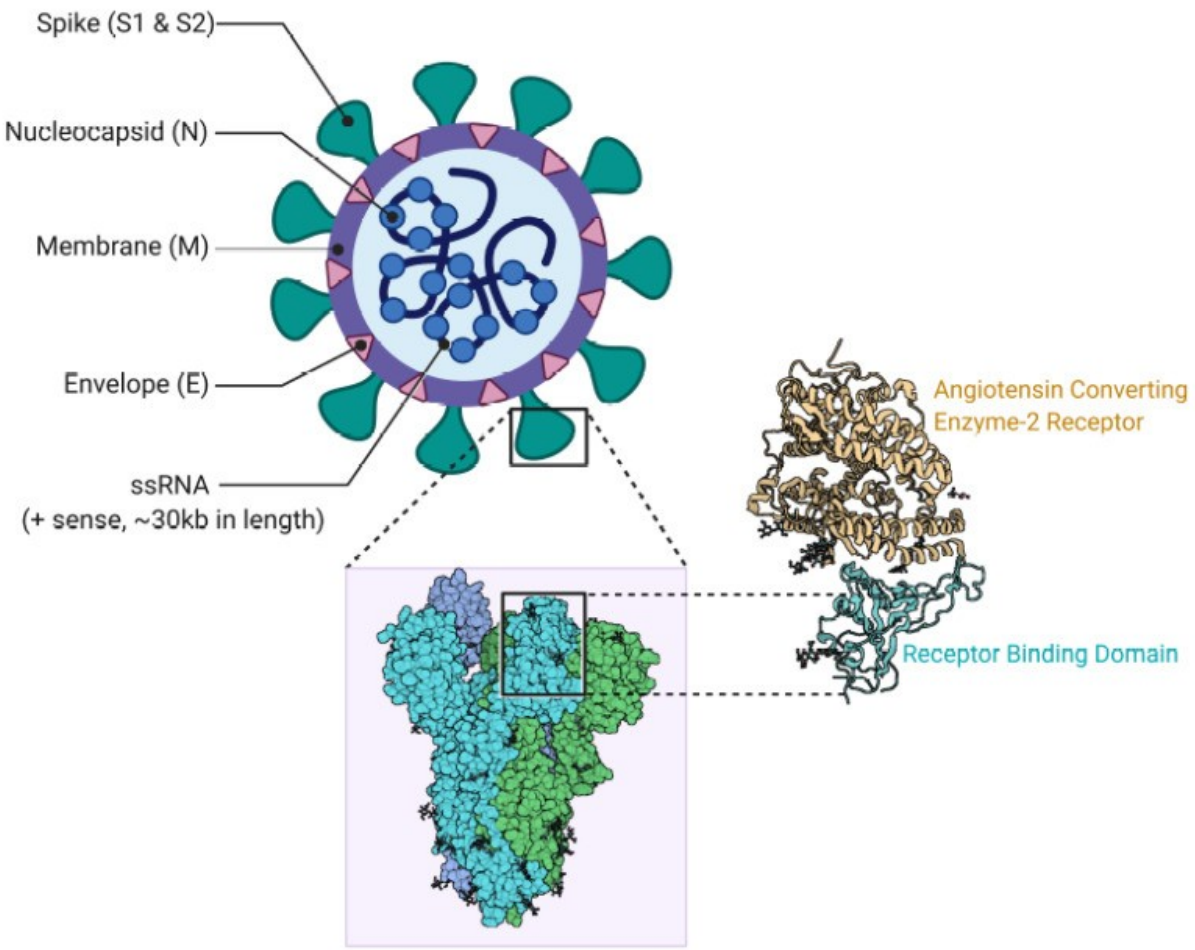
Aminoácidos

Contribuição slides : Evelyn Ayumi Onga (PAE 2020)
Profª Drª Tie Koide

SARS-CoV 2 Structure



Covid: Variante brasileira corresponde a 90% dos casos em SP, diz estudo

Análise identificou a variante P.1 corresponde em 90% dos sequenciamentos genéticos realizados; 21 linhagens já foram encontradas em São Paulo

Imagem: Divulgação/Governo do Estado de São Paulo

Colaboração para o UOL

28/04/2021 13h31 | Atualizada em 28/04/2021 14h25

Um estudo do Instituto Adolfo Lutz concluiu que a variante brasileira, a P.1, que surgiu em Manaus, corresponde a 90% casos analisados de infecção pelo novo coronavírus no estado de São Paulo.

VARIANTE 'BRASILEIRA' P1 PODE TER CARGA VIRAL ATÉ 10 VEZES MAIOR QUE OUTRAS CEPAS, DIZ CIENTISTA DA FIOCRUZ

Descoberta consta em estudo de epidemiologia genômica assinado por 29 pesquisadores brasileiros da área de virologia
Época abril 2021

Covid-19: Variante brasileira faz explodir intubações de jovens

A maioria dos casos do novo coronavírus em São Paulo se concentra entre pessoas de 20 a 54 anos

Brasil, um possível celeiro de novas variantes do coronavírus

Grande número de casos, medidas de restrição não respeitadas, falta de sequenciamento do vírus e vacinação lenta fazem do país um caldeirão de mutações

Veja saúde abril 2021

Ácidos e Bases

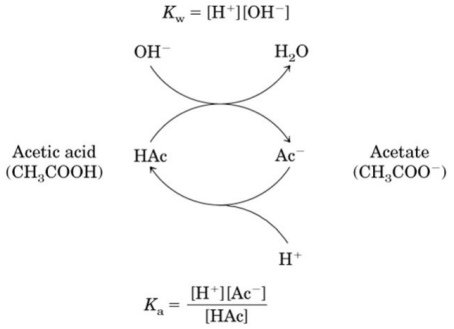
Definição de Brönsted & Lowry

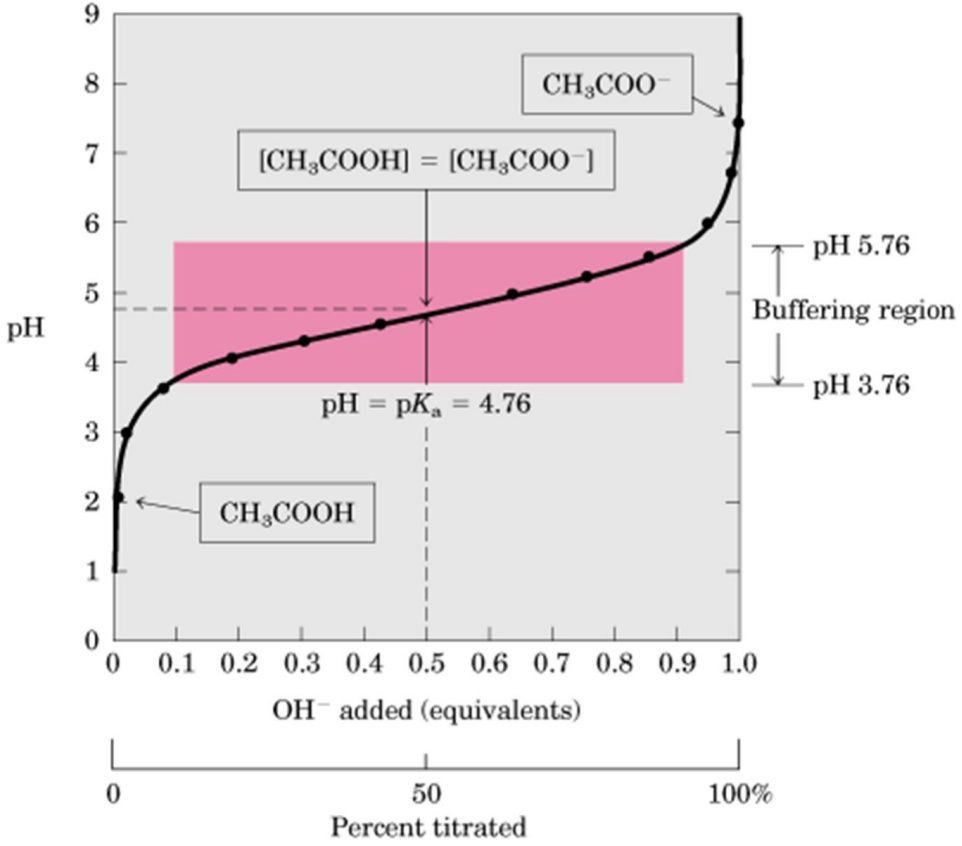
Ácido: capaz de doar H^+
Base: capaz de receber H^+

$$Keq = \frac{[H^+][A]}{[HA]} = K_a$$

Constante de dissociação

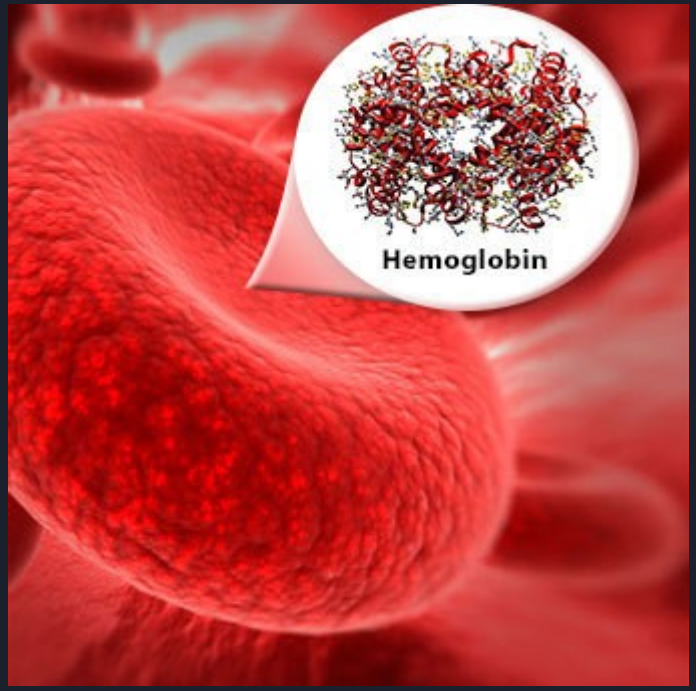
$$pK_a = log\frac{1}{K_a} = -logK_a$$



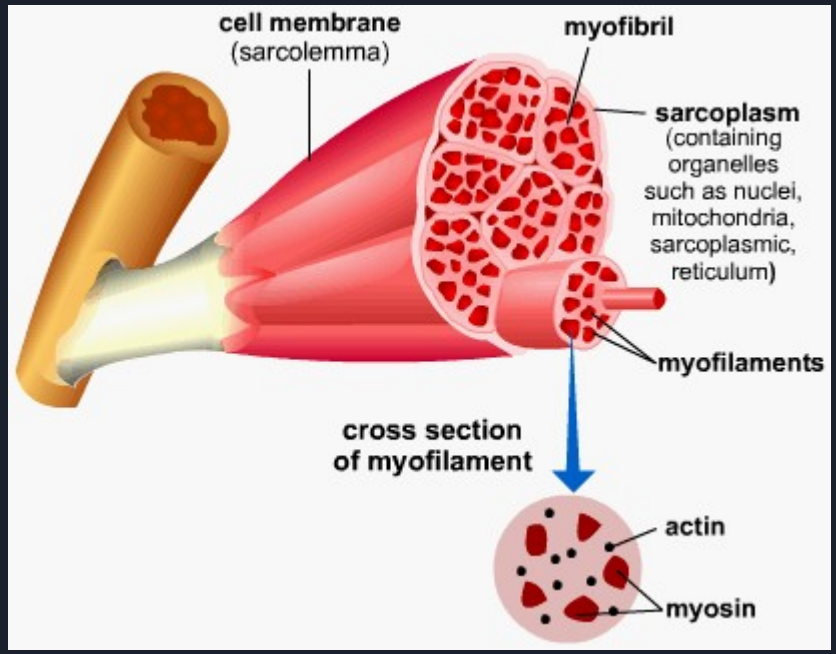


$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

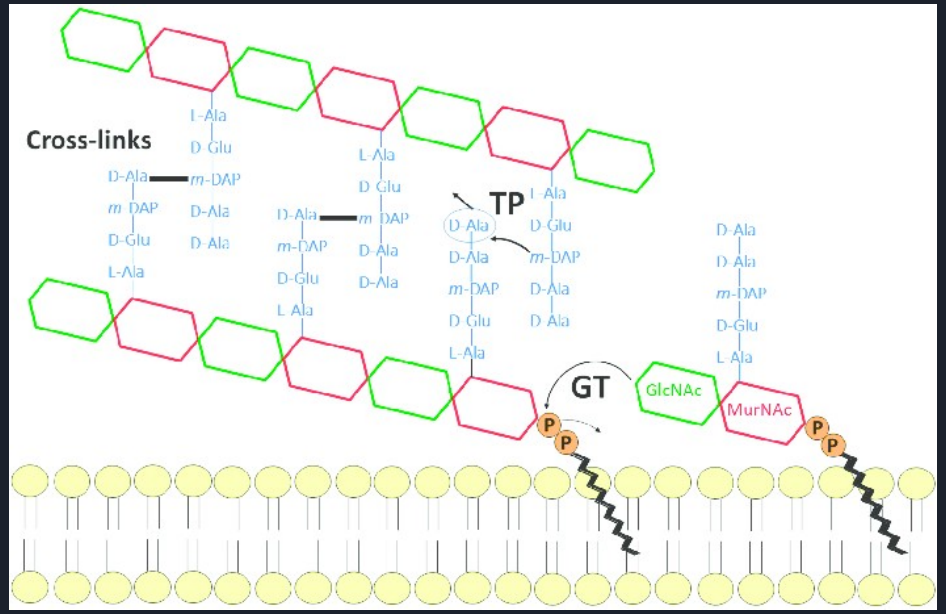
Um ácido fraco está 50% dissociado num pH igual ao seu pKa

