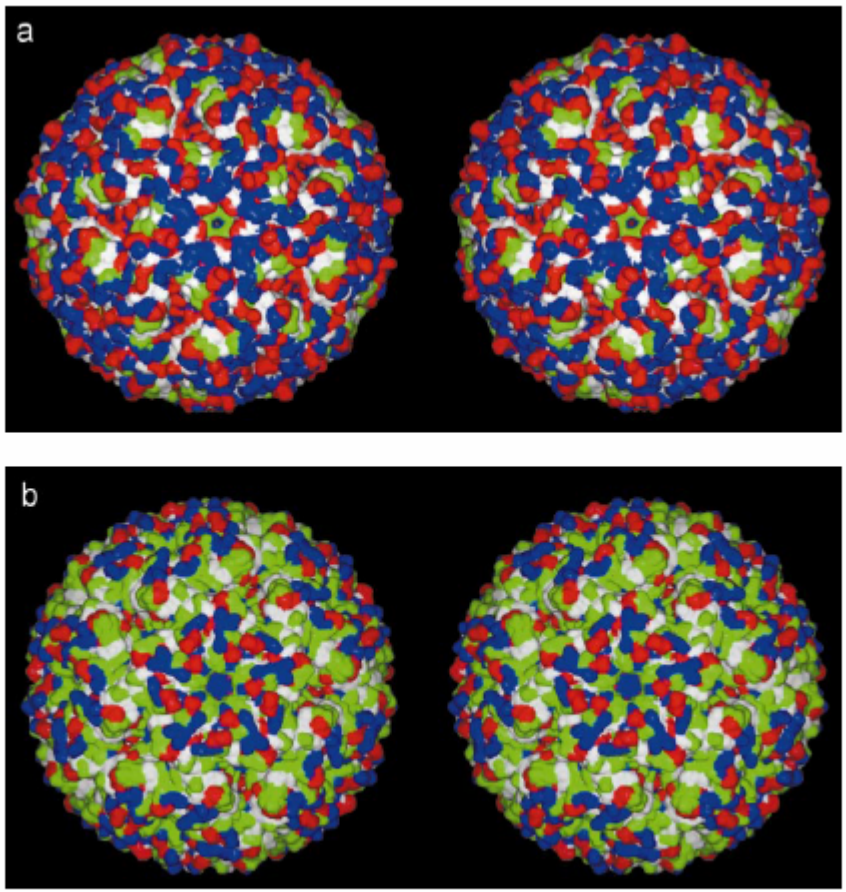
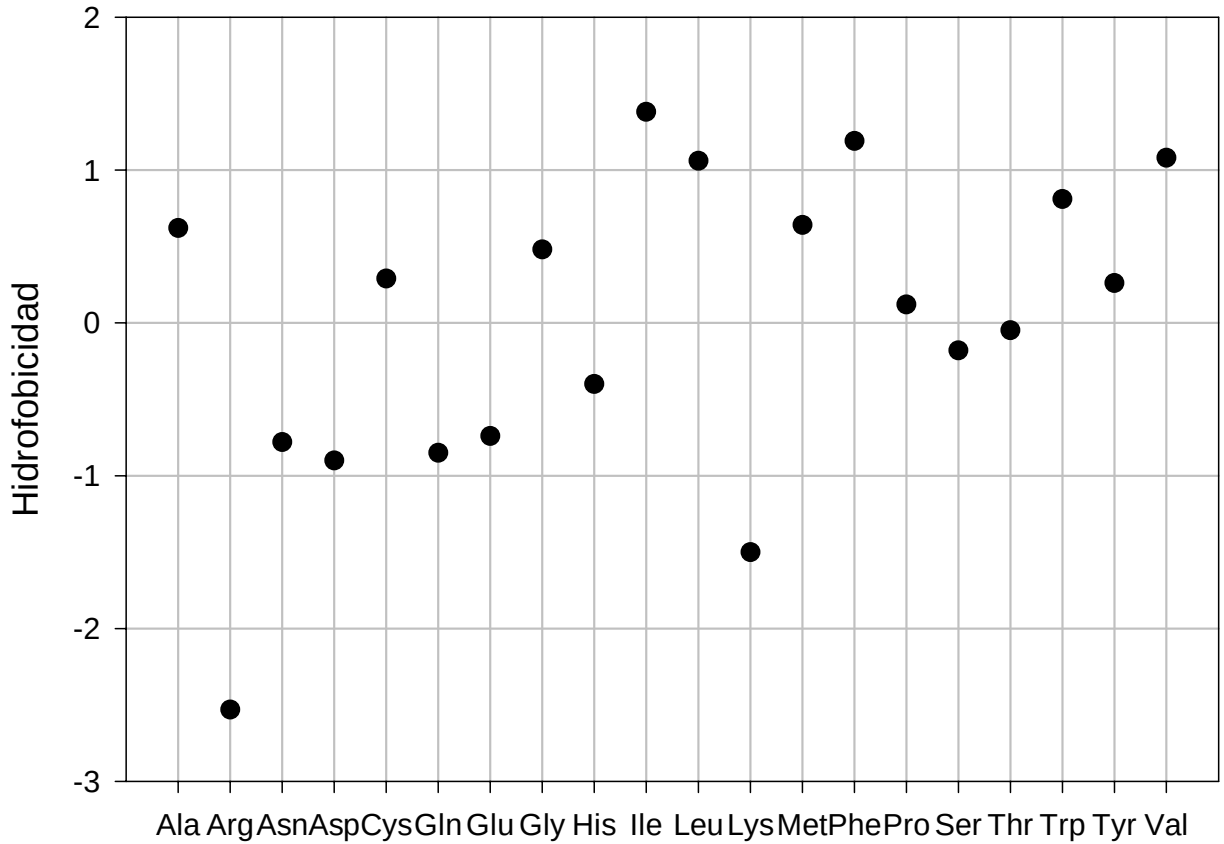
