



QBQ 0204 – Bioquímica: Estrutura e Metabolismo de Biomoléculas

Aula 3.1

**Titulação de aminoácidos,
estruturas primária e
secundária de proteínas**

SISTEMAS TAMPÃO



- Os ácidos fracos quando em solução estão em um equilíbrio entre as concentrações de HA, A⁻ e de H⁺. Este equilíbrio é regido por uma constante de equilíbrio denominada de K.

$$K = \frac{[A^-][H^+]}{[HA]}$$

- A constante K é conhecida como constante de dissociação ou de ionização, e no caso dos ácidos é chamada de K_a.

Equação de Henderson-Hasselbalck

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

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

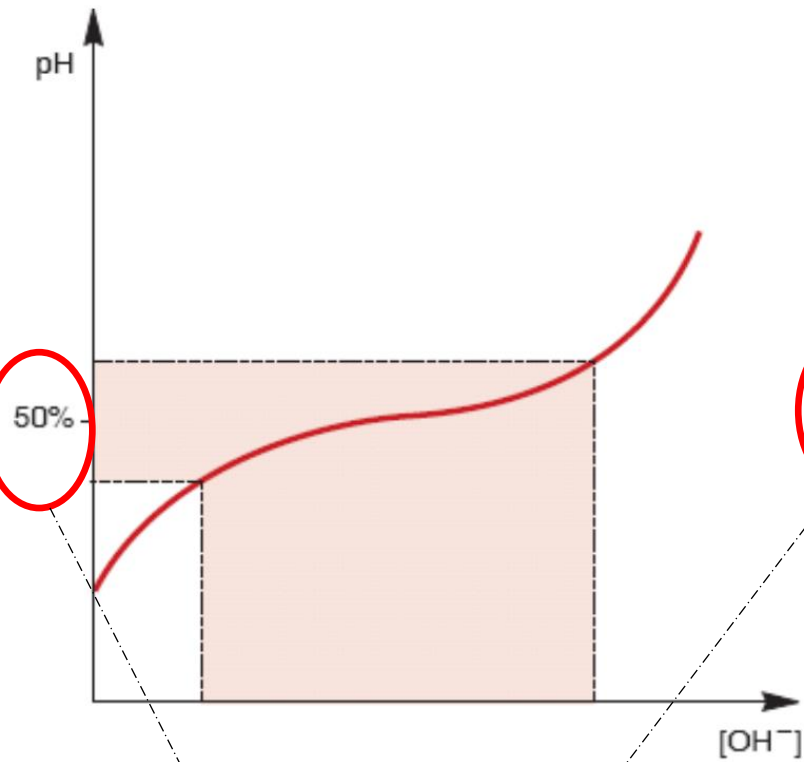
$$\log [H^+] = \log K_a + \log \frac{[HA]}{[A]}$$

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

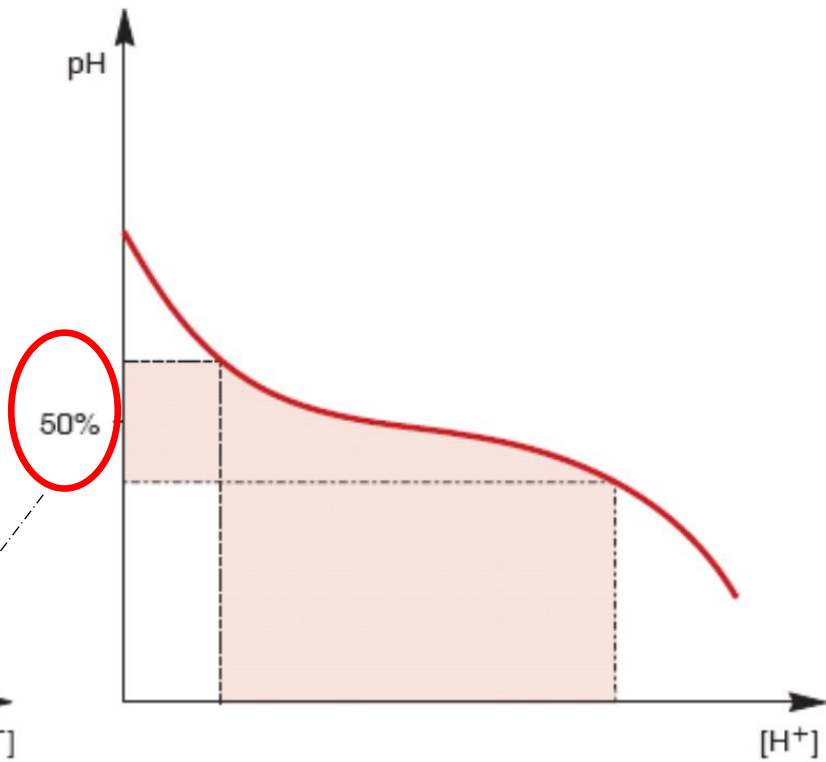
$$-\log [H^+] = -\log K_a + \log \frac{[A]}{[HA]}$$

$$\text{pH} = \text{p}K_a + \log \frac{[A]}{[HA]}$$

Base conjugada
Ácido conjugado



(a)



(b)

50% de HA e 50% de A
Ou seja
HA = A

As concentrações de ácido e base conjugadas são iguais

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

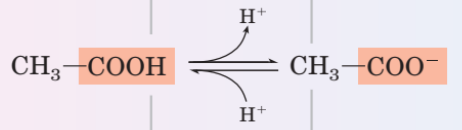
Base conjugada
Ácido conjugado

log 1 = 0

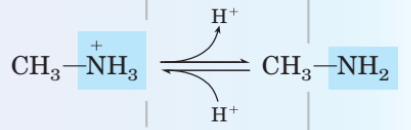
Portanto, no $pH = pK_a$
o tampão tem sua máxima eficiência

pK_a 2 4 6 8 10 12

Grupos carboxila e amino substituídos por metil

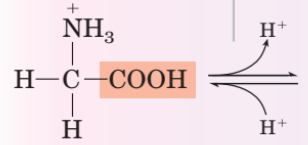


Ácido acético
O pK_a normal para um grupo carboxila é de cerca de 4,8.

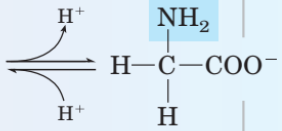
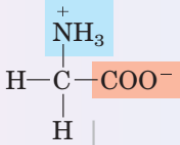


Metilamina
O pK_a normal para um grupo amino é de cerca de 10,6.

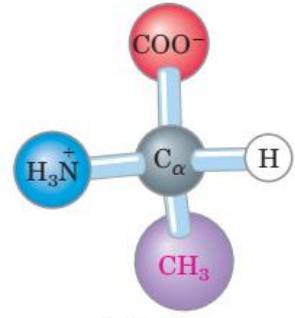
Grupos amino e carboxil na glicina



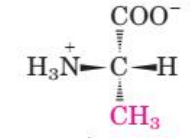
α-Aminoácido (glicina)
pK_a = 2,34
Grupos com cargas opostas diminuem o pK_a pela estabilização do zwitterión.



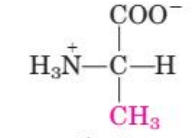
α-Aminoácido (glicina)
pK_a = 9,60
Átomos de oxigênio eletronegativos no grupo carboxila puxam os elétrons para longe do grupo amino, reduzindo seu pK_a.



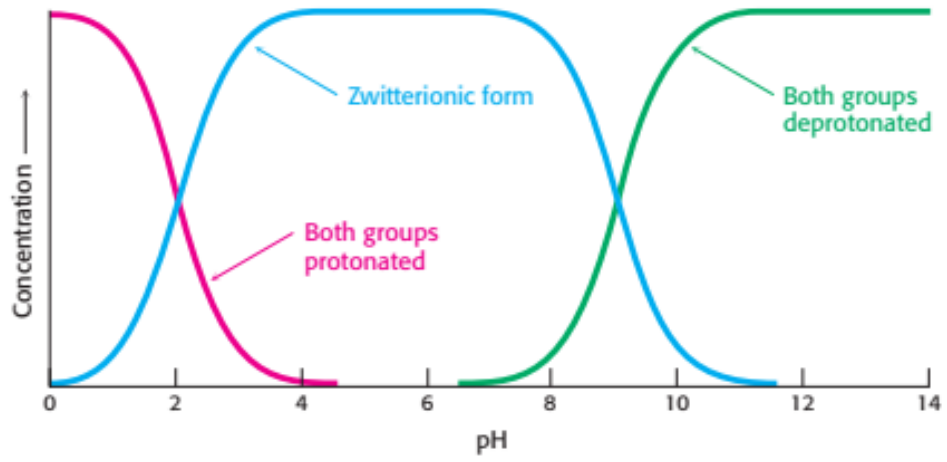
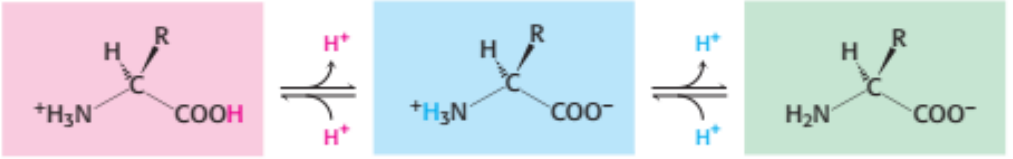
(a) L-Alanina



(b) L-Alanina



(c) L-Alanina



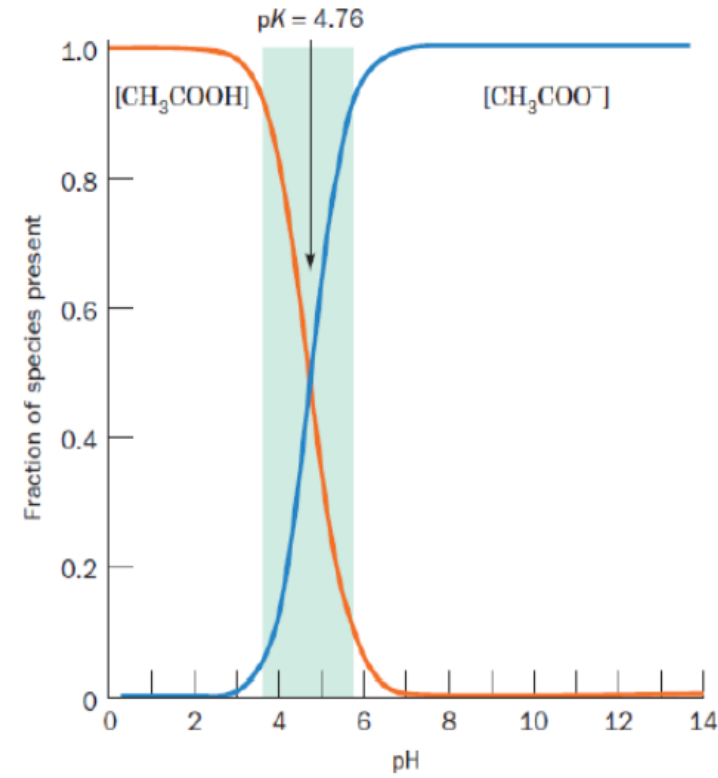
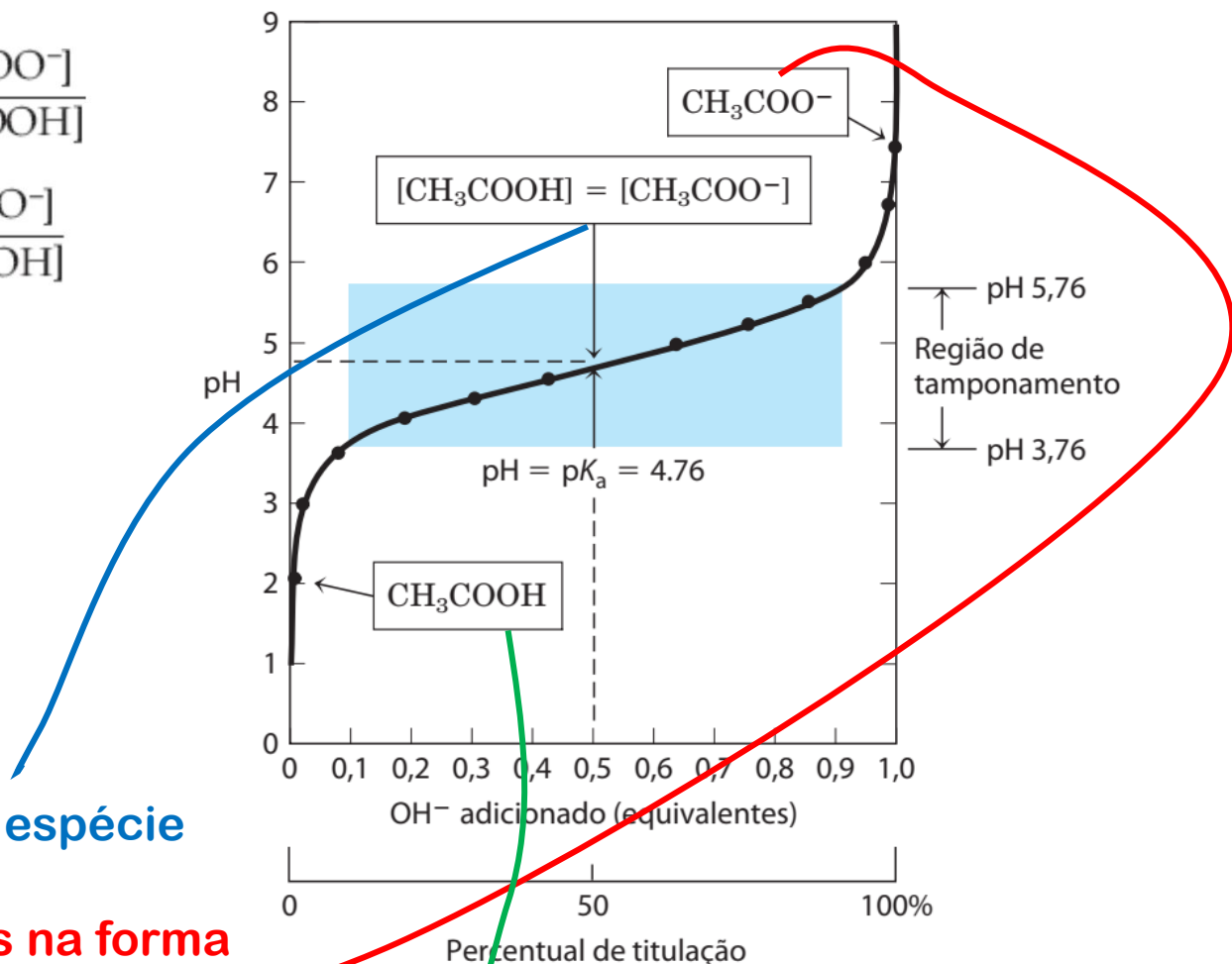
Proporção entre as espécies uma unidade de pH acima do pK_a para o ácido acético.

$$pH = pK_a + \log \frac{[H_3C-COO^-]}{[H_3C-COOH]}$$

$$5,7 = 4,7 + \log \frac{[H_3C-COO^-]}{[H_3C-COOH]}$$

$$1 = \log \frac{[H_3C-COO^-]}{[H_3C-COOH]}$$

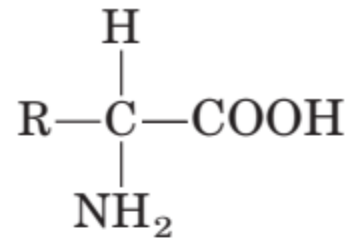
$$\frac{[H_3C-COO^-]}{[H_3C-COOH]} = 10$$



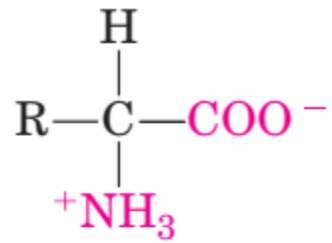
pH = pKa , 50% de cada espécie

pH > pKa, mais espécies na forma desprotonada

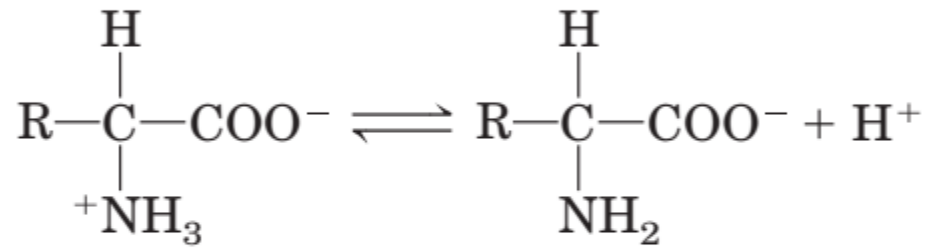
pH < pKa, mais espécies na forma protonada



