

Gli aminoacidi

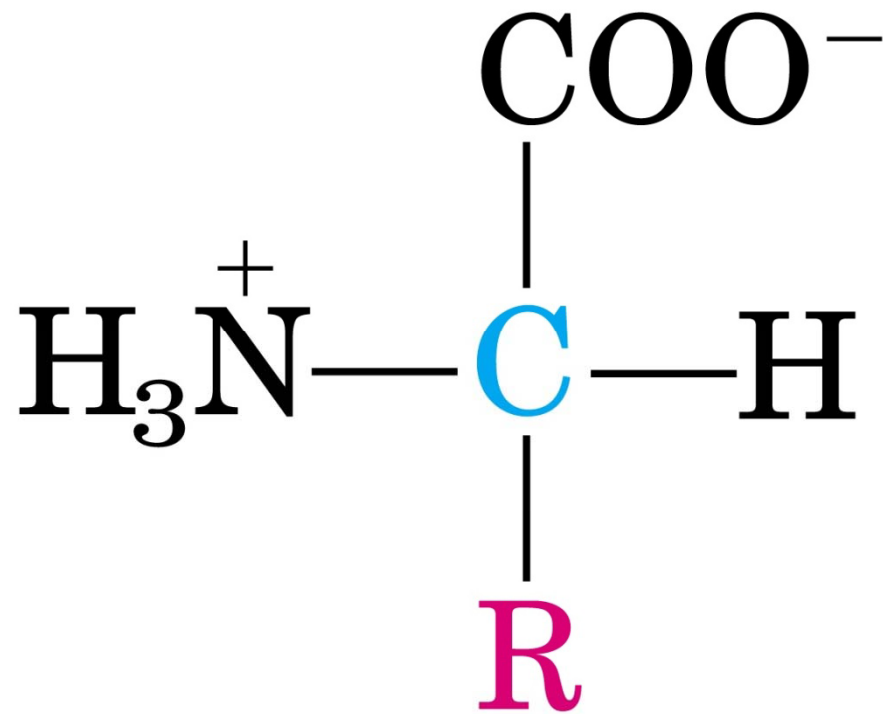


table 5–1

Properties and Conventions Associated with the Standard Amino Acids

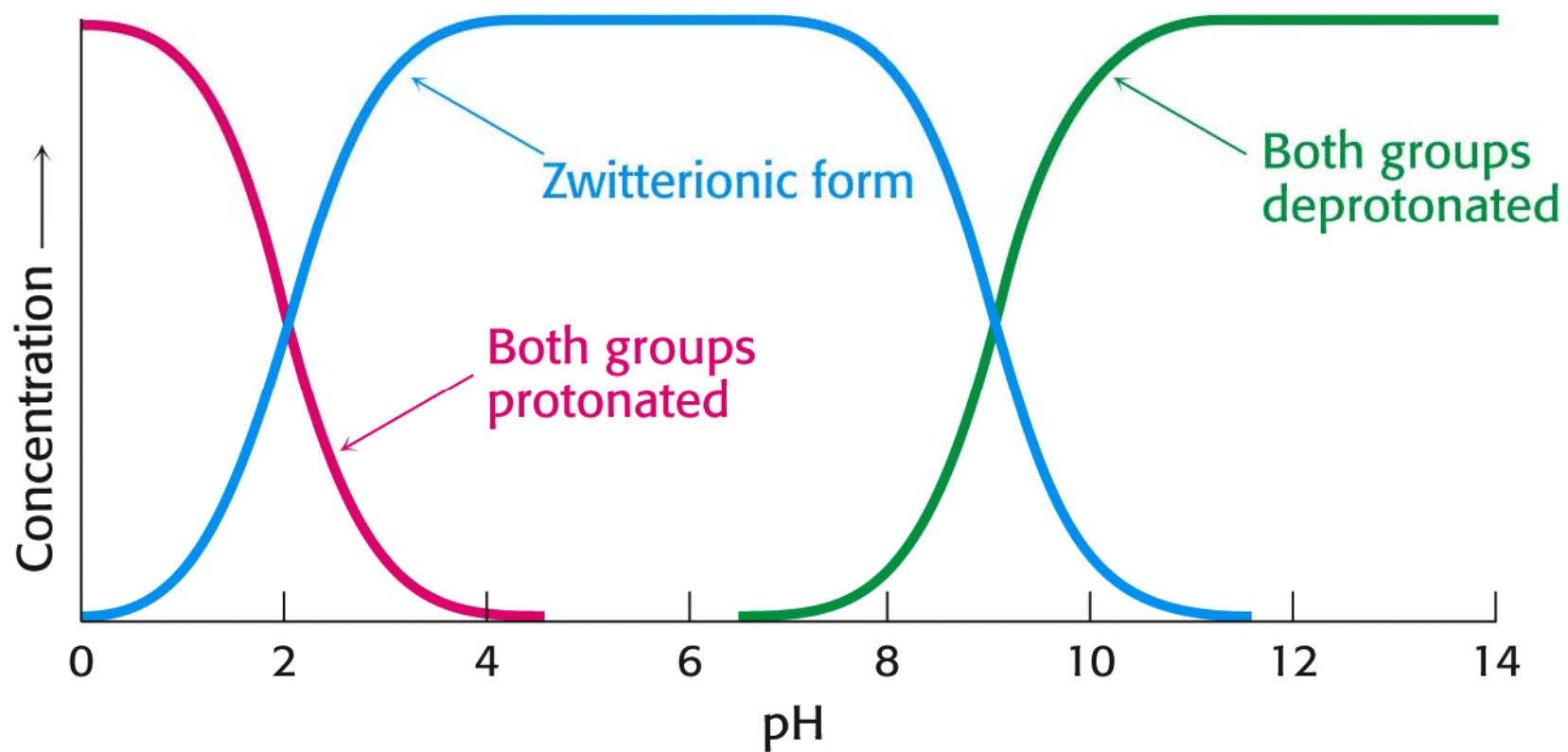
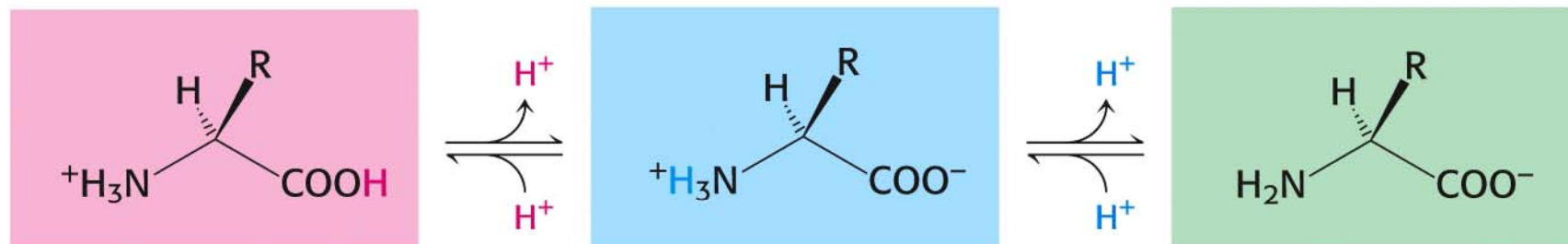
Amino acid	Abbreviated names		M_r	pK_a values			pI	Hydropathy index*	Occurrence in proteins (%)
				pK_1 (—COOH)	pK_2 (—NH ₃ ⁺)	pK_R (R group)			
Nonpolar, aliphatic R groups									
Glycine	Gly	G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala	A	89	2.34	9.69		6.01	1.8	7.8
Valine	Val	V	117	2.32	9.62		5.97	4.2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