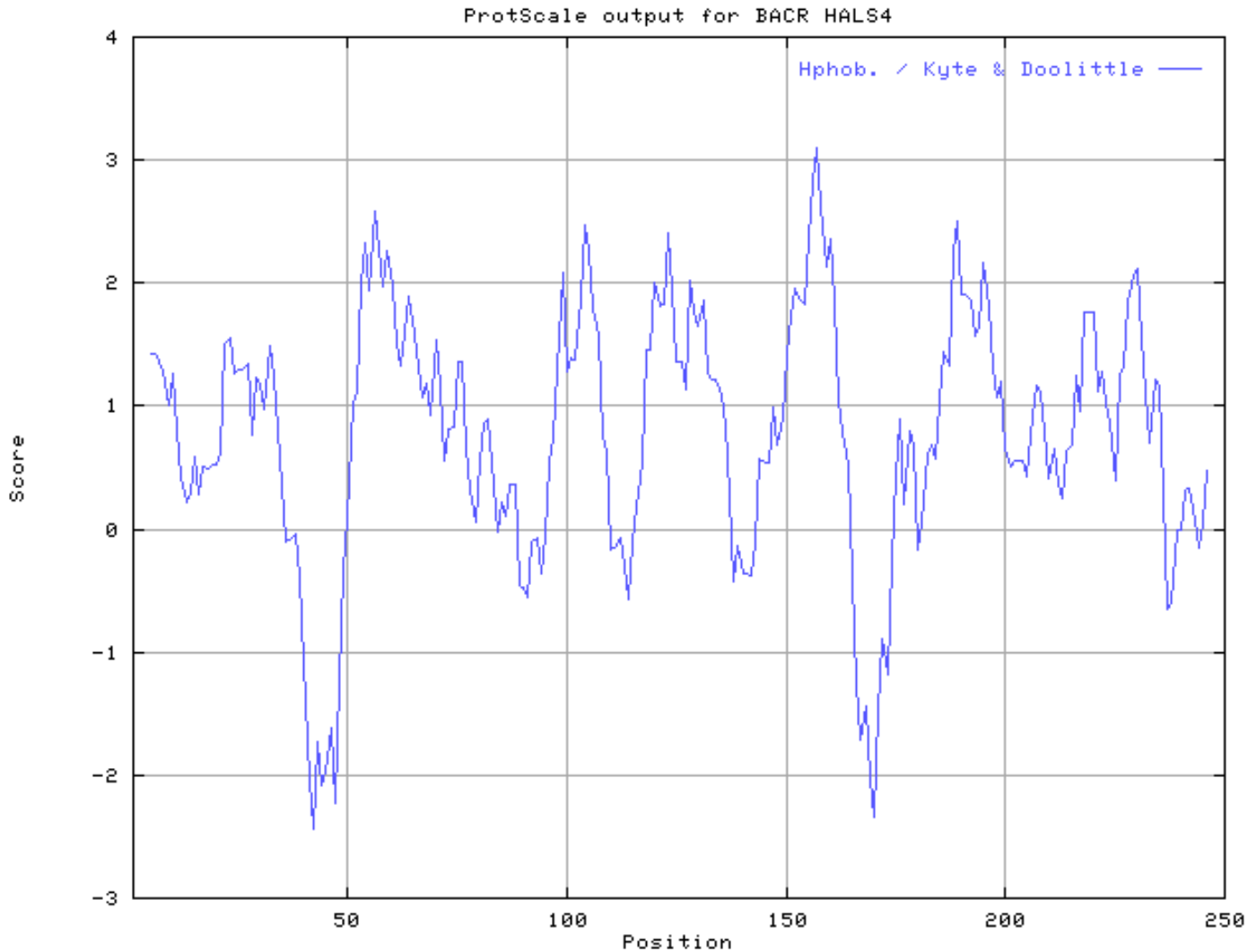


