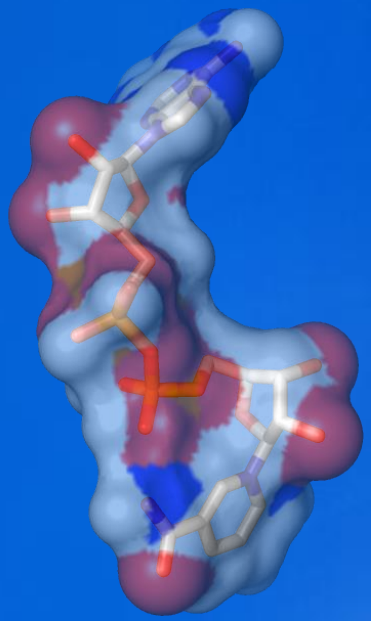
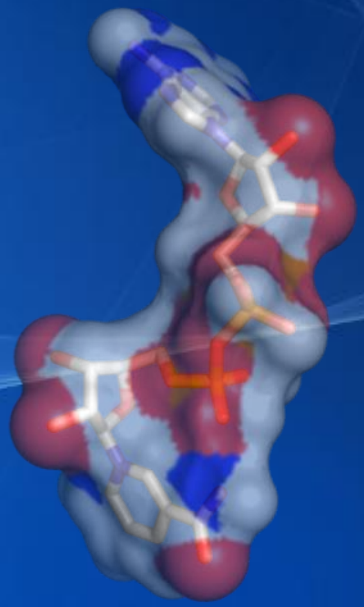
FFI0750 – Biologia Molecular Estrutural





Prof. Rafael V. C. Guido

rvcguido@ifsc.usp.br

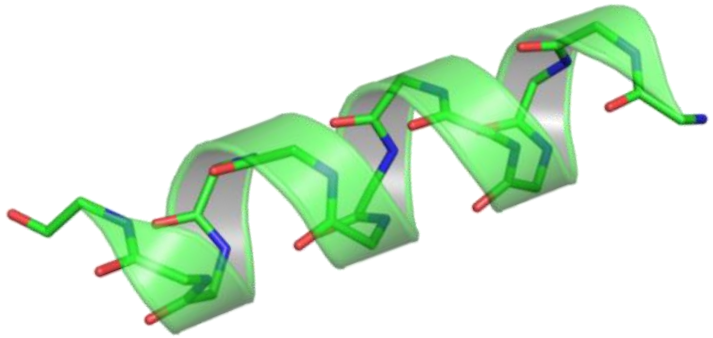
Aula 05

Bacharelado em Ciências Físicas e Biomoleculares

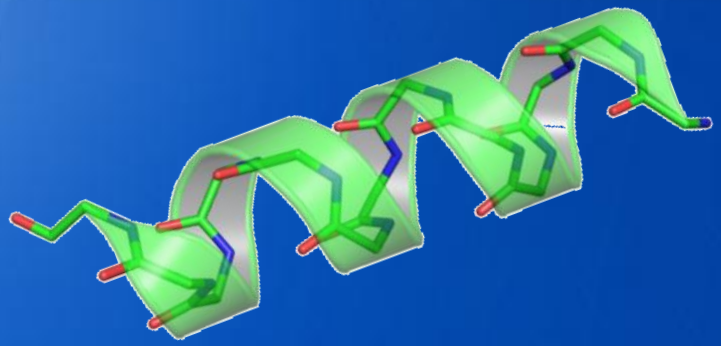
Instituto de Física de São Carlos - USP

Objetivos

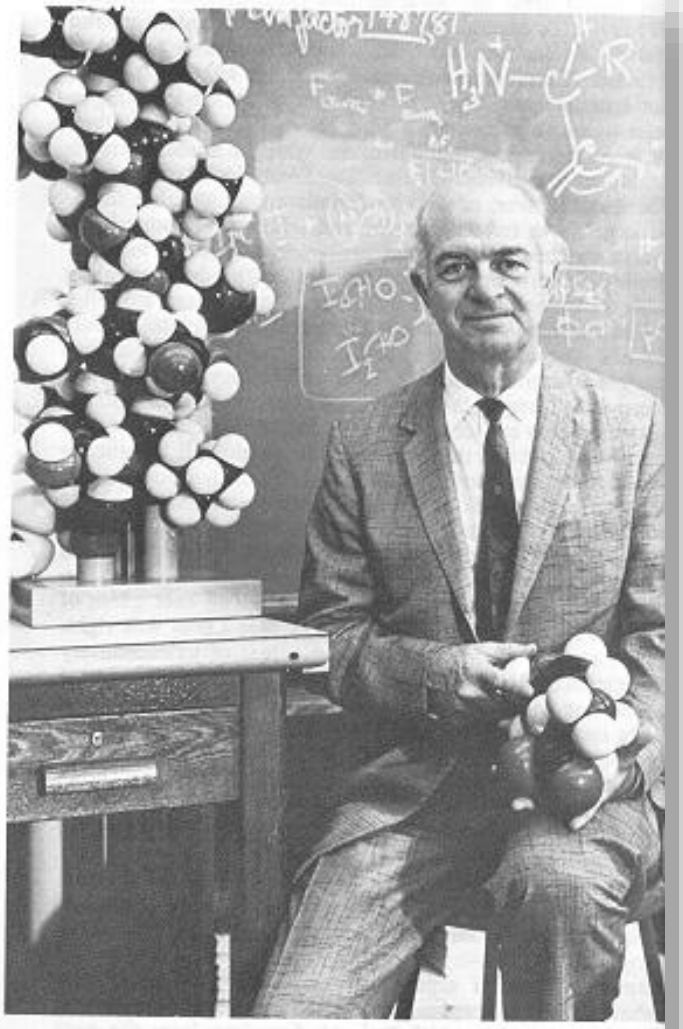
- Hélices em proteínas
  - Aspectos históricos
  - Características estruturais



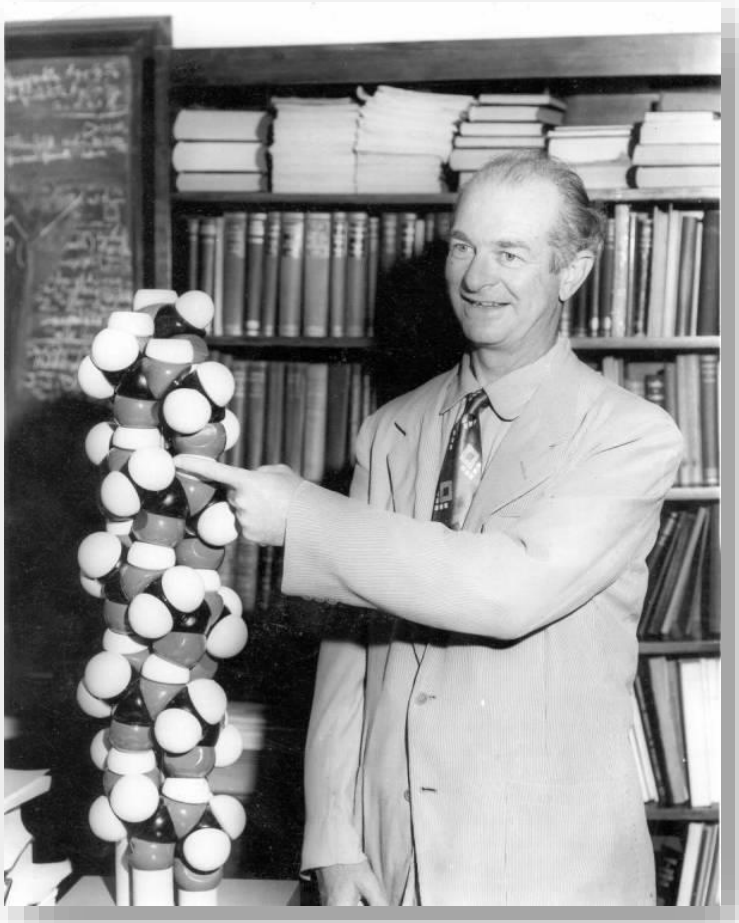
Estrutura de Proteínas – Alfa-hélices



Linus Pauli e alfa-hélice (1951)



Linus Pauling with his atomic models.



Jonh Kendrew – Mioglobina (1958)

662 NATURE March 8, 1958 Vol. 181

A THREE-DIMENSIONAL MODEL OF THE MYOGLOBIN MOLECULE OBTAINED BY X-RAY ANALYSIS

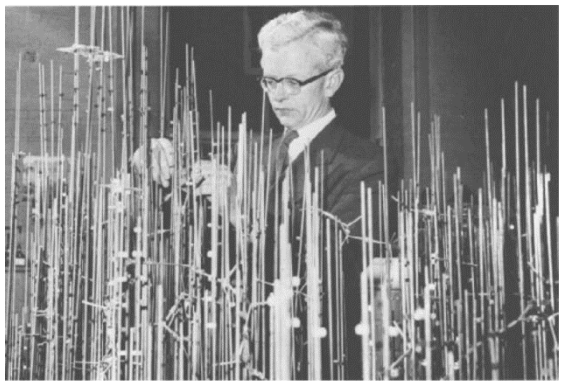
By Drs. J. C. KENDREW, G. BODO, H. M. DINTZIS, R. G. PARRISH and H. WYCKOFF
Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge
AND
D. C. PHILLIPS
Davy Faraday Laboratory, The Royal Institution, London