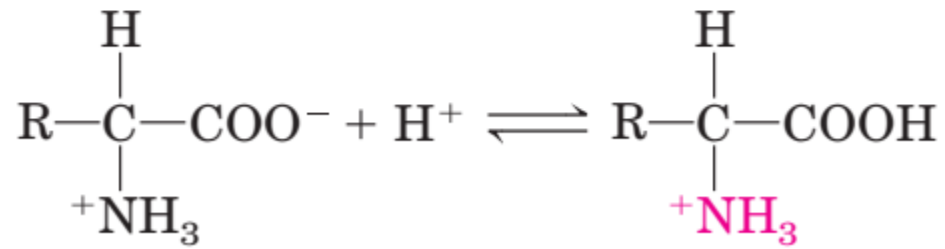
Forma não iônica



Forma zwitteriônica



Zwitterión
como ácido



Zwitterión
como base

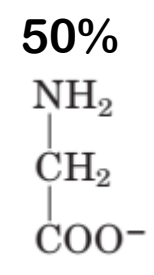
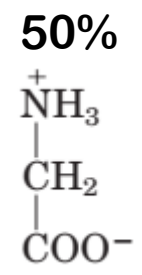
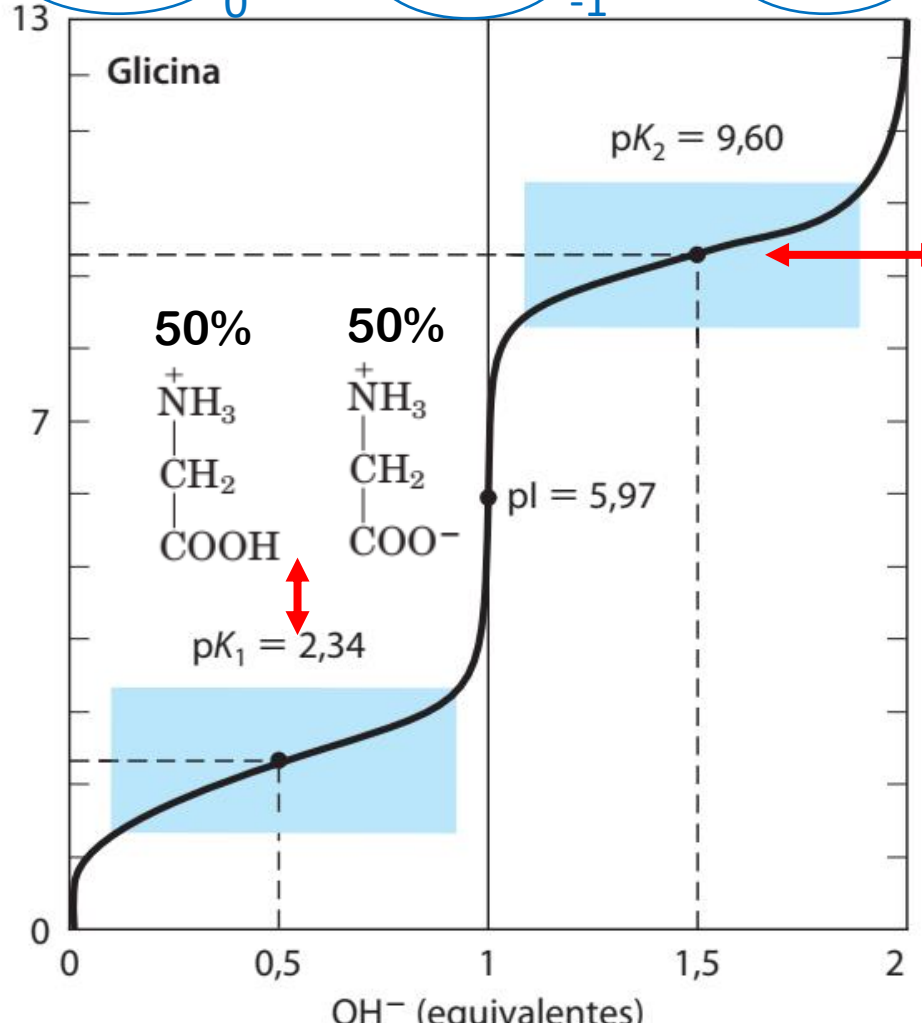
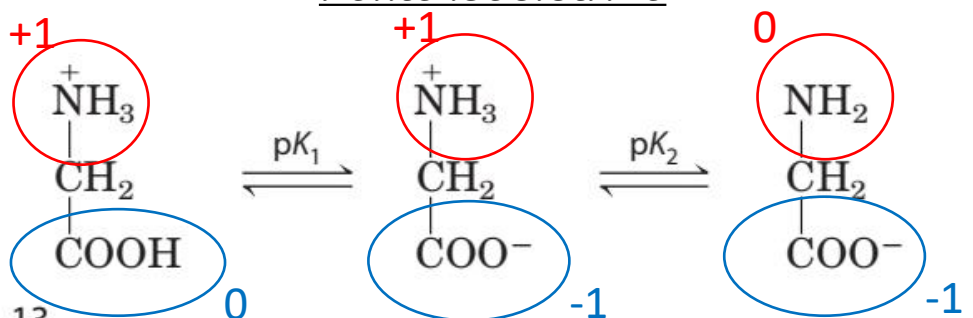
TABELA 3-1 Propriedades e convenções associadas a aminoácidos comuns encontrados em proteínas

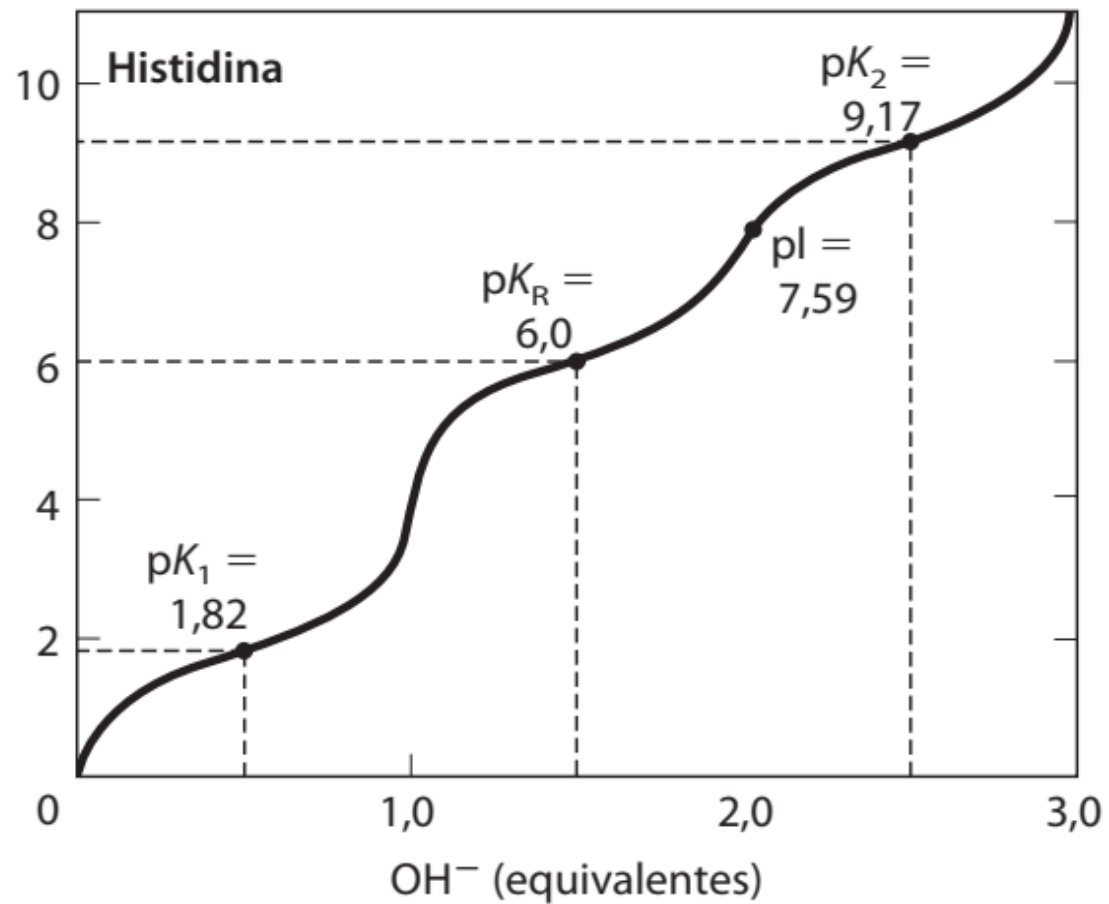
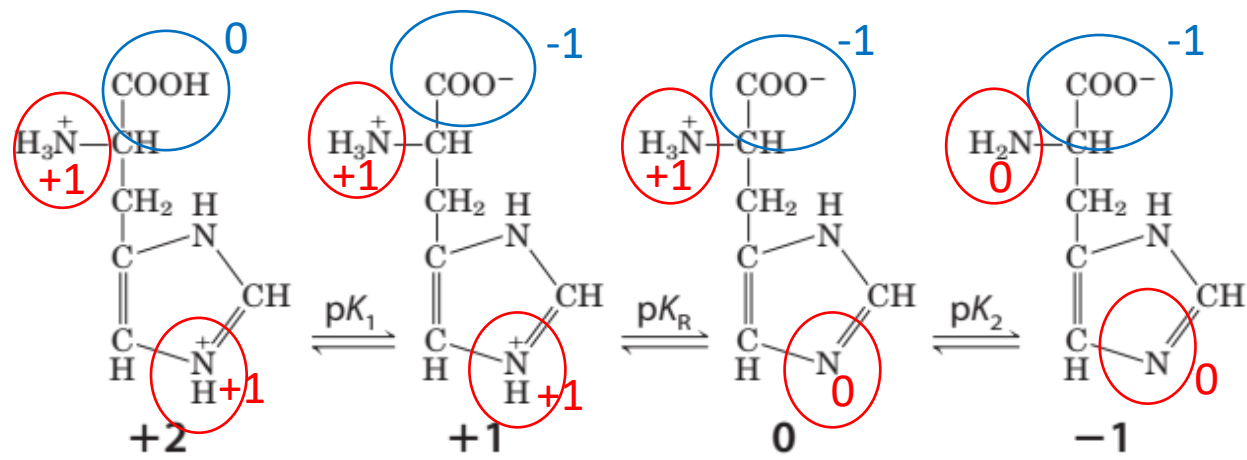
Aminoácido	Abreviação/ símbolo	M_r^*	Valores de pK_a			pI	Índice de hidropatia [†]	Ocorrência em proteínas (%) [‡]
			pK_1 (—COOH)	pK_2 (—NH ₃ ⁺)	pK_R (grupo R)			
Grupos R alifáticos, apolares								
Glicina	Gly G	75	2,34	9,60		5,97	-0,4	7,2
Alanina	Ala A	89	2,34	9,69		6,01	1,8	7,8
Prolina	Pro P	115	1,99	10,96		6,48	-1,6	5,2
Valina	Val V	117	2,32	9,62		5,97	4,2	6,6
Leucina	Leu L	131	2,36	9,60		5,98	3,8	9,1
Isoleucina	Ile I	131	2,36	9,68		6,02	4,5	5,3
Metionina	Met M	149	2,28	9,21		5,74	1,9	2,3
Grupos R aromáticos								
Fenilalanina	Phe F	165	1,83	9,13		5,48	2,8	3,9
Tirosina	Tyr Y	181	2,20	9,11	10,07	5,66	-1,3	3,2
Triptofano	Trp W	204	2,38	9,39		5,89	-0,9	1,4
Grupos R polares, não carregados								
Serina	Ser S	105	2,21	9,15		5,68	-0,8	6,8
Treonina	Thr T	119	2,11	9,62		5,87	-0,7	5,9
Cisteína [¶]	Cys C	121	1,96	10,28	8,18	5,07	2,5	1,9
Asparagina	Asn N	132	2,02	8,80		5,41	-3,5	4,3
Glutamina	Gln Q	146	2,17	9,13		5,65	-3,5	4,2
Grupos R carregados positivamente								
Lisina	Lys K	146	2,18	8,95	10,53	9,74	-3,9	5,9
Histidina	His H	155	1,82	9,17	6,00	7,59	-3,2	2,3
Arginina	Arg R	174	2,17	9,04	12,48	10,76	-4,5	5,1
Grupos R carregados negativamente								
Aspartato	Asp D	133	1,88	9,60	3,65	2,77	-3,5	5,3
Glutamato	Glu E	147	2,19	9,67	4,25	3,22	-3,5	6,3

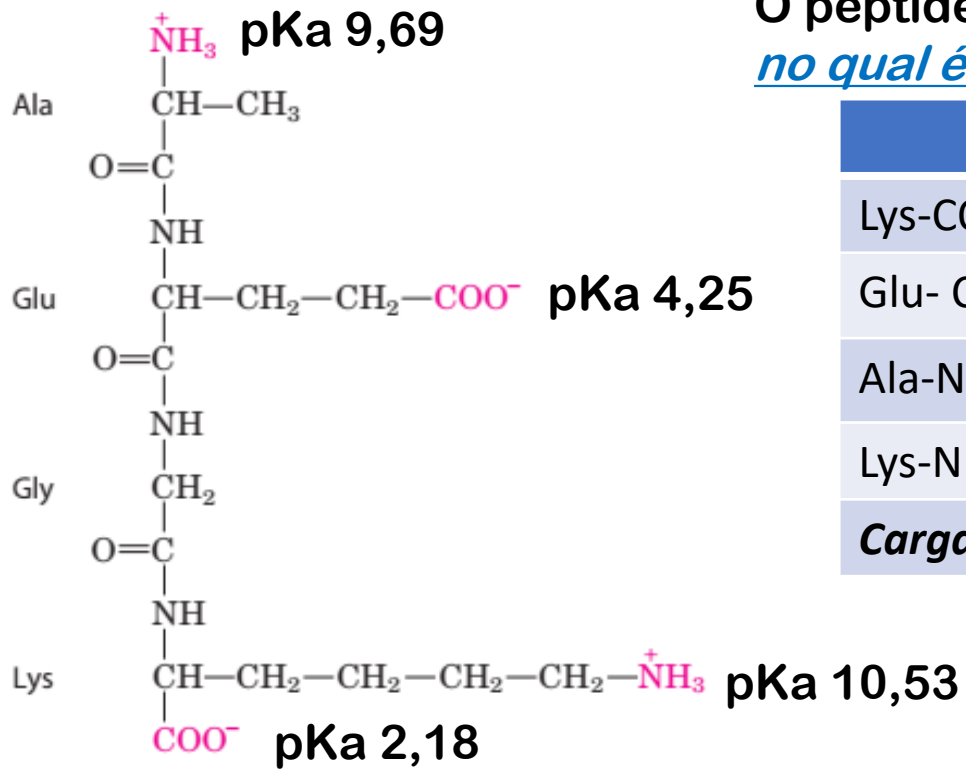
Carga total +1

Carga total 0
Ponto isoelétrico

Carga total -1



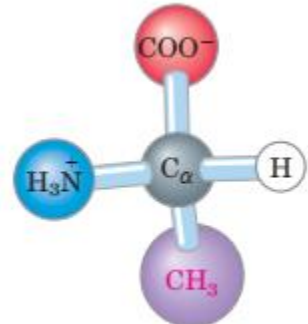




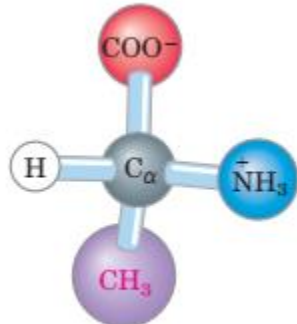
O peptídeo passa de uma molécula **carregada positivamente**, por estágios **no qual é neutra (ponto isoelétrico)**, até ter **uma carga total negativa**.

	2,18	4,25	9,69	10,53
Lys-COOH	-0,5	-1	-1	-1
Glu- COOH (lateral)	0	-0,5	-1	-1
Ala-NH3	+1	+1	+0,5	0
Lys-NH3 (lateral)	+1	+1	+1	+0,5
Carga do peptídeo	+1,5	+0,5	-0,5	-1,5

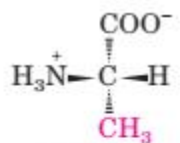
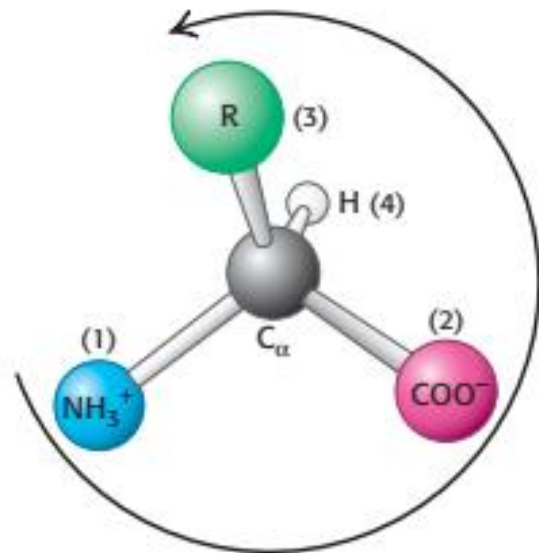
Região de pH na qual a molécula estará neutra, portanto, a média entre esses valores de pH = **pl (Ponto isoelétrico)**



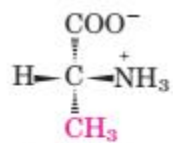
(a) L-Alanina



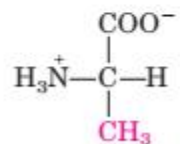
D-Alanina



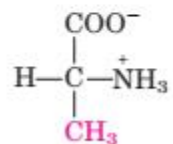
L-Alanina



D-Alanina



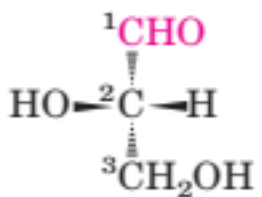
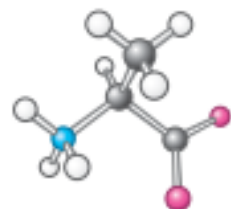
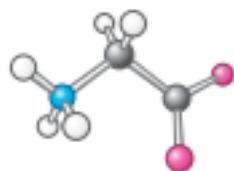
L-Alanina



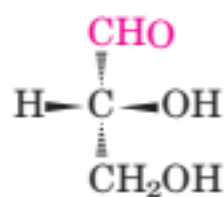
D-Alanina

Glycine
(Gly, G)

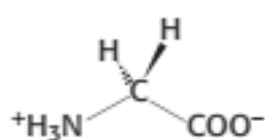
Alanine
(Ala, A)



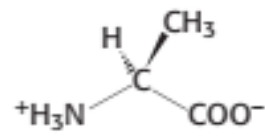
L-Gliceraldeído



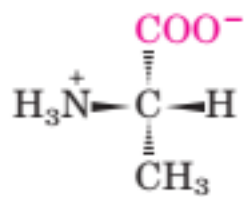
D-Gliceraldeído



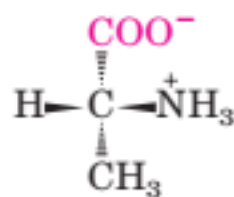
Glycine
(Gly, G)



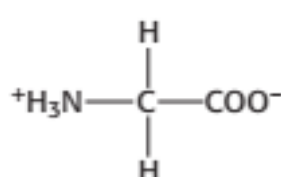
Alanine
(Ala, A)



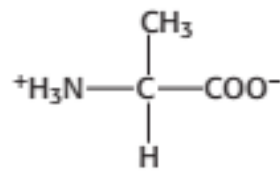
L-Alanina



D-Alanina



Glycine
(Gly, G)



Alanine
(Ala, A)