Figure 4. Accessible surface comparison of LS from (a) *A. aeolicus* and (b) *B. subtilis*. Color codes are: red for Asp and Glu; blue for Lys, His and Arg; green for Asn, Gln, Ser, Thr, Cys, Tyr and Gly; white for Ala, Val, Leu, Ile, Met, Pro, Phe and Trp. The image was generated by SPOCK (J. A. Christopher, The Center for Macromolecular Design, Texas A&M University).


Hidrofobicidad
2
1
0
-1
-2
-3
Ala Arg Asn Asp Cys Gln Glu Gly His Ile Leu Lys Met Phe Pro Ser Thr Trp Tyr Val


ProtScale output for BACR HALS4
Hphob. / Kyte & Doolittle
Score
Position
4
3
2
1
0
-1
-2
-3
50
100
150
200
250

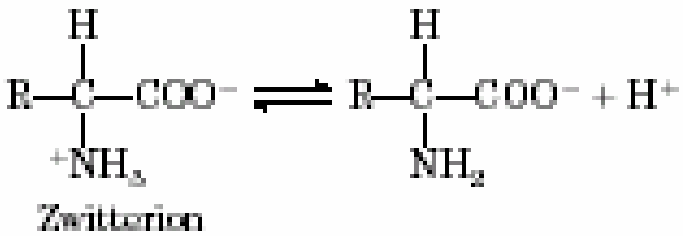
Propiedades ácido-base

Porque estudiarlas?

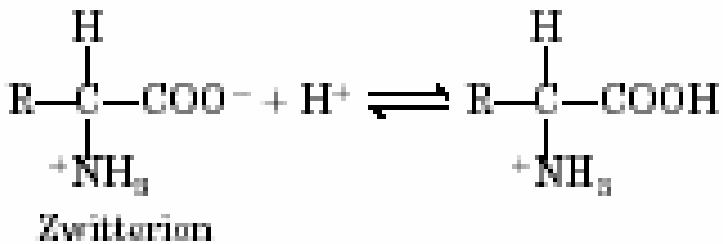
- del estado ácido-base de una molécula se deduce su carga neta
- de la carga de una molécula dependerá su energía y así su conformación
- la actividad biológica depende de la conformación y (en algunos casos) de la presencia de cargas en el sitio activo
- permite la cuantificación (titulación), identificación y purificación

Propiedades Acido-Base

(Bronsted-Lowry)