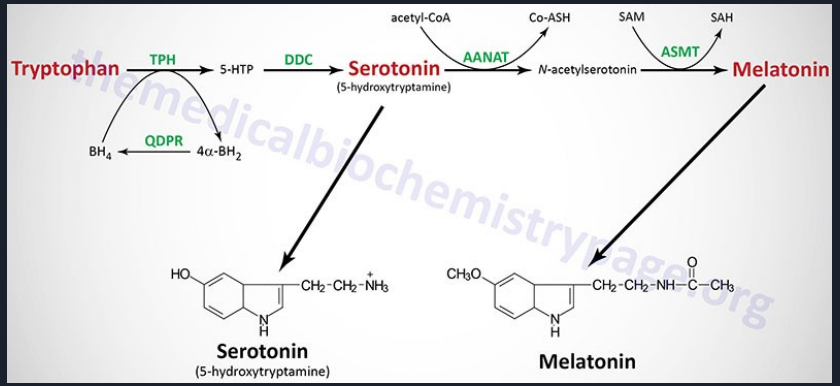


Transporte

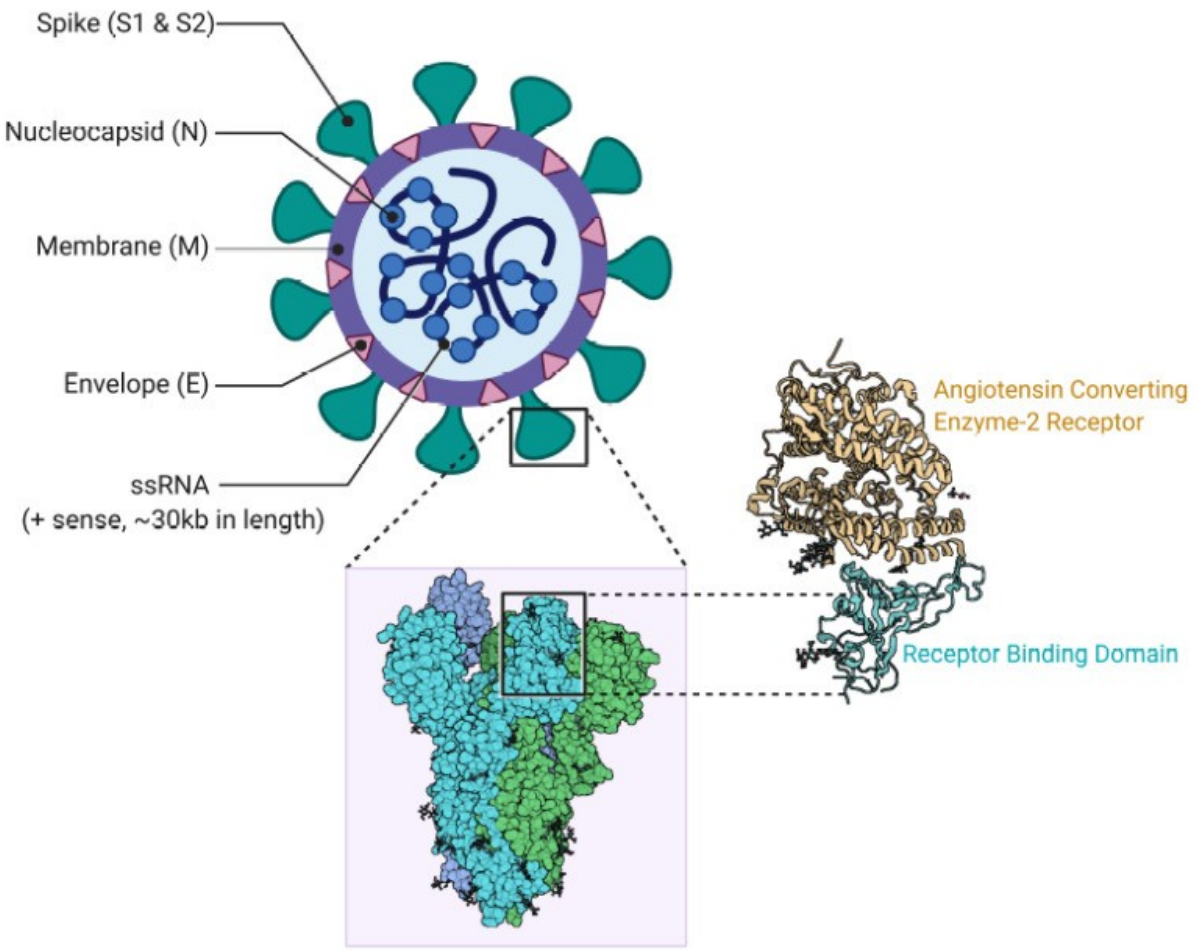


Estrutura
Contração muscaular

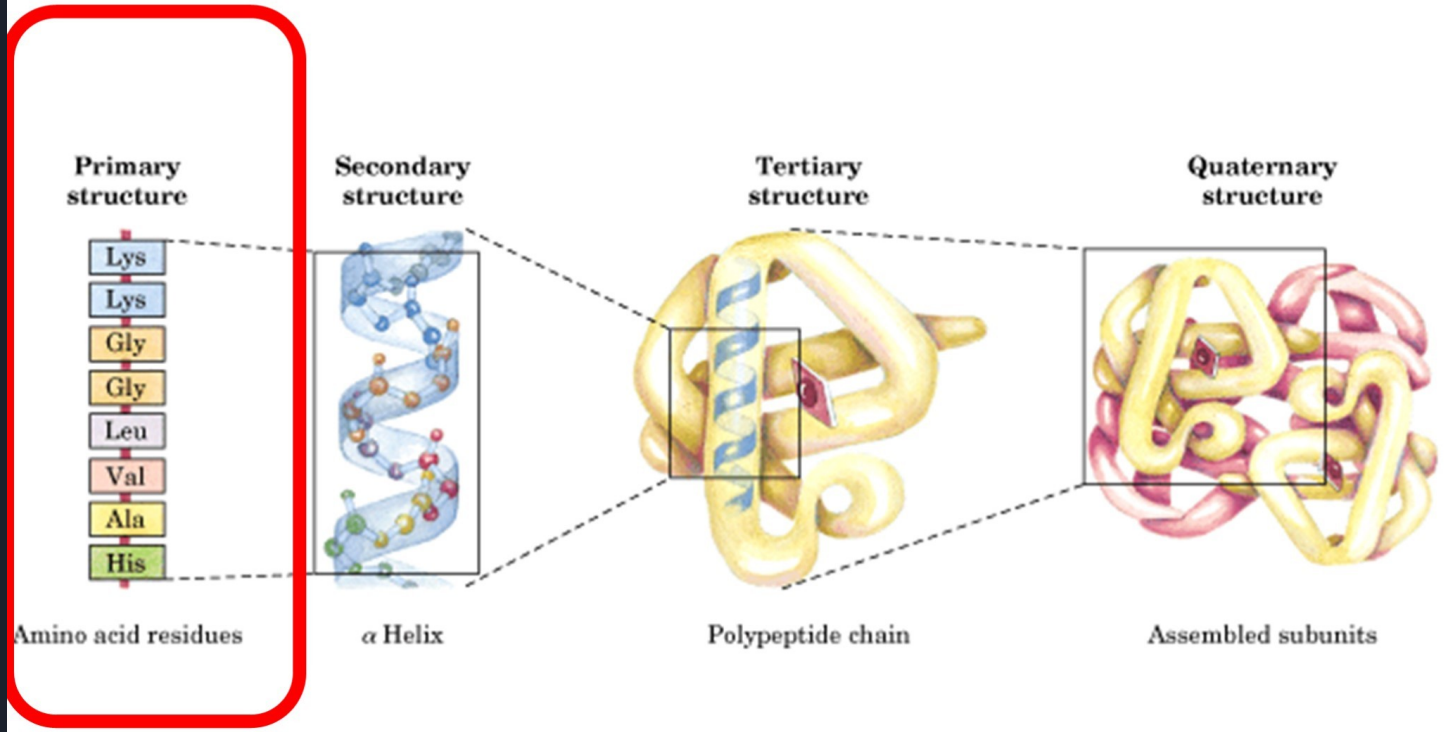

Cross-links
L-Ala
D-Glu
D-Ala
m-DAP
D-Ala
D-Ala
TP
GT
GlcNAc
MurNAc
P
P
P
P

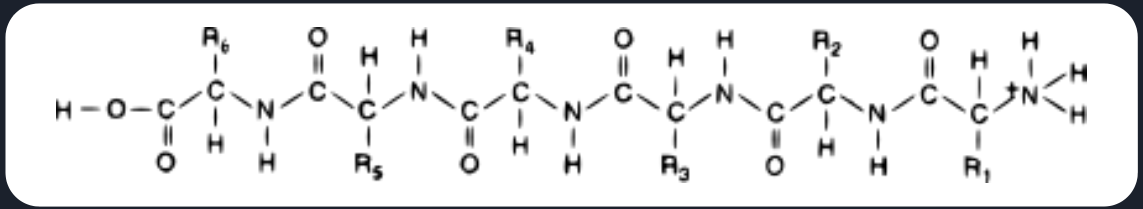

Tryptophan
TPH
5-HTP
DDC
Serotonin
(5-hydroxytryptamine)
acetyl-CoA
Co-ASH
AANAT
N-acetylserotonin
SAM
SAH
ASMT
Melatonin
QDPR
BH4
4α-BH2
HO
CH2-CH2-NH3
CH3O
CH2-CH2-NH-C-CH3
O
Serotonin
(5-hydroxytryptamine)
Melatonin

SARS-CoV 2 Structure

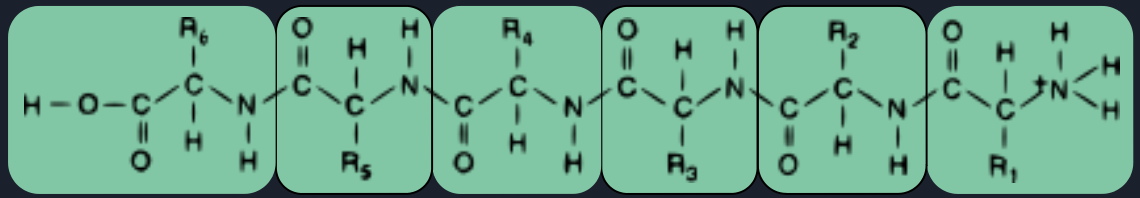


Proteínas: polímeros de aminoácidos





Aminoácidos - Unidades monoméricas que formam as proteínas (polímeros).



Aminoácidos - Unidades monoméricas que formam as proteínas (polímeros de aminoácidos).

Formação de proteína hipotética, com 20 aa, um de cada tipo = 2.4 X 10^{18} moléculas diferentes

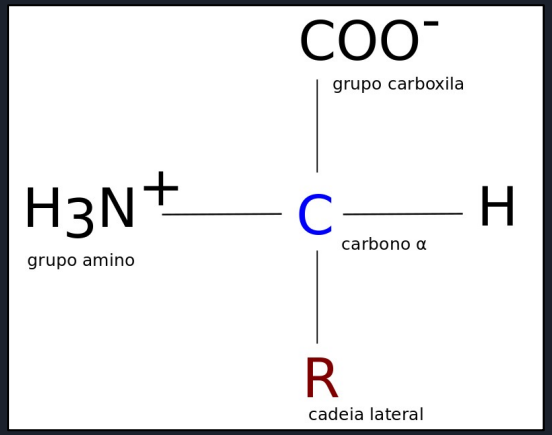
table 5–2

Molecular Data on Some Proteins

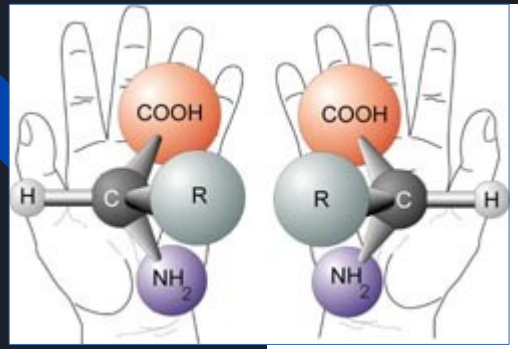
	Molecular weight	Number of residues	Number of polypeptide chains
Cytochrome *c* (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (*E. coli*)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (*E. coli*)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

1. Conceito e estrutura geral de um AMINOÁCIDO

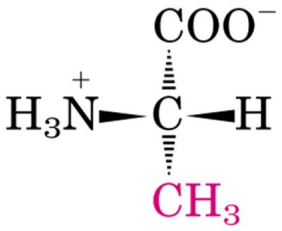
Substâncias que apresentam grupos funcionais **amino** e **ácido carboxílico**.



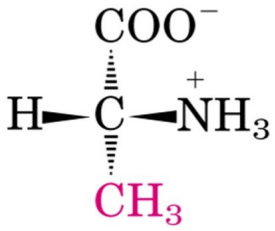
- **Cadeia lateral** ou **grupo R** variável: pode conter grupos funcionais, carbonos ou hidrogênio.



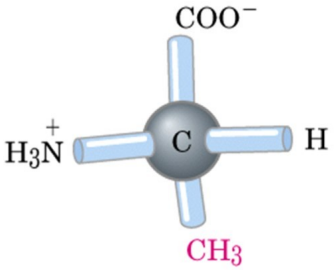
As proteínas são constituídas de L-aminoácidos



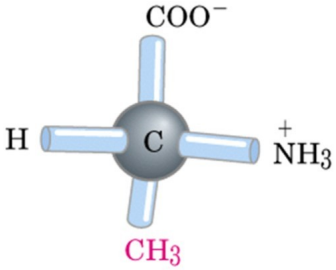
L-Alanine



D-Alanine



L-Alanine

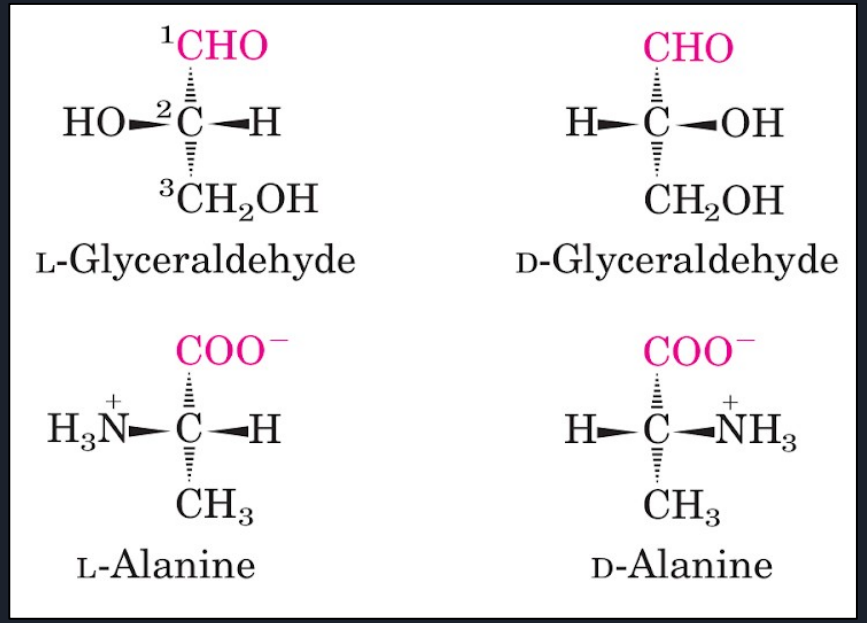


D-Alanine

Isomeria

A maioria dos aminoácidos, com exceção à glicina, apresentam **isomeria óptica** e existem como um par de **enantiômeros**.

- Aminoácidos são L-enantiômeros nas proteínas.



Nomenclatura

- 20 aminoácidos mais comuns nas proteínas.
- Nomeados por semelhança com os objetos de pesquisa.

Trivial name[a]	Symbols[b]	
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn[d]	N[d]
Aspartic acid	Asp[d]	D[d]
Cysteine	Cys	C
Glutamine	Gln[d]	Q[d]
Glutamic acid	Glu[d]	E[d]
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

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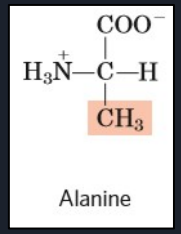
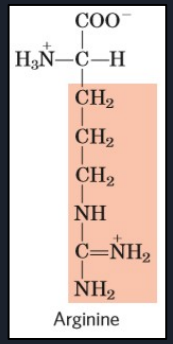
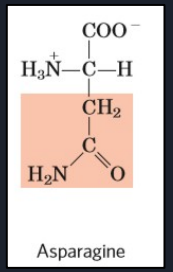
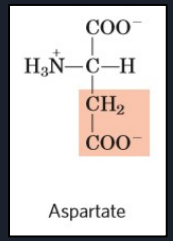
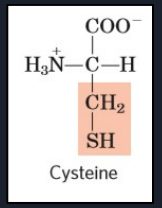
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn[d]	N[d]
Aspartic acid	Asp[d]	D[d]
Cysteine		
Glutamine		
Glutamic acid		
Glycine		
Histidine		
Isoleucine		
Leucine		
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