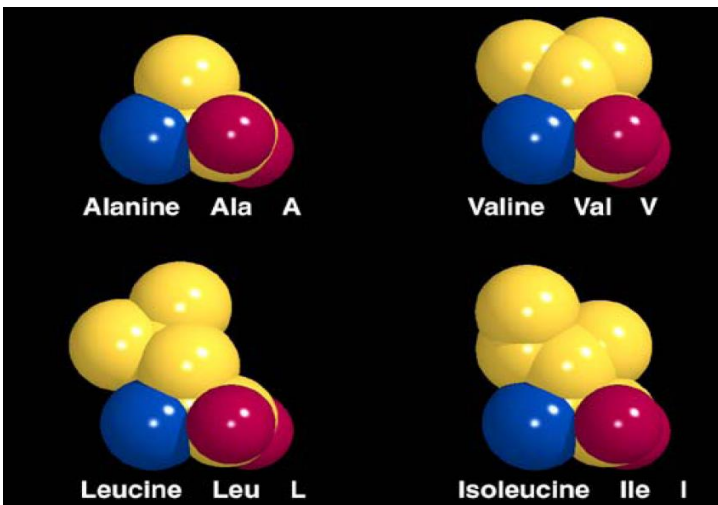
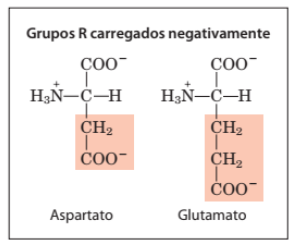
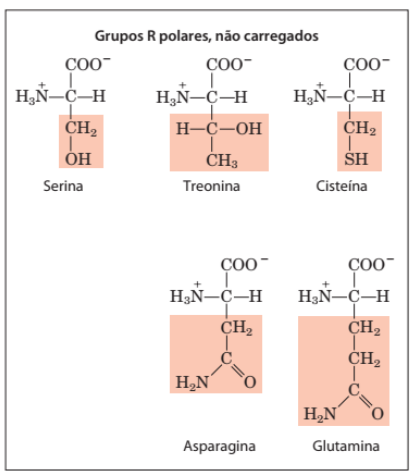
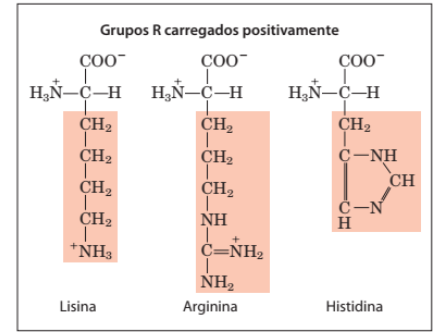
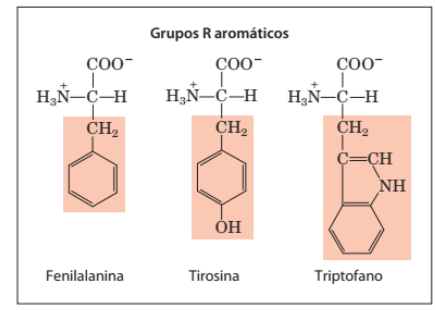
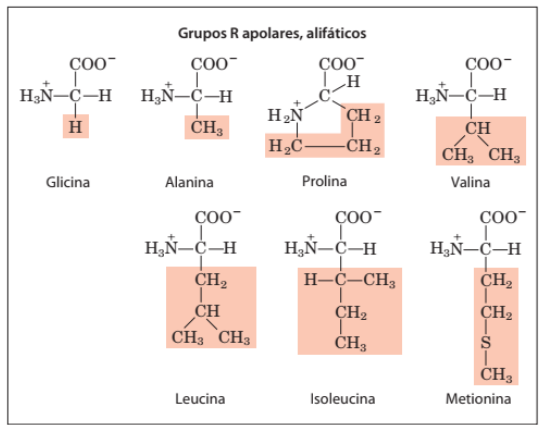
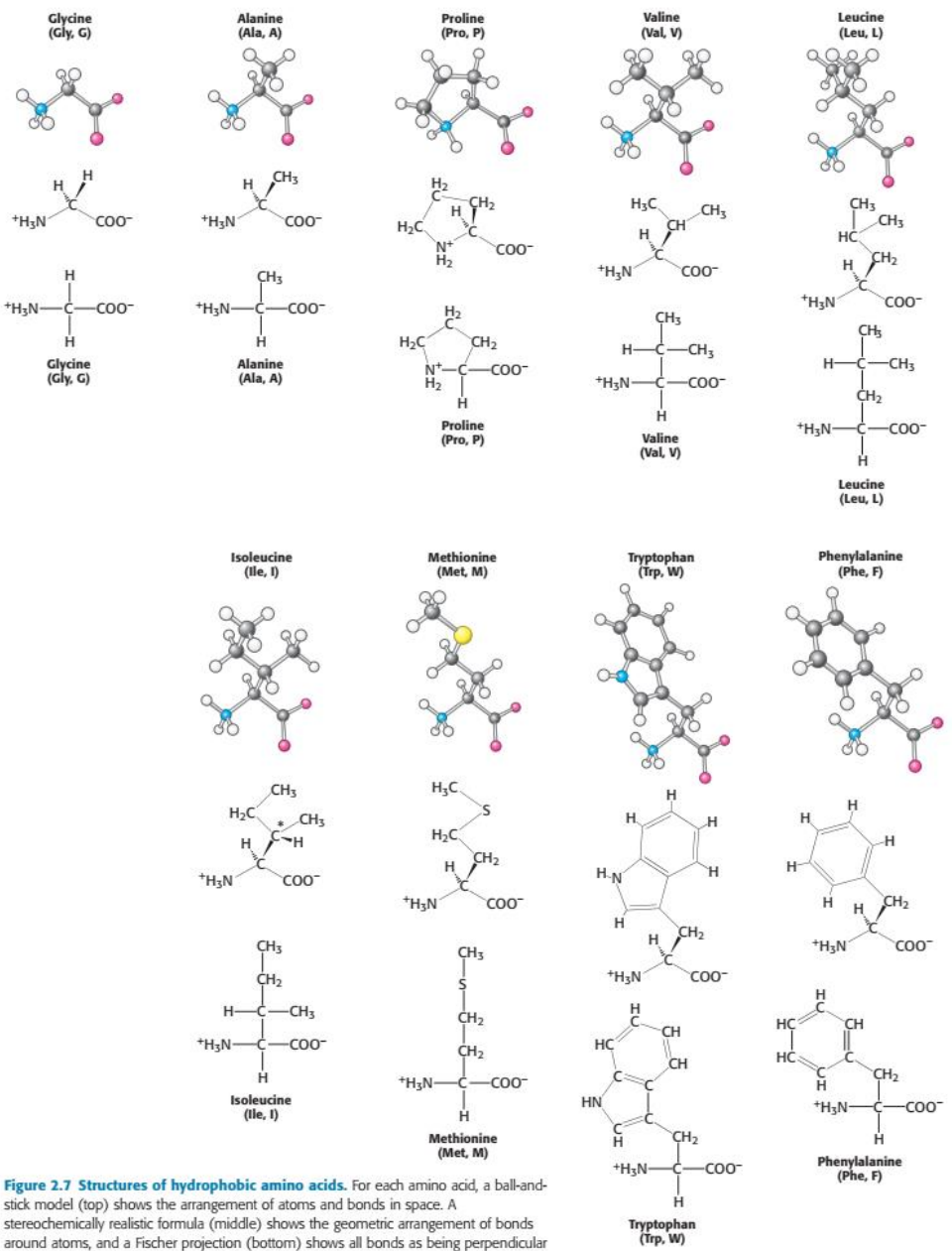


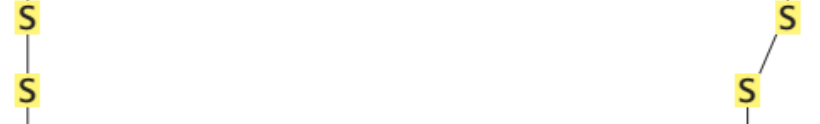
Figure 2.7 Structures of hydrophobic amino acids. For each amino acid, a ball-and-stick model (top) shows the arrangement of atoms and bonds in space. A stereochemically realistic formula (middle) shows the geometric arrangement of bonds around atoms, and a Fischer projection (bottom) shows all bonds as being perpendicular for a simplified representation (see the Appendix to Chapter 1).

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Aminoácido	Abreviação/ símbolo	M_r^*	Valores de pK_a			pI	Índice de hidropatia [†]	Ocorrência em proteínas (%) [‡]
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Grupos R carregados positivamente								
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Arginina	Arg R	174	2,17	9,04	12,48	10,76	-4,5	5,1
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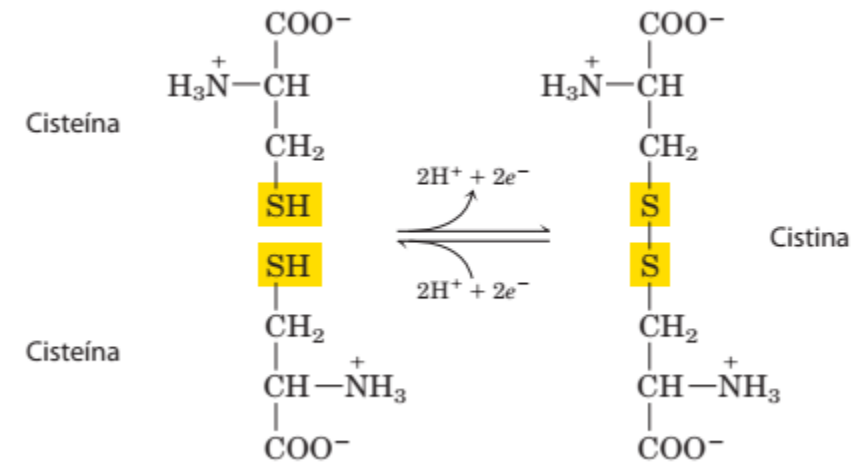
A chain
 Gly-Ile-Val-Glu-Gln-Cys-Cys-Ala-Ser-Val-Cys-Ser-Leu-Tyr-Gln-Leu-Glu-Asn-Tyr-Cys-Asn

5 10 15 21



B chain
 Phe-Val-Asn-Gln-His-Leu-Cys-Gly-Ser-His-Leu-Val-Glu-Ala-Leu-Tyr-Leu-Val-Cys-Gly-Glu-Arg-Gly-Phe-Phe-Tyr-Thr-Pro-Lys-Ala

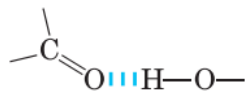
5 10 15 20 25 30



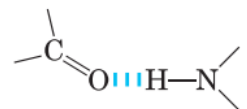
As pontes dissulfeto (caso ocorram), juntamente com as interações abaixo, são as responsáveis pela manutenção da estrutura da proteína.

Ligações de hidrogênio

Entre grupos neutros



Entre ligações peptídicas



Interações iônicas

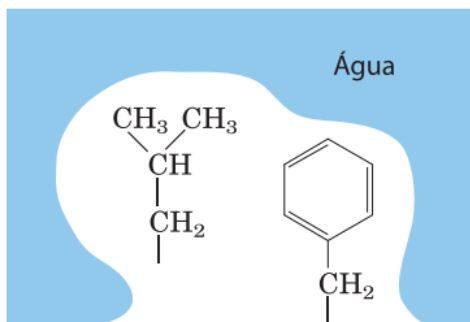
Atração



Repulsão

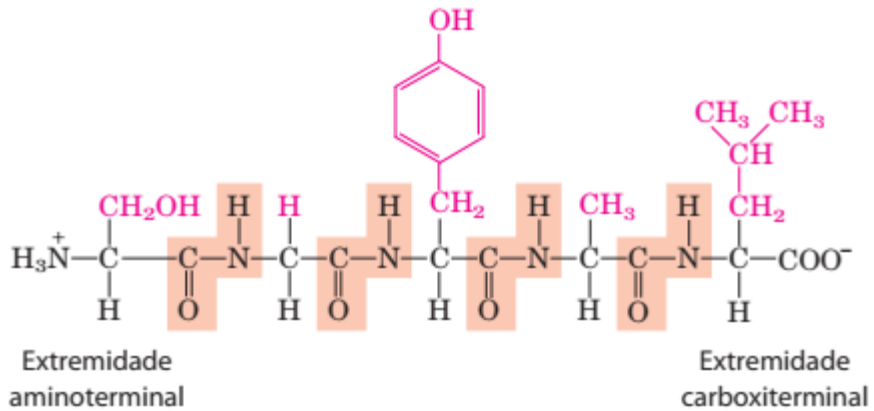
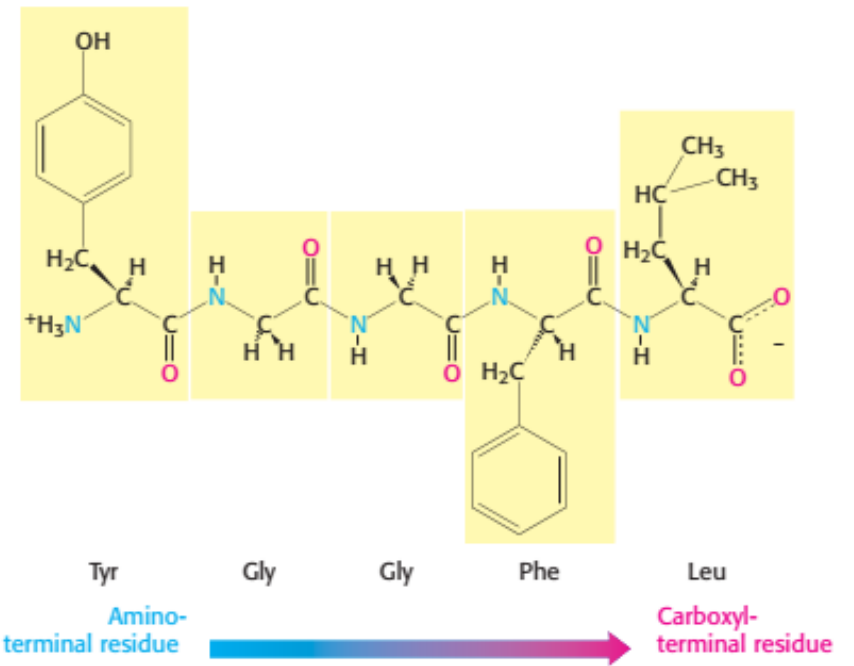
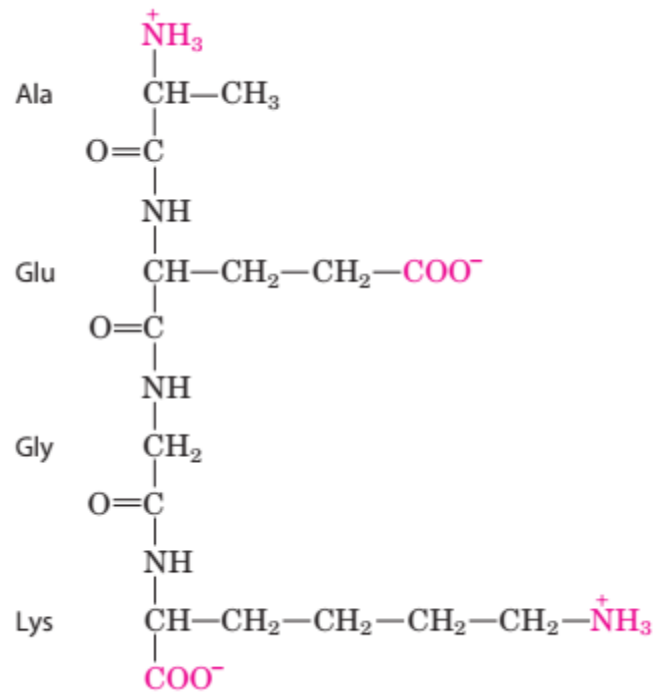
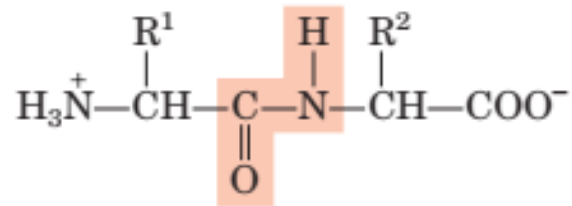
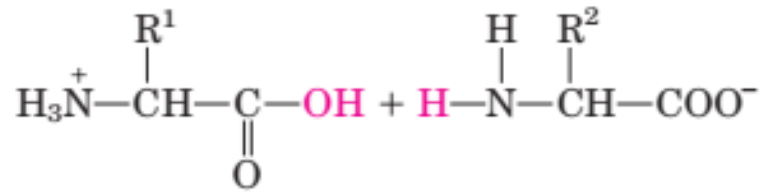


Interações hidrofóbicas



Interações de van der Waals

Dois átomos quaisquer bem próximos um do outro



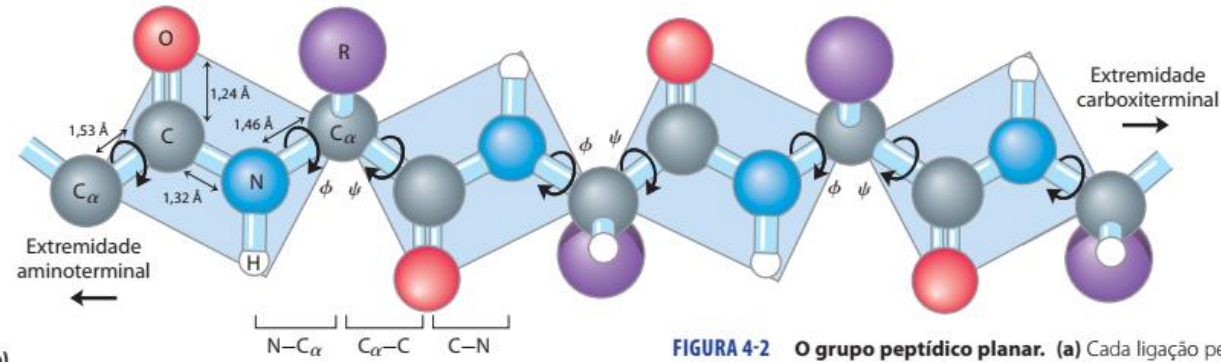
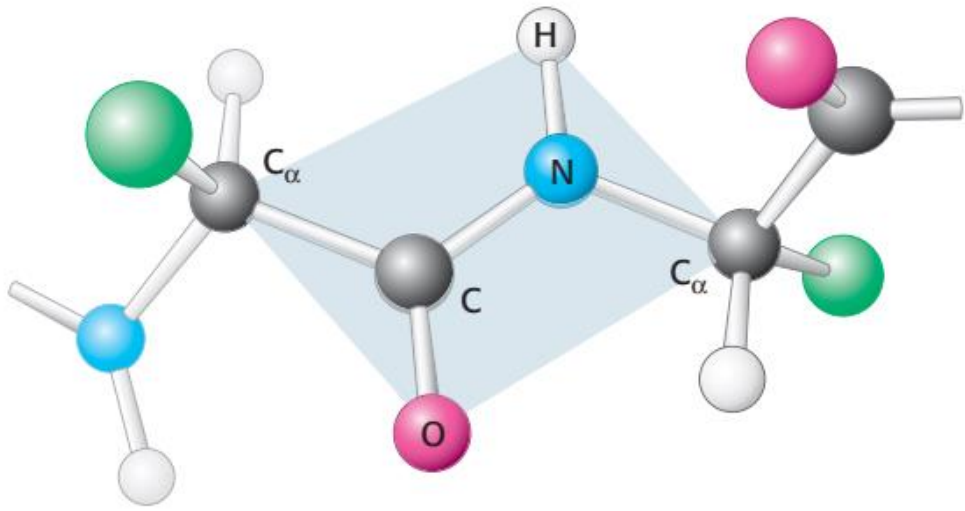
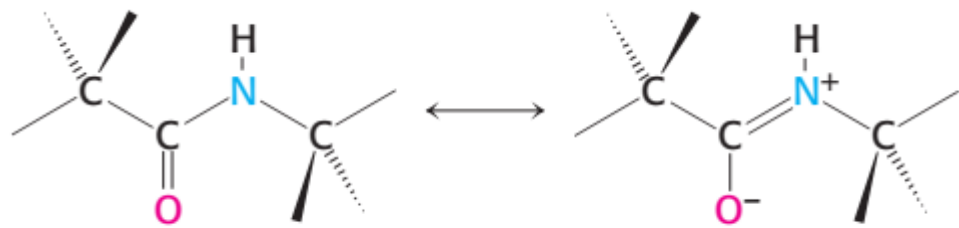