Comportamiento ácido

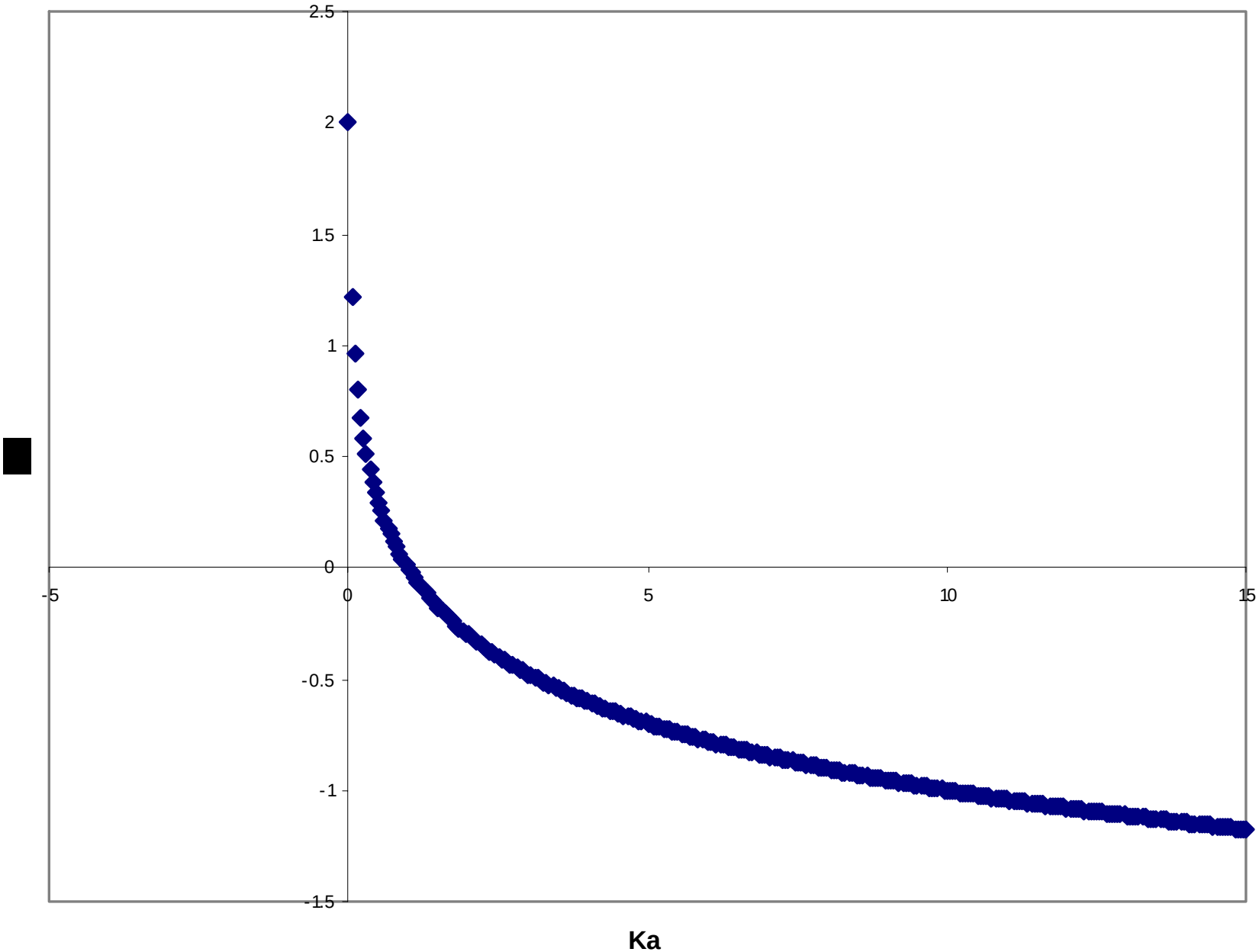


Comportamiento básico

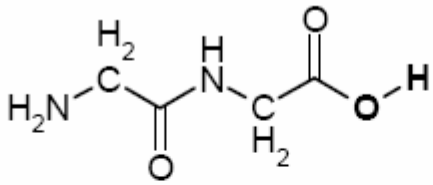
$$HA \rightleftharpoons H^+ + A^-$$

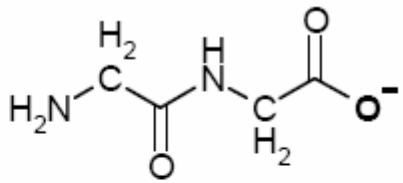
$$K_{eq} = \frac{[H^+][A^-]}{[HA]} = K_a$$