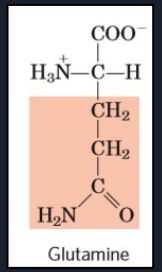

Alanine

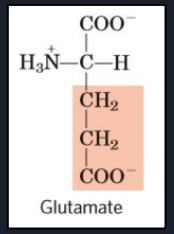

Arginine

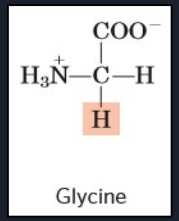

Asparagine

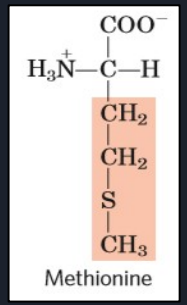

Aspartate

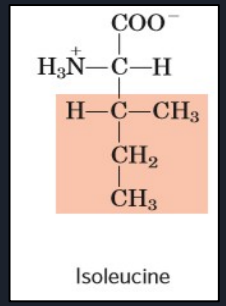

Cysteine

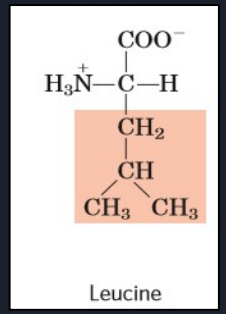

Glutamine

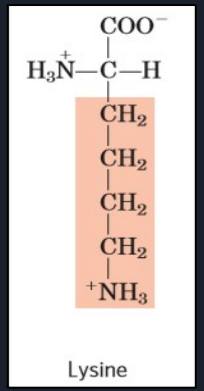

Glutamate

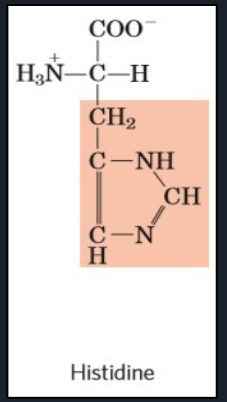

Glycine

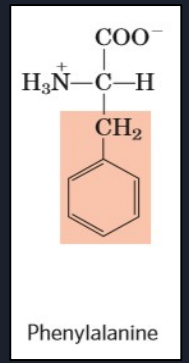

Methionine

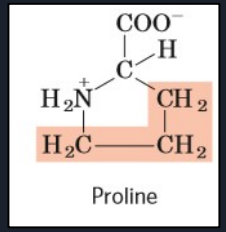

Isoleucine

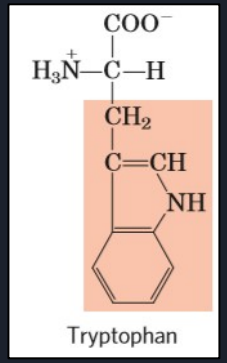

Leucine

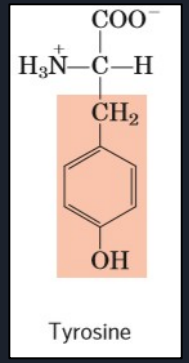

Lysine

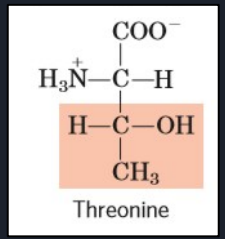

Histidine

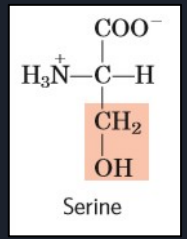

Phenylalanine

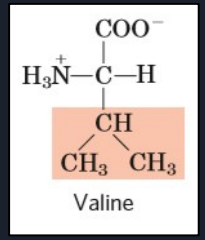

Proline


Tryptophan

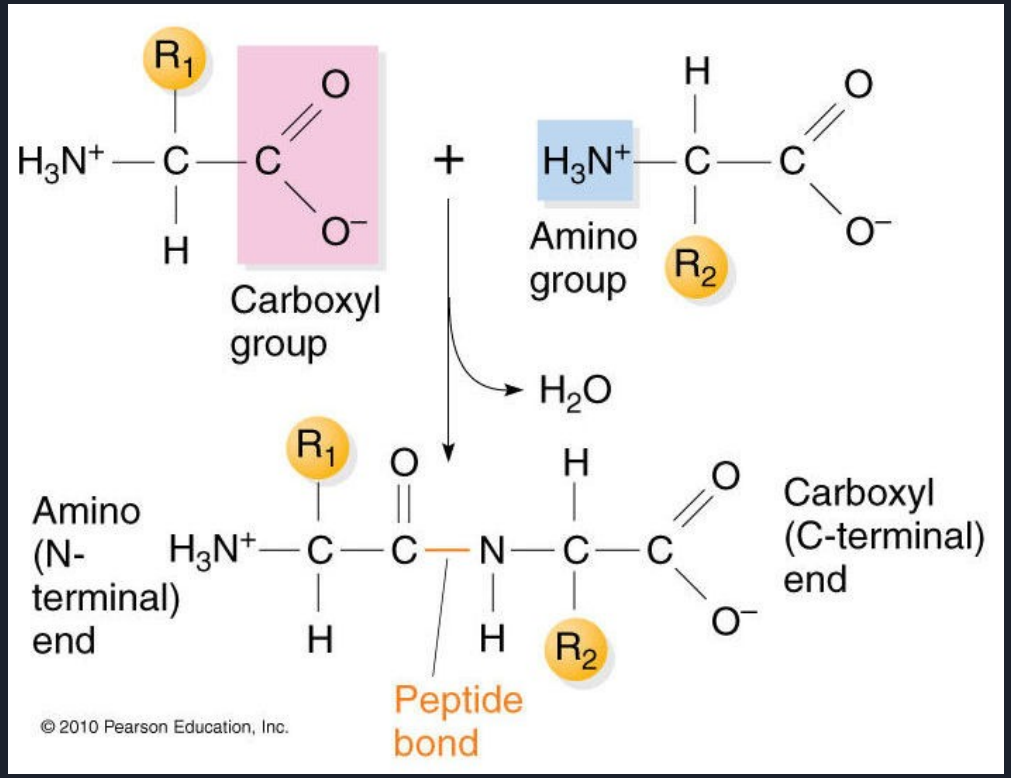

Tyrosine


Threonine

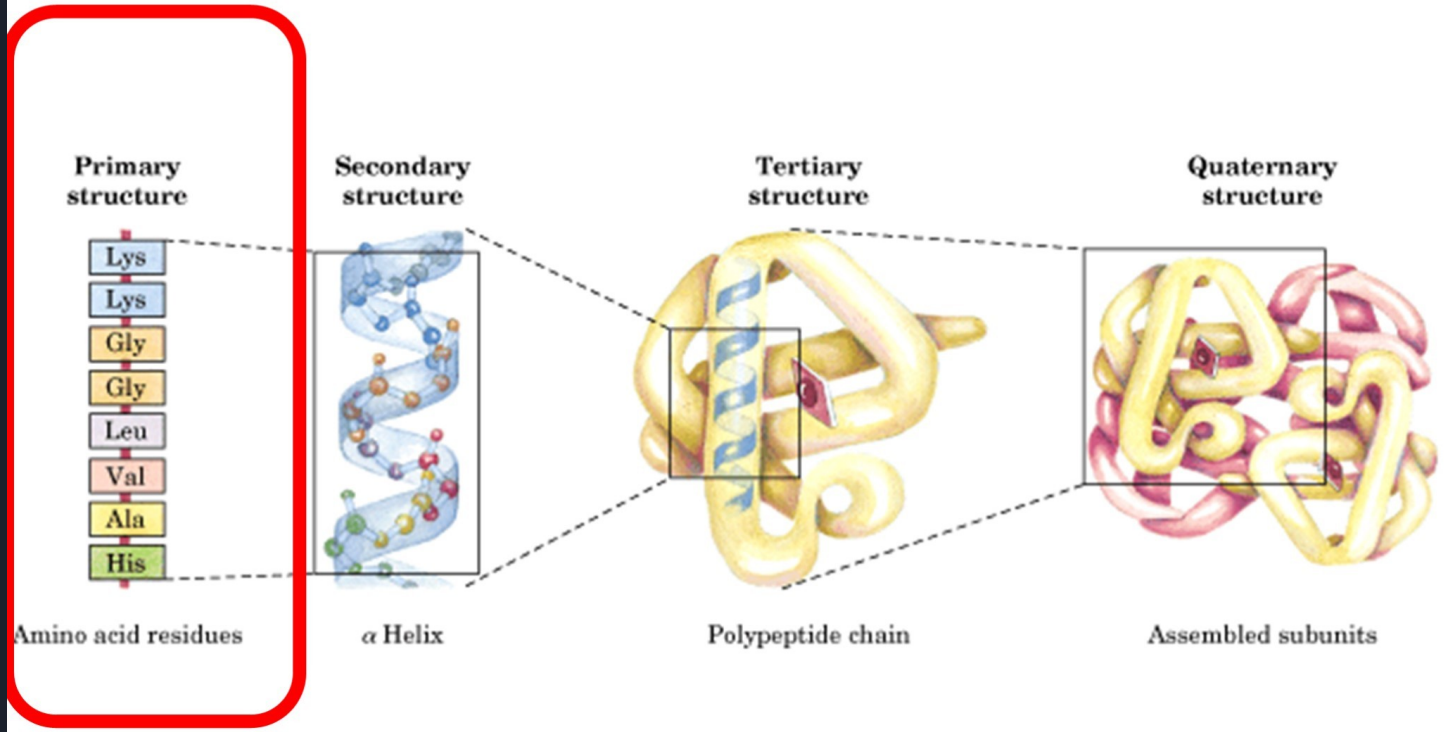

Serine


Valine

Por que caracterizar as cadeias laterais?



Proteínas: polímeros de aminoácidos



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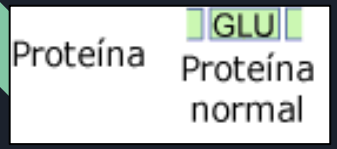
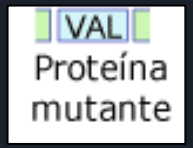
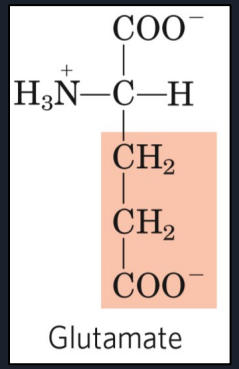
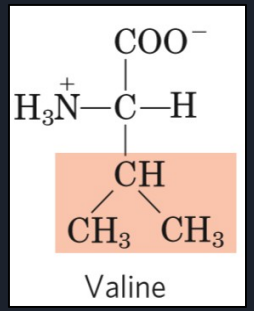
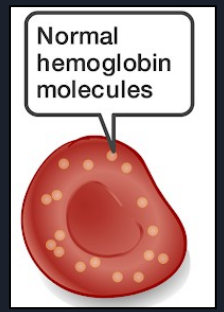


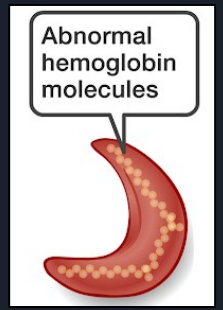








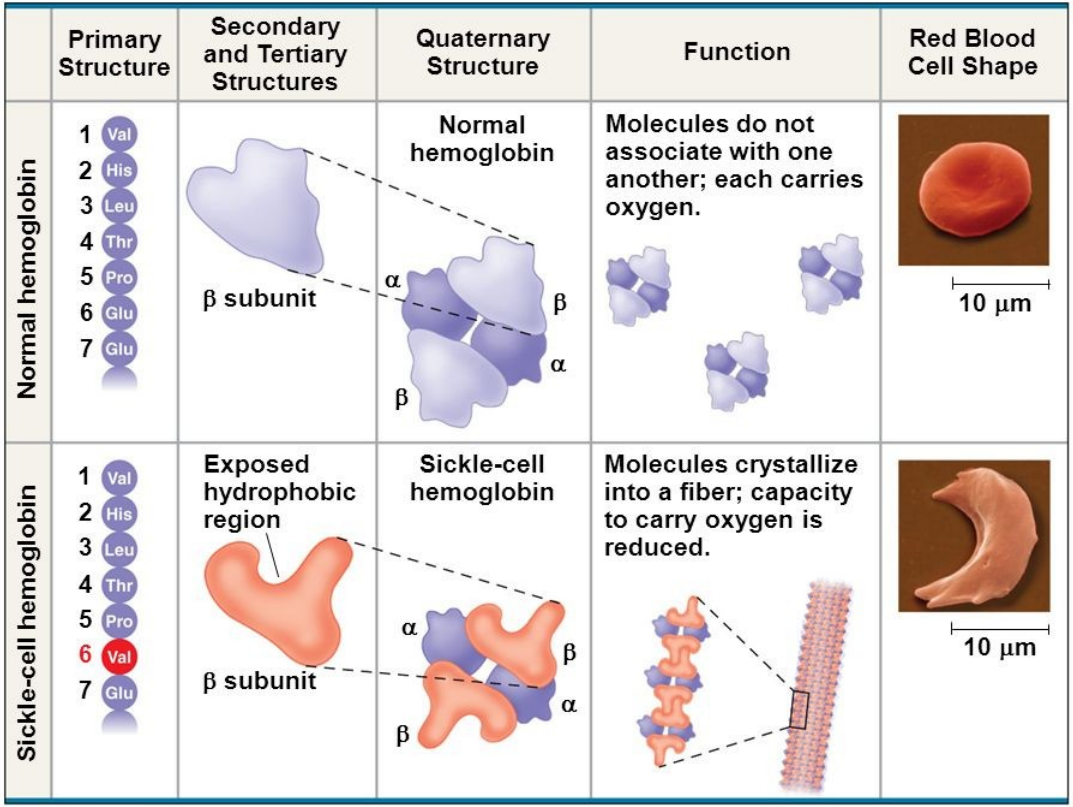
Eritrócito



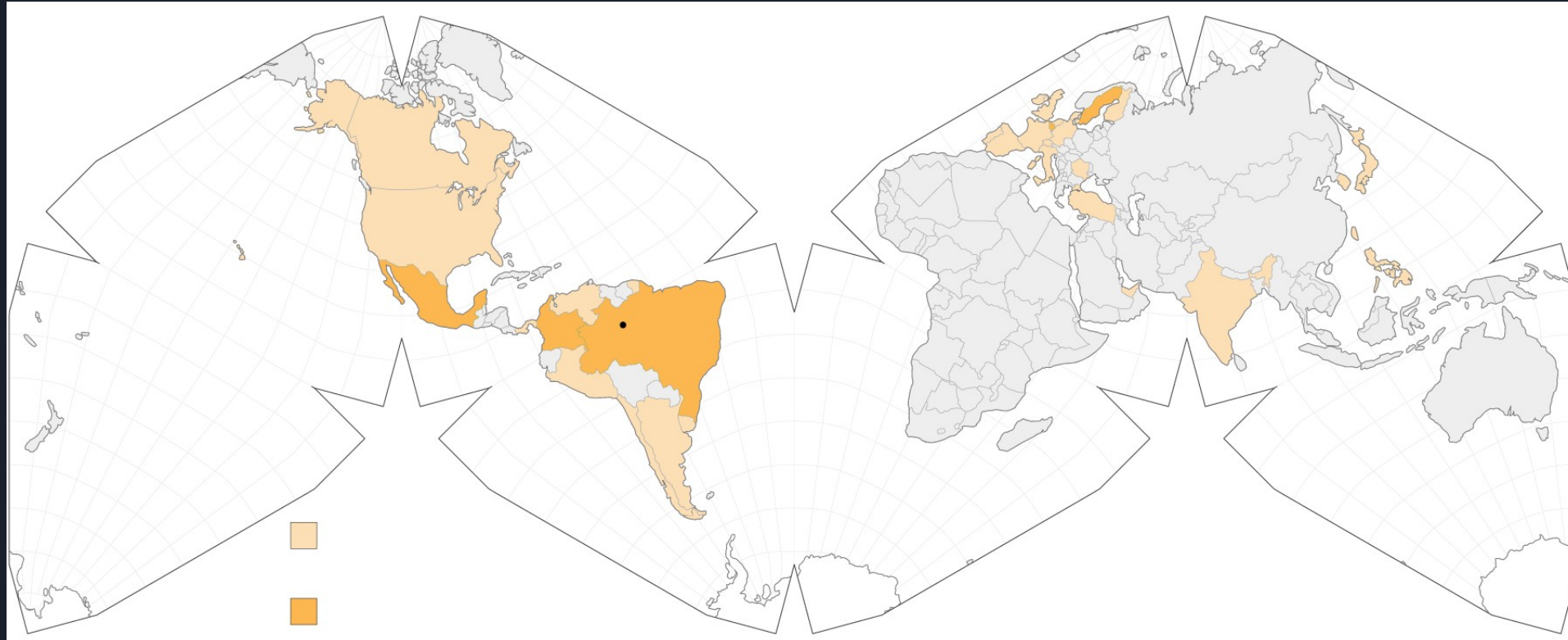
Anemia Falciforme

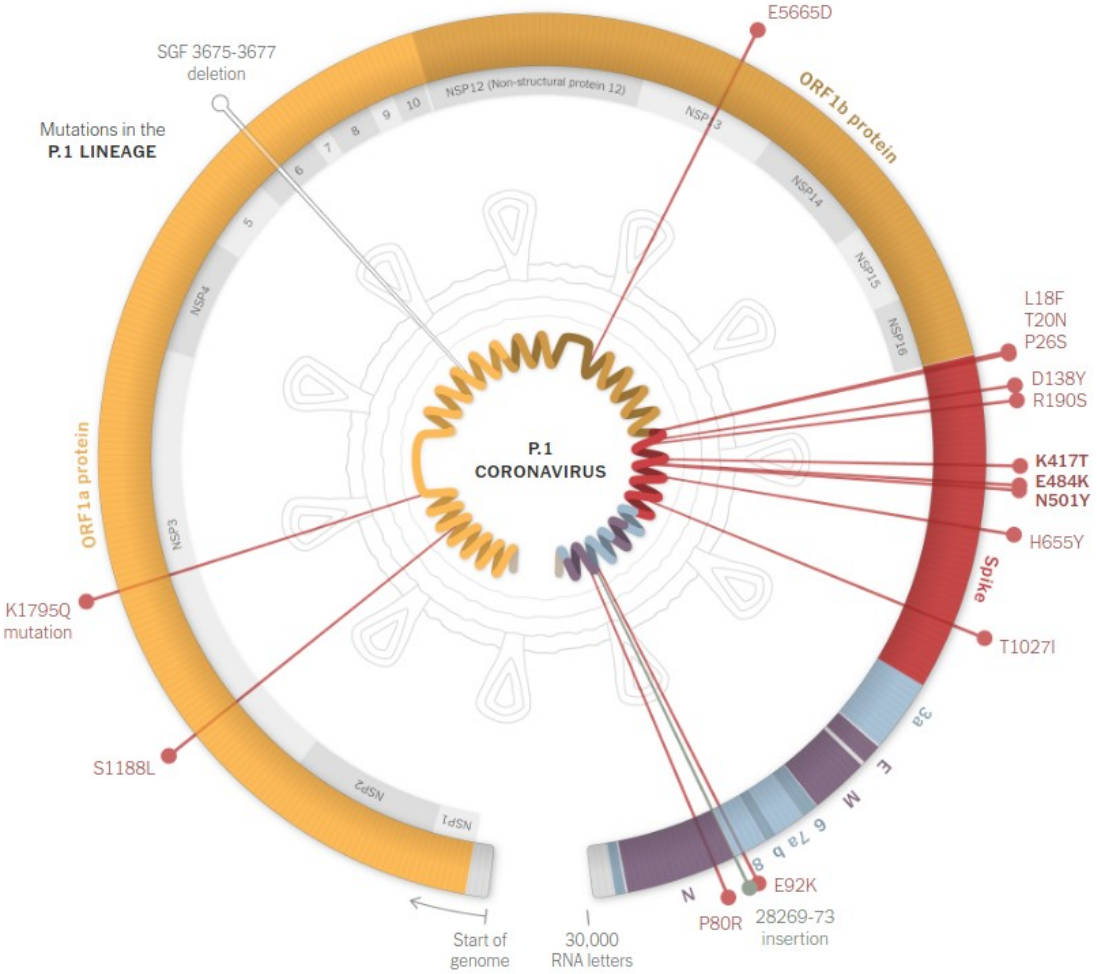
- Falta de oxigenação nos tecidos;
- Tendência a infecções;
- Problemas neurológicos, cardiovasculares, pulmonares e renais;

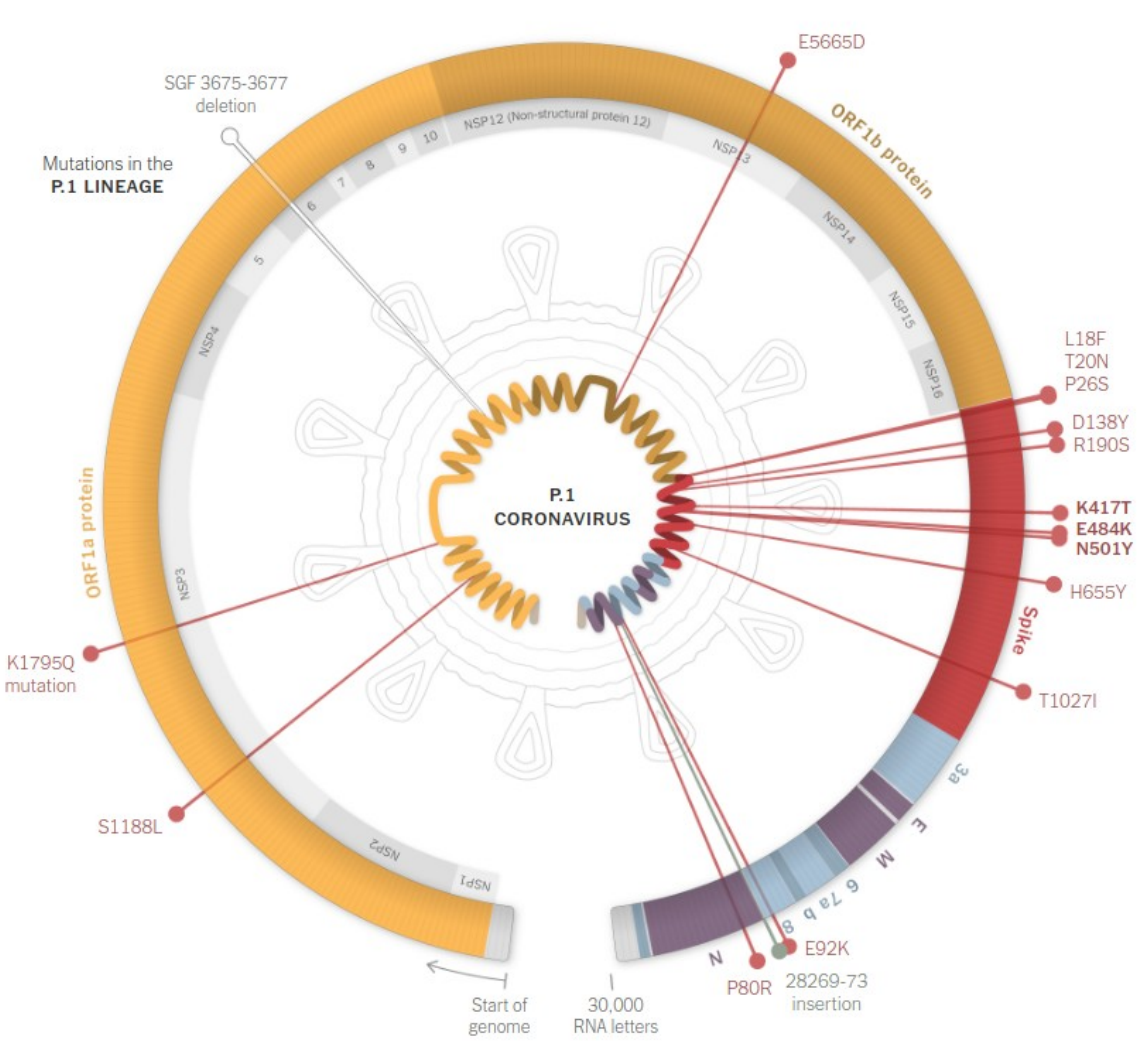
Por que caracterizar as cadeias laterais?