FIGURA 4-2 O grupo peptídico planar. (a) Cada ligação peptídica



Peptide-bond resonance structures

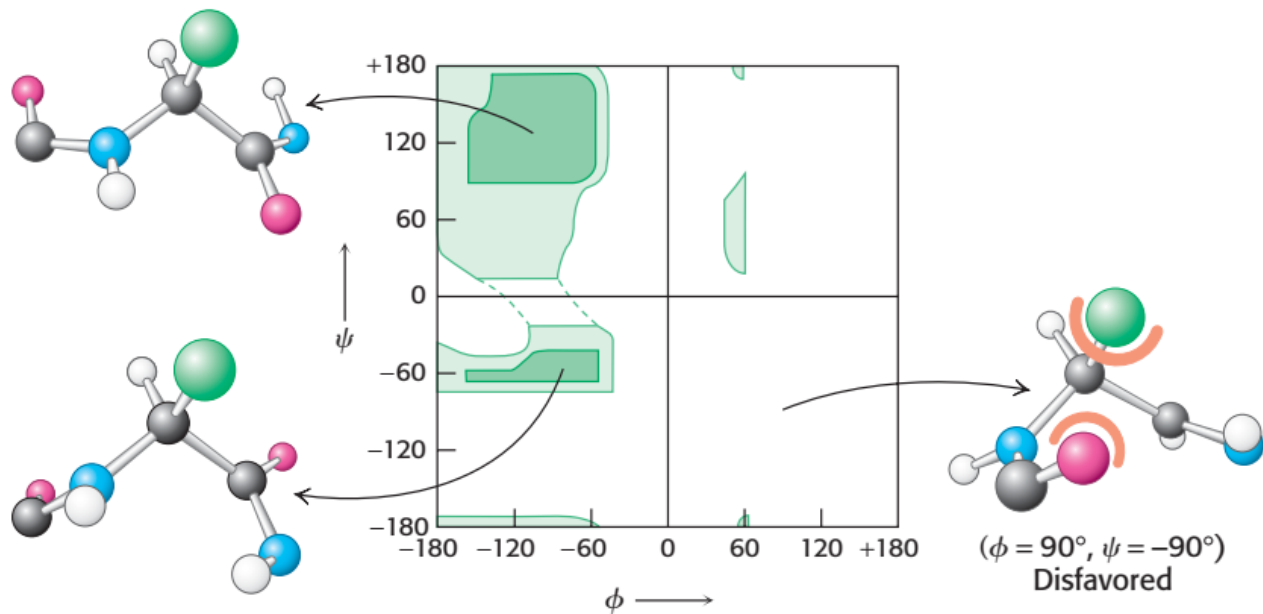
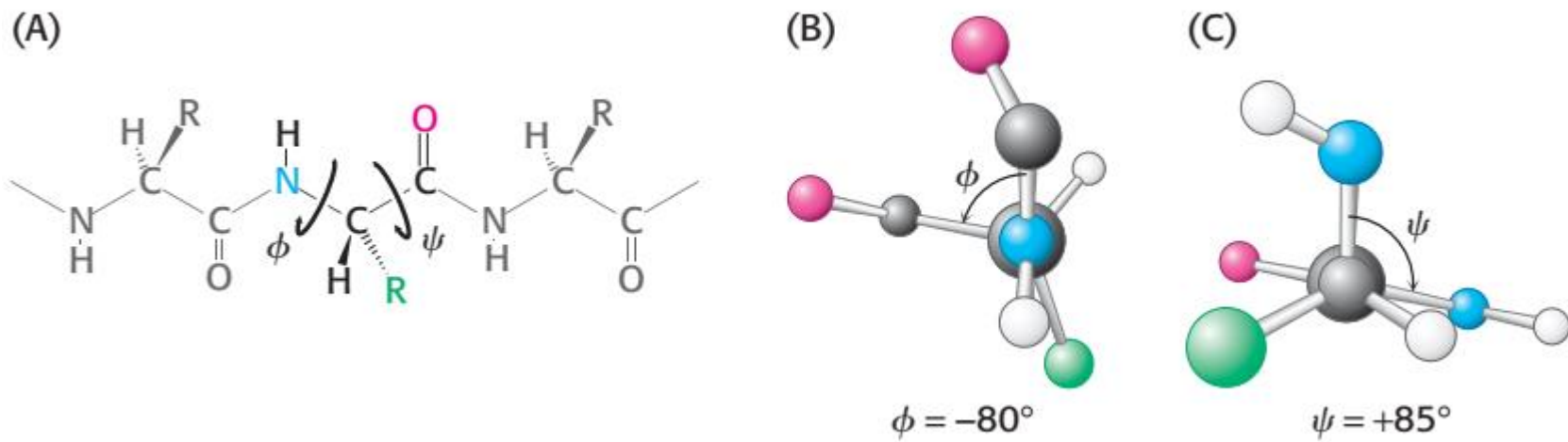


Figure 2.23 A Ramachandran diagram showing the values of ϕ and ψ . Not all ϕ and ψ values are possible without collisions between atoms. The most favorable regions are shown in dark green; borderline regions are shown in light green. The structure on the right is disfavored because of steric clashes.

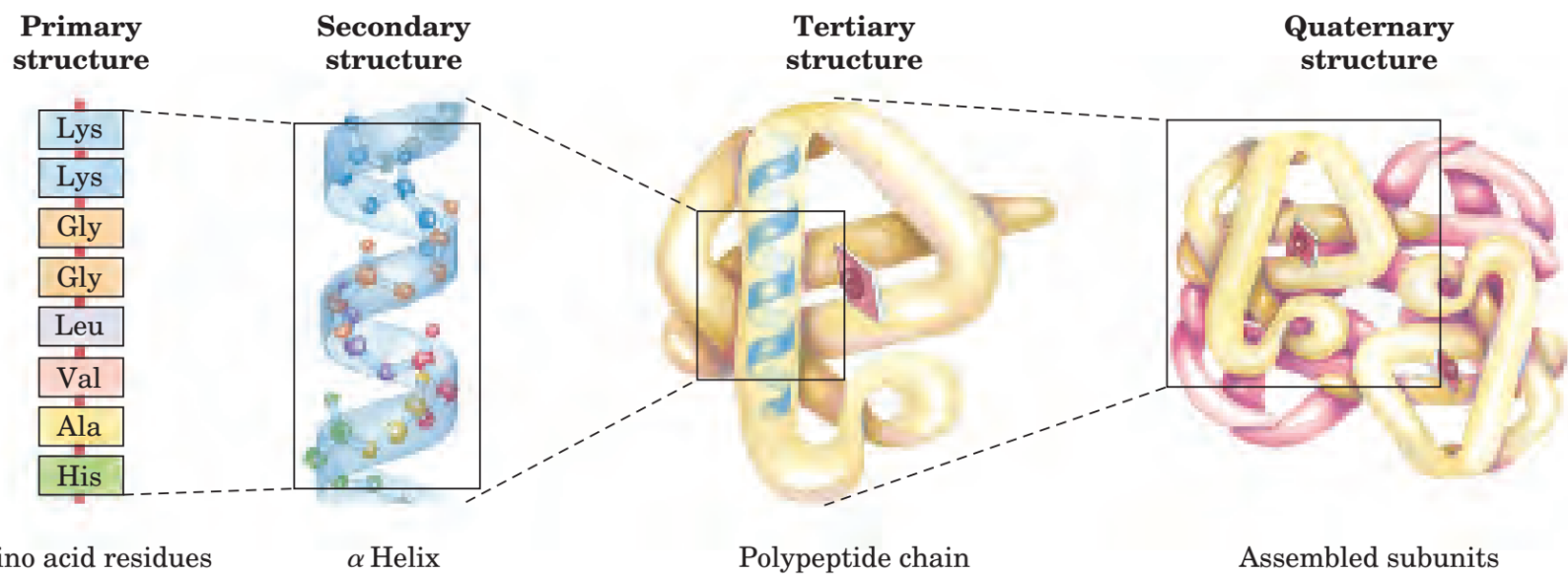
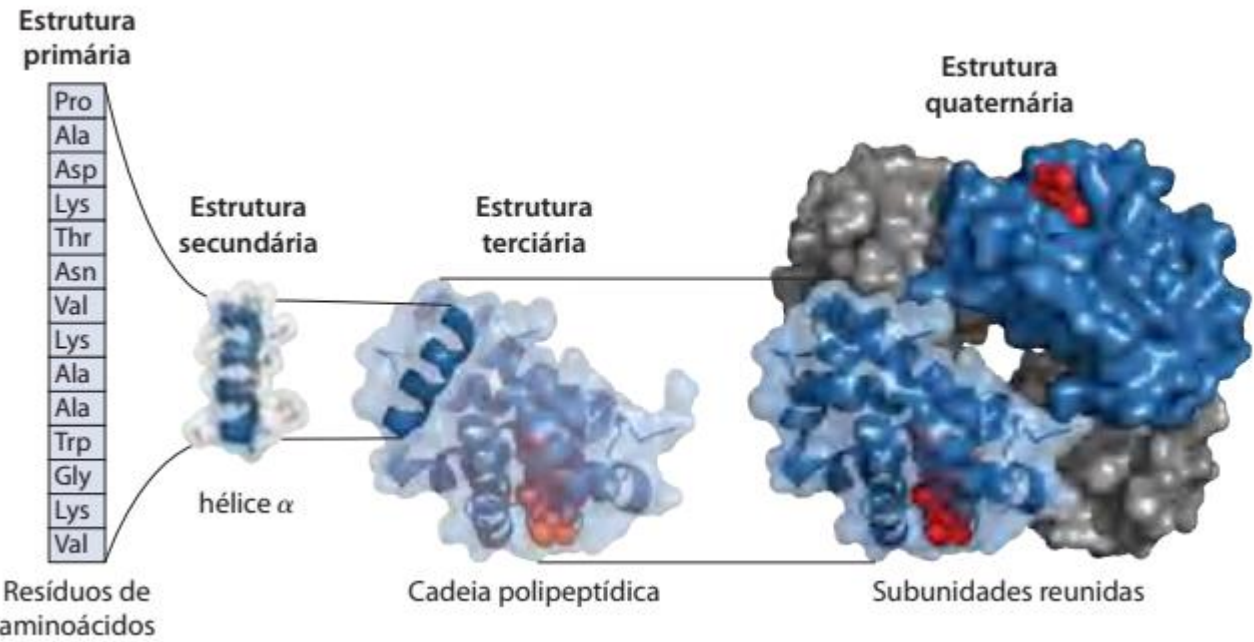
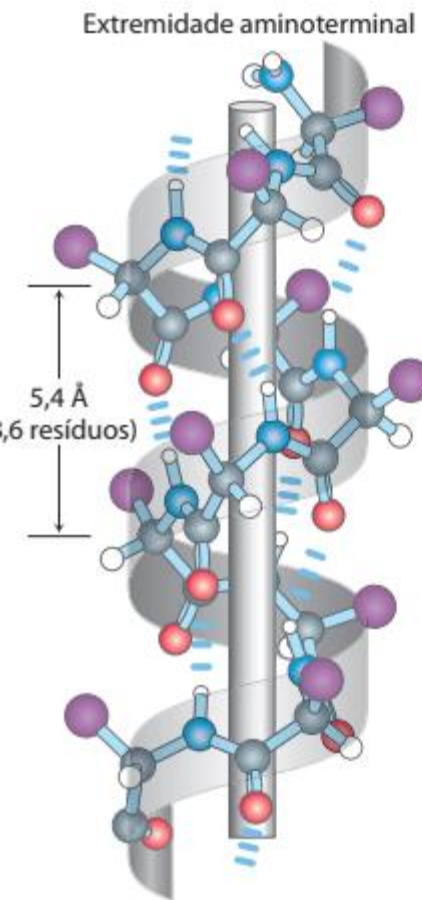


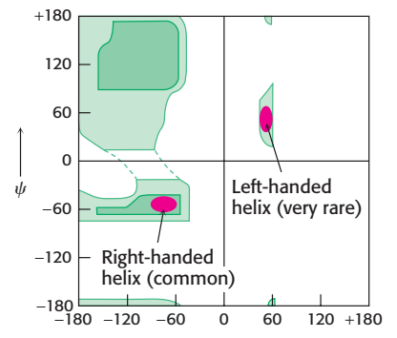
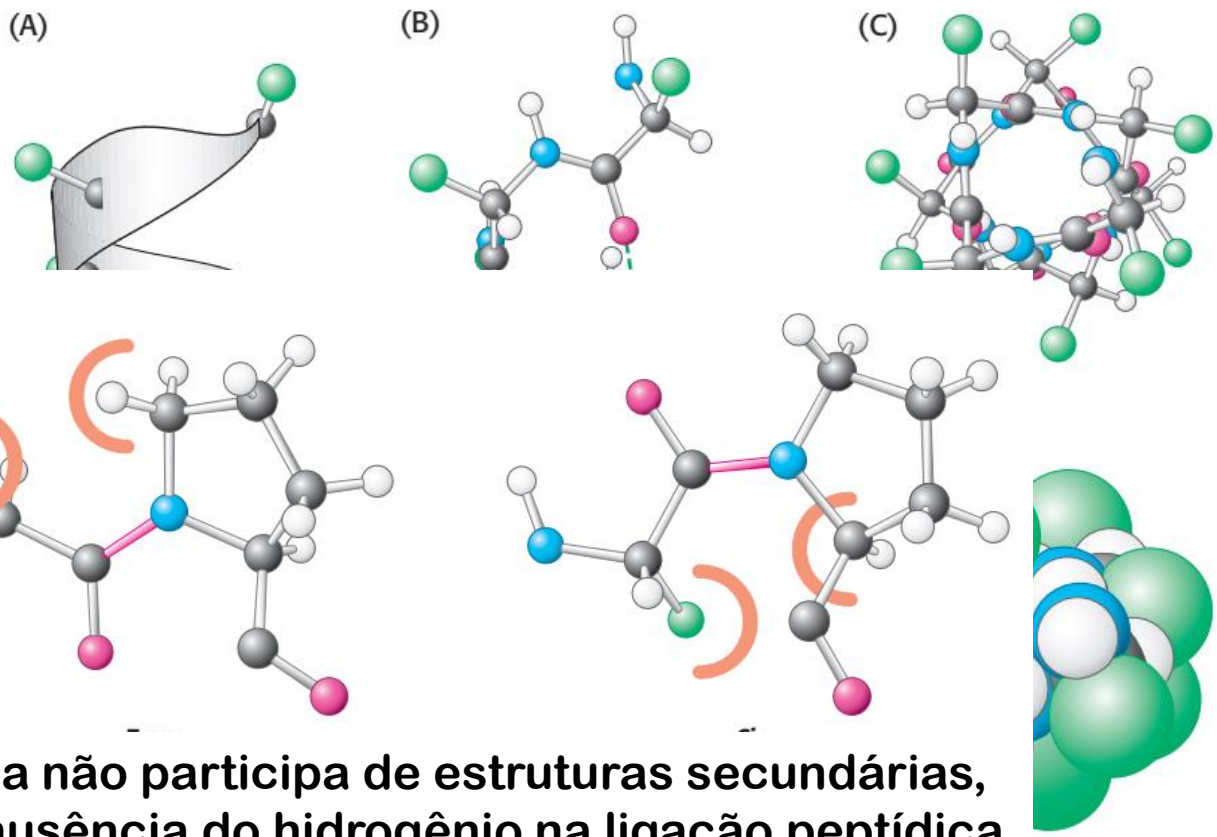
FIGURE 3-16 Levels of structure in proteins. The *primary structure* consists of a sequence of amino acids linked together by peptide bonds and includes any disulfide bonds. The resulting polypeptide can be

lix is a part of the *tertiary structure* of the folded polypeptide, which is itself one of the subunits that make up the *quaternary structure* of the multisubunit protein, in this case hemoglobin.

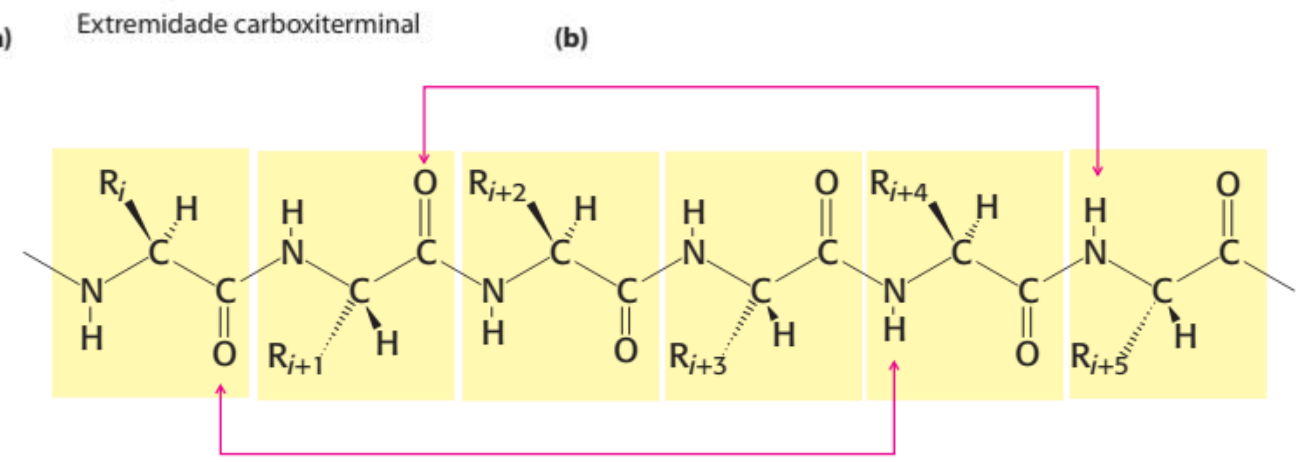


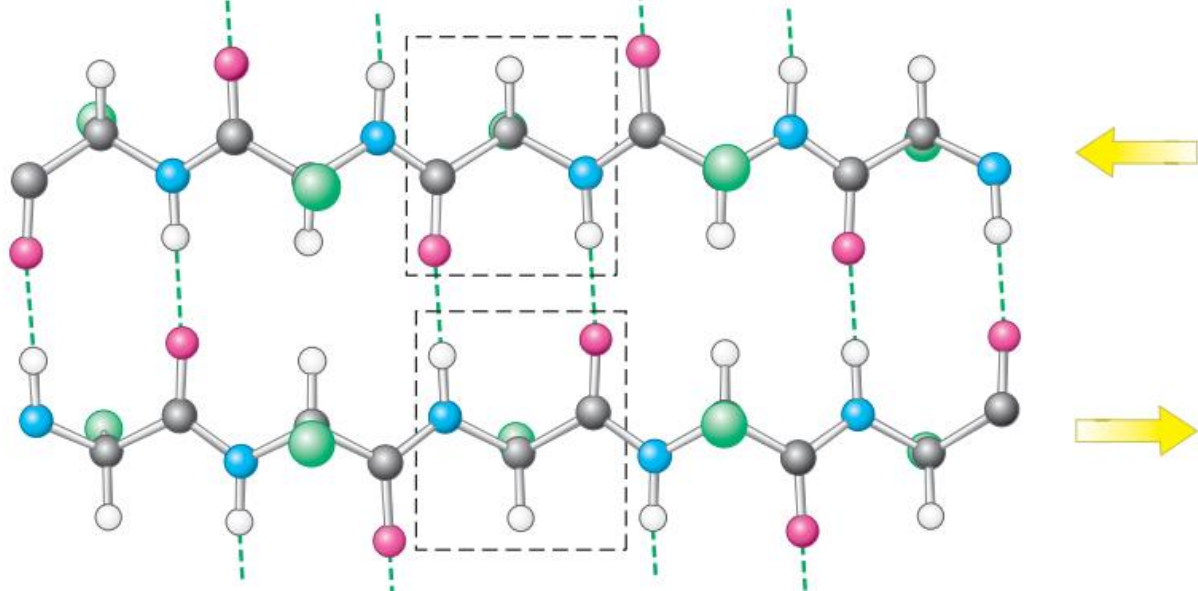


- Carbono
- Hidrogênio
- Oxigênio
- Nitrogênio
- Grupo R

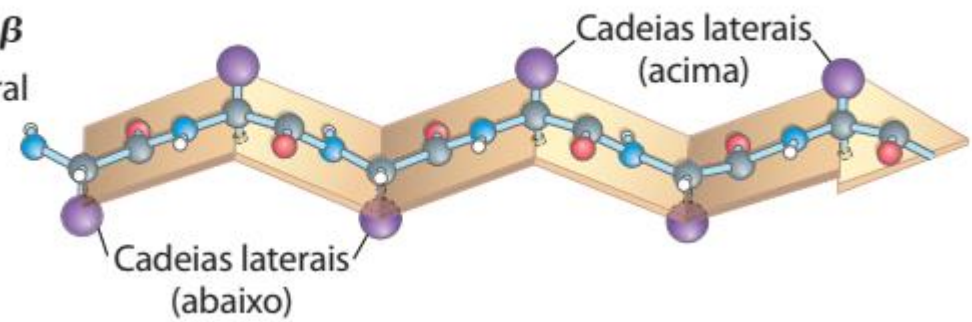


Prolina não participa de estruturas secundárias, pela ausência do hidrogênio na ligação peptídica