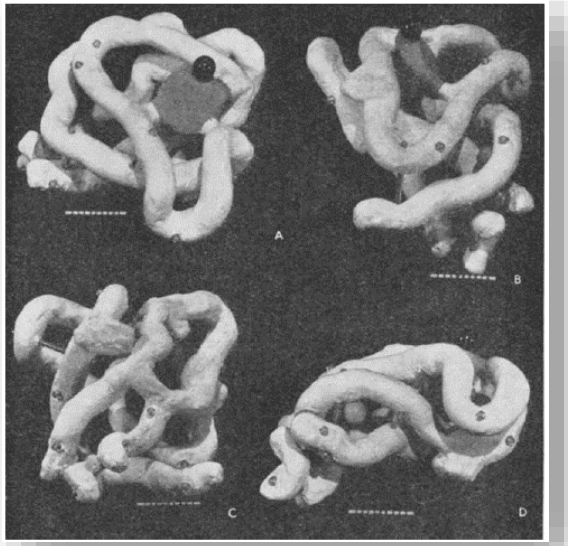
422 NATURE February 13, 1960 Vol. 185

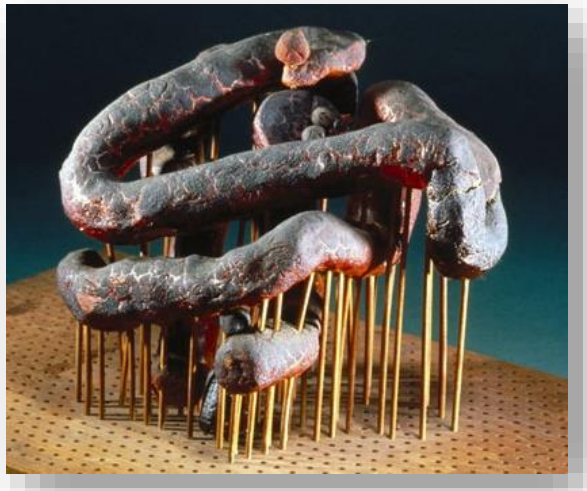
STRUCTURE OF MYOGLOBIN

A THREE-DIMENSIONAL FOURIER SYNTHESIS AT 2 Å. RESOLUTION

By Drs. J. C. KENDREW, R. E. DICKERSON, B. E. STRANDBERG, R. G. HART and D. R. DAVIES*
Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge
AND
D. C. PHILLIPS and V. C. SHORE
Davy Faraday Laboratory, The Royal Institution, London







Alfa-hélice: Definição

Alfa hélice (α-hélice) é uma estrutura secundária cuja conformação em espiral posiciona o grupo C=O do resíduo *n* da cadeia polipeptídica em geometria favorável para receber ligação de hidrogênio do grupo NH do resíduo localizado quatro posições a frente (*n* + 4) na cadeia polipeptídica.

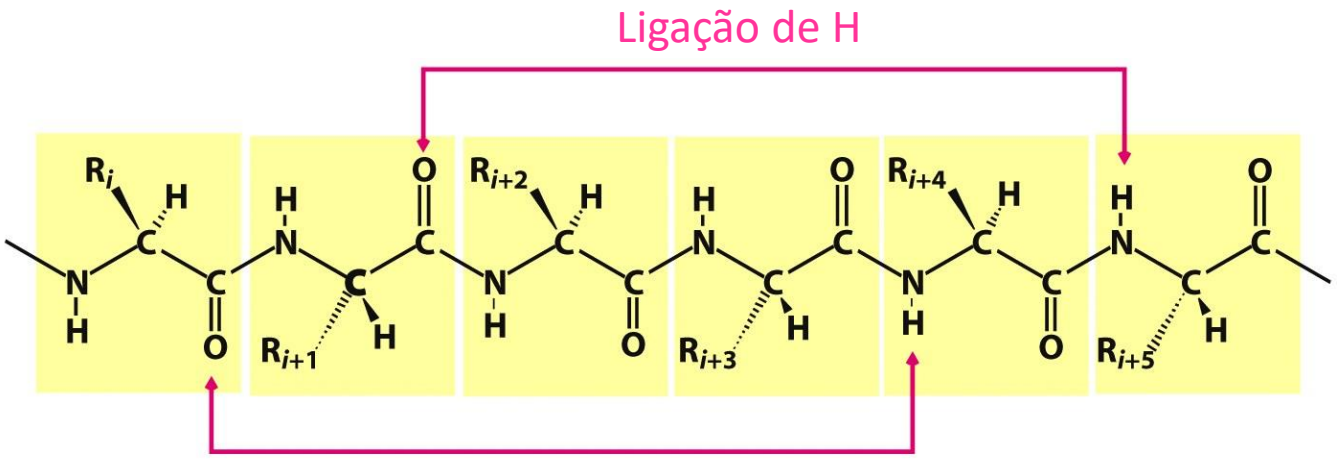
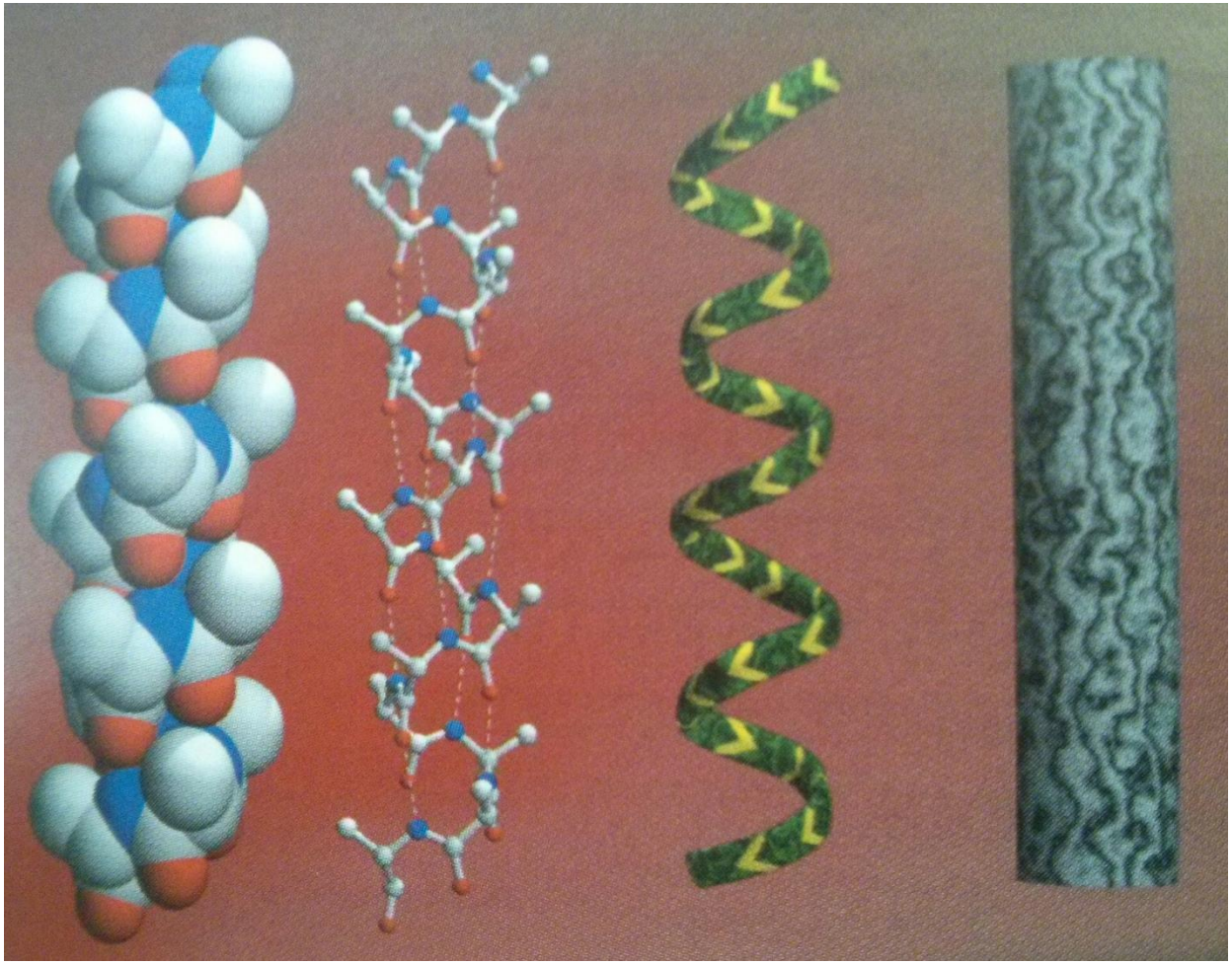


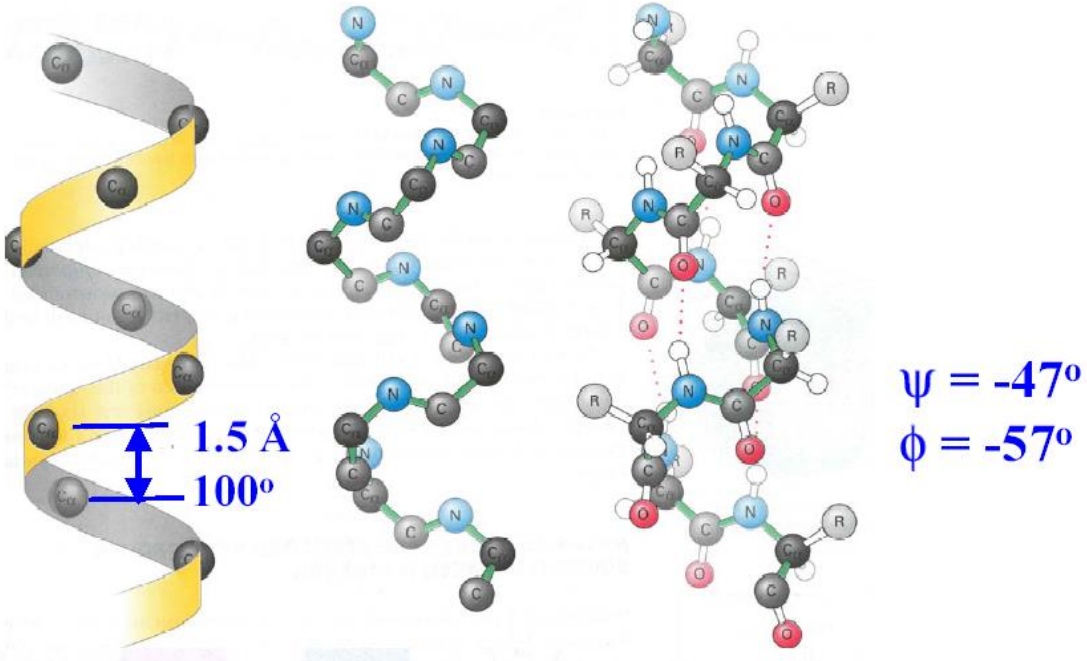
Figure 2.25
***Biochemistry*, Seventh Edition**