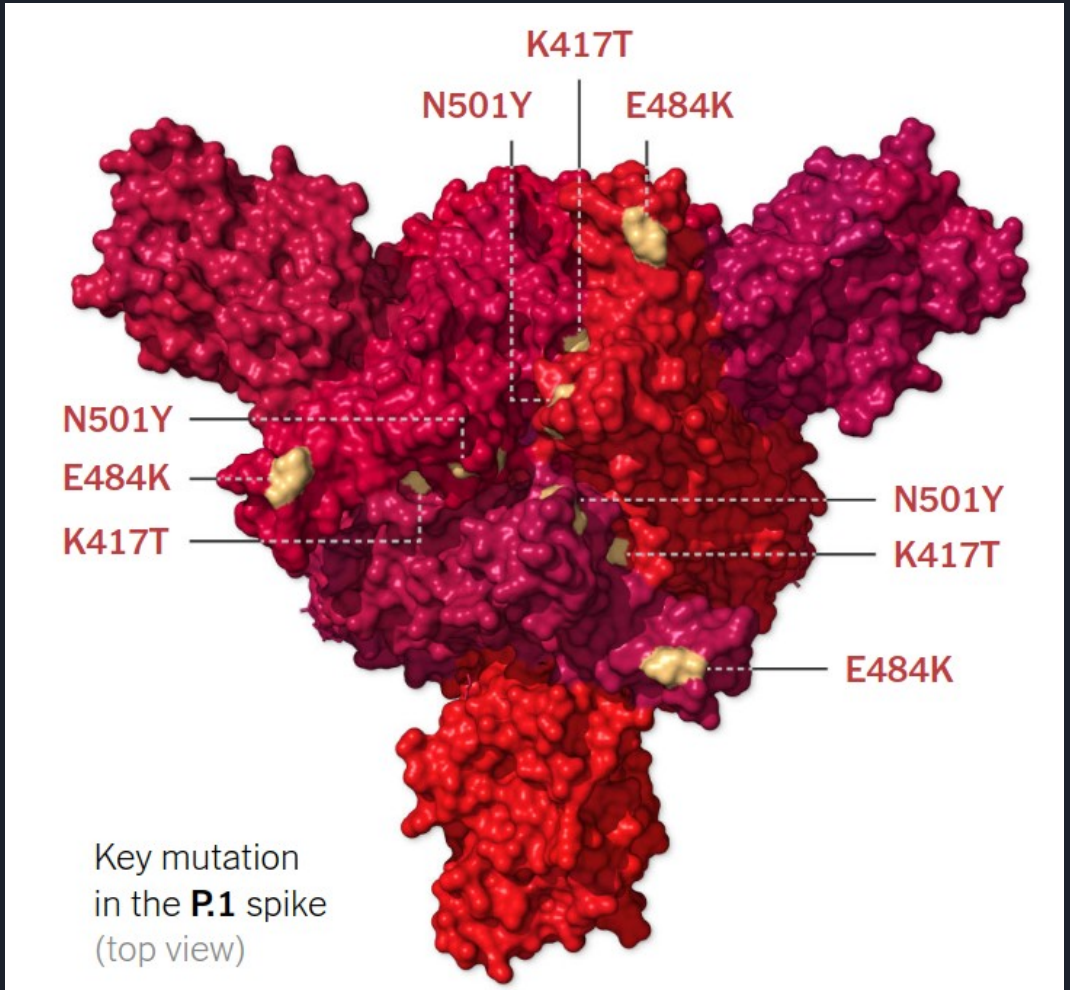
Distribuição mundial da variante P1 SARS-Cov2




Mutations in the
P.1 LINEAGE
SGF 3675-3677
deletion
E5665D
ORF1b protein
NSP12 (Non-structural protein 12)
NSP13
NSP14
NSP15
NSP16
L18F
T20N
P26S
D138Y
R190S
K417T
E484K
N501Y
H655Y
T1027I
Spike
3a
E
M
6
7a
b
8
N
E92K
P80R
28269-73
insertion
30,000
RNA letters
Start of
genome
S1188L
NSP2
NSP1
K1795Q
mutation
ORF1a protein
NSP3
NSP4
5
6
7
8
9
10
P.1
CORONAVIRUS



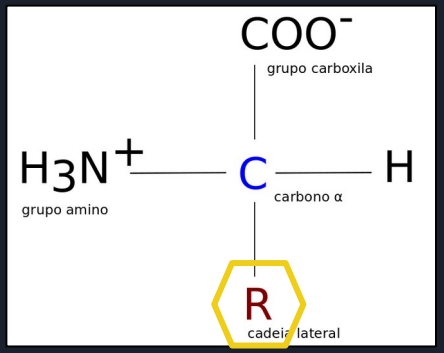
Trivial name[a]	Symbols[b]	
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn[d]	N[d]
Aspartic acid	Asp[d]	D[d]
Cysteine	Cys	C
Glutamine	Gln[d]	Q[d]
Glutamic acid	Glu[d]	E[d]
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



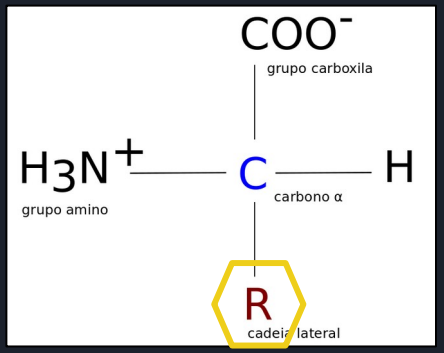
https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html#P1

— N501Y, which helps the virus latch on more tightly to human cells. This mutation also appears in the B.1.1.7 and B.1.351 lineages.
— K417T, which is the same site as the K417N mutation in the B.1.351 lineage. It may also help the virus latch on tighter.
— E484K, which may help the virus evade some kinds of antibodies.

Classificação dos aminoácidos

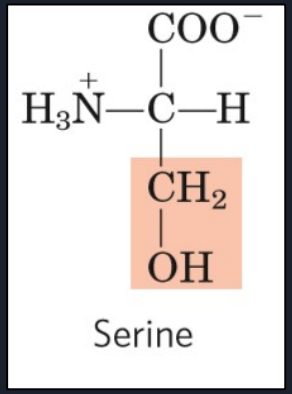


Classificação dos aminoácidos

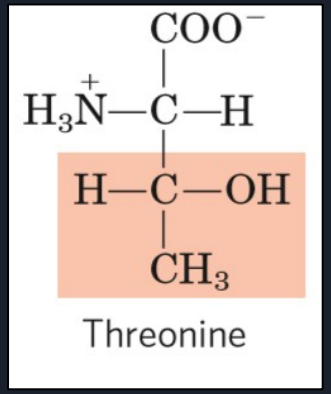


Polares não carregados

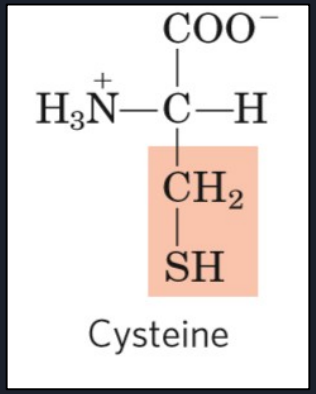
Hidrofílicos, capazes de formar ligações de hidrogênio com a água.



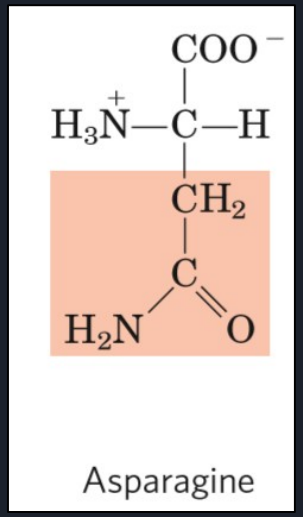
Serine



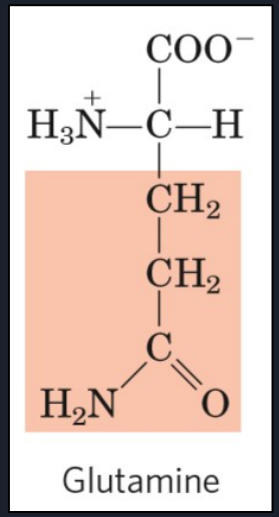
Threonine



Cysteine

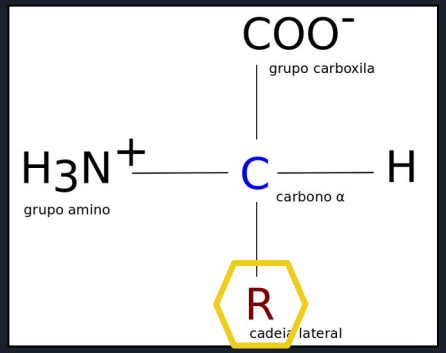


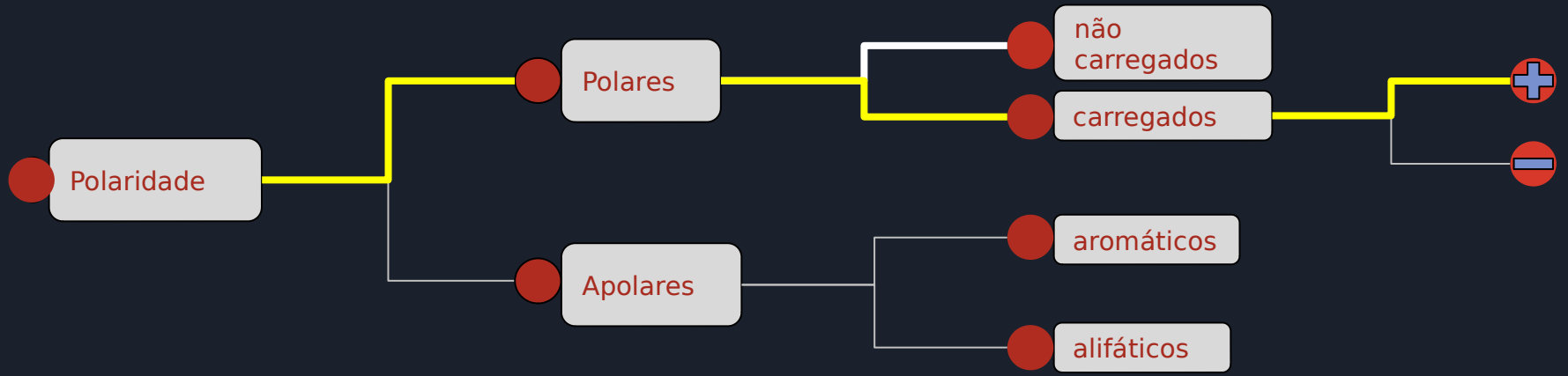
Asparagine



Glutamine

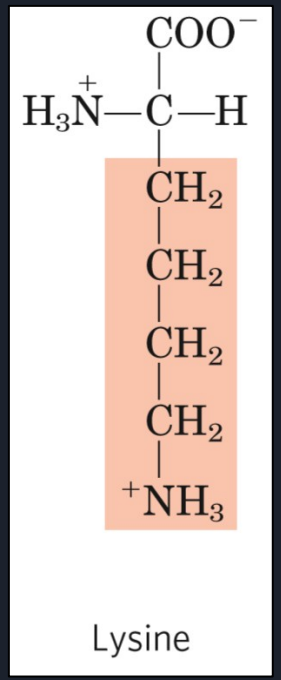
4. Classificação dos aminoácidos



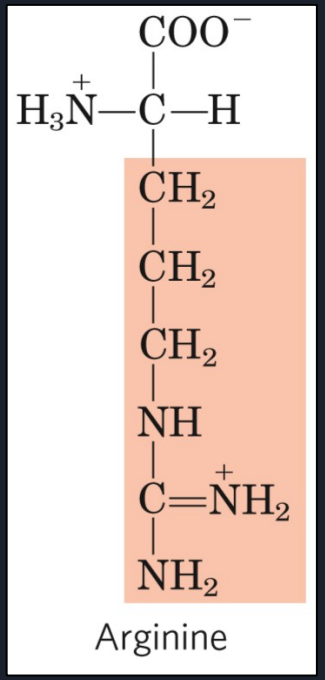


Polares carregados positivamente

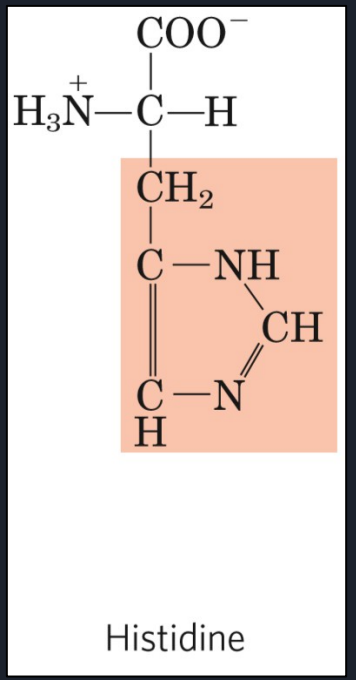
Mais hidrofílicos que os polares não carregados.



Lysine

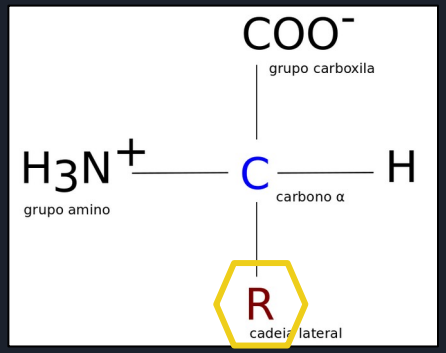


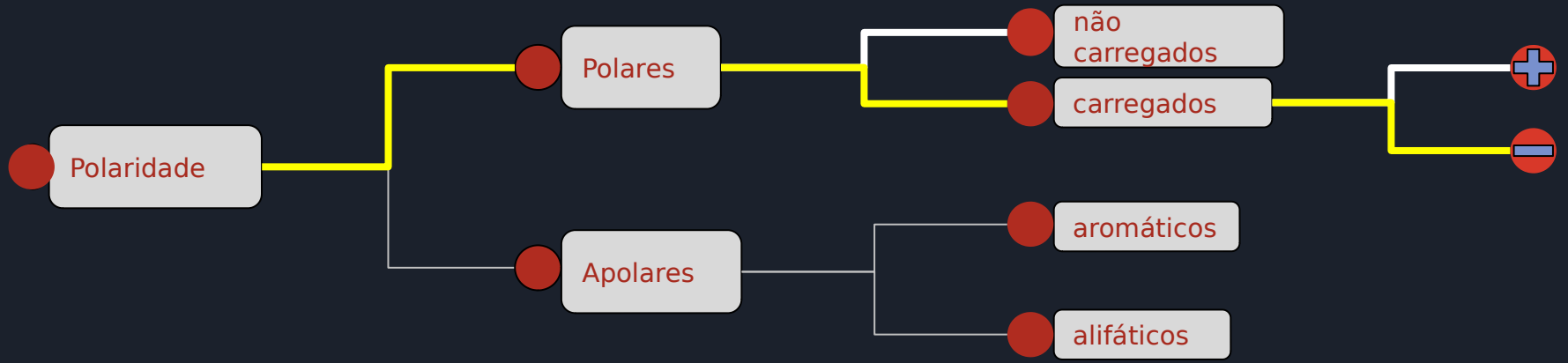
Arginine



Histidine

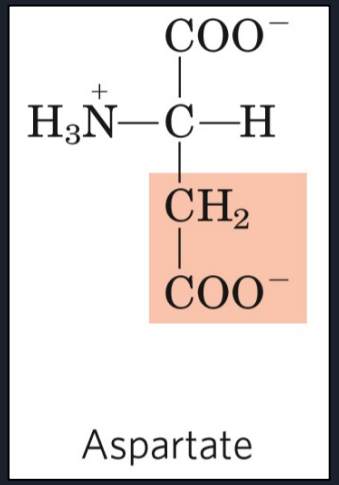
4. Classificação dos aminoácidos



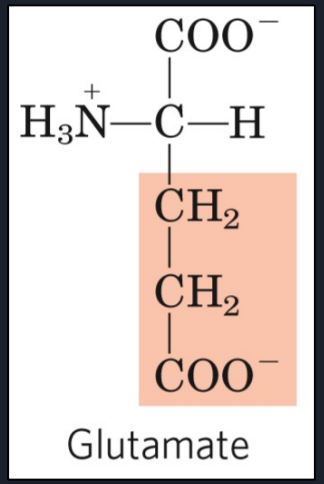


Polares carregados negativamente

Hidrofílicos.