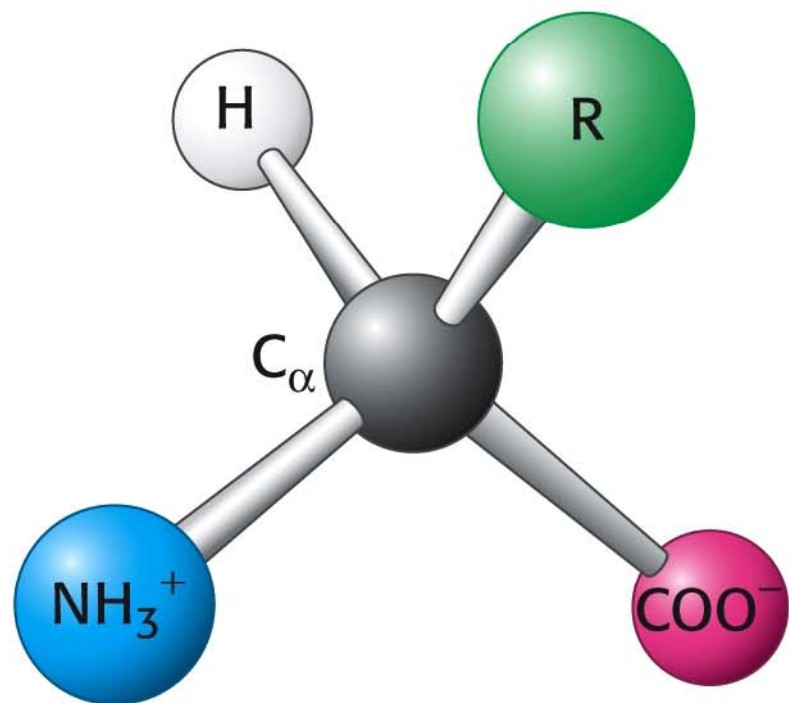
*A scale combining hydrophobicity and hydrophilicity of R groups; it can be used to measure the tendency of an amino acid to seek an aqueous environment (– values) or a hydrophobic environment (+ values). See Chapter 12. From Kyte, J. & Doolittle, R.F. (1982) *J. Mol. Biol.* **157**, 105–132.

†Average occurrence in over 1150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed) Plenum Press, NY, pp. 599–623.

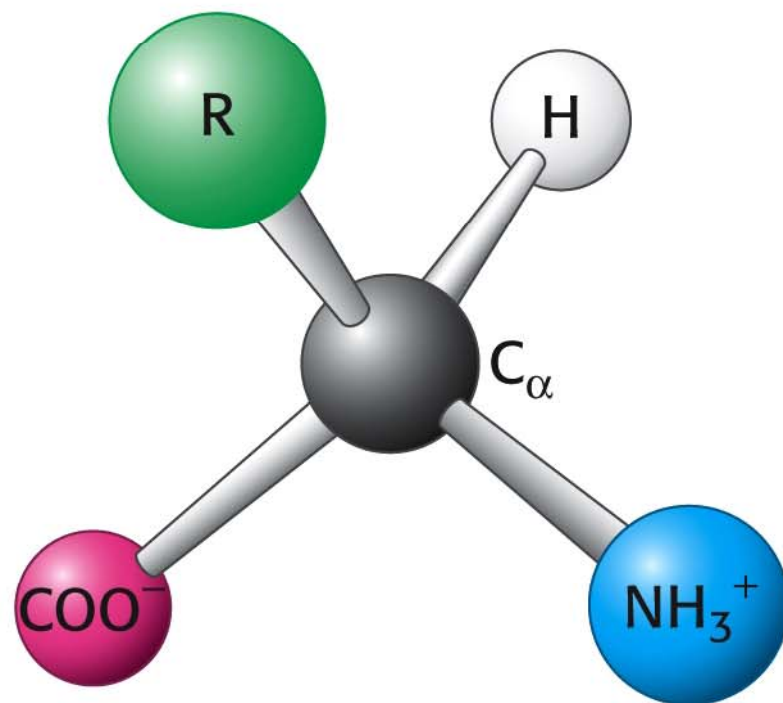
Proprietà comuni

- Il gruppo α -carbossilico è un acido più forte del gruppo carbossilico degli acidi alifatici paragonabili
- Il gruppo α -aminico è un acido più forte (o una base più debole del gruppo aminico di amine alifatiche corrispondenti
- Tutti gli aminoacidi con gruppi R privi di carica hanno valori pK_1 e pK_2 molto simili tra loro
- L'unico aminoacido con una capacità tampone degna di nota a pH fisiologico è l'istidina





L isomer



D isomer

table 5-3

Amino Acid Composition of Two Proteins*		
Amino acid	Number of residues per molecule of protein	
	Bovine cytochrome c	Bovine chymotrypsinogen
Ala	6	22
Arg	2	4
Asn	5	15
Asp	3	8
Cys	2	10
Gln	3	10
Glu	9	5
Gly	14	23
His	3	2
Ile	6	10
Leu	6	19
Lys	18	14
Met	2	2
Phe	4	6
Pro	4	9
Ser	1	28
Thr	8	23
Trp	1	8
Tyr	4	4
Val	3	23
Total	104	245

*Note that standard procedures for the acid hydrolysis of proteins convert Asn and Gln to Asp and Glu, respectively. In addition, Trp is destroyed. Special procedures must be employed to determine the amounts of these amino acids.

table 5–4

Conjugated Proteins