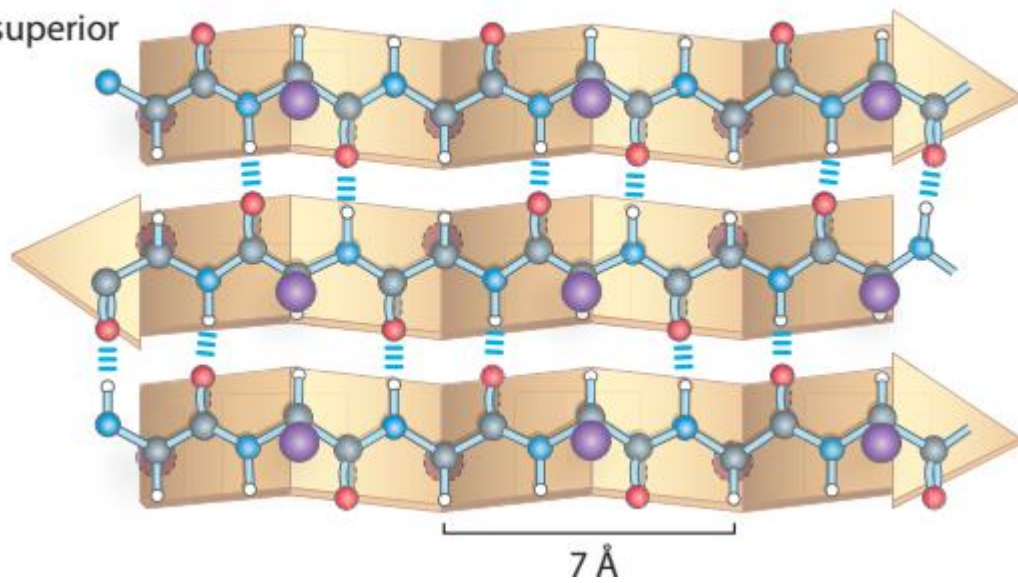


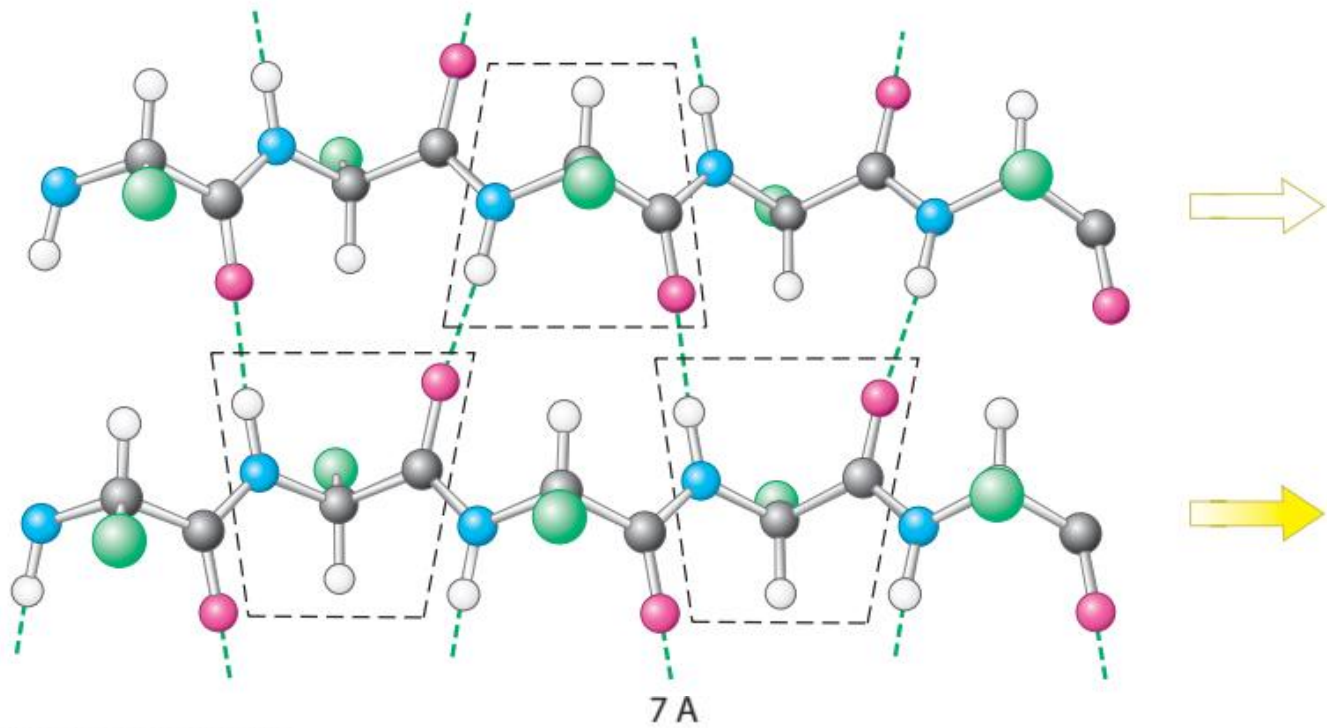
(a) Folha β
Visão lateral



(b) Folha β antiparalela

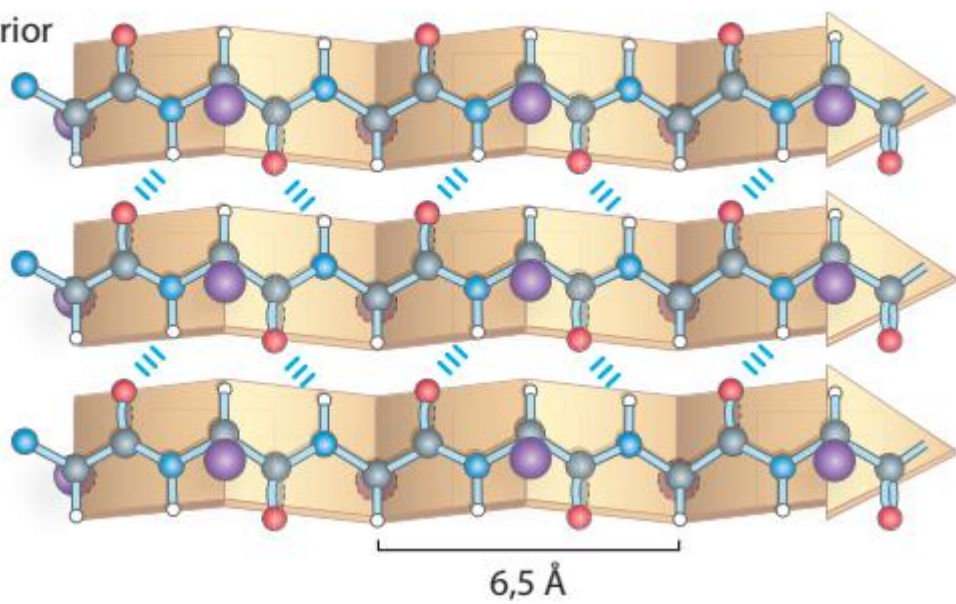
Visão superior



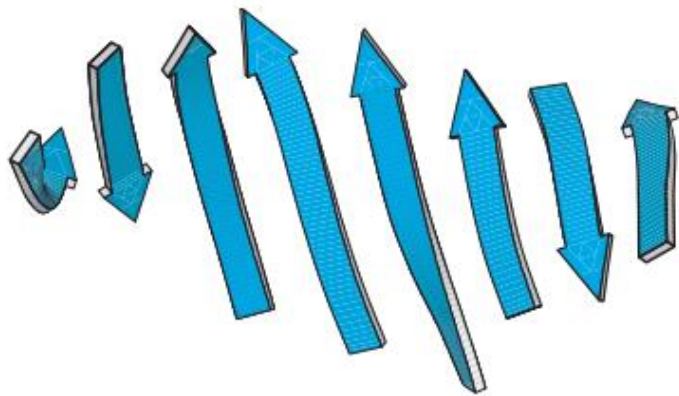


(c) Folha β paralela

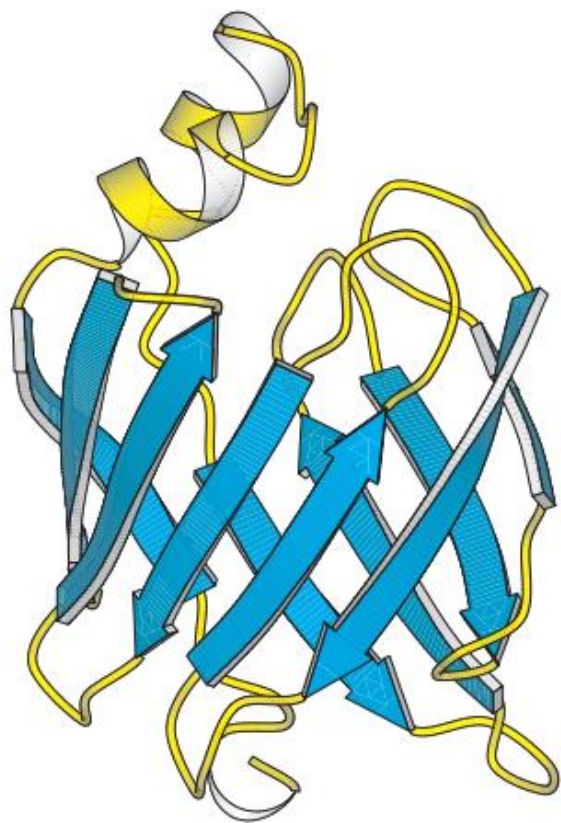
Visão superior



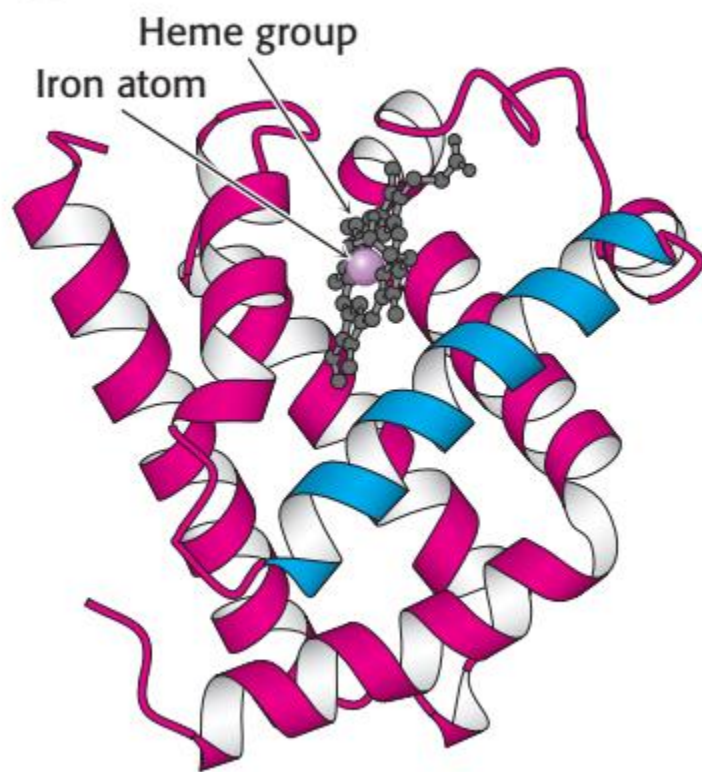
(A)

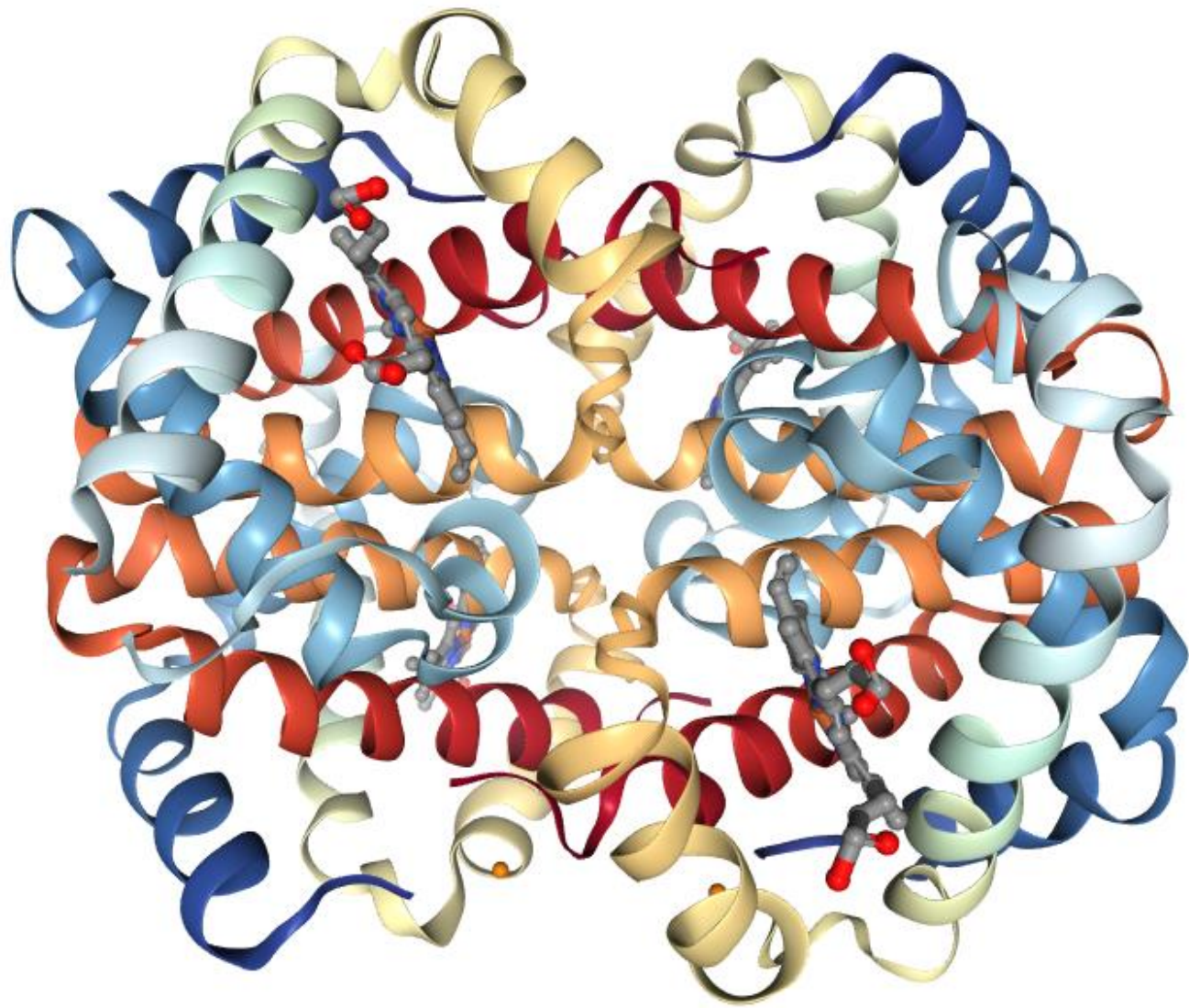


(B)



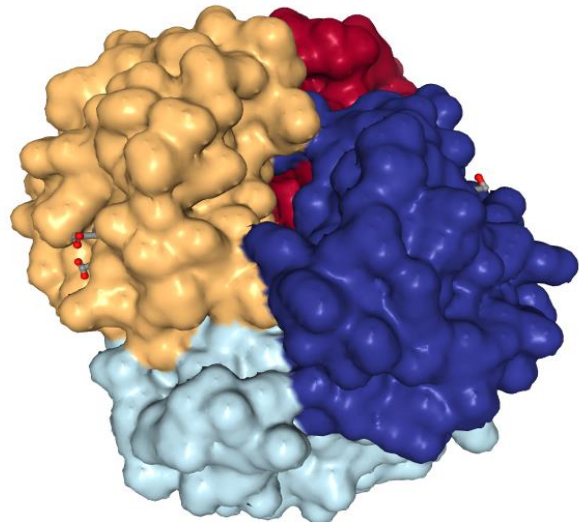
(A)