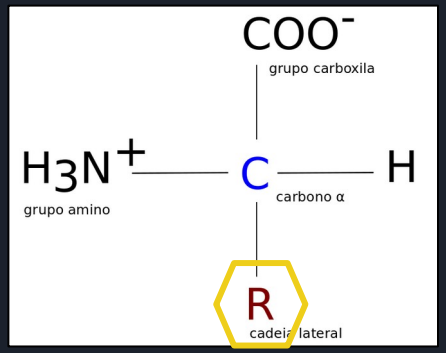


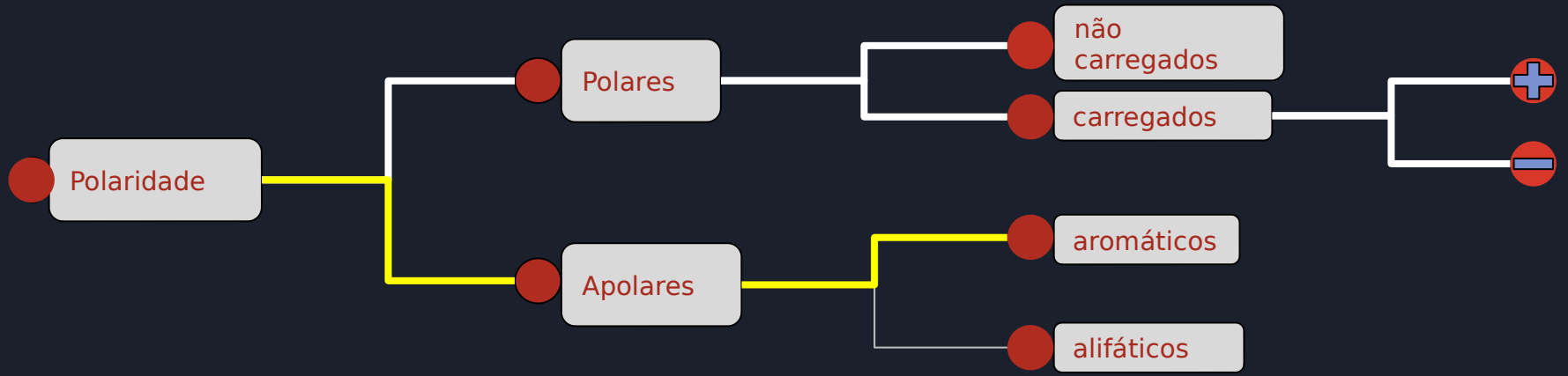
Aspartate



Glutamate

4. Classificação dos aminoácidos



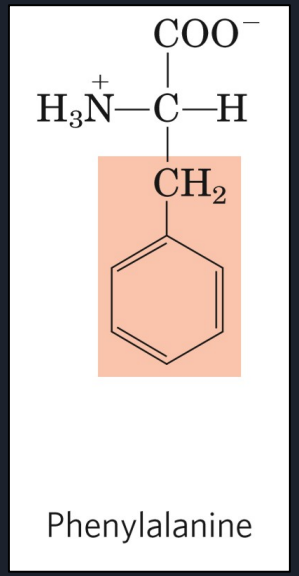


Apolares aromáticos

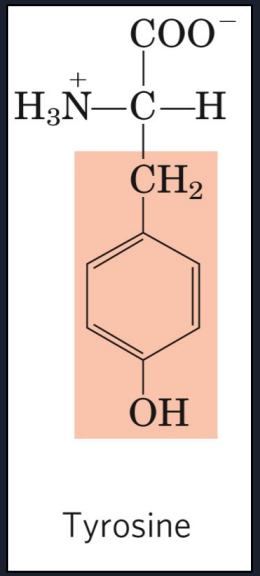
Participam de interações hidrofóbicas.

Tyr e Trp mais polares que Phe.

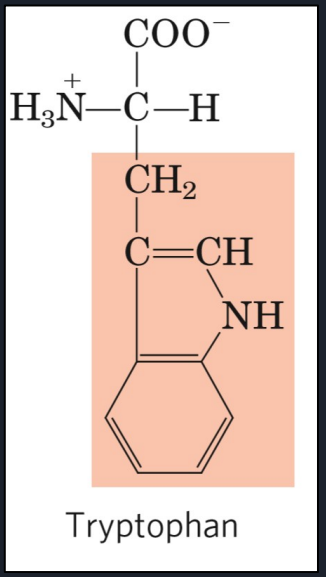
Podem absorver luz UV.



Phenylalanine

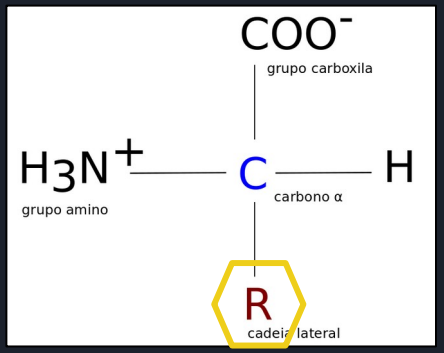


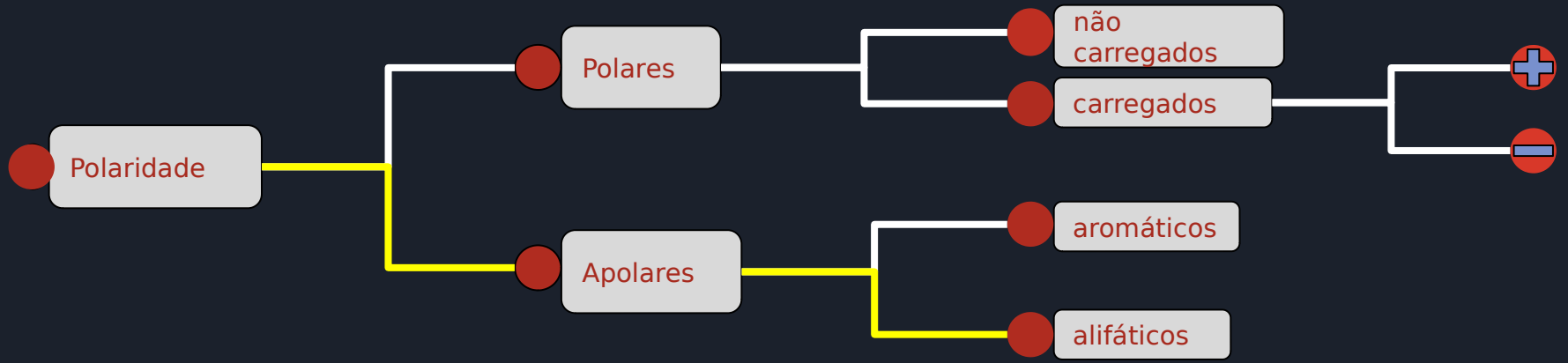
Tyrosine



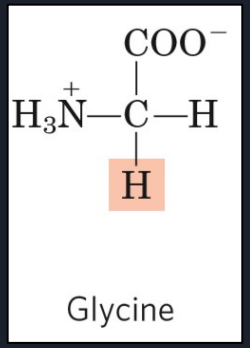
Tryptophan

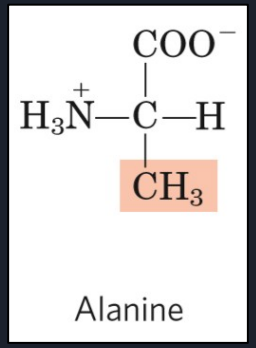
Classificação dos aminoácidos

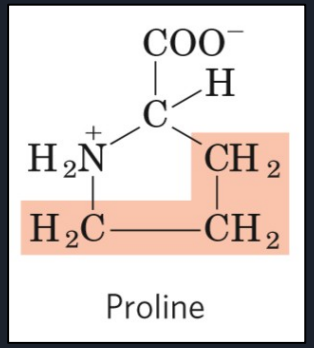


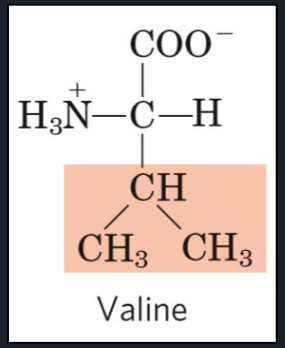


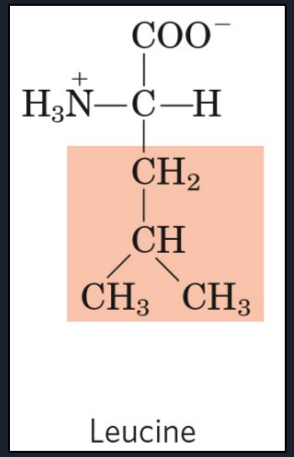
Apolares alifáticos

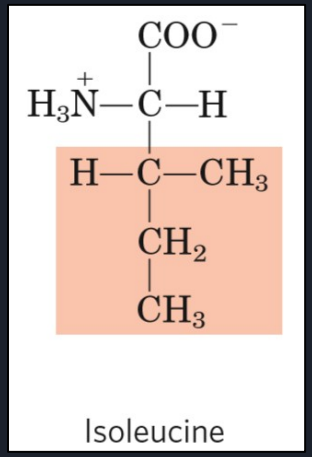


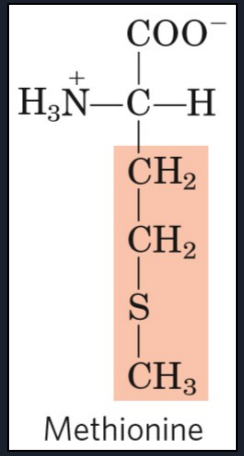






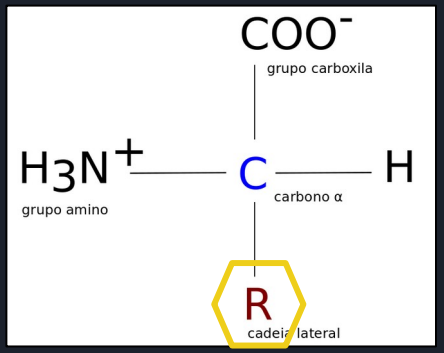


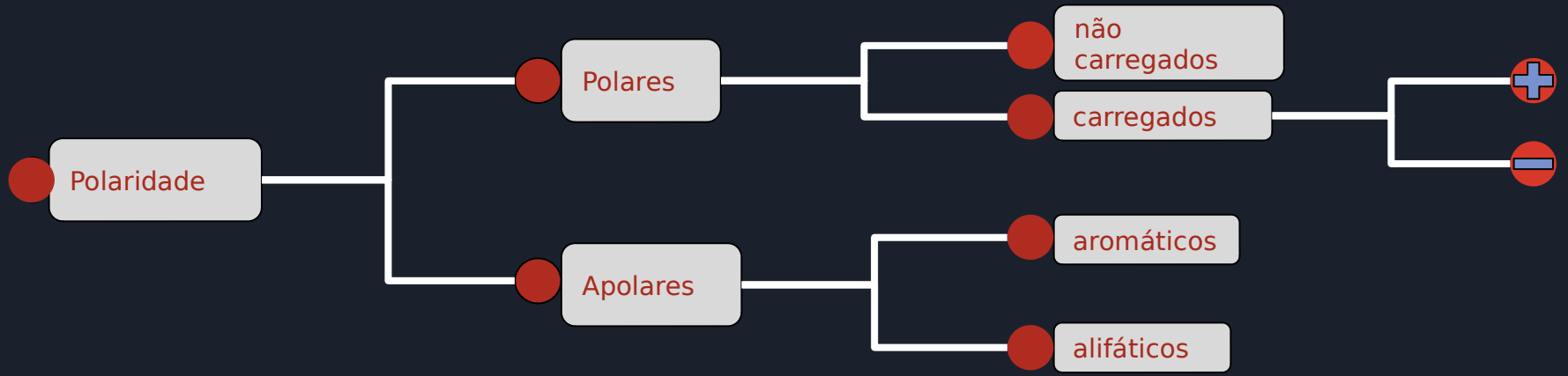




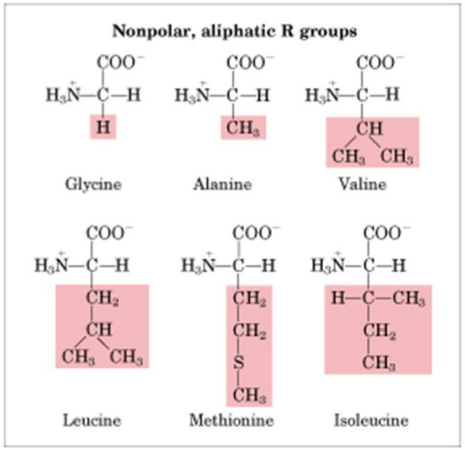
Participam de interações hidrofóbicas.

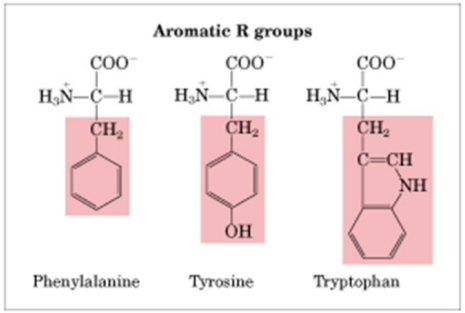
Classificação dos aminoácidos

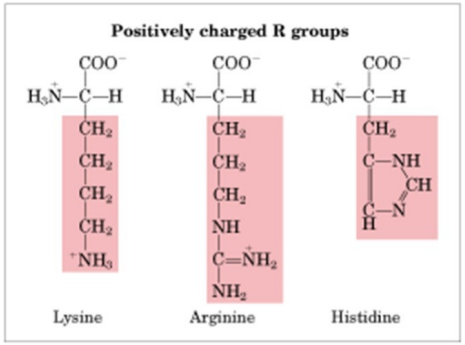


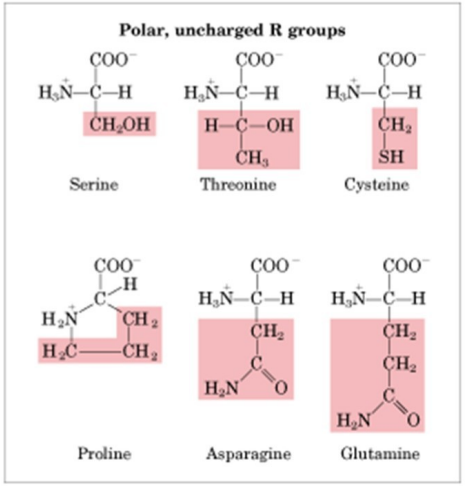


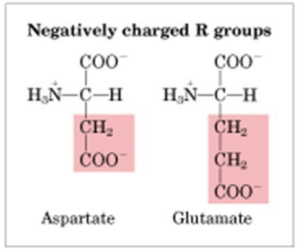
Os 20 aminoácidos

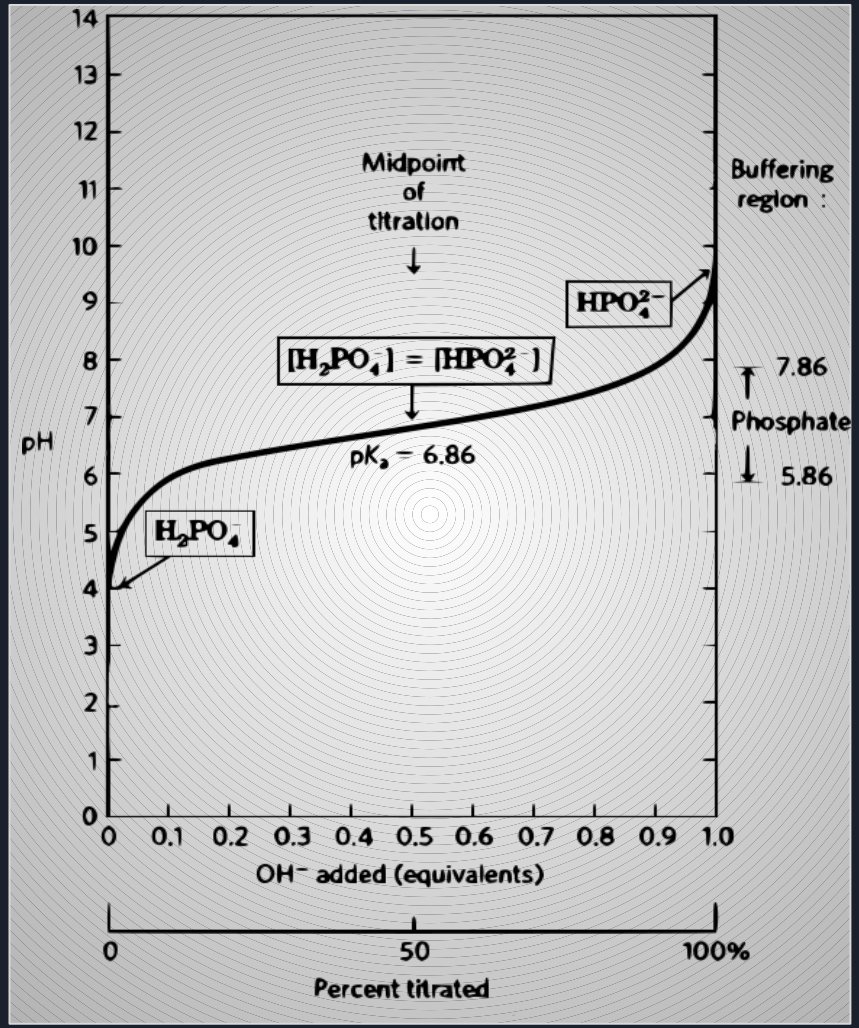










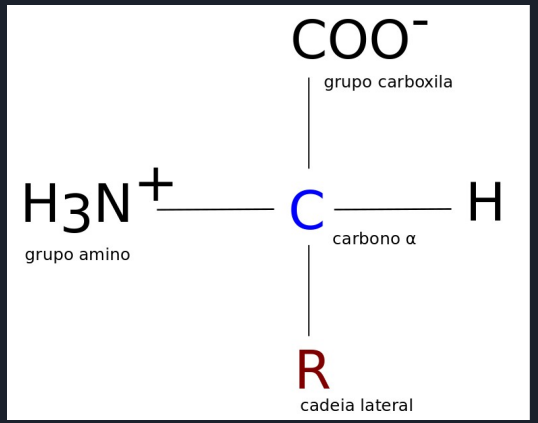


$$\mathrm{pH} = \mathrm{p}K_\mathrm{a} + \log \frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

Equação de Henderson-Hasselbalch

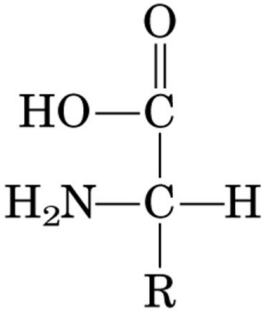
Ionização dos aminoácidos

- Aminoácidos podem ter carga positiva, negativa ou neutra.
- Zwitterions - ácido ou base.
- pKa - constante de dissociação e faixa de tamponamento.