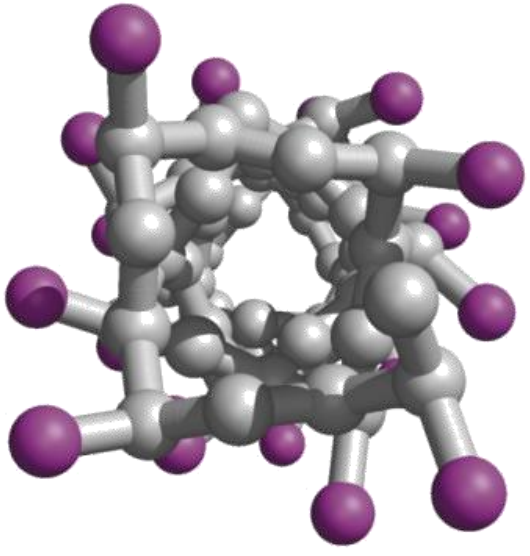
Alfa-hélice



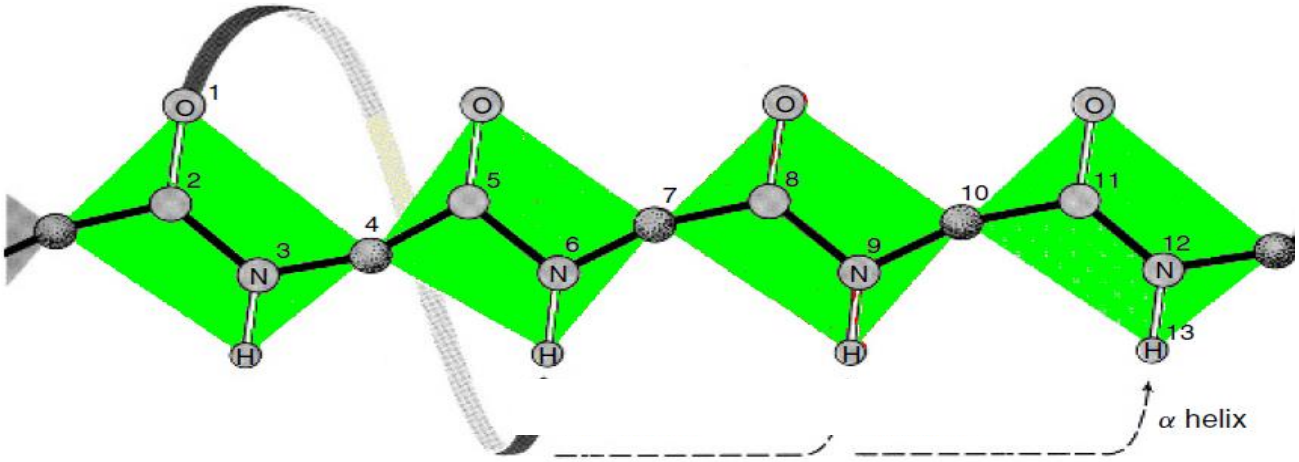
Estrutura secundária – α hélices

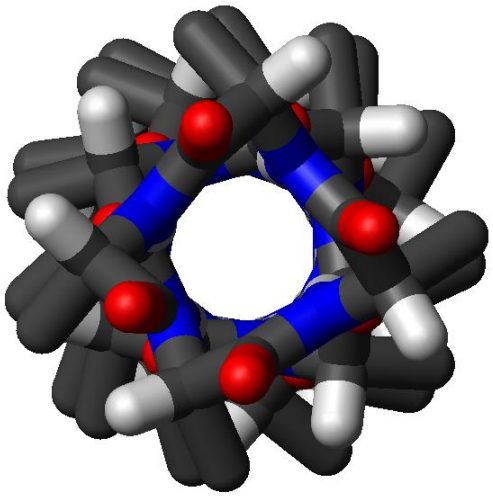
- Estrutura regular e energeticamente estável, pois todas as ligações de H possíveis entre a cadeia principal são estabelecidas ao longo do eixo da hélice;
- Em proteínas globulares o comprimento das α-hélices varia consideravelmente (desde 4,5 até > 40 resíduos)
- O comprimento médio das α-hélices é 10-15 resíduos (12-22 Å)