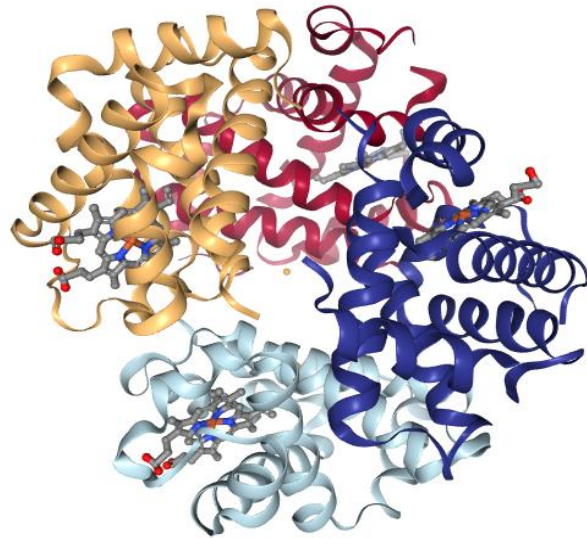


Estrutura da Hemoglobina. Acessada em <http://www.rcsb.org/>, 20/03/2018

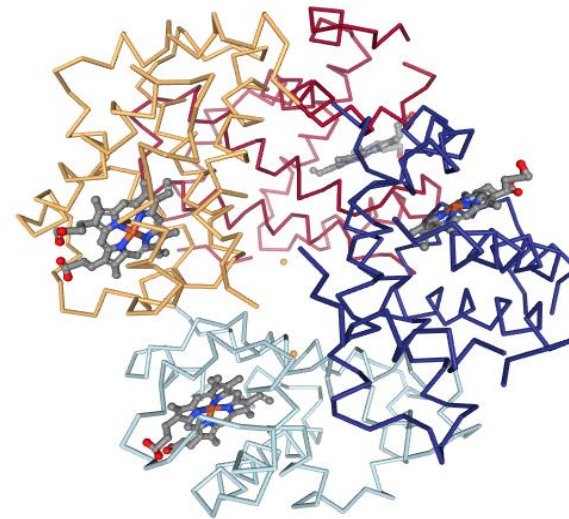
Tipos de representação da estrutura



Superfície



Desenho



Esqueleto peptídico

RCSB **PDB** 138878 Biological
PROTEIN DATA BANK Macromolecular Structures
Enabling Breakthroughs in
Research and Education

RCSB PDB-101 WORLDWIDE PDB PROTEIN DATA BANK EMDatabank Unified Data Resource for 2020 ndb NUCLEIC ACID DATABASE Worldwide Protein Data Bank Foundation

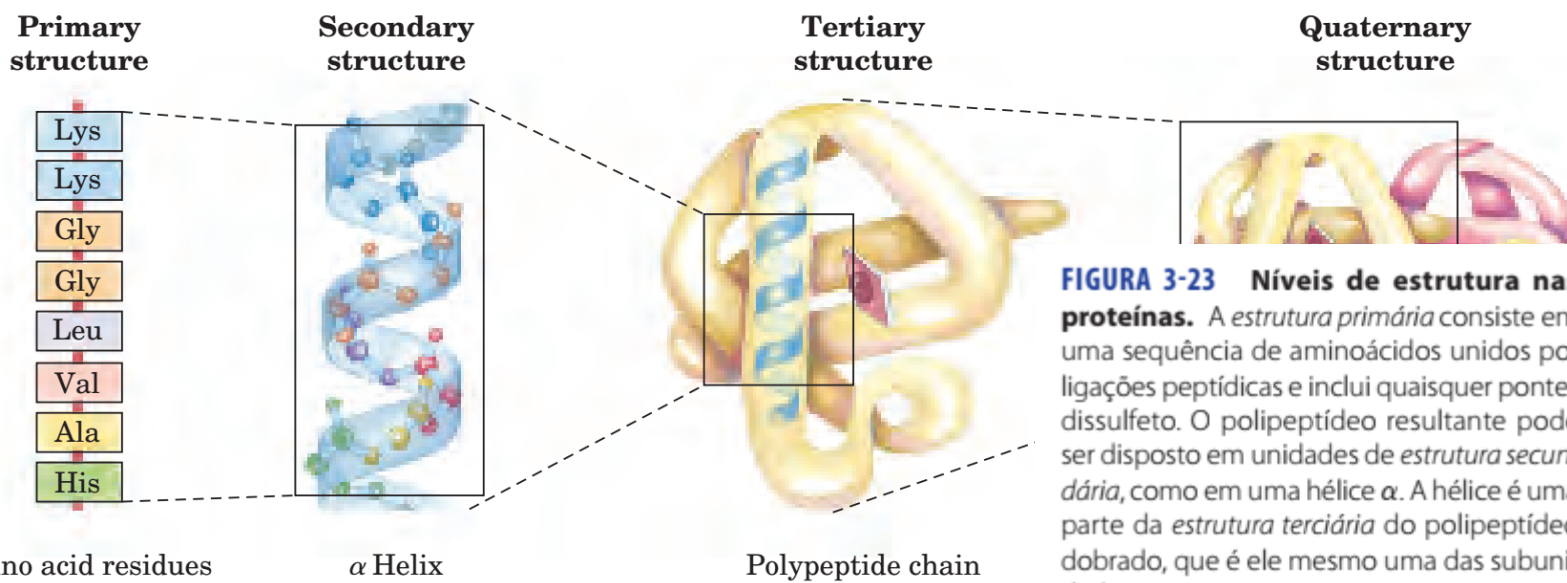


FIGURA 3-23 Níveis de estrutura nas proteínas. A *estrutura primária* consiste em uma sequência de aminoácidos unidos por ligações peptídicas e inclui quaisquer pontes dissulfeto. O polipeptídeo resultante pode ser disposto em unidades de *estrutura secundária*, como em uma hélice α . A hélice é uma parte da *estrutura terciária* do polipeptídeo dobrado, que é ele mesmo uma das subunidades que compõem a *estrutura quaternária* da proteína multissubunidade, nesse caso a hemoglobina.

Amino acid residues

α Helix

Polypeptide chain

FIGURE 3-16 Levels of structure in proteins. The *primary structure* consists of a sequence of amino acids linked together by peptide bonds and includes any disulfide bonds. The resulting polypeptide can be

lix is a part is itself one the multisubunit protein, in this case hemoglobin.

ptide, which structure of

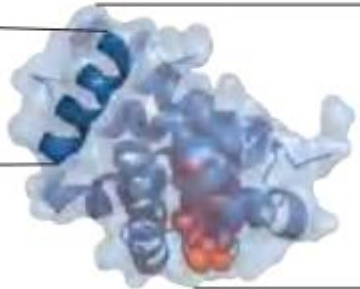
Estrutura primária

- Pro
- Ala
- Asp
- Lys
- Thr
- Asn
- Val
- Lys
- Ala
- Ala
- Trp
- Gly
- Lys
- Val

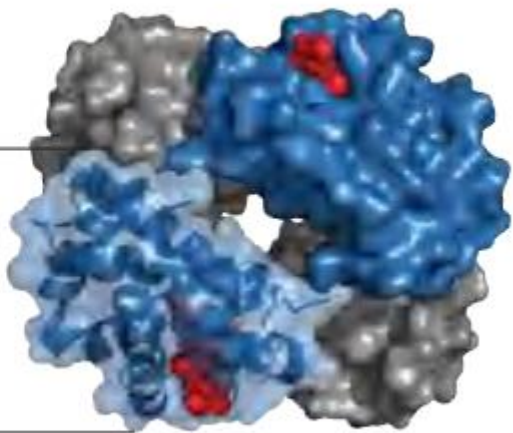
Estrutura secundária



Estrutura terciária



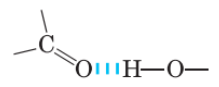
Estrutura quaternária



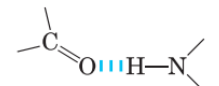
Resíduos de aminoácidos

As pontes dissulfeto (caso ocorram), juntamente com as interações abaixo, são as responsáveis pela manutenção da estrutura da proteína.

Ligações de hidrogênio
Entre grupos neutros



Entre ligações peptídicas



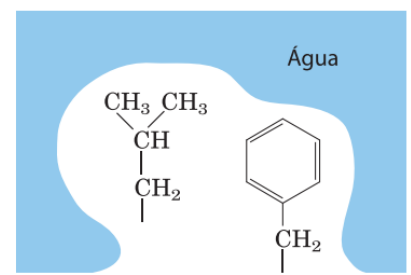
Interações iônicas
Atração



Repulsão

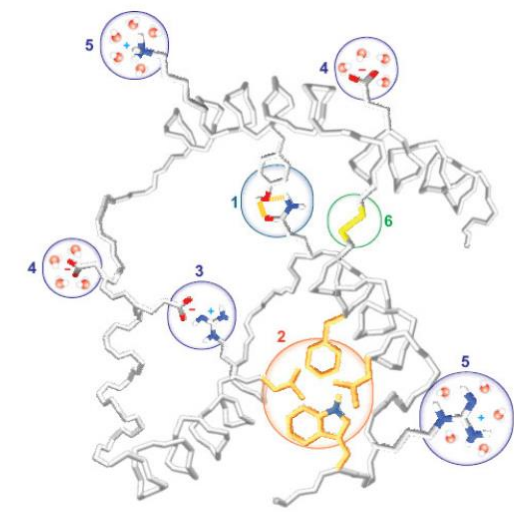


Interações hidrofóbicas

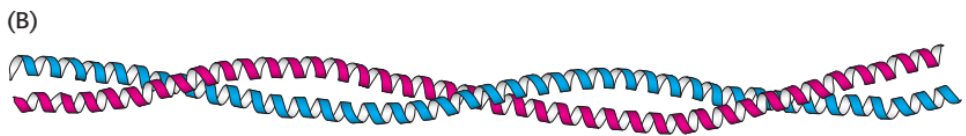
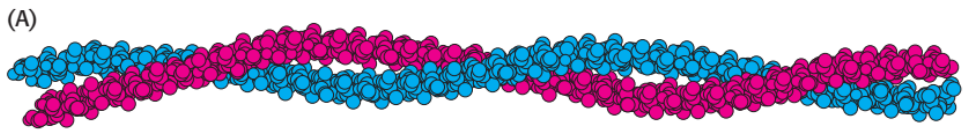


Interações de van der Waals

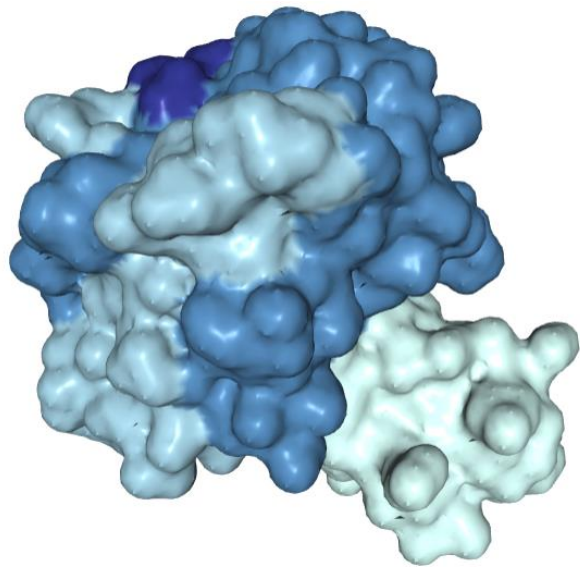
Dois átomos quaisquer bem próximos um do outro



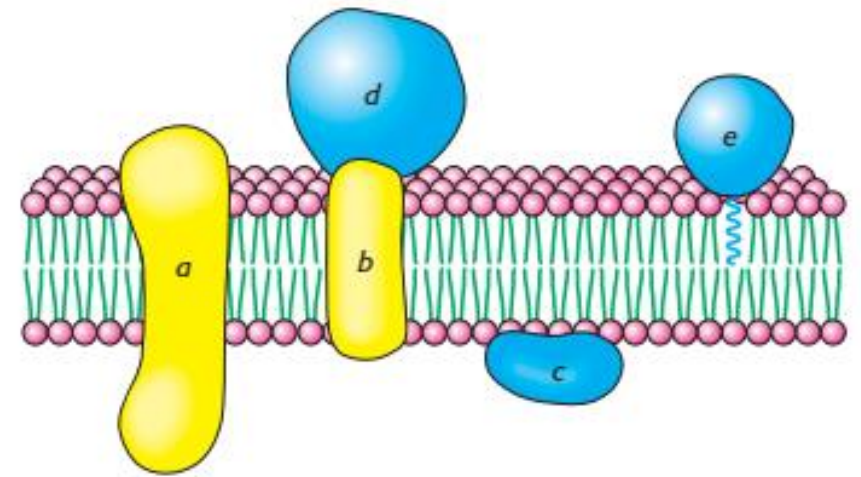
Ligações de hidrogênio	Interações hidrofóbicas	Ligações iônicas	Ponte dissulfeto
1 	2 	3 	6
4 		5 	



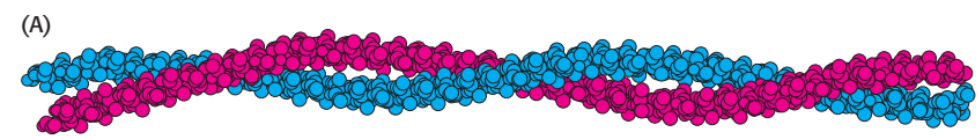
Proteínas fibrosas



Proteínas globulares



Proteínas de membrana



Hélice α de queratina



Duas cadeias em
espiral enrolada



Protofilamento

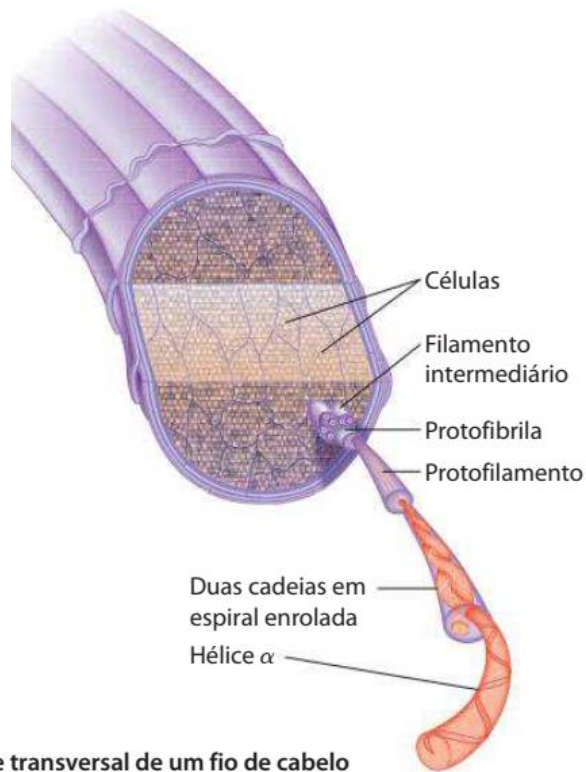
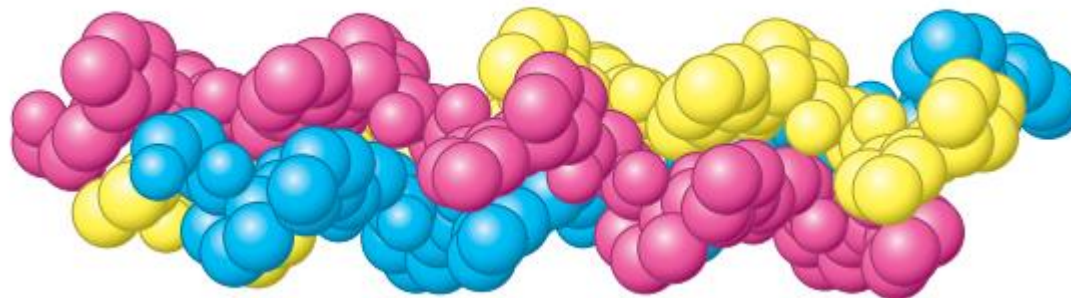


20-30 Å

Protofibrila



(A)



(b) Corte transversal de um fio de cabelo

**Queratina,
exemplo de
proteína fibrosa**

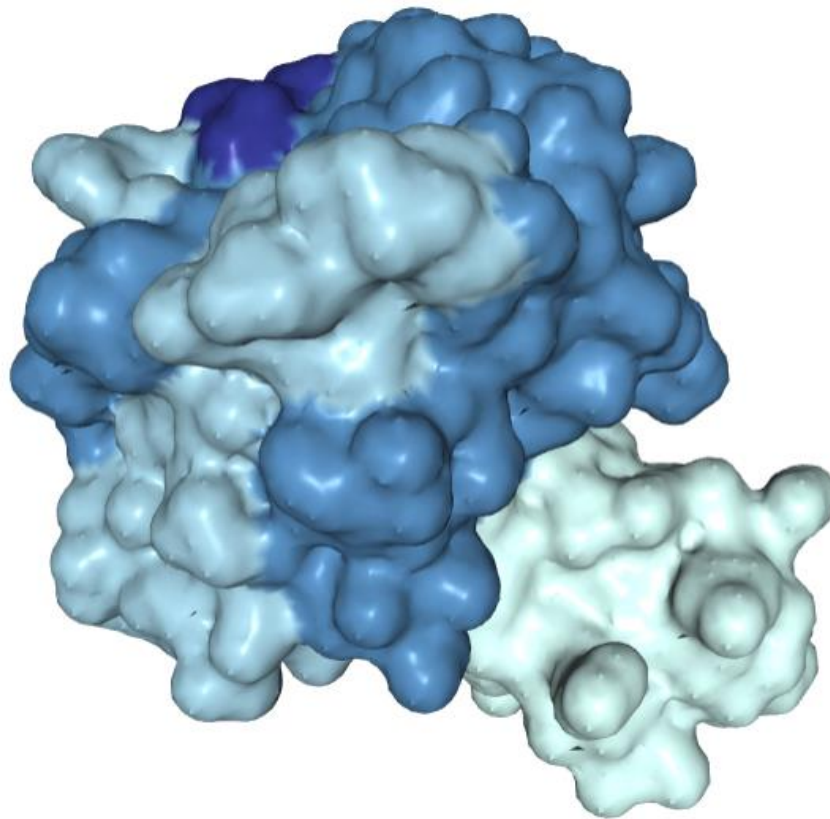
Estrutura Terciária

Proteínas Globulares:

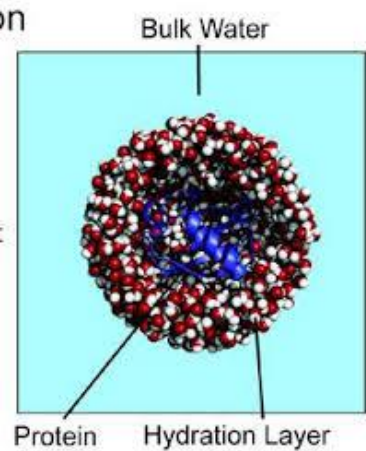
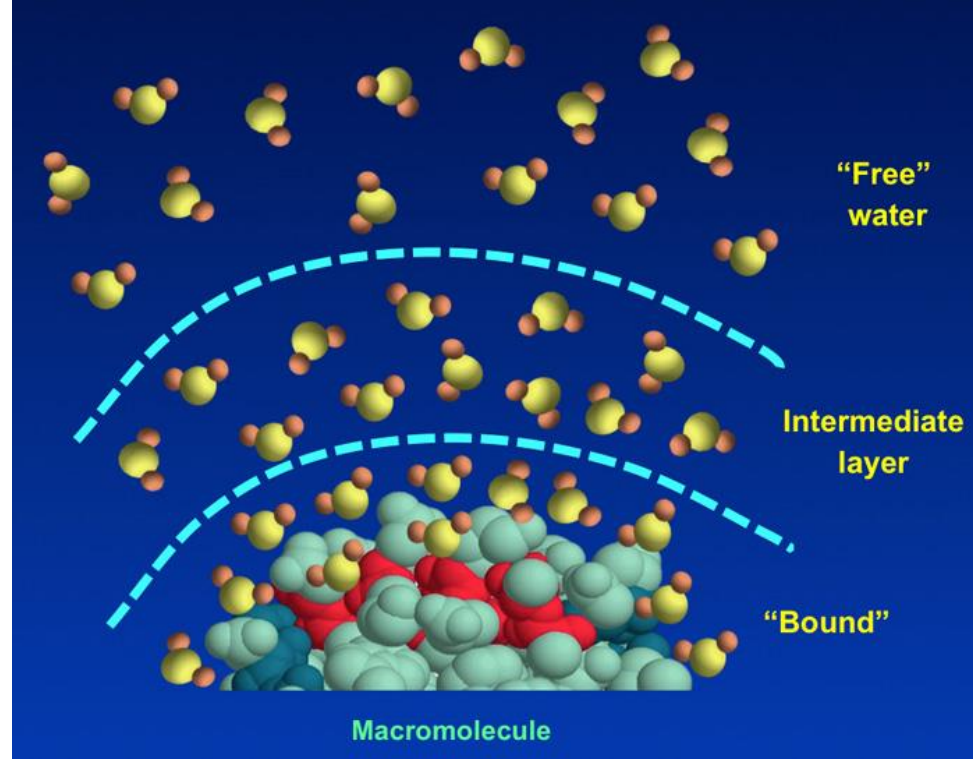
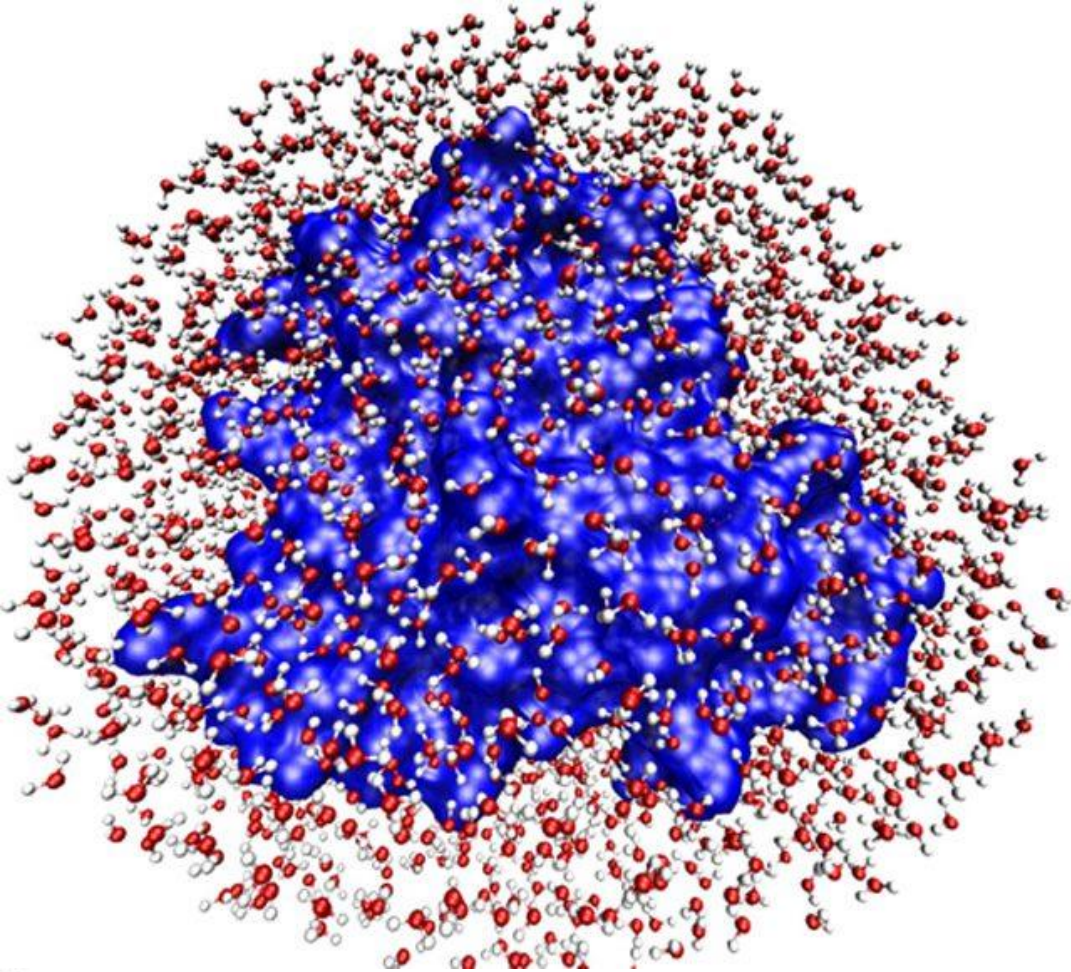
*Interior hidrofóbico e exterior hidrofílico

*Solúveis em água

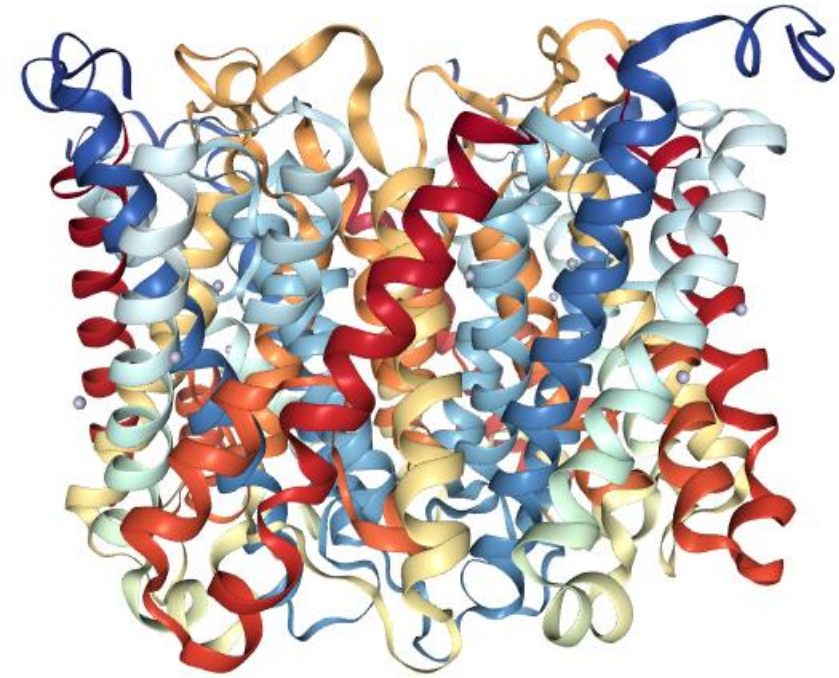
*Associadas às mais variadas funções:
enzimas, transporte, imunoglobulinas



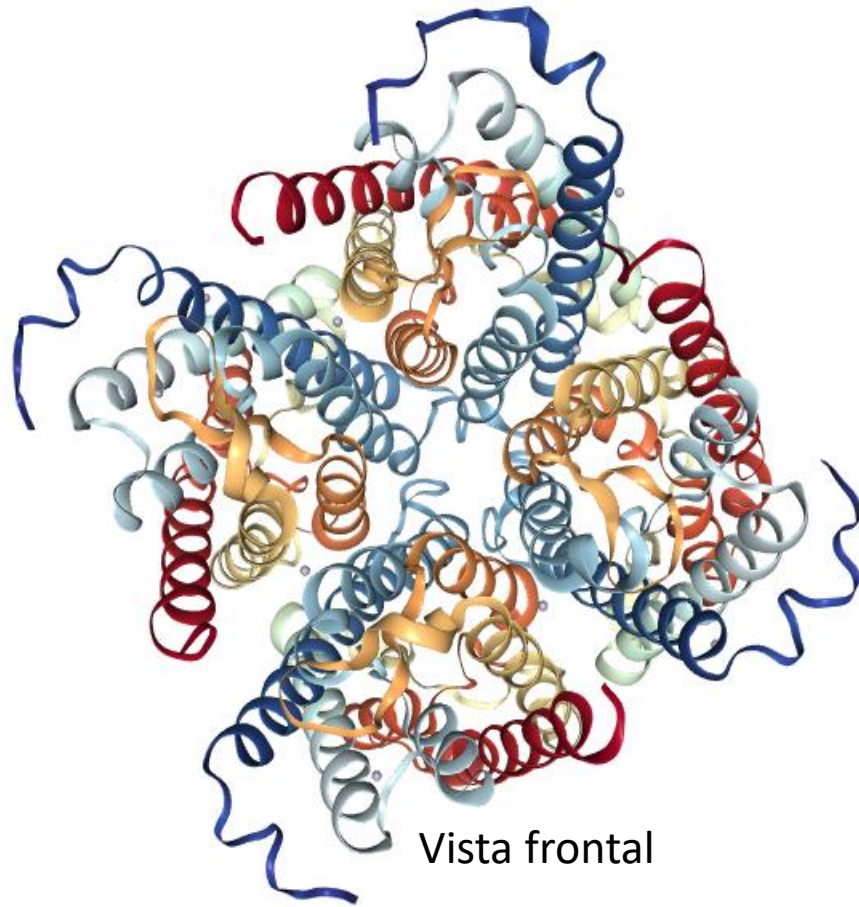
Estrutura da Quimotripsina. Acessada em <http://www.rcsb.org/>



Proteínas de Membrana – Canais/transportadores

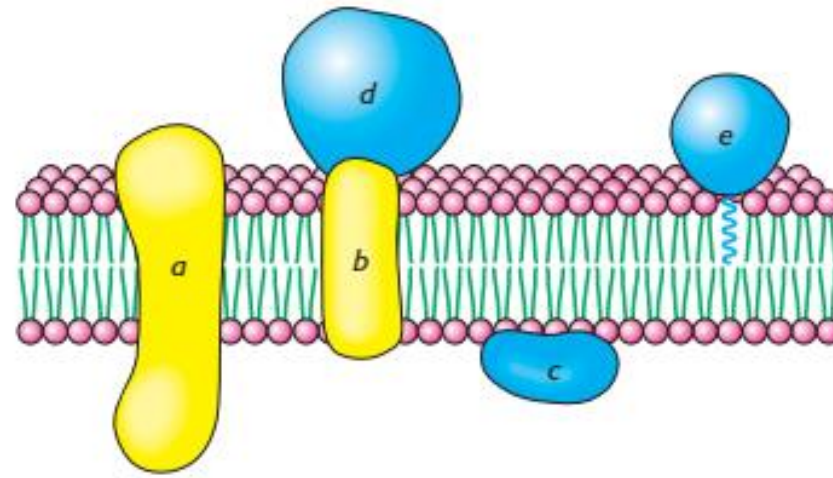
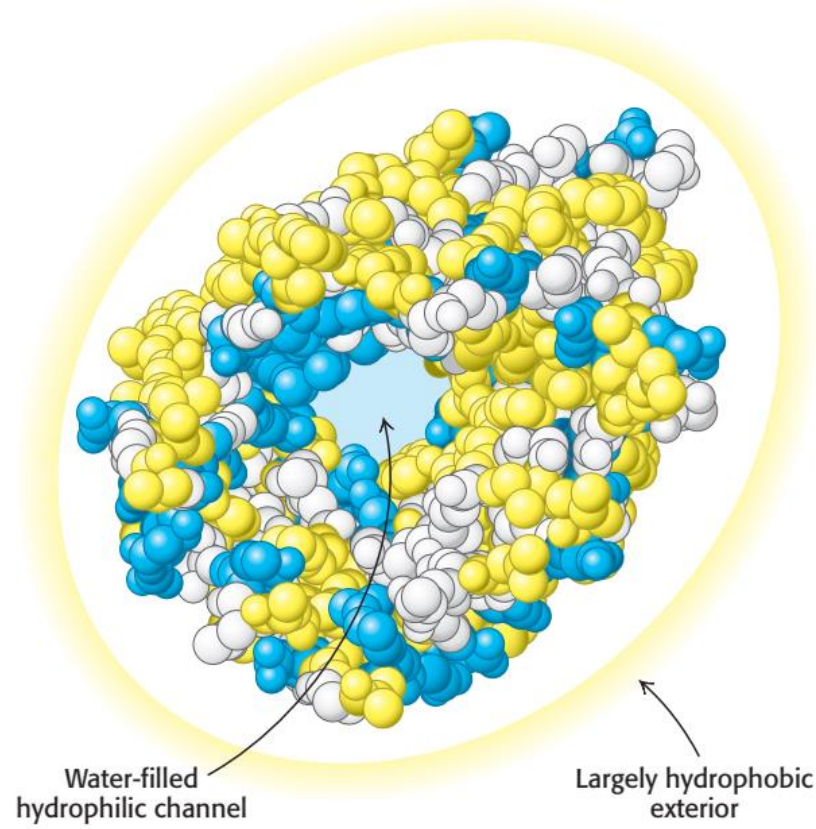


Vista lateral



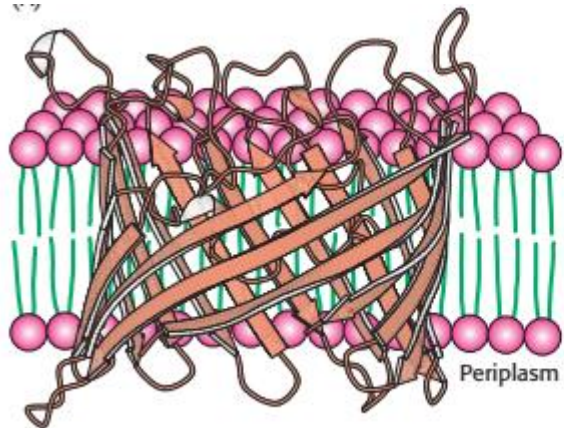
Vista frontal

Aquaporina de espinafre.



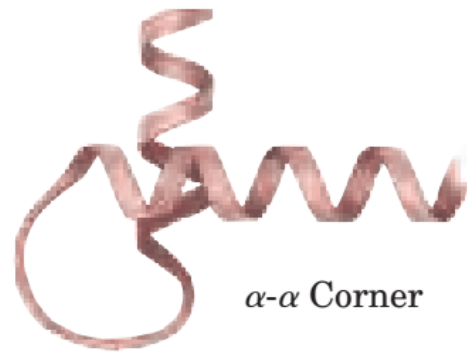
Proteínas de membrana

Figure 2.45 "Inside out" amino acid distribution in porin. The outside of porin (which





(a) β - α - β Loop



α - α Corner

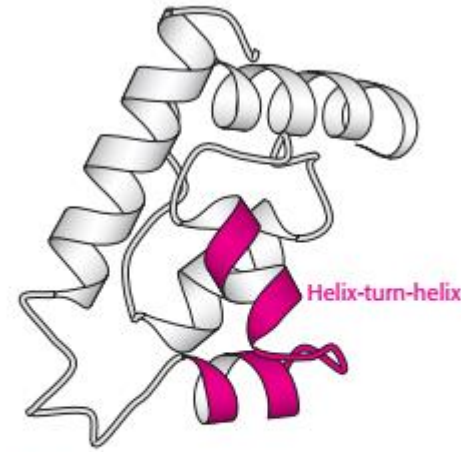


Figure 2.46 The helix-turn-helix motif, a supersecondary structural element. Helix-turn-helix motifs are found in many DNA-binding proteins. [Drawn from 1LMB.pdb.]



(b) Typical connections in an all- β motif



Crossover connection (not observed)



(c) Right-handed connection between β strands



Left-handed connection between β strands (very rare)
Alguns exemplos de motivos

Domínios

- Unidades estruturais estáveis em um polipeptídeo
- Mantêm a estrutura (e função) mesmo após separação da cadeia principal

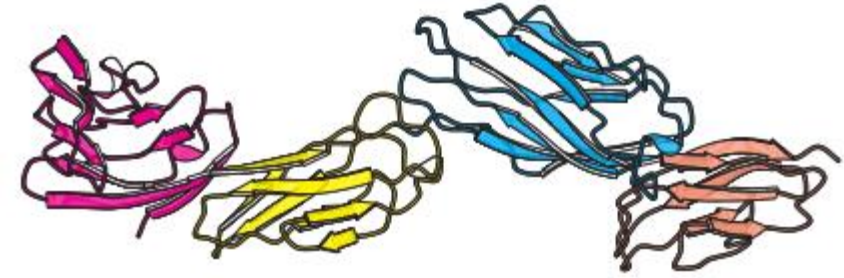


Figure 2.47 Protein domains. The cell-surface protein CD4 consists of four similar domains. [Drawn from 1WIO.pdb.]