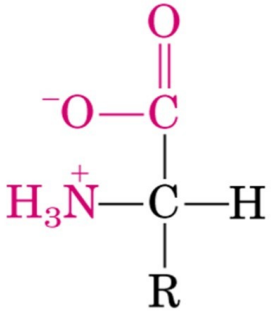


aa não carregado em pH próx. 7.

Ionização de aminoácidos



Nonionic form

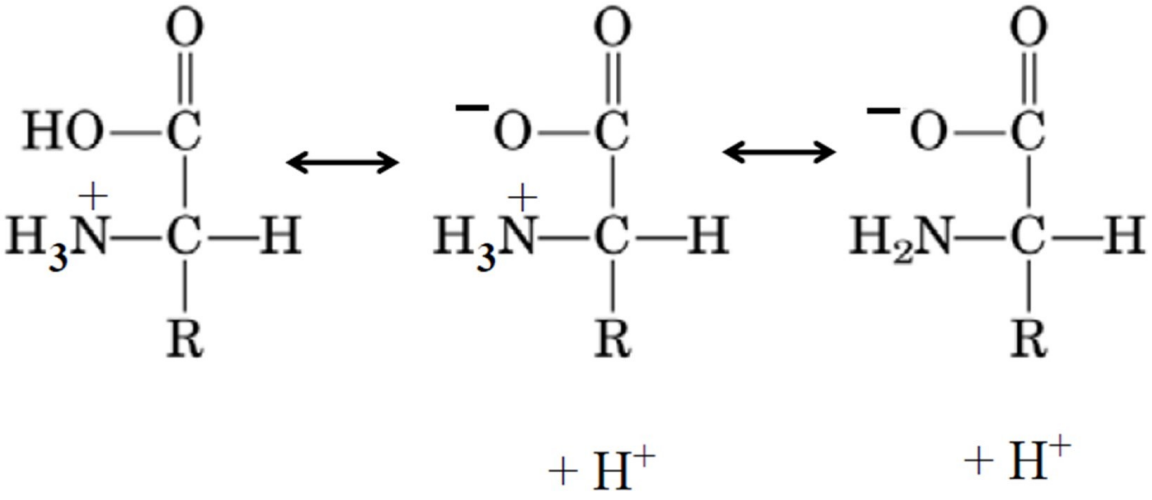


Zwitterionic form

Forma anfótera ou zwitteriônica

Aminoácidos podem funcionar como ácidos ou bases

zwitterion



Carga líquida em cada uma das formas?

ácido → básico

pH

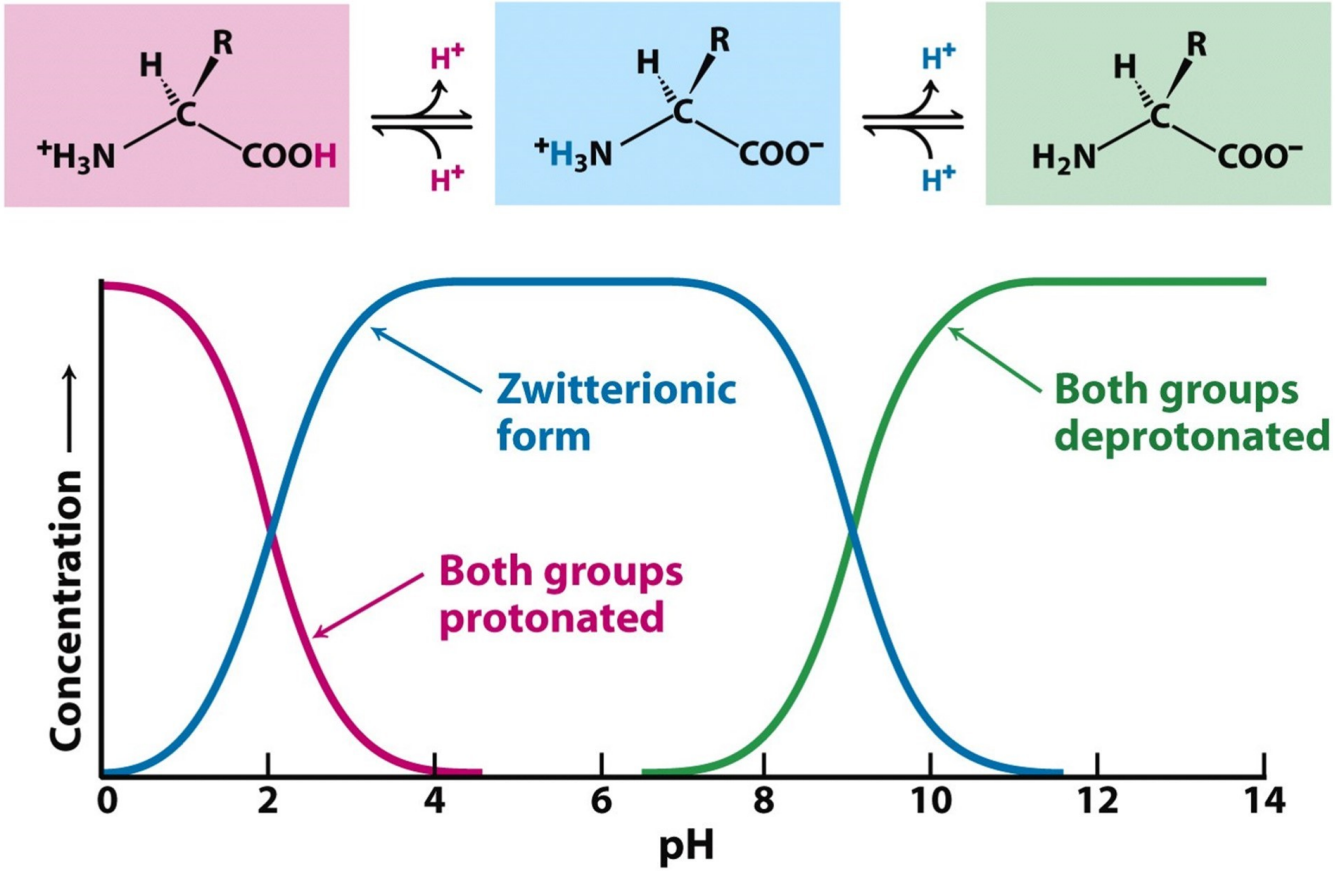
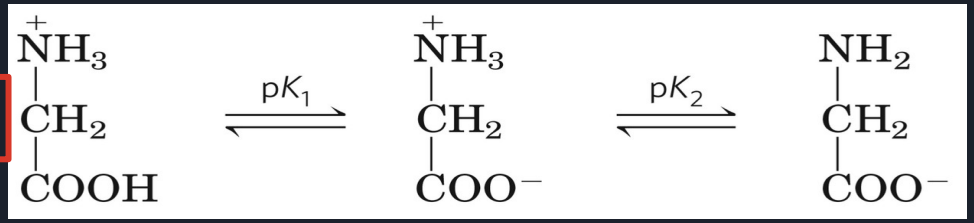
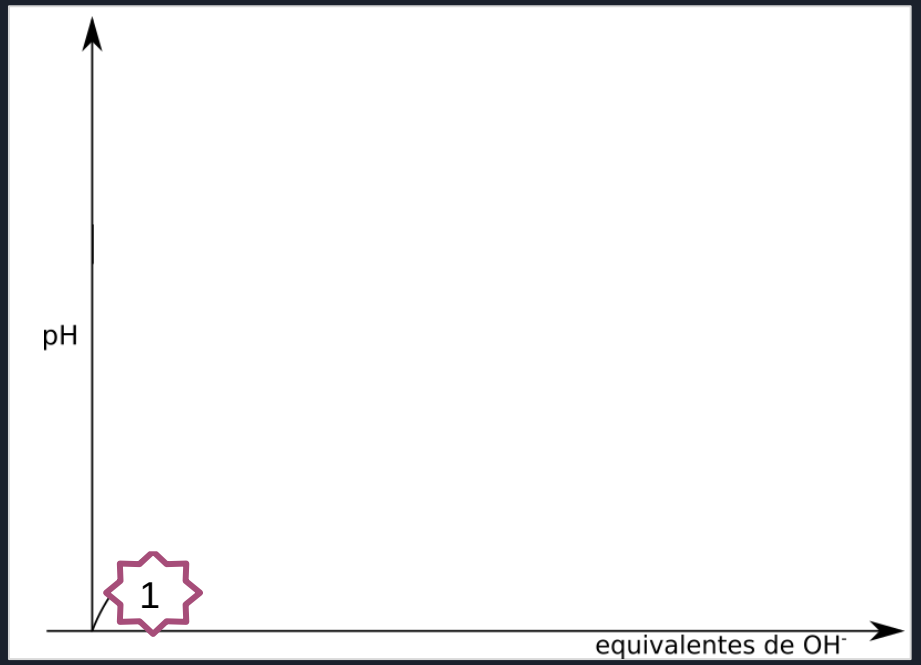
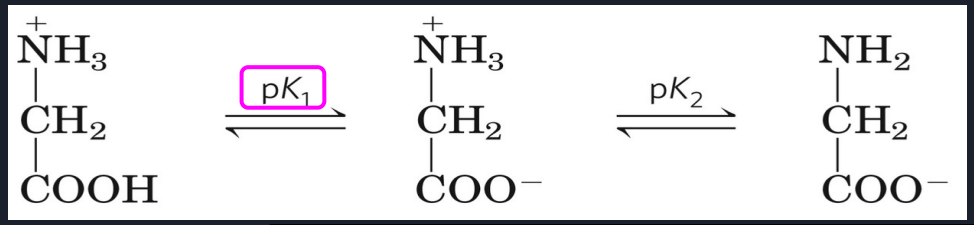


Figure 2-6
Biochemistry, Sixth Edition





Ionização da Glicina



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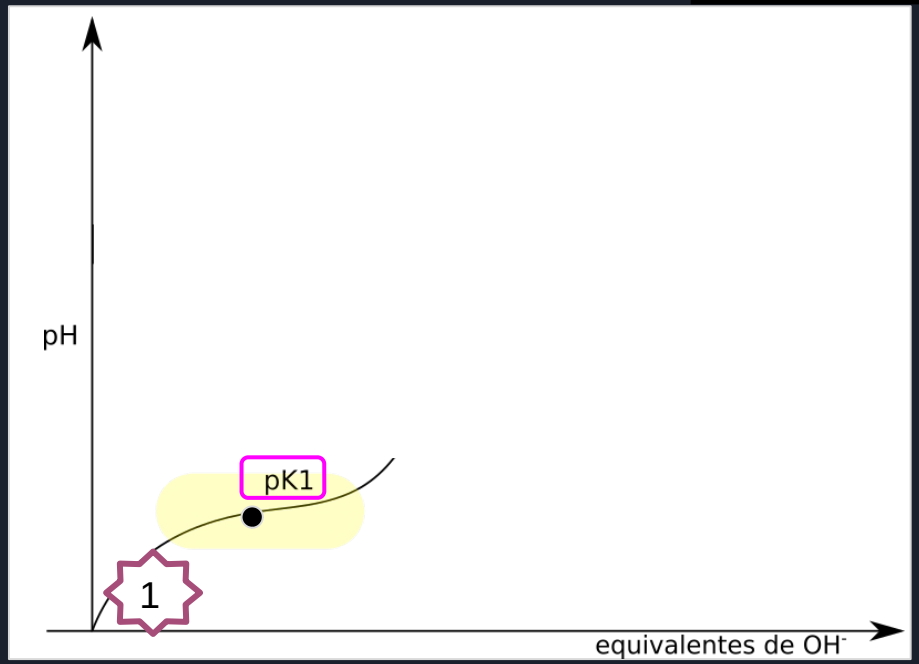
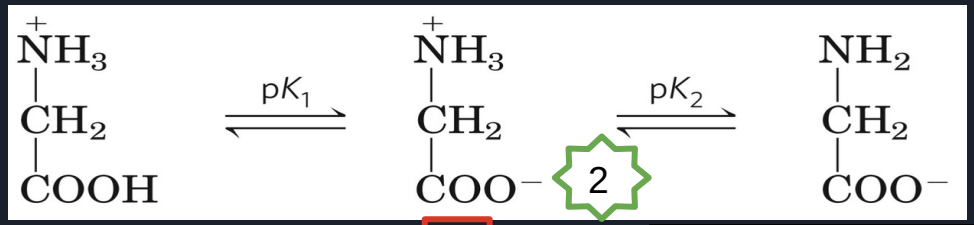
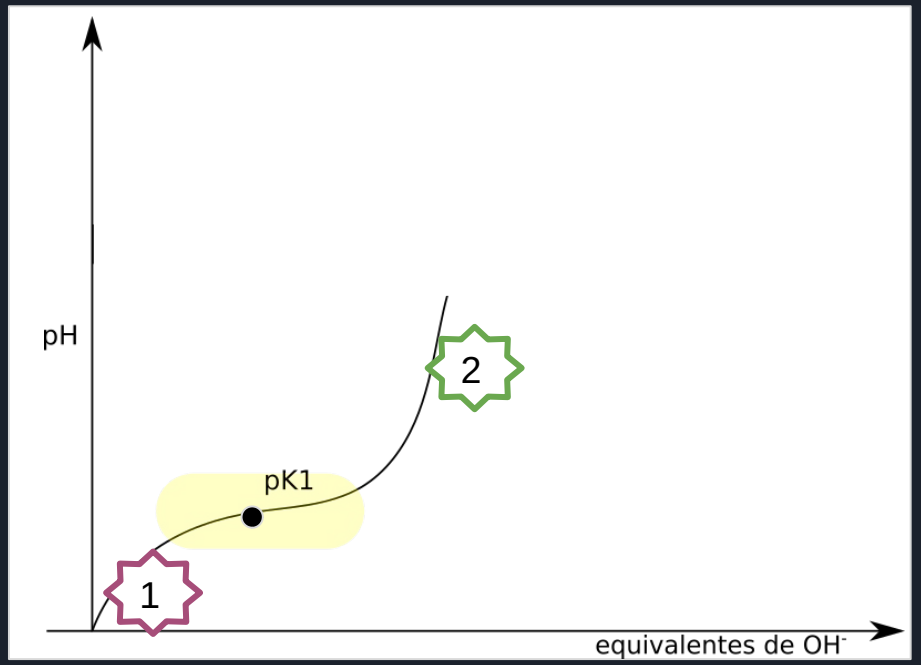


Ionização da Glicina

Faixas de tamponamento:

1. De pk1 -1 até pk1 +1

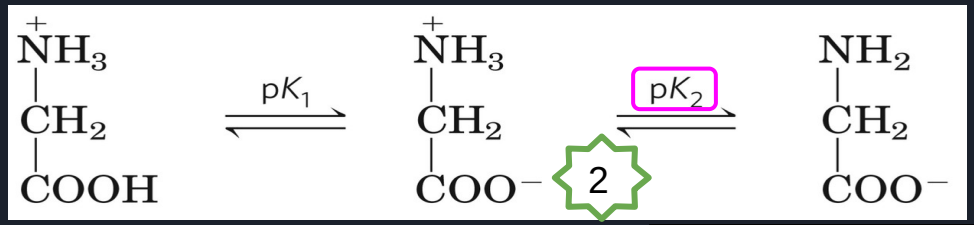




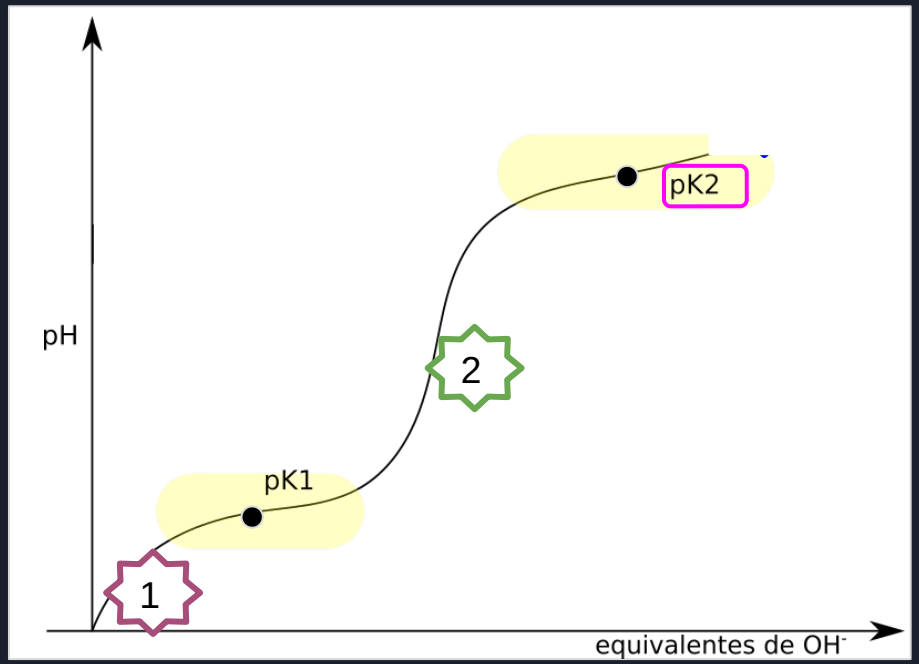
Ionização da Glicina

Faixas de tamponamento:

1. De pk1 -1 até pk1 +1



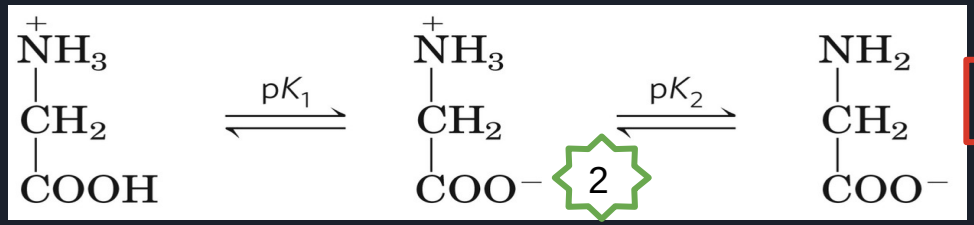
1

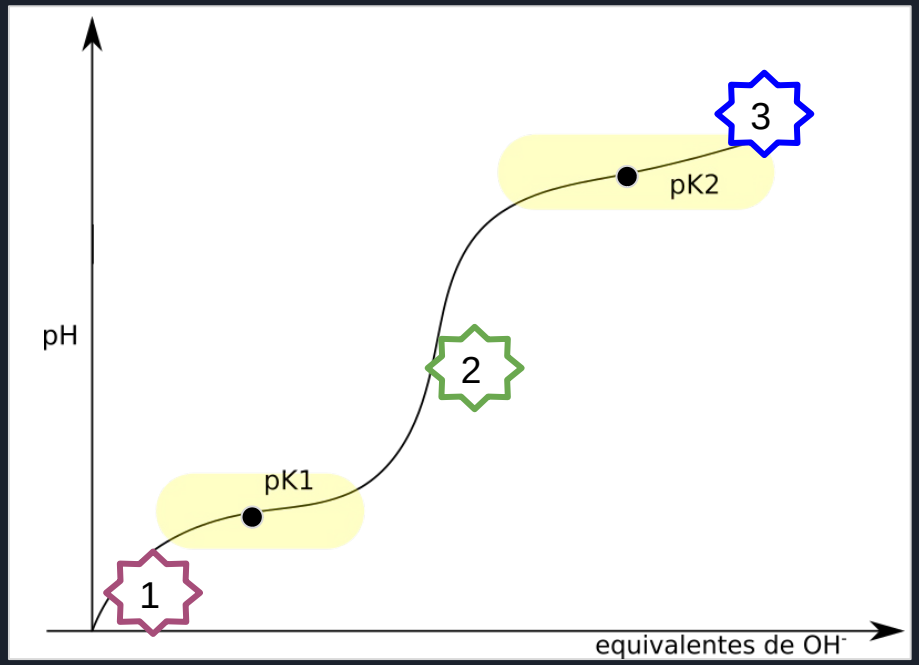


Ionização da Glicina

Faixas de tamponamento:

1. De pk1 -1 até pk1 +1
2. De pk2 -1 até pk2 +1

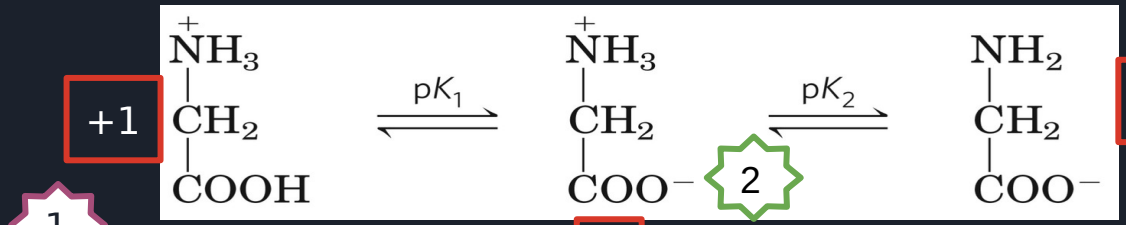


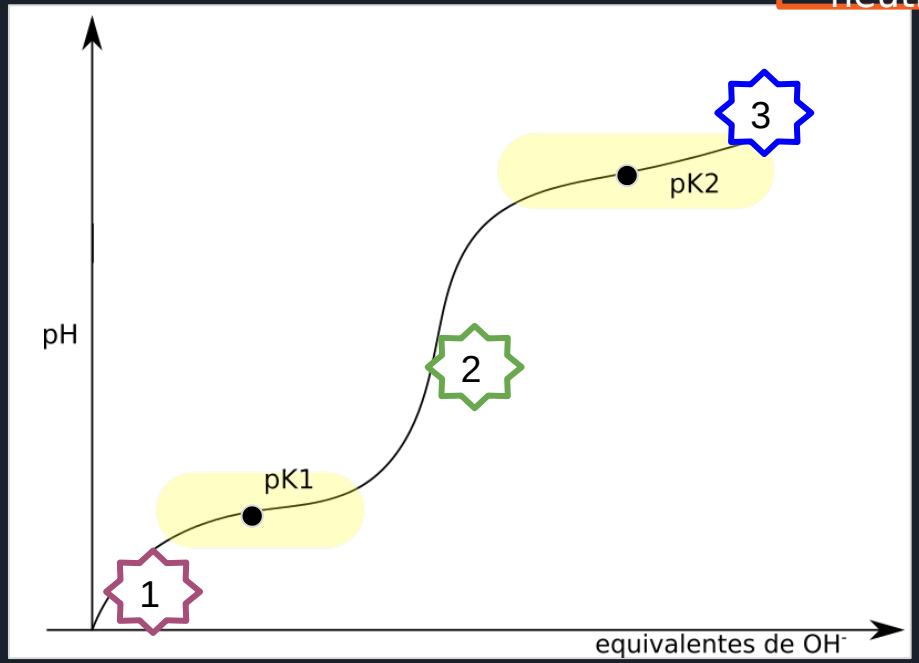


Ionização da Glicina

Faixas de tamponamento:

1. De pk1 -1 até pk1 +1
2. De pk2 -1 até pk2 +1





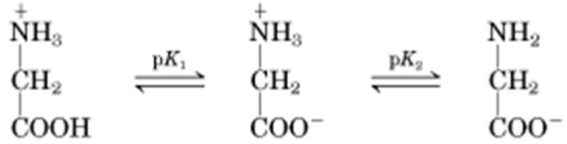
Ionização da Glicina

Faixas de tamponamento:

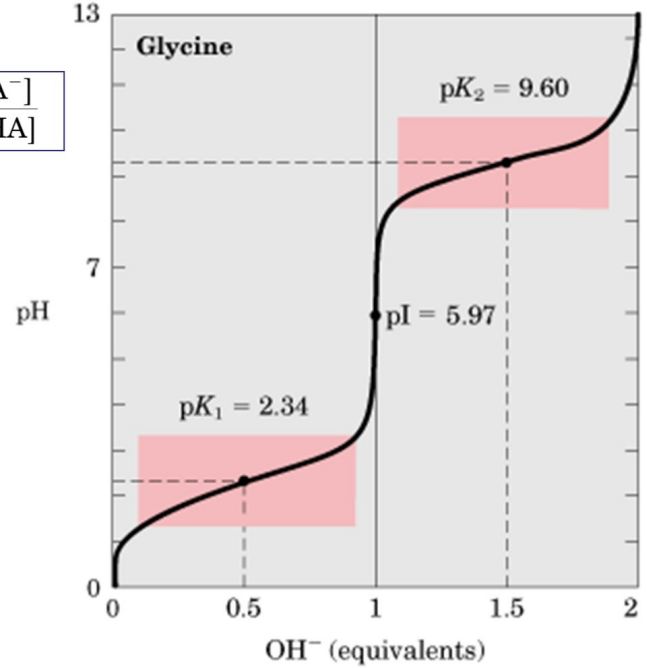
1. De pk1 -1 até pk1 +1 => 1 a 3
2. De pk2 -1 até pk2 +1 => 8 a 10

pka amino ≅ 9
pka ácido carboxílico ≅ 2

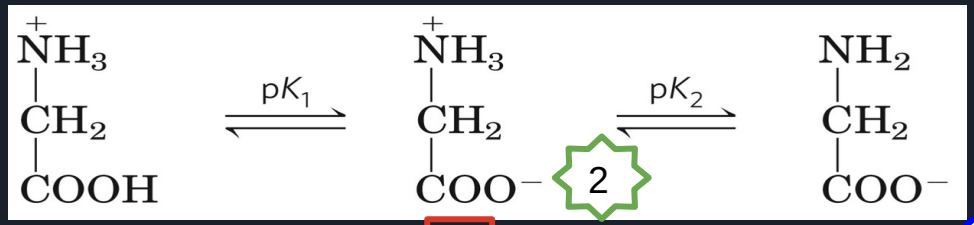
Titulação de aminoácidos

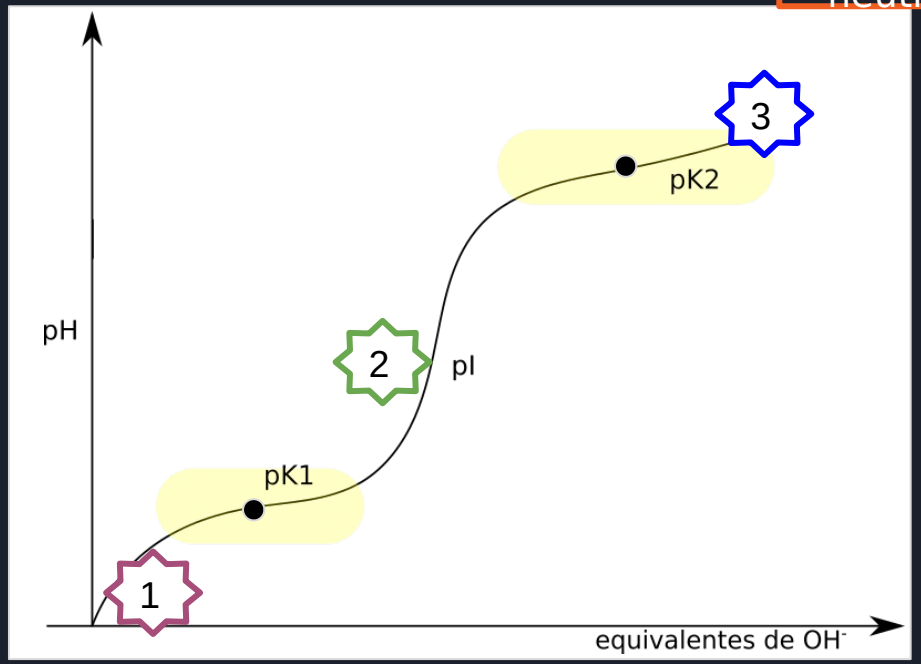


$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$



pI = ponto isoelétrico
pH em que a carga líquida das moléculas de uma
solução é igual a zero





Ponto Isoelétrico

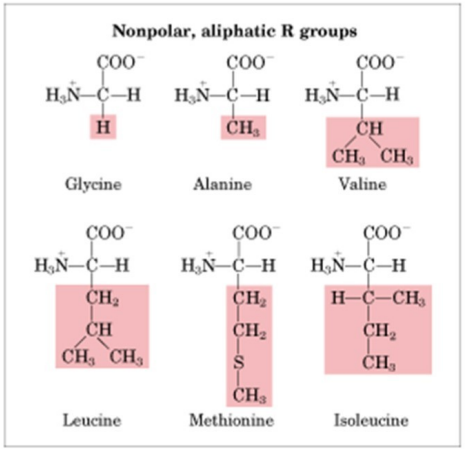
$$pI = \frac{pK_1 + pK_2}{2}$$

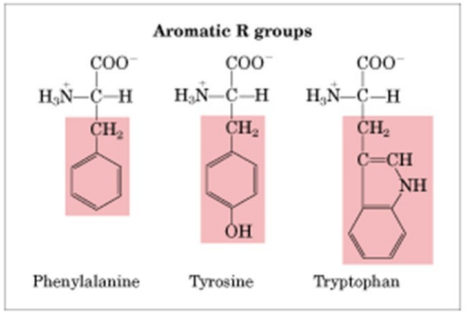
2

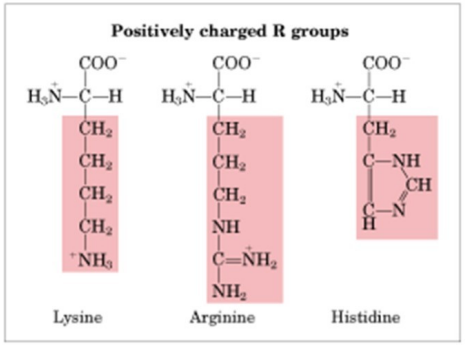
Média dos valores de pk que contribuem para a formação da molécula com soma de cargas igual a 0.

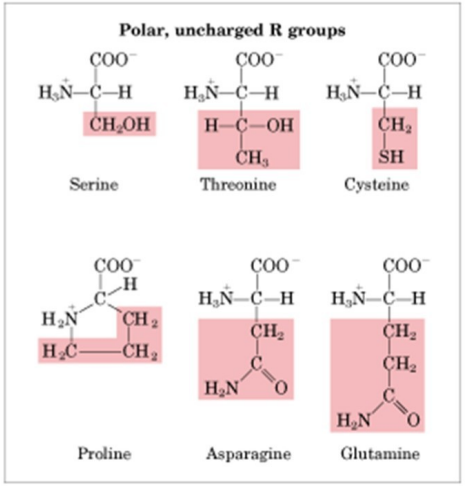
pka amino ≅ 9
pka ácido carboxílico ≅ 2

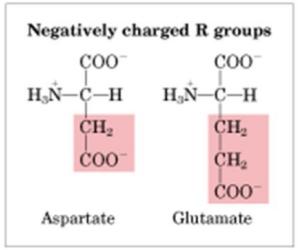
Os 20 aminoácidos











Amino acid	Abbreviation/ symbol	M_r*	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI
Nonpolar, aliphatic R groups						
Glycine	Gly G	75	2.34	9.60		5.97
Alanine	Ala A	89	2.34	9.69		6.01
Proline	Pro P	115	1.99	10.96		6.48
Valine	Val V	117	2.32	9.62		5.97
Leucine	Leu L	131	2.36	9.60		5.98
Isoleucine	Ile I	131	2.36	9.68		6.02
Methionine	Met M	149	2.28	9.21		5.74
Aromatic R groups						
Phenylalanine	Phe F	165	1.83	9.13		5.48
Tyrosine	Tyr Y	181	2.20	9.11	10.07	5.66
Tryptophan	Trp W	204	2.38	9.39		5.89
Polar, uncharged R groups						
Serine	Ser S	105	2.21	9.15		5.68
Threonine	Thr T	119	2.11	9.62		5.87
Cysteine¶	Cys C	121	1.96	10.28	8.18	5.07
Asparagine	Asn N	132	2.02	8.80		5.41
Glutamine	Gln Q	146	2.17	9.13		5.65
Positively charged R groups						
Lysine	Lys K	146	2.18	8.95	10.53	9.74
Histidine	His H	155	1.82	9.17	6.00	7.59
Arginine	Arg R	174	2.17	9.04	12.48	10.76
Negatively charged R groups						
Aspartate	Asp D	133	1.88	9.60	3.65	2.77
Glutamate	Glu E	147	2.19	9.67	4.25	3.22

Amino acid	Abbreviation/ symbol	M_r*	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI
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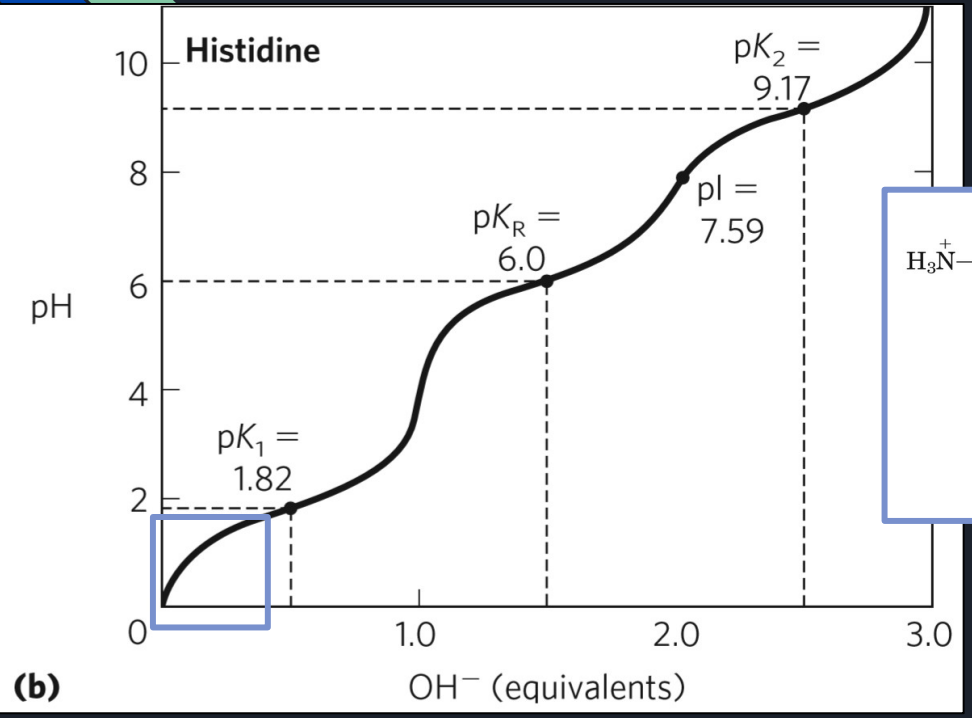
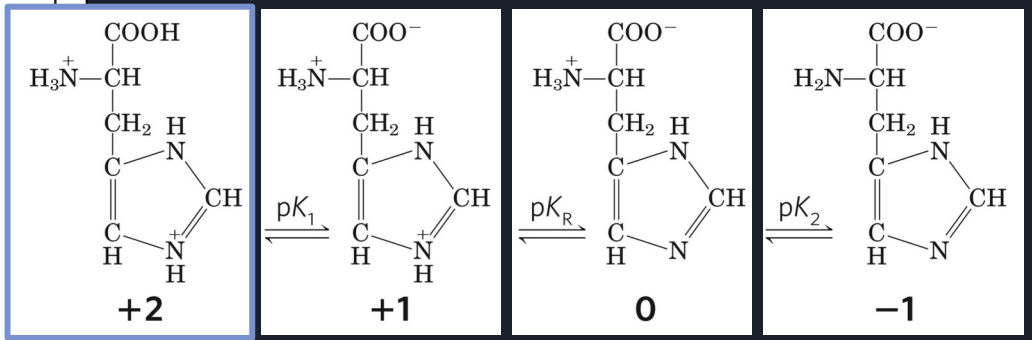
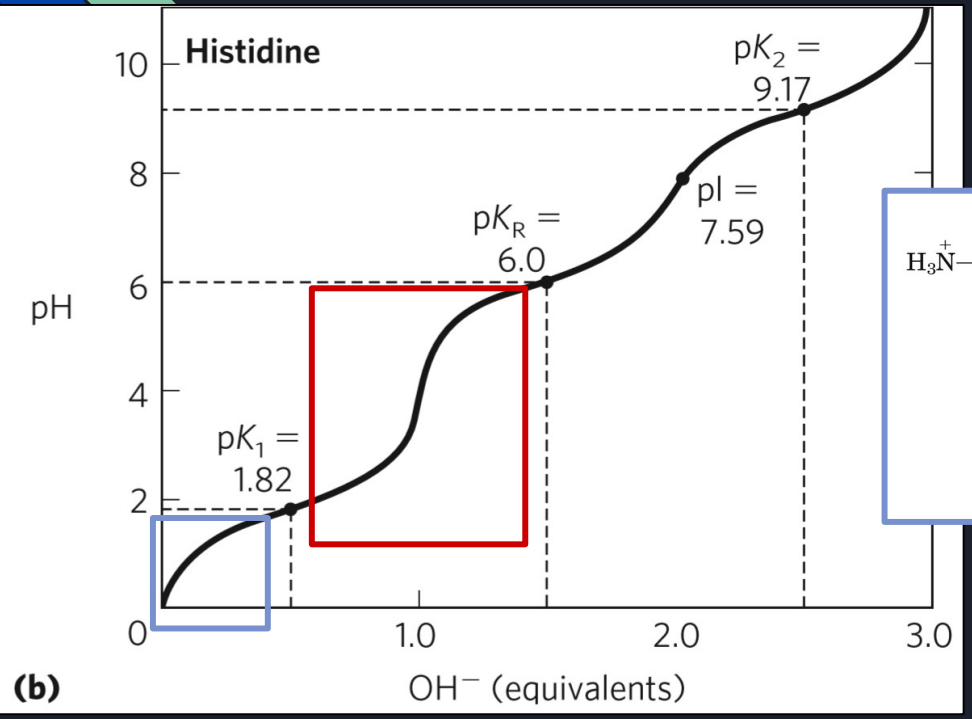
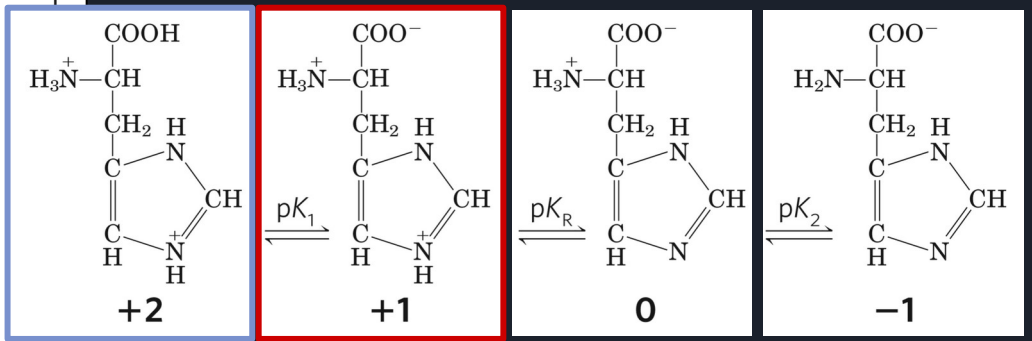




Faixas de tamponamento:

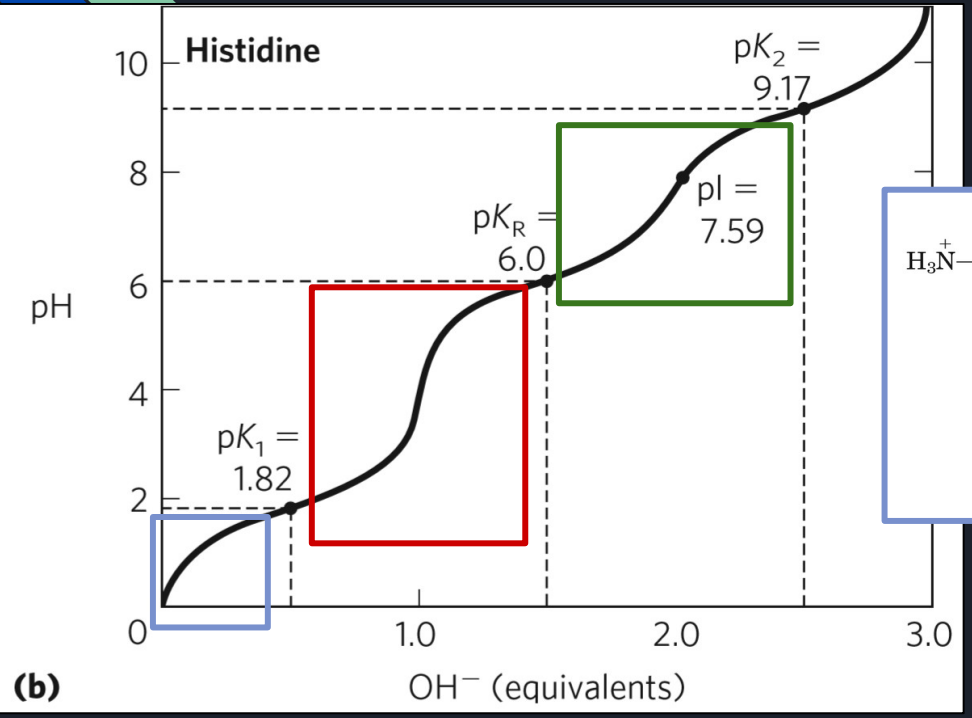
1. .
2. .
3. .

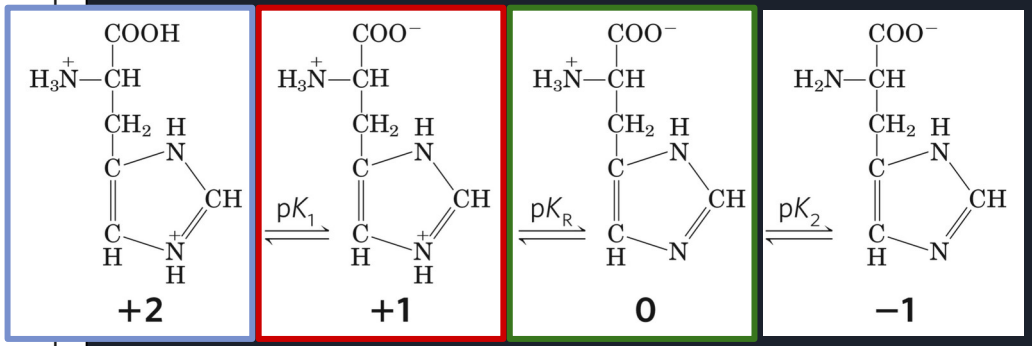




Faixas de tamponamento:

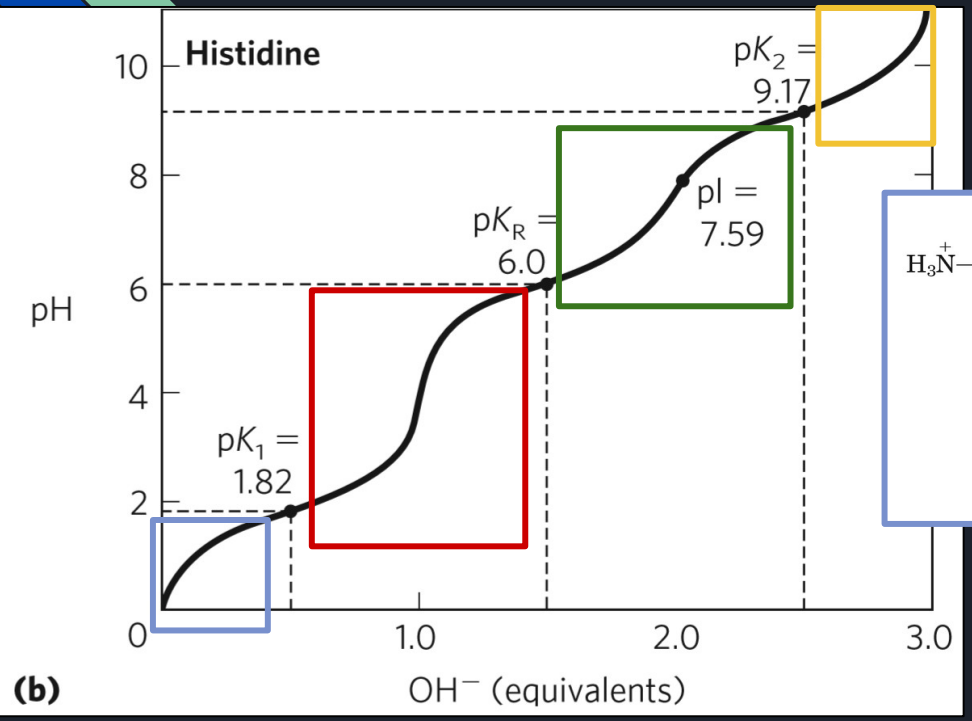
1. De pk1 -1 até pk1 +1 => 0,82 a 2.82
2. .
3. .

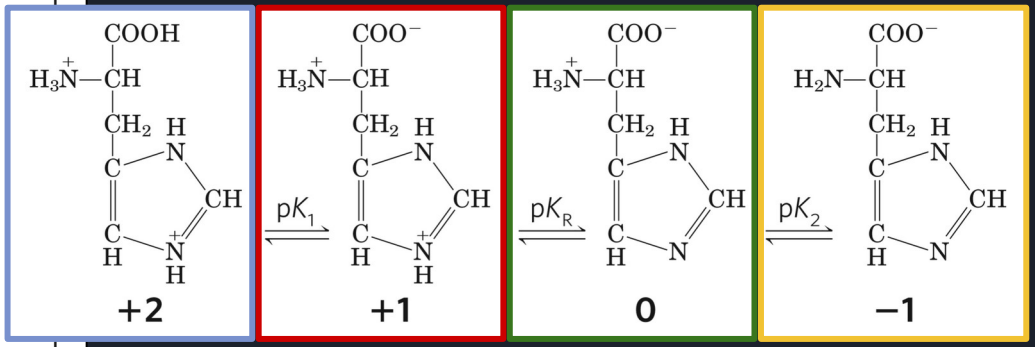




Faixas de tamponamento:

1. De pk1 -1 até pk1 +1 => 0,82 a 2.82
2. De pkR -1 até pkR +1 => 5,0 a 7,0
3. .

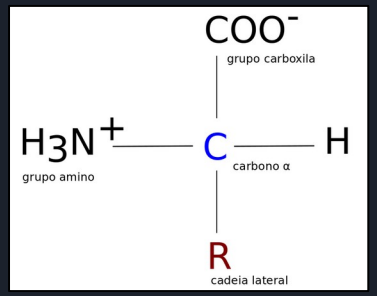




Faixas de tamponamento:

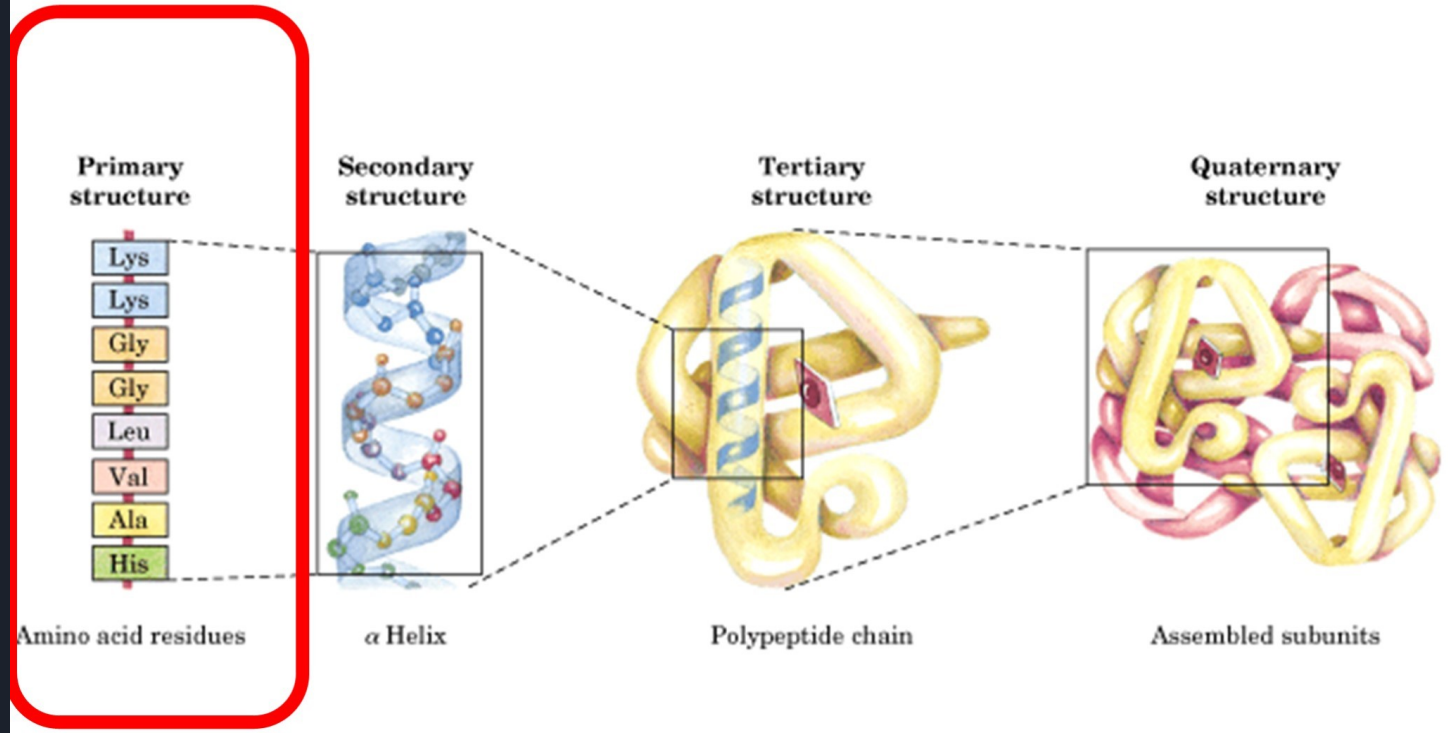
1. De pk1 -1 até pk1 +1 => 0,82 a 2.82
2. De pkR -1 até pkR +1 => 5,0 a 7,0
3. De pk2 -1 até pk2+1 =>8,17 a 10,17

Vimos que os aminoácidos ...



- Estruturas comuns e **cadeia lateral** variável.
- Existem como enantiômeros D e L.
- Alguns ocorrem mas são menos comuns nas proteínas.
- **Polaridade** das cadeias laterais.
- Têm propriedades ácido-básicas que variam.
- Podem ser usados como **tampões** e têm curvas de titulação características.

Proteínas: polímeros de aminoácidos



Proteínas: pIs característicos

The Isoelectric Points of Some Proteins

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

Peptídeos de importância biológica

Peptídeo	Número de aa	Efeito principal
Encefalina	5	Analgesia
Oxitocina	9	Contração da musculatura uterina no parto e glândulas mamárias na lactação
Vasopressina	9	Aumento da pressão sangüínea
Glucagon	29	Aumento da produção de glicose pelo fígado no jejum
Gramicidina	10	Antibiótico

Ligação peptídica