Alfa-hélice



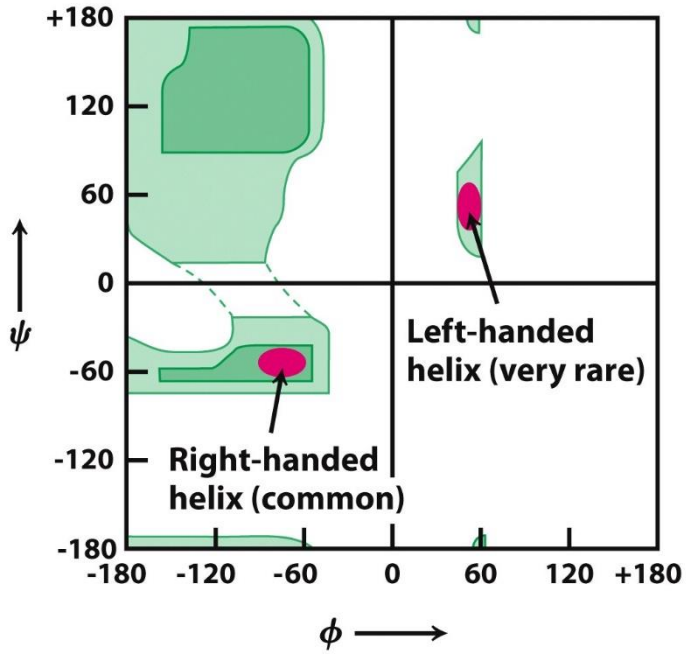


α hélice

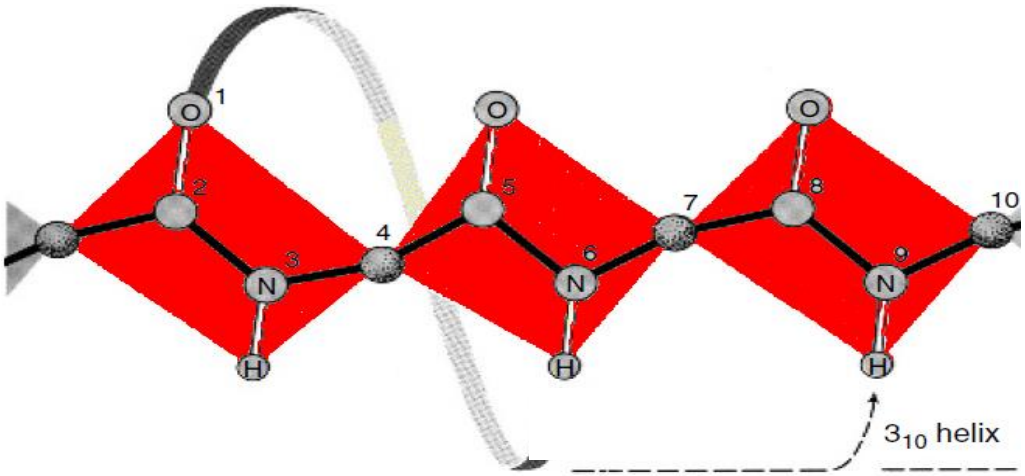
Ligação de H = *n* – *n*+4

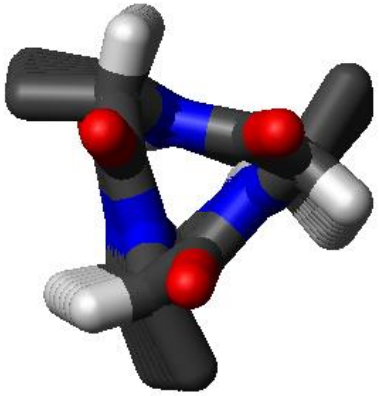
Período = 3,6 aa/volta

Mão direita	**Mão Esquerda**
Φ = -57º	Φ = 60º
Ψ = -47º	Ψ = 60º



Hélice 3_{10}





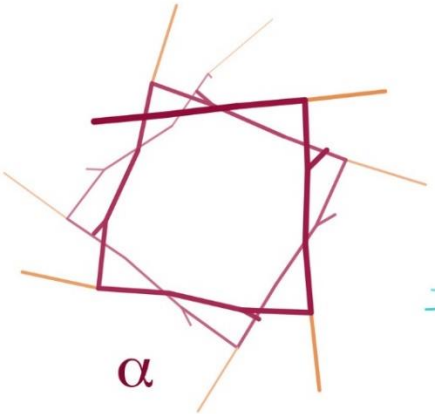
hélice 3_{10}

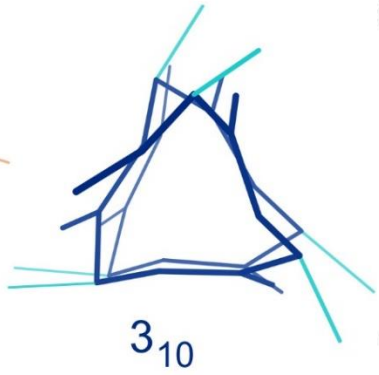
Ligação de H = $n - n+3$

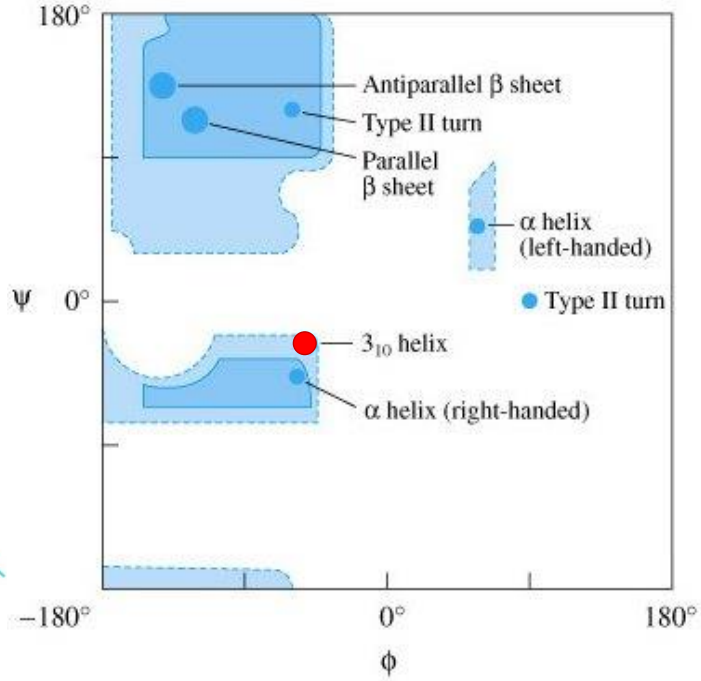
Período = 3,0 aa/volta

Φ = -49º

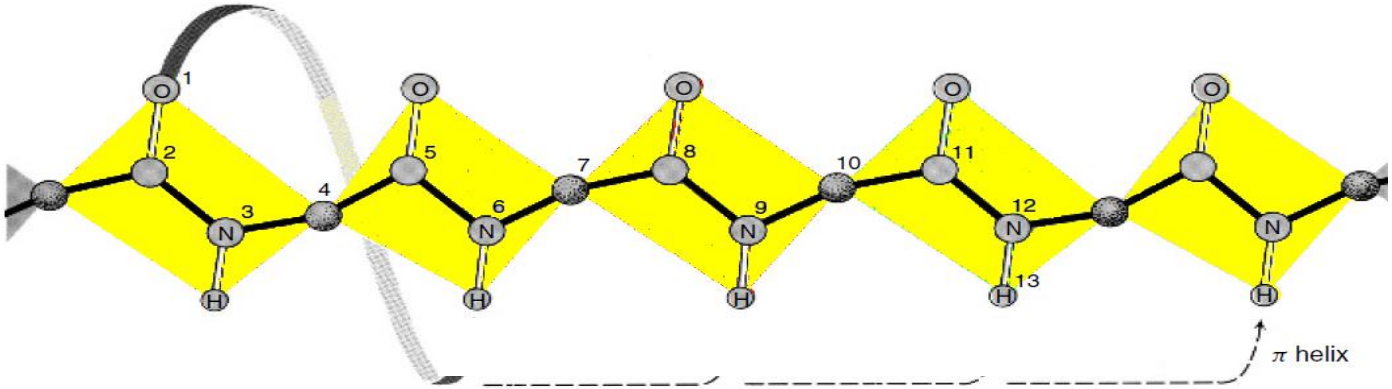
Ψ = -26º

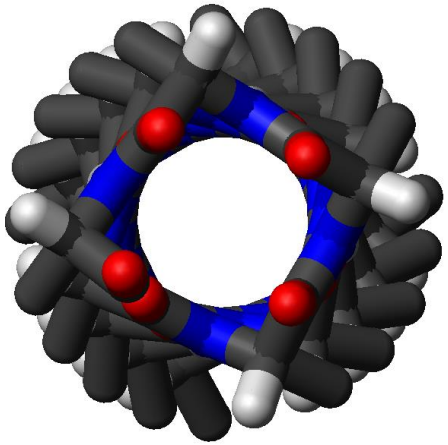






Pi-Hélice





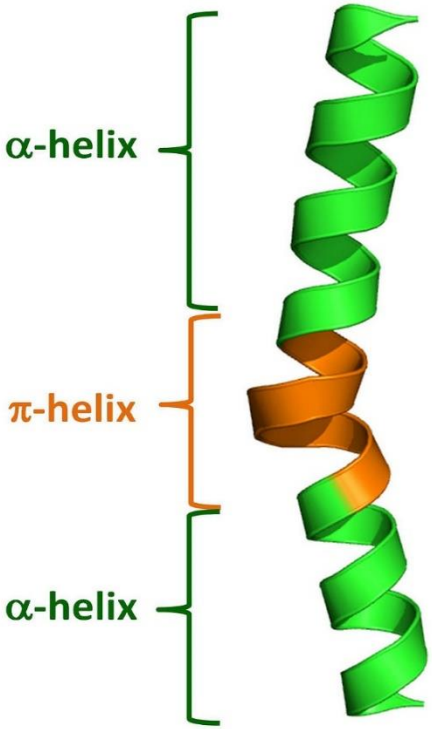
π hélice

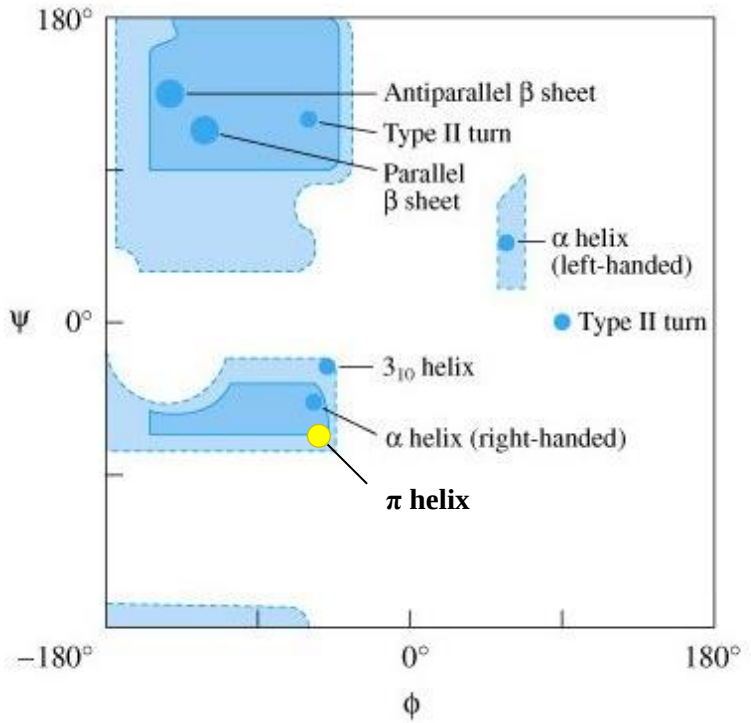
Ligação de H = *n* – *n*+5

Período = 4,4 aa/volta

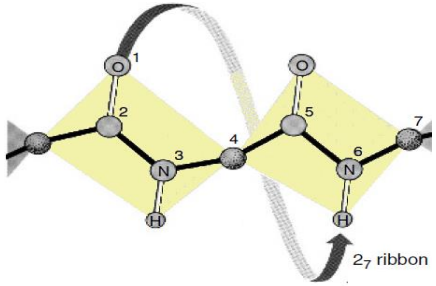
Φ = -57º

Ψ = -70º

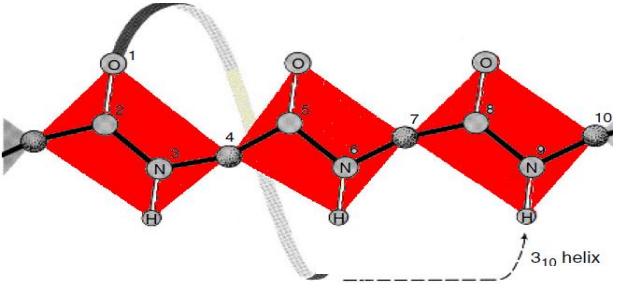




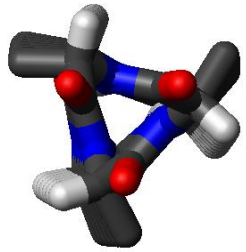
Hélices em proteínas: Resumo

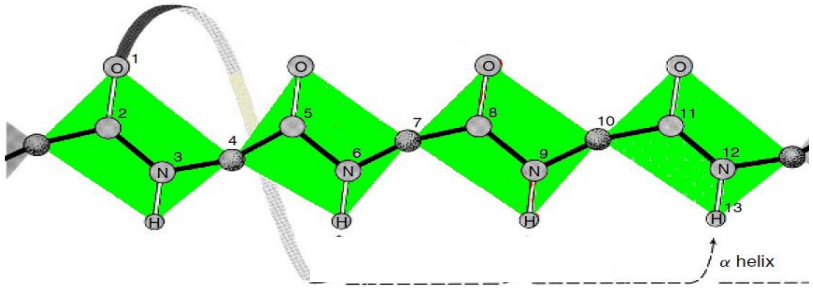


2_7 ribbon
Ligação de H = *n* – *n*+2
Período = 2,0 aa/volta

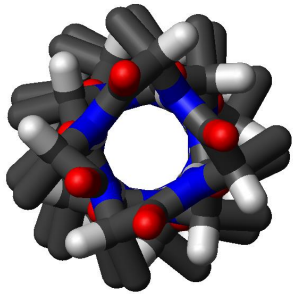


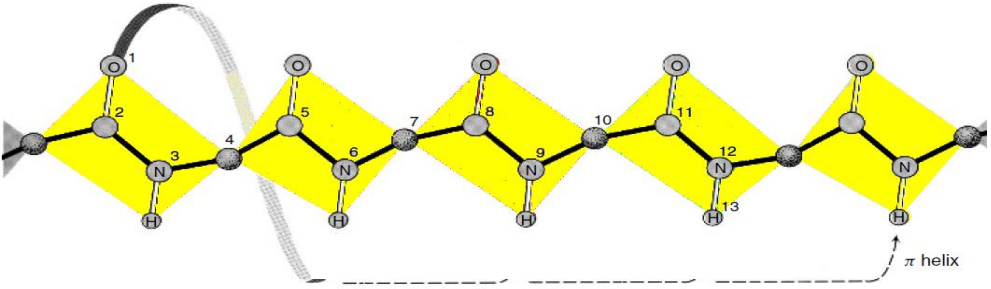
hélice 3_{10}
Ligação de H = *n* – *n*+3
Período = 3,0 aa/volta