$$pK_a = \log\frac{1}{K_a} = -\log K_a$$

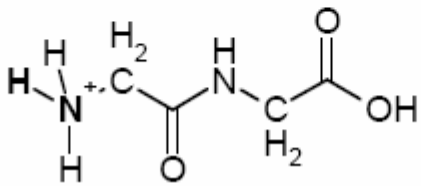

2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
-5
0
5
10
15
Ka

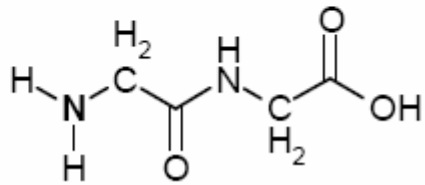
Carboxy-Terminus
pKa=2



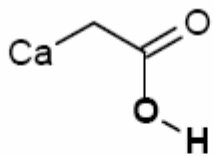


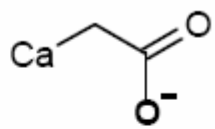
Amino-Terminus
pka=10



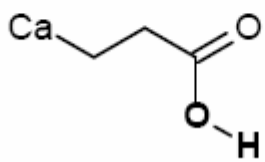


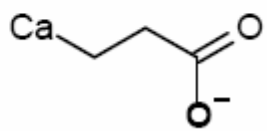
Aspartic Acid (Asp)
pKa=4



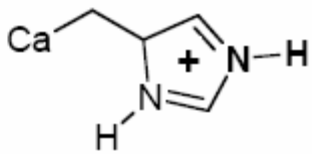


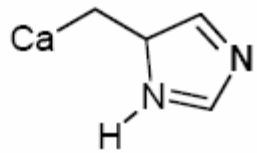
Glutamic Acid (Glu)
pKa=4



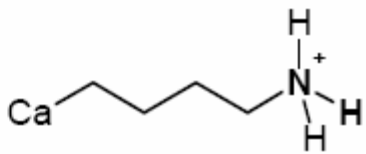


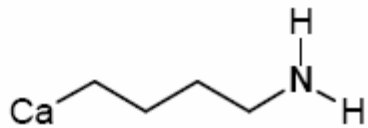
Histidine (His)
pKa=6



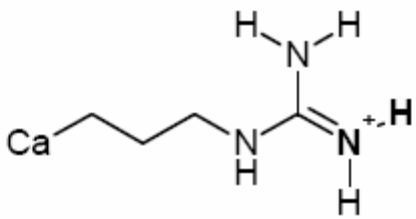


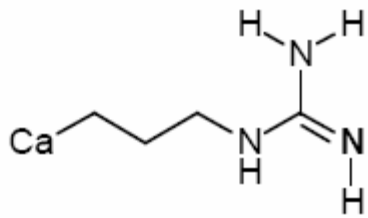
Lysine (Lys)
pKa=10



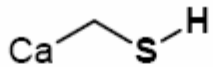


Arginine (Arg)
pKa=12.5

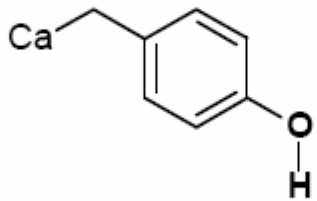




Cysteine (Cys)
pKa=8



Tyrosine (Tyr)
pKa=10



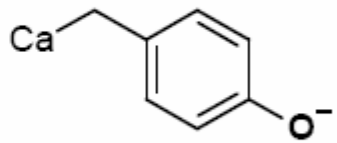


table 5–1

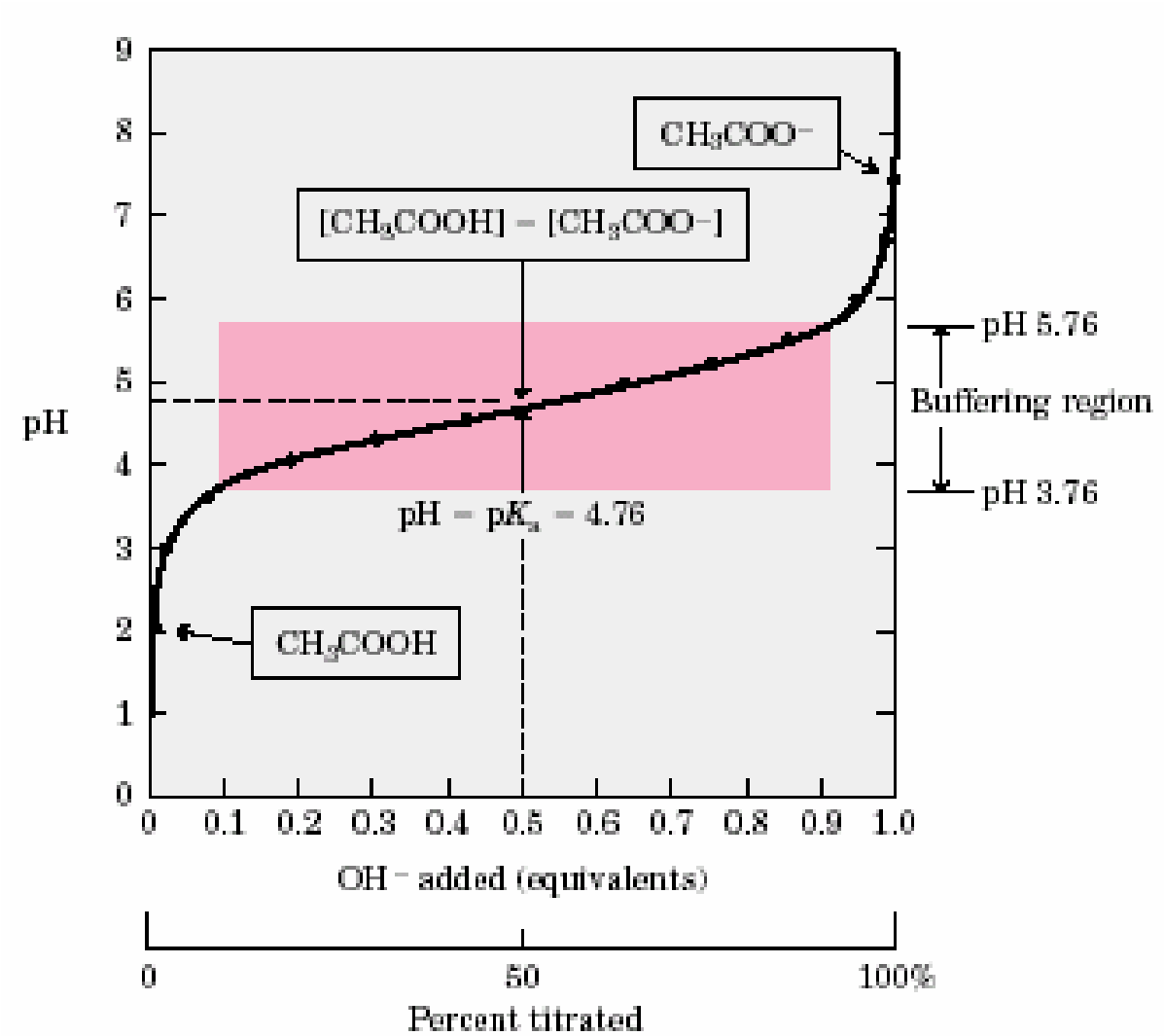
Properties and Conventions Associated with the Standard Amino Acids

Amino acid	Abbreviated names		M_r	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI	Hydropathy index*	Occurrence in proteins (%)†
Nonpolar, aliphatic R groups									
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
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
Aromatic R groups									
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	17	5.89	−0.9	1.4
Polar, uncharged R groups									
Serine	Ser	S	105	2.21	9.15	14	5.68	−0.8	6.8
Proline	Pro	P	115	1.99	10.96		6.48	1.6	5.2
Threonine	Thr	T	119	2.11	9.62	14	5.87	−0.7	5.9
Cysteine	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
Positively charged R groups									
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
Negatively charged R groups									
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

*A scale combining hydrophobicity and hydrophilicity of R groups; it can be used to measure the tendency of an amino acid to seek an aqueous environment (− values) or a hydrophobic environment (+ values). See Chapter 12. From Kyte, J. & Doolittle, R.F. (1982) *J. Mol. Biol.* **157**, 105–132.