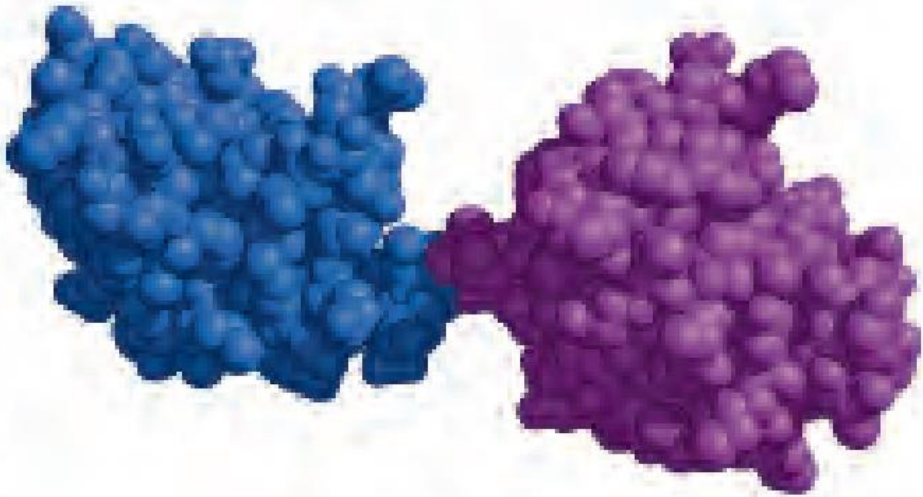
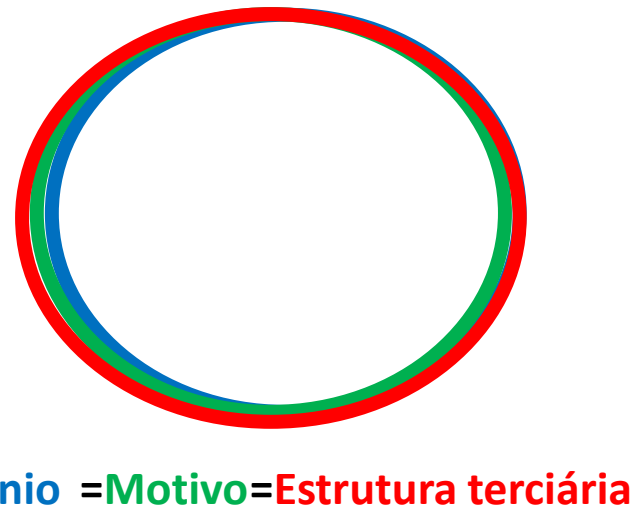
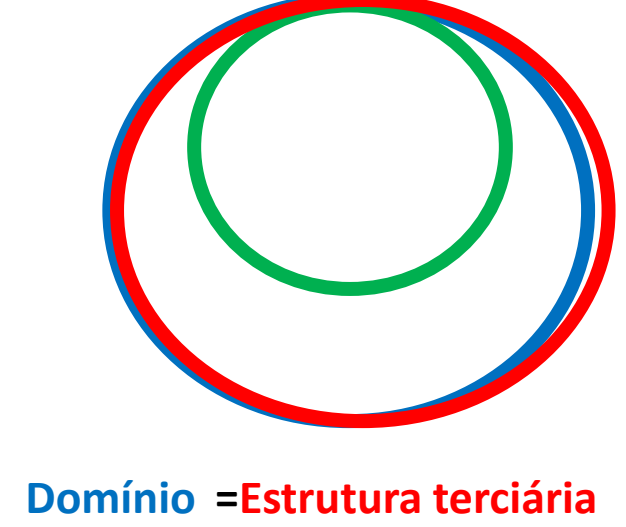
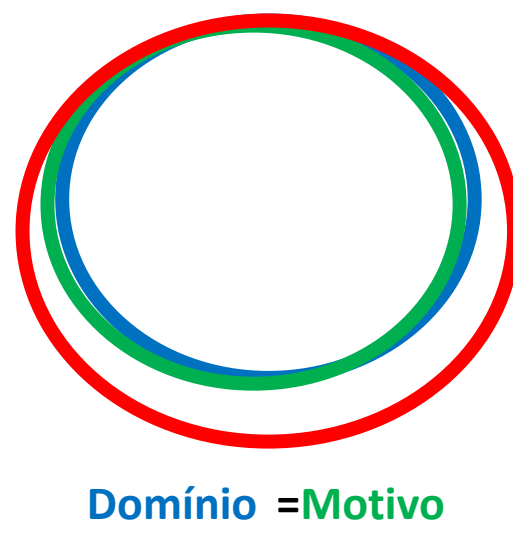
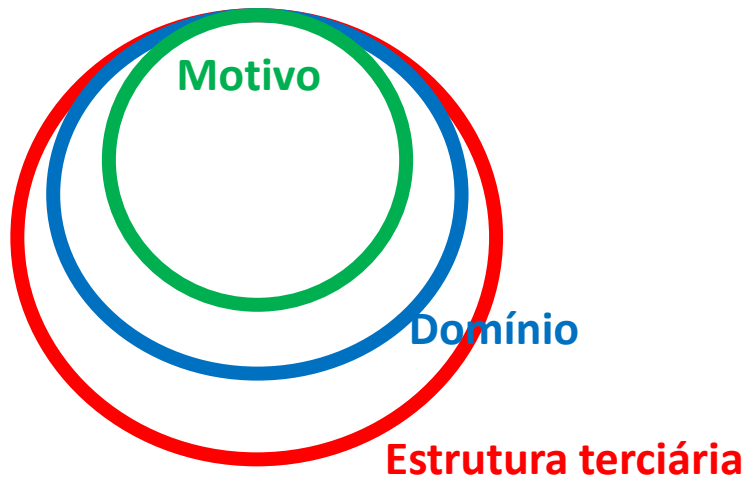
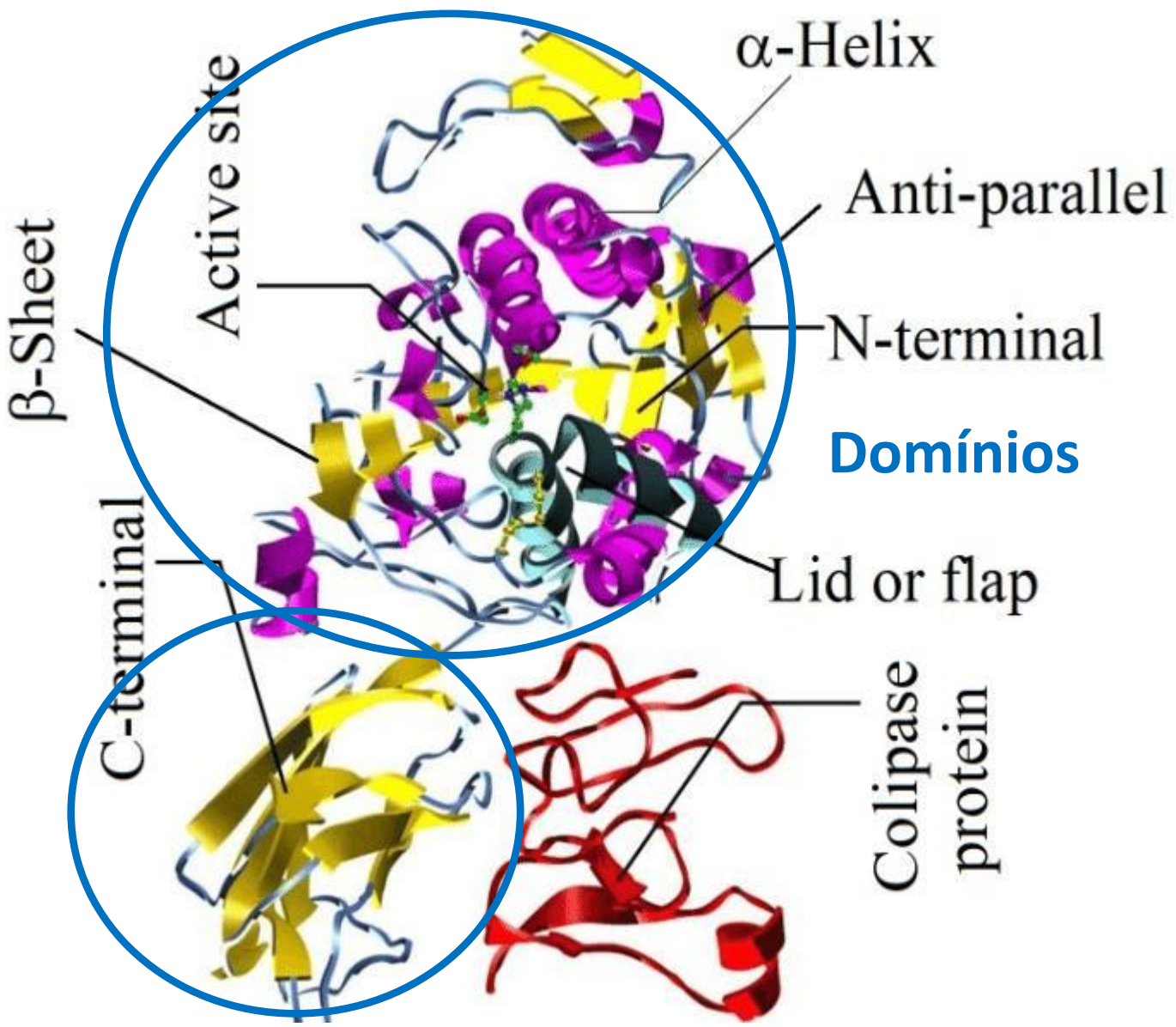


FIGURE 4-19 Structural domains in the polypeptide troponin C. (PDB ID 4TNC) This calcium-binding protein associated with muscle has separate calcium-binding domains, indicated in blue and purple.



Exemplo- Lipase humana



Estrutura Quaternária

- Interação entre cadeias polipeptídicas distintas
- Não-covalente (hidrofóbica, pontes de hidrogênio, interação iônica, van der Waals) ou covalente (Ponte dissulfeto)
- Oligômeros e multímeros- monômero é o nome que se dá a subunidade

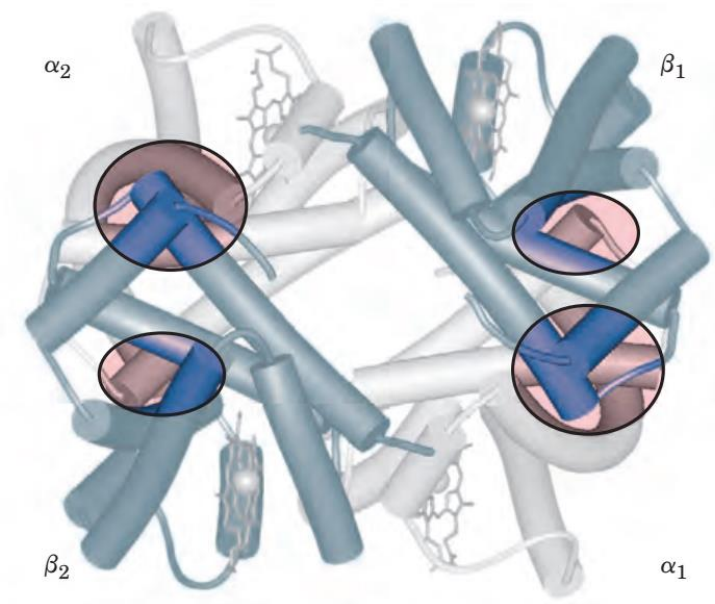


FIGURE 5-8 Dominant interactions between hemoglobin subunits. In this representation, α subunits are light and β subunits are dark. The strongest subunit interactions (highlighted) occur between unlike subunits. When oxygen binds, the $\alpha_1\beta_1$ contact changes little, but there is a large change at the $\alpha_1\beta_2$ contact, with several ion pairs broken (PDB ID 1HGA).

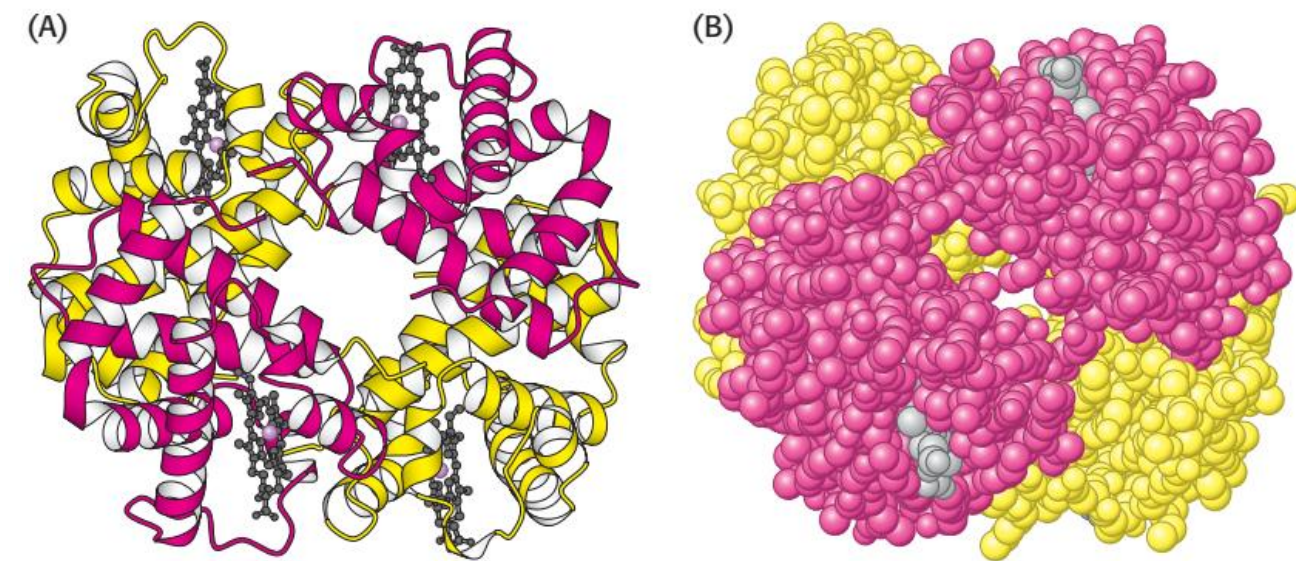
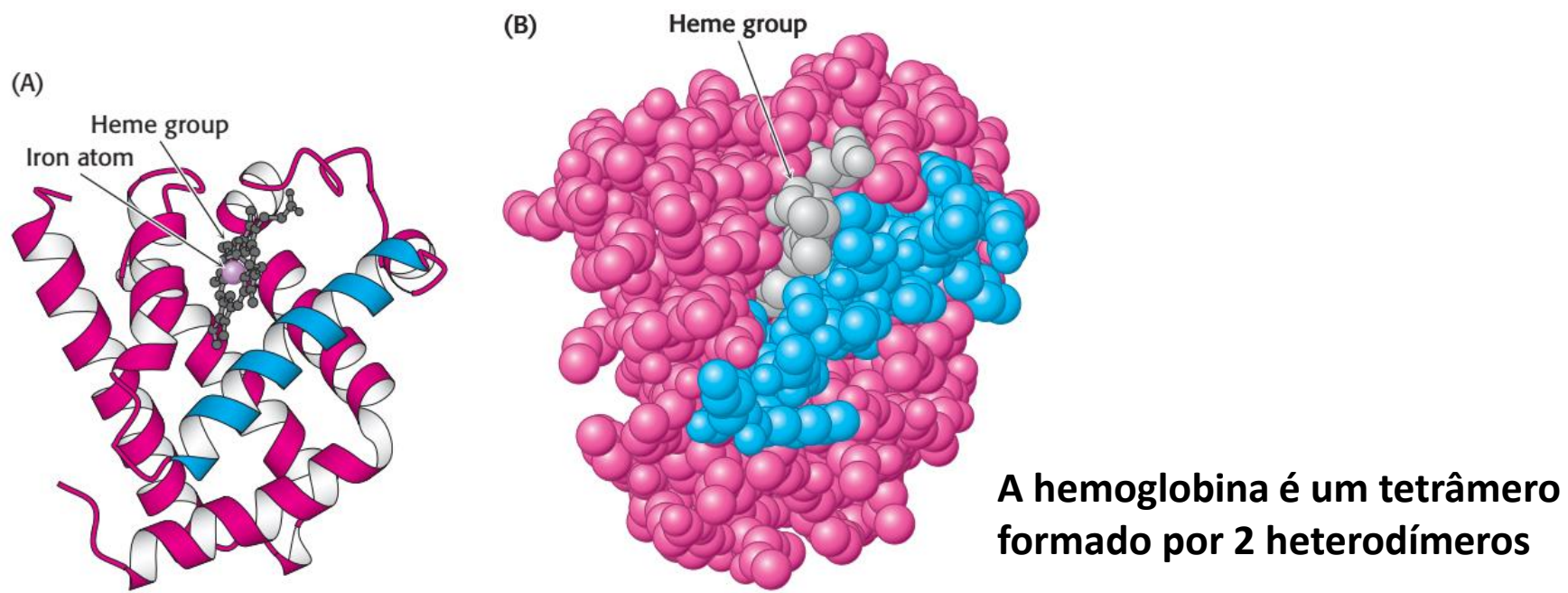


Figure 2.49 The $\alpha_2\beta_2$ tetramer of human hemoglobin. The structure of the two identical

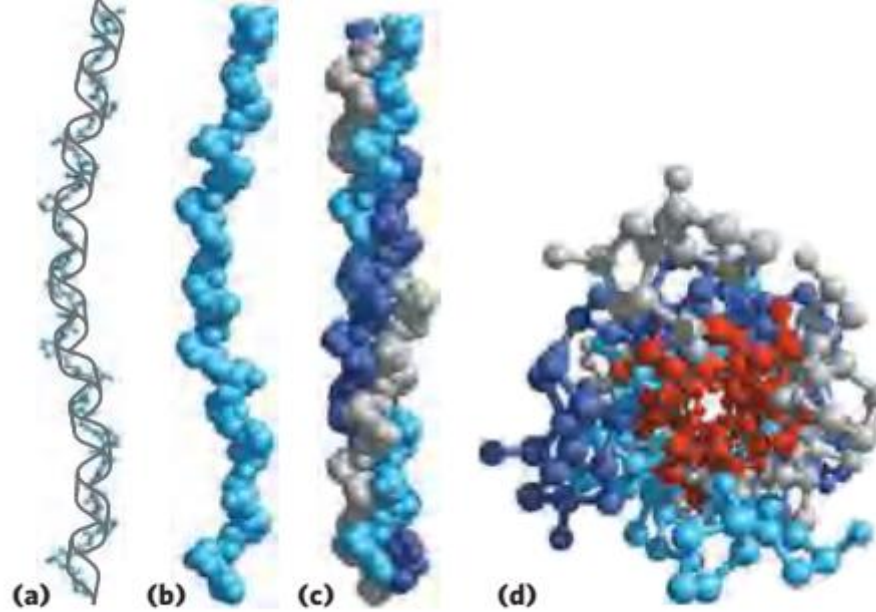


FIGURA 4-12 Estrutura do colágeno. (Obtida do PDB ID 1CGD.) (a) A c

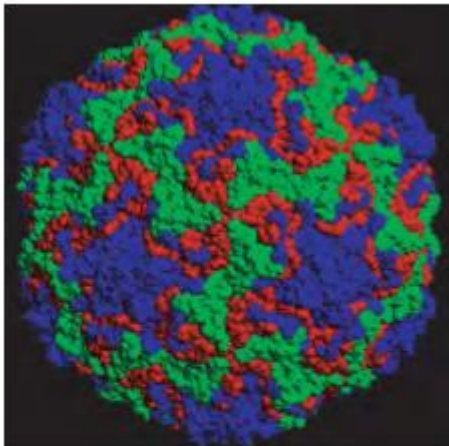
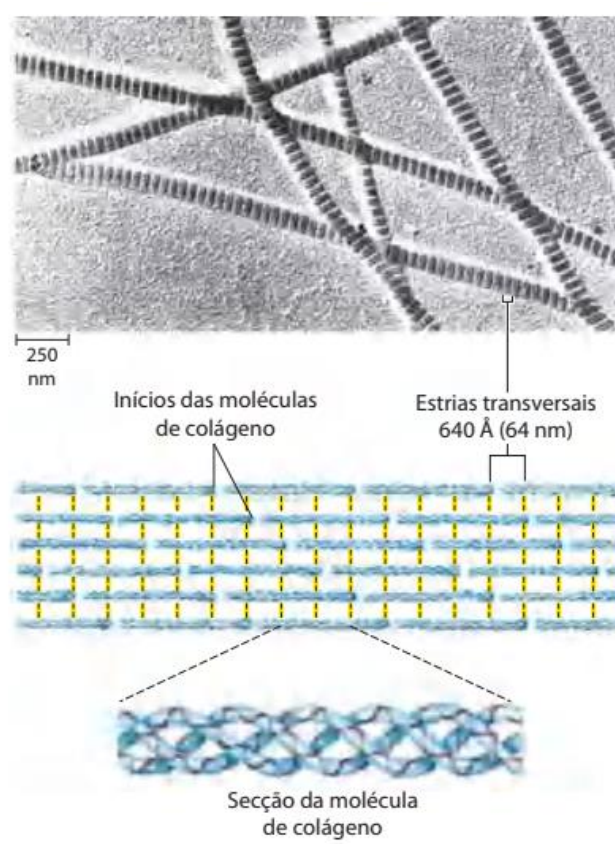


Figure 2.50 Complex quaternary structure. The coat of human rhinovirus, the cause of the common cold, comprises 60 copies of each of four subunits. The three most prominent subunits are shown as different colors.