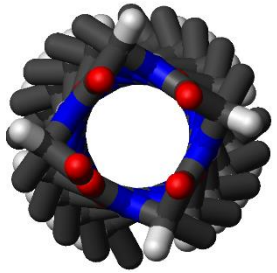


α hélice
Ligação de H = *n* – *n*+4
Período = 3,6 aa/volta

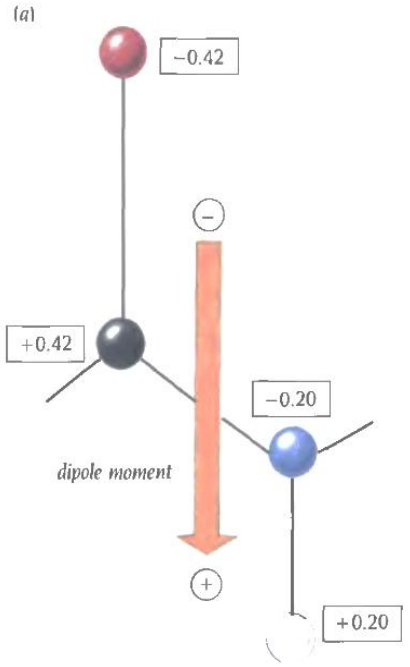


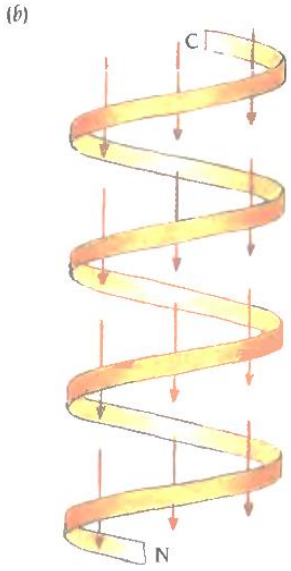


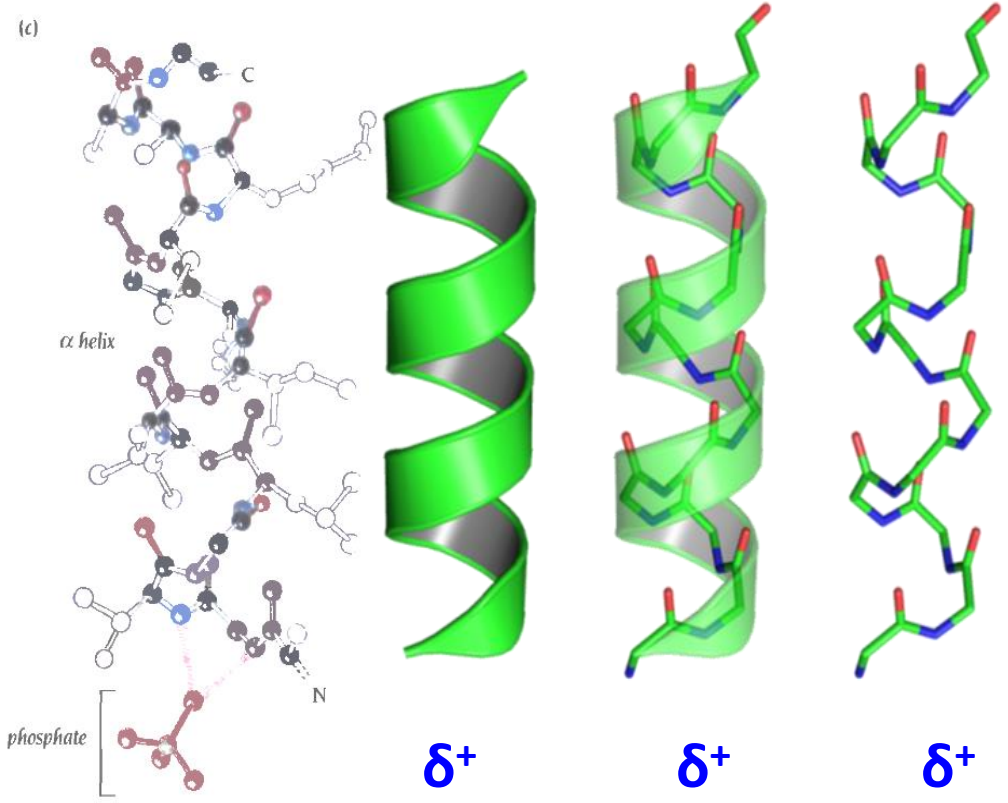
π hélice
Ligação de H = *n* – *n*+5
Período = 4,4 aa/volta



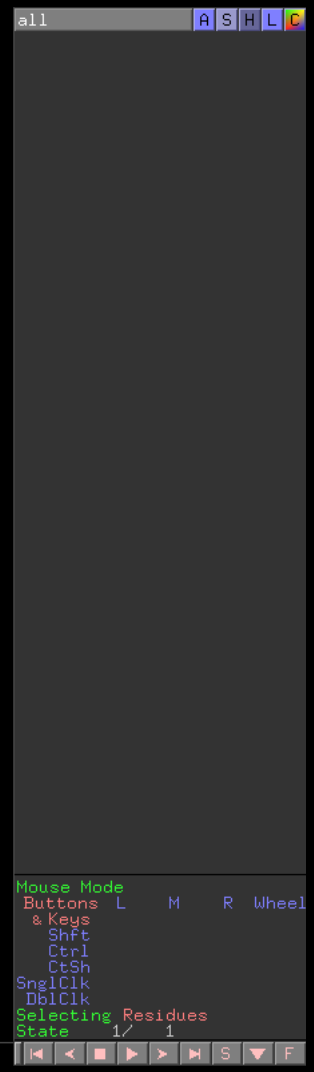
Alfa-hélice: dipolos

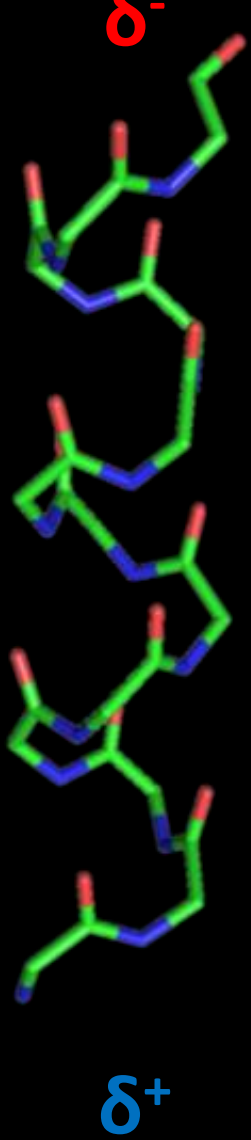






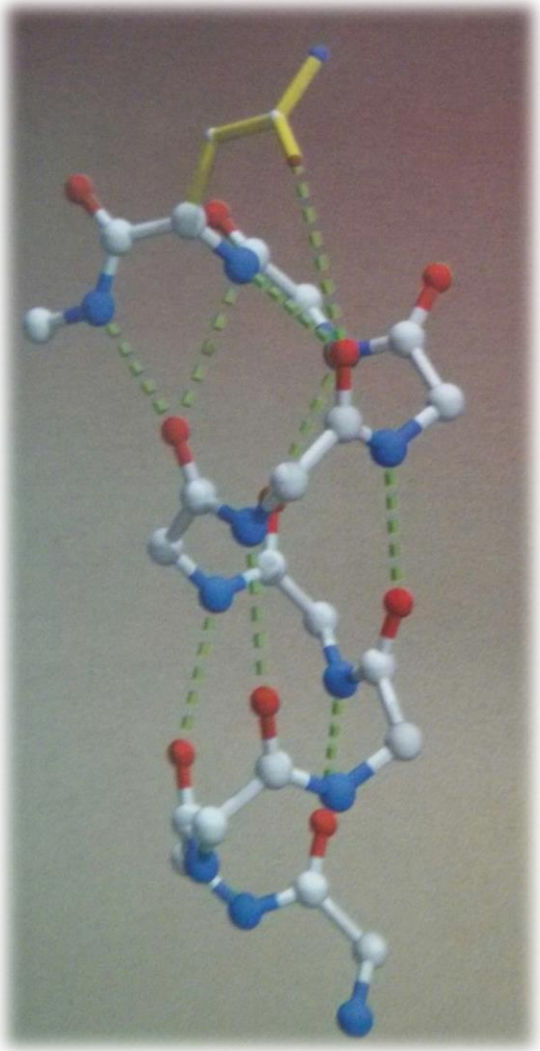
Alfa-hélices: dipolo



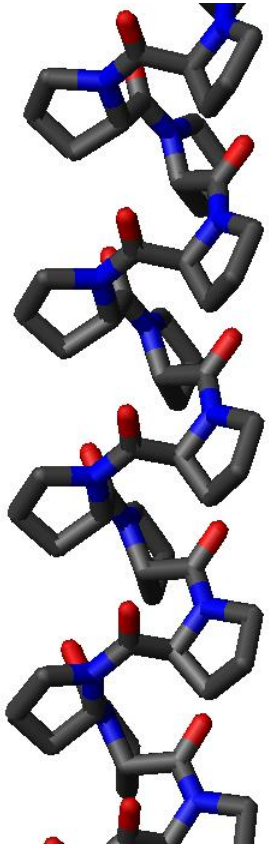


Hélices

Hélice “caps”