†Average occurrence in over 1150 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) Plenum Press, NY, pp. 599–623.

Titulación de un ácido débil



Ecuación de Henderson-Hasselbalch

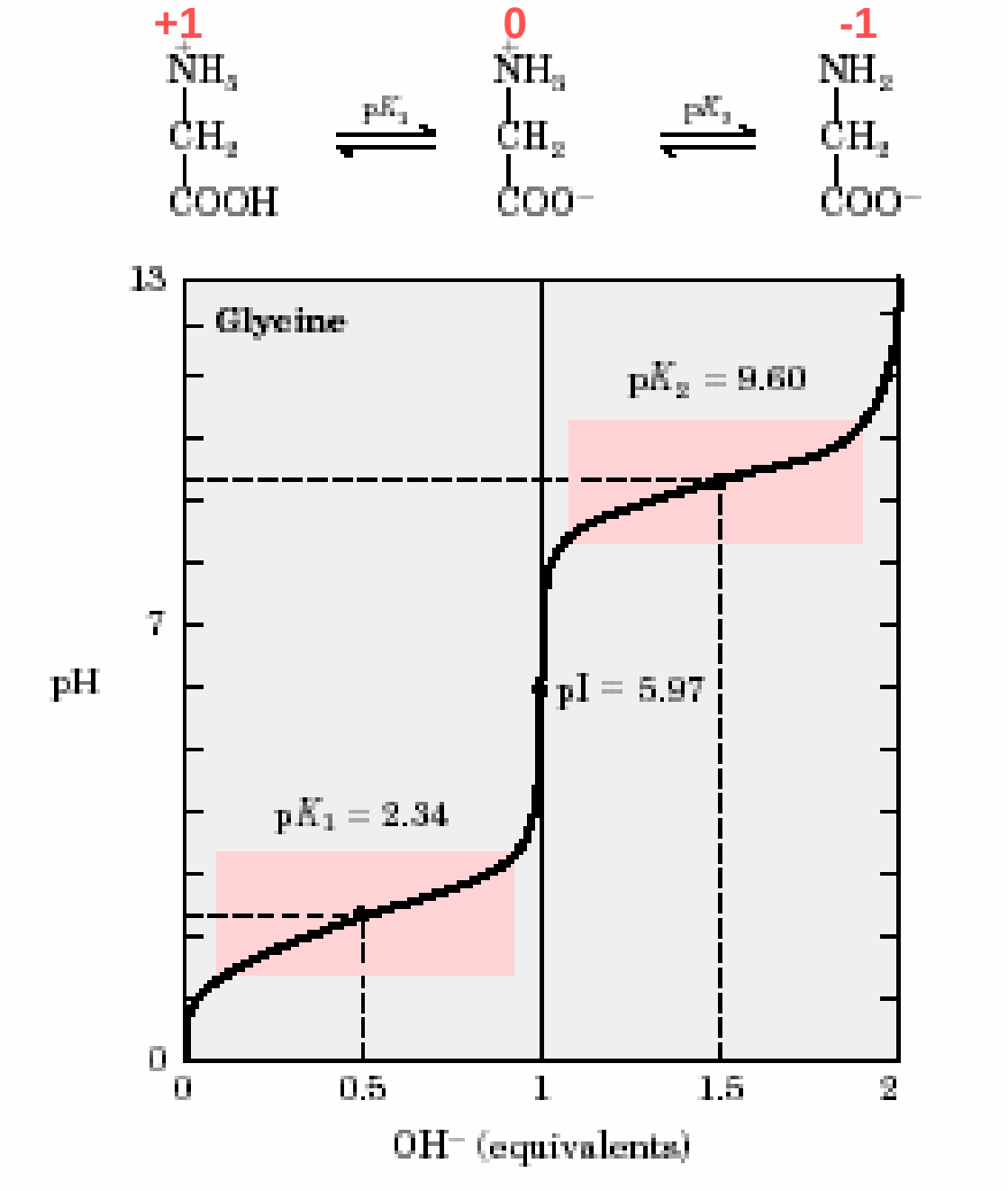
$$K_a = \frac{a_{H^+} a_{A^-}}{a_{AH}}$$