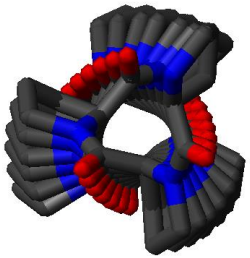
Hélice poliprolina I



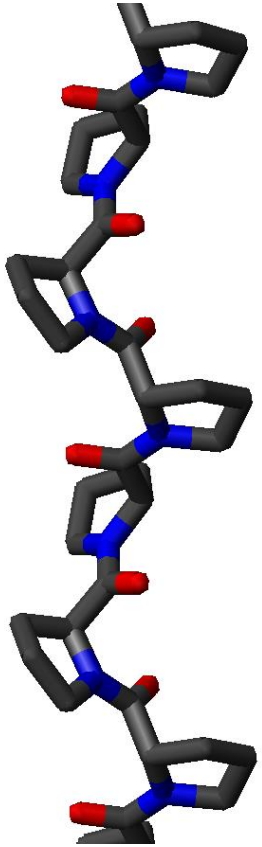
cys

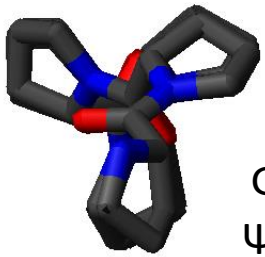
Φ = -75º

Ψ = 160º



Hélice poliprolina II





trans

Φ = -75º

Ψ = 150º

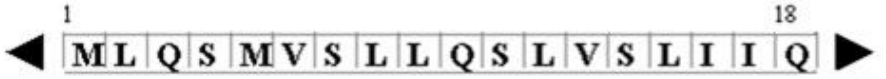
Alfa-hélice

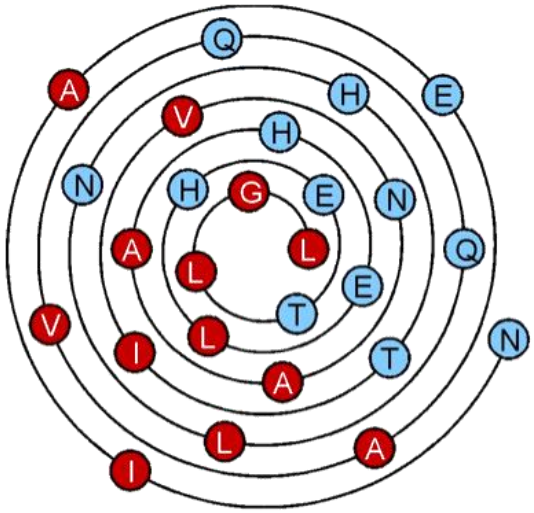
Resíduos de **Ala, Leu, Glu, Lys, Arg e Met (MALERK)** são encontrados mais frequentemente em **hélices alfa**, enquanto **Pro, Gly e Asp** são encontrados com menos frequência que a média.

Residue	Helix propensity, ΔG (kJ mol^{-1})	Residue	Helix propensity, ΔG (kJ mol^{-1})
Ala	0	Ile	0.41
Arg	0.21	Leu	0.21
Asn	0.65	Lys	0.26
Asp^0	0.43	Met	0.24
Asp^-	0.69	Phe	0.54
Cys	0.68	Pro	3.16
Gln	0.39	Ser	0.50
Glu^0	0.16	Thr	0.66
Glu^-	0.40	Tyr	0.53
Gly	1.00	Trp	0.49
His^0	0.56	Val	0.61
His^+	0.66		

Alfa-hélices

- Uma maneira conveniente de ilustrar as sequências de aminoácidos em hélices é a roda helicoidal (“helical wheel”)
- Cada uma volta em hélice alfa contém 3,6 resíduos de comprimento, logo, cada resíduo pode ser indicado a cada 360 / 3,6 = 100º ao redor de um círculo ou uma espiral.
- A roda helicoidal representa uma projeção da posição dos resíduos de aminoácidos sobre um plano perpendicular ao eixo helicoidal da hélice





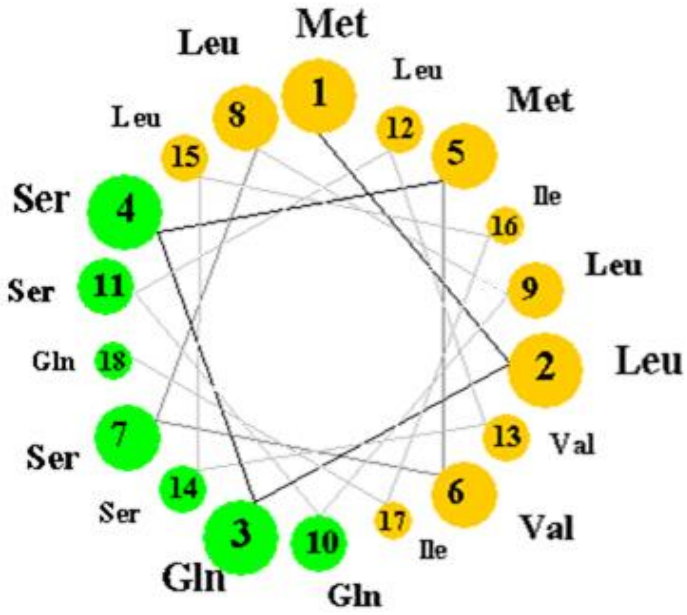


Diagrama Wenxiang

http://www.jci-bioinfo.cn/wenxiang2

Wenxiang: A web-server to draw Wenxiang diagram

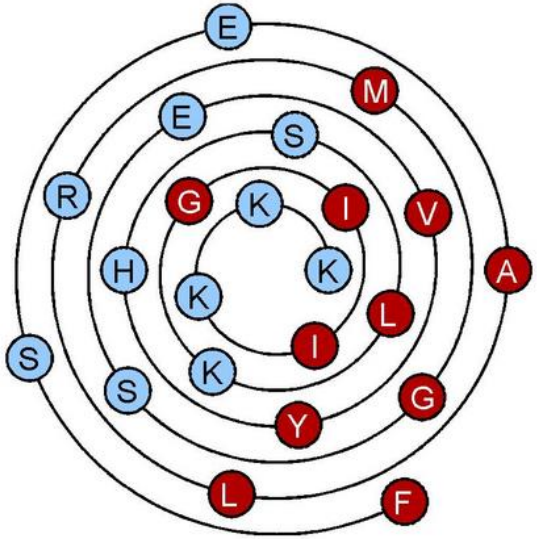
| Read Me | Citation |

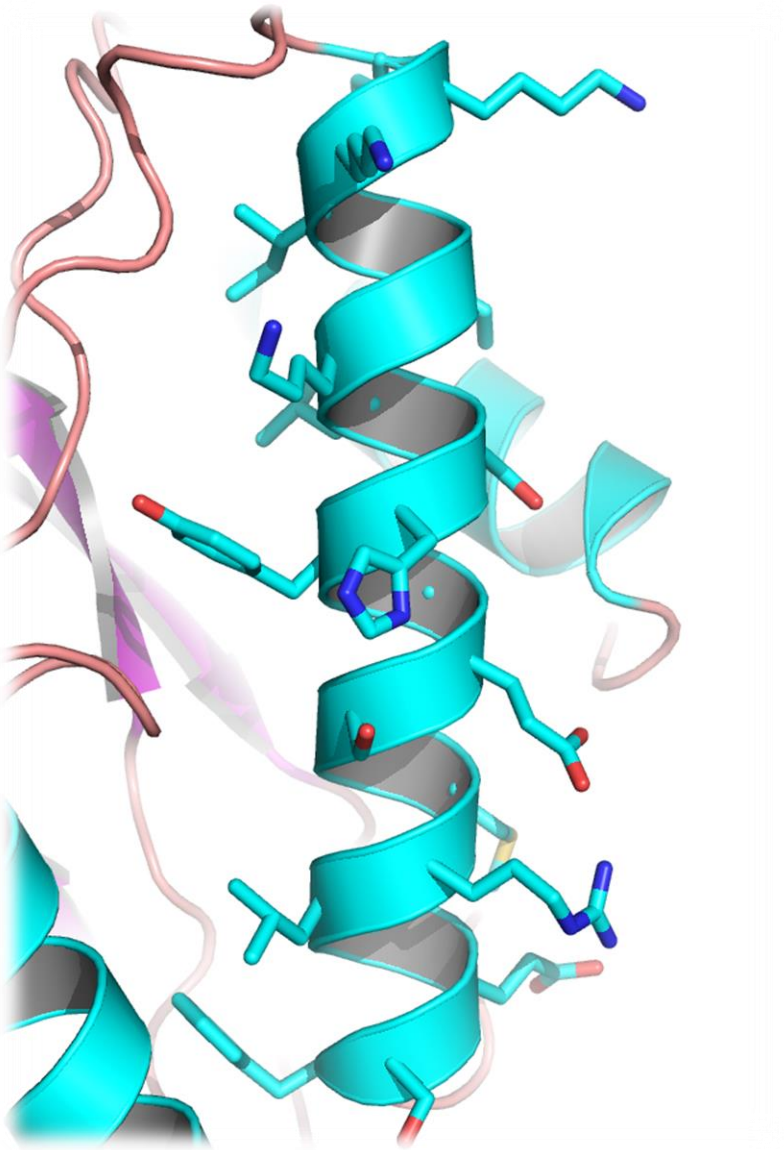
Input the sequence of an α-helix (Example)

FSEALRMGSEVYHSLKGIIKKK

Black&White Color Cancel

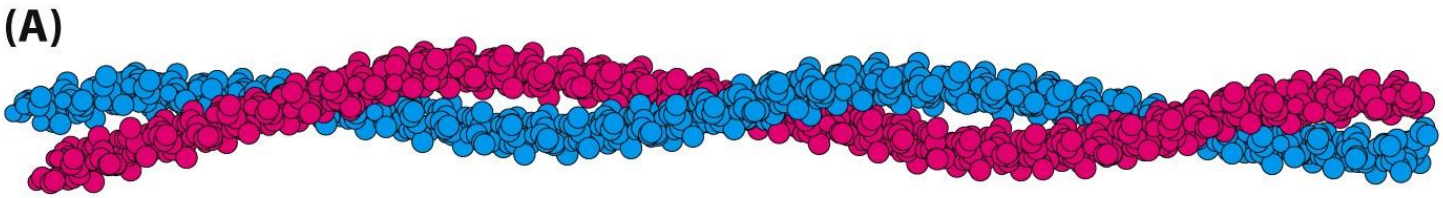
00428

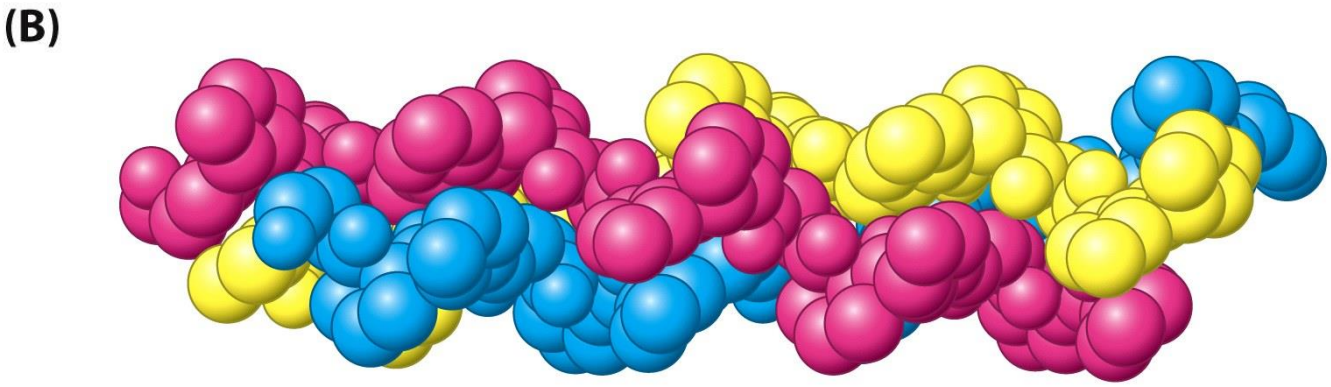


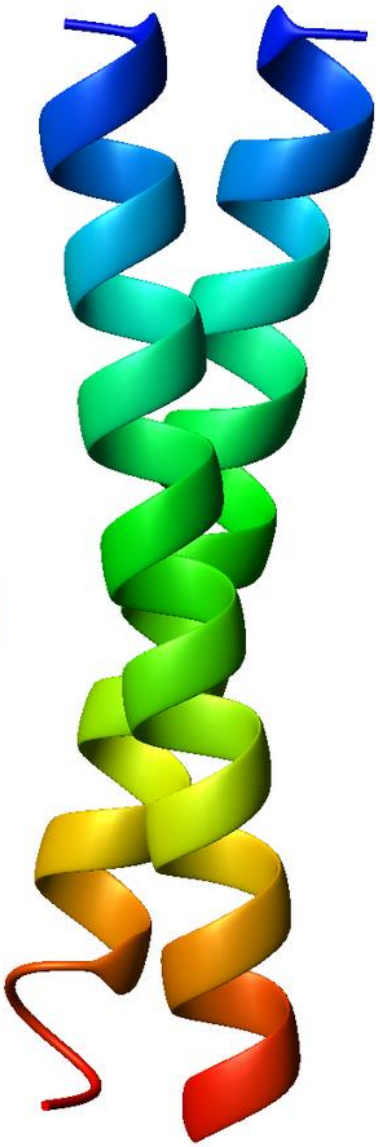


Coiled-coil

- *Coiled-coil* (“bobina em espiral”) é um motivo estrutural em proteínas em que 2 a 7 alfa-hélices são enroladas em conjunto como os fios de um cabo
- Dímeros e trímeros são os tipos mais comuns



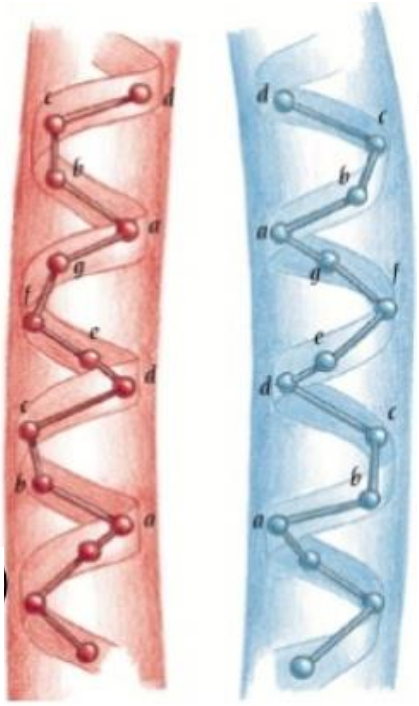


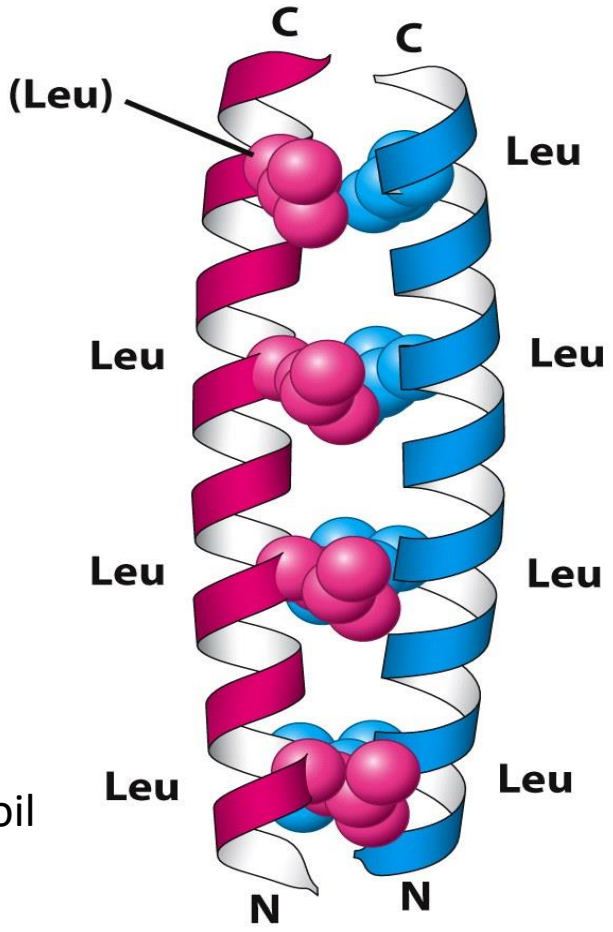


Repetição Hepta “Heptad repeat”

The heptad repeat

	a	b	c	d	e	f	g
1	Met	Lys	Gln	**Leu**	Glu	Asp	Lys
8	Val	Glu	Glu	**Leu**	Leu	Ser	Lys
15	Asn	Tyr	His	**Leu**	Glu	Asn	Glu
22	Val	Ala	Arg	**Leu**	Lys	Lys	Leu





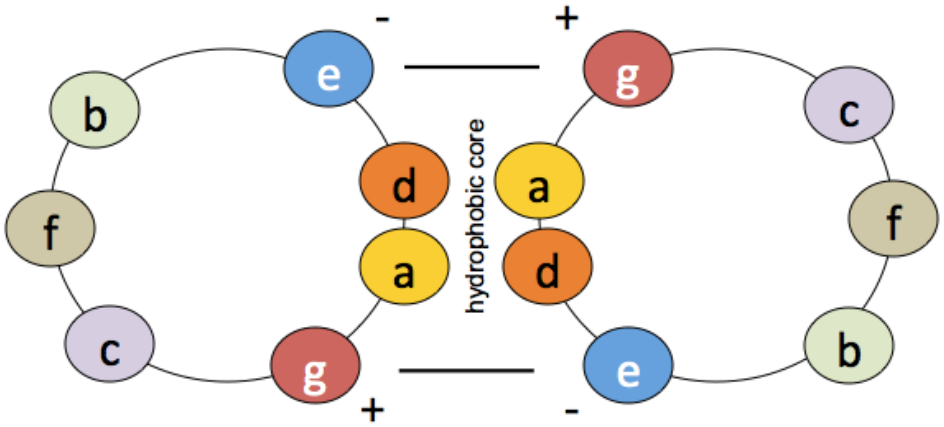
- d: frequentemente Leu ou Ile
- a: frequentemente hidrofóbico
- e,g: frequentemente carregado
- b,c,f : carregado ou polar
- essas características são utilizadas para predição de coiled-coil em estruturas de proteínas

Por que hepta?

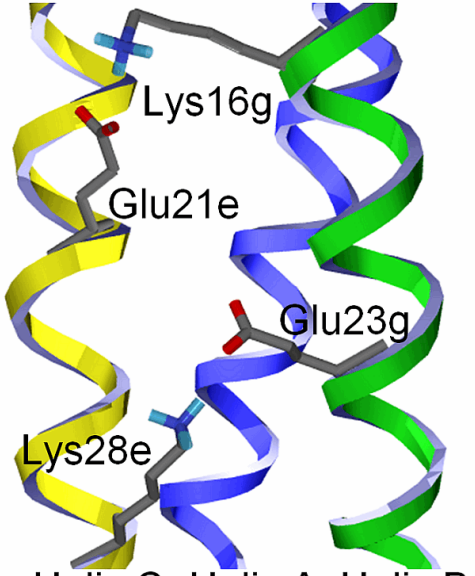
- hélice α: 3,6 resíduos/volta
- hélice 3_{10}: 3 resíduos/volta
- hélices α em “coiled-coil” são ligeiramente distorcidas e apresentam 3,5 resíduos/volta
- 3,5 x 2 = 7, portanto, a cada duas voltas forma-se uma repetição hepta

Interações em Coiled-coil

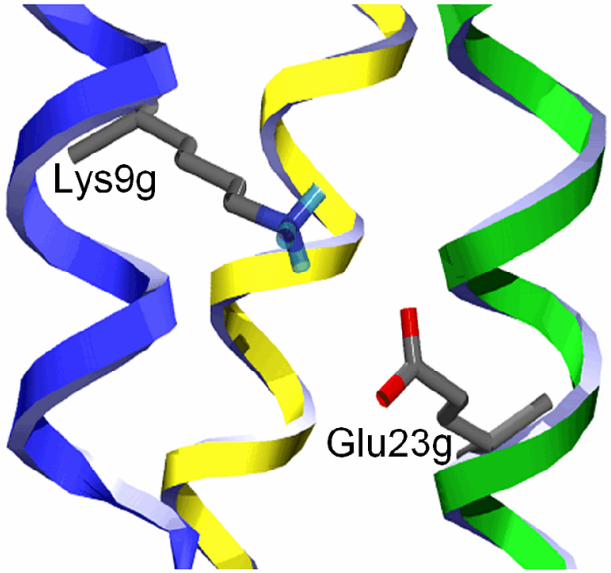
	a	b	c	d	e	f	g
1	Met	Lys	Gln	**Leu**	Glu	Asp	Lys
8	Val	Glu	Glu	**Leu**	Leu	Ser	Lys
15	Asn	Tyr	His	**Leu**	Glu	Asn	Glu
22	Val	Ala	Arg	**Leu**	Lys	Lys	Leu



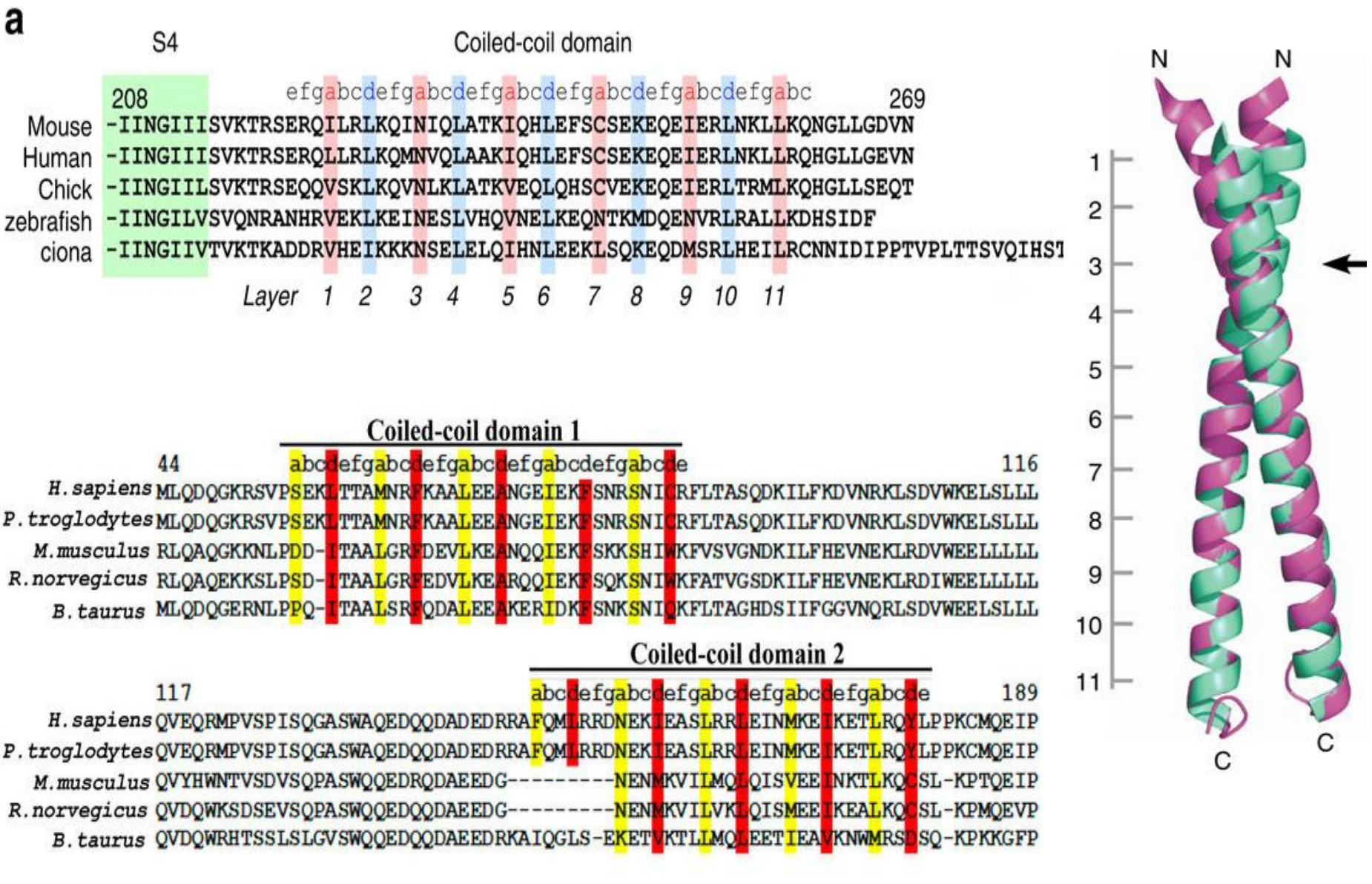
e/g in Parallel face



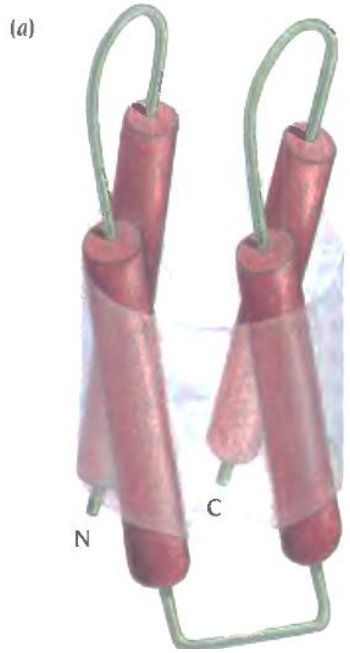
g/g in Antiparallel face

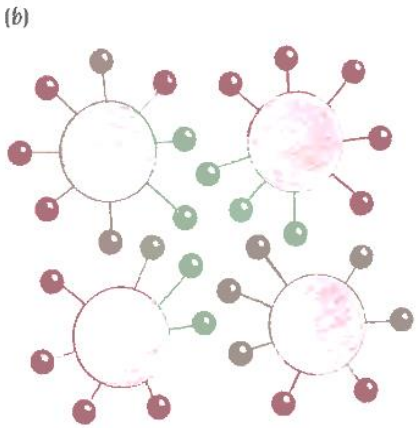


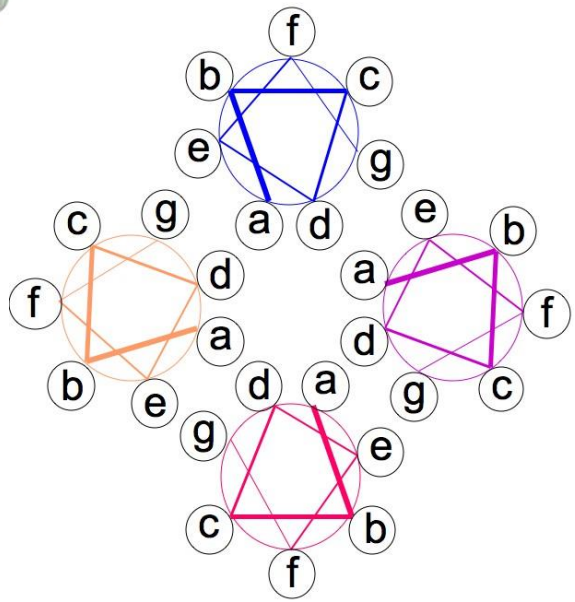
Repetição Hepta “Heptad repeat”

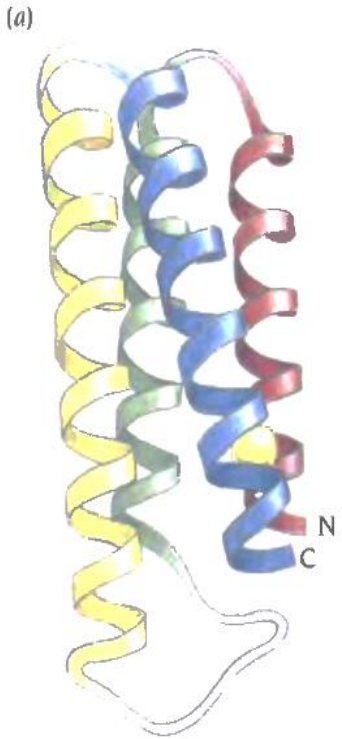


Four-helix bundle "pacote de 4 hélices"

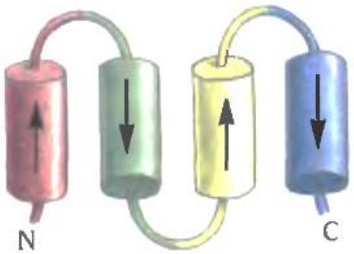


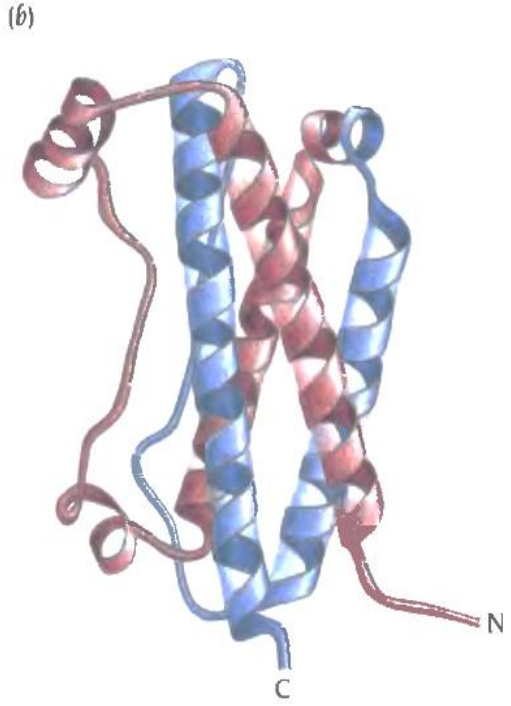




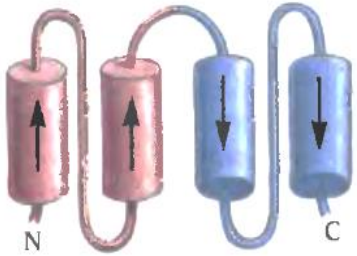


cytochrome b_{562}





human growth hormone



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