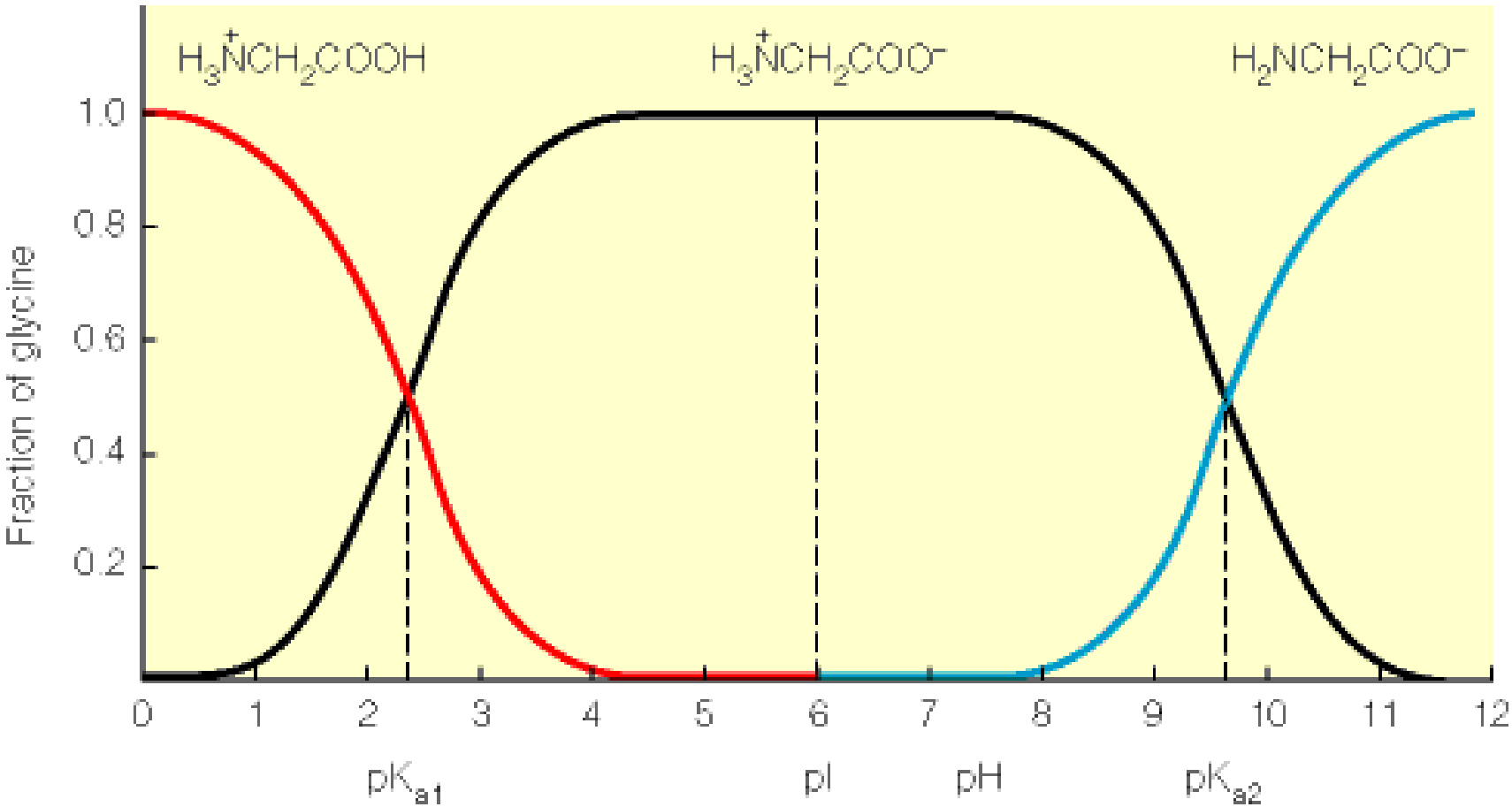
$$-\log(K_a) = -\log\left(\frac{a_{H^+} a_{A^-}}{a_{AH}}\right)$$

$$pK_a = -\log(a_{H^+}) - \log\left(\frac{a_{A^-}}{a_{AH}}\right)$$

$$pK_a = pH - \log\left(\frac{a_{A^-}}{a_{AH}}\right)$$

$$pH = pK_a + \log\left(\frac{a_{A^-}}{a_{AH}}\right)$$


+1
0
-1
NH_3^+
CH_2
COOH
pK_1
NH_3^+
CH_2
COO^-
pK_2
NH_2
CH_2
COO^-
Glycine
$pK_2 = 9.60$
pI = 5.97
$pK_1 = 2.34$
pH
13
7
0
0
0.5
1
1.5
2
OH^- (equivalents)

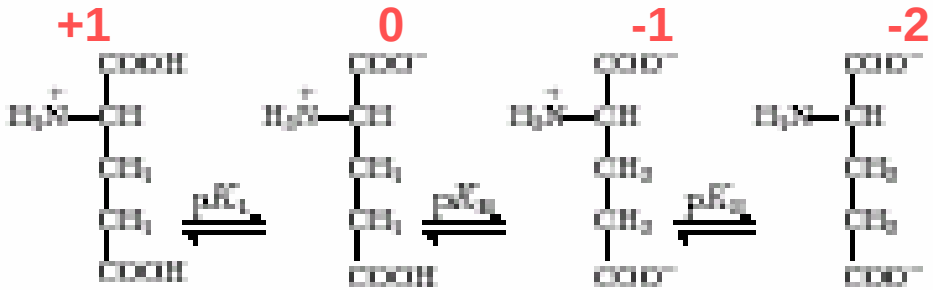

$H_3\overset{+}{N}CH_2COOH$
$H_3\overset{+}{N}CH_2COO^-$
$H_2NCH_2COO^-$
Fraction of glycine
1.0
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
10
11
12
pK_{a1}
pI
pH
pK_{a2}

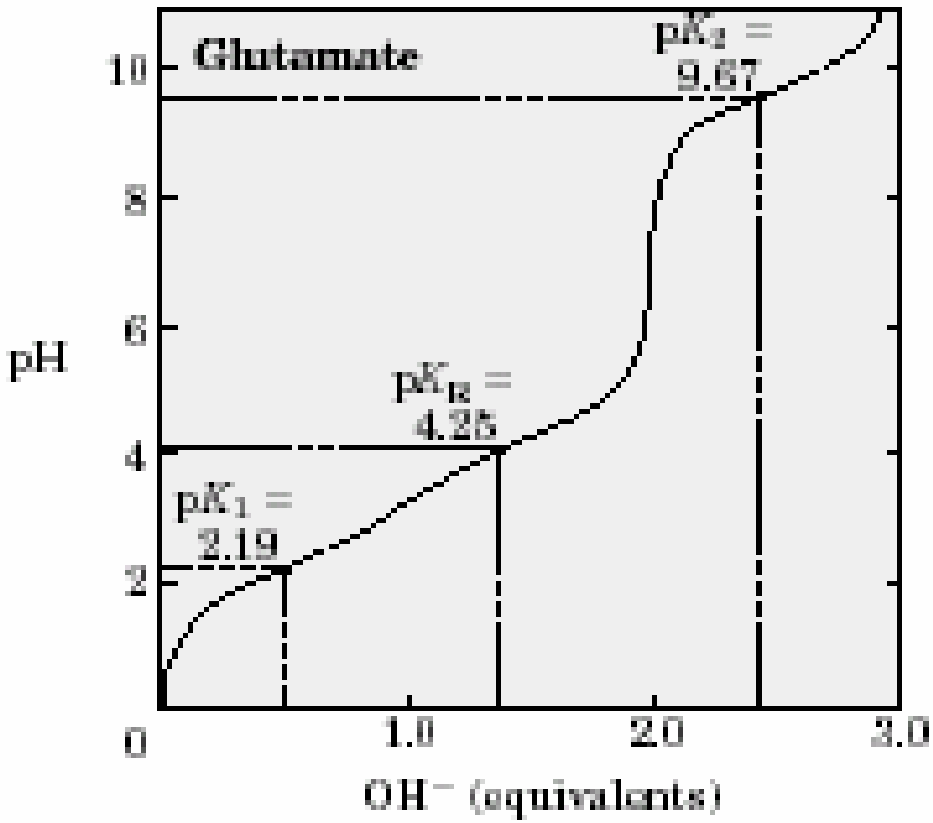
Punto isoiónico e isoeléctrico

El punto *isoiónico* (PI) es el pH en el cual el número de cargas positivas es igual al número de cargas negativas

El punto isoeléctrico (PE) es el pH en el cual una molécula puesta en un campo eléctrico no presenta movilidad (ya que tiene carga neta igual a cero)

Para moléculas pequeñas (aminoácidos y péptidos) el PI=PE

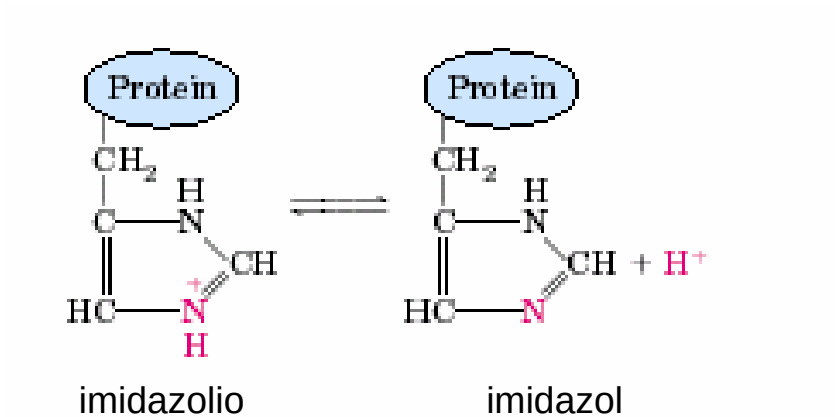

+1
0
-1
-2
pK1
pK2
pK3


Glutamate
pK3 = 9.67
pKR = 4.25
pK1 = 2.19
pH
10
8
6
4
2
0
1.0
2.0
3.0
OH⁻ (equivalents)

Sistemas Buffer

- Son sistemas formados por una ácido y una base conjugadas que mantienen constante el ph dentro de ciertos límites
- La capacidad buffer es la variación del ph con respecto al agregado de H^+ u OH^-
- La capacidad buffer es máxima cuando la actividad del ácido sea igual al de la base conjugada (pka)
- Para obtener un buffer efectivo en un determinado pH debemos elegir un par acido/base conjugada con un pka cercano al pH deseado

Buffers de importancia biológica



pK= 6.0

$$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$$

pK= 6.86

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$CO_2(d) + H_2O \rightleftharpoons H_2CO_3$$

$$CO_2(g) \rightleftharpoons CO_2(d)$$

pK= 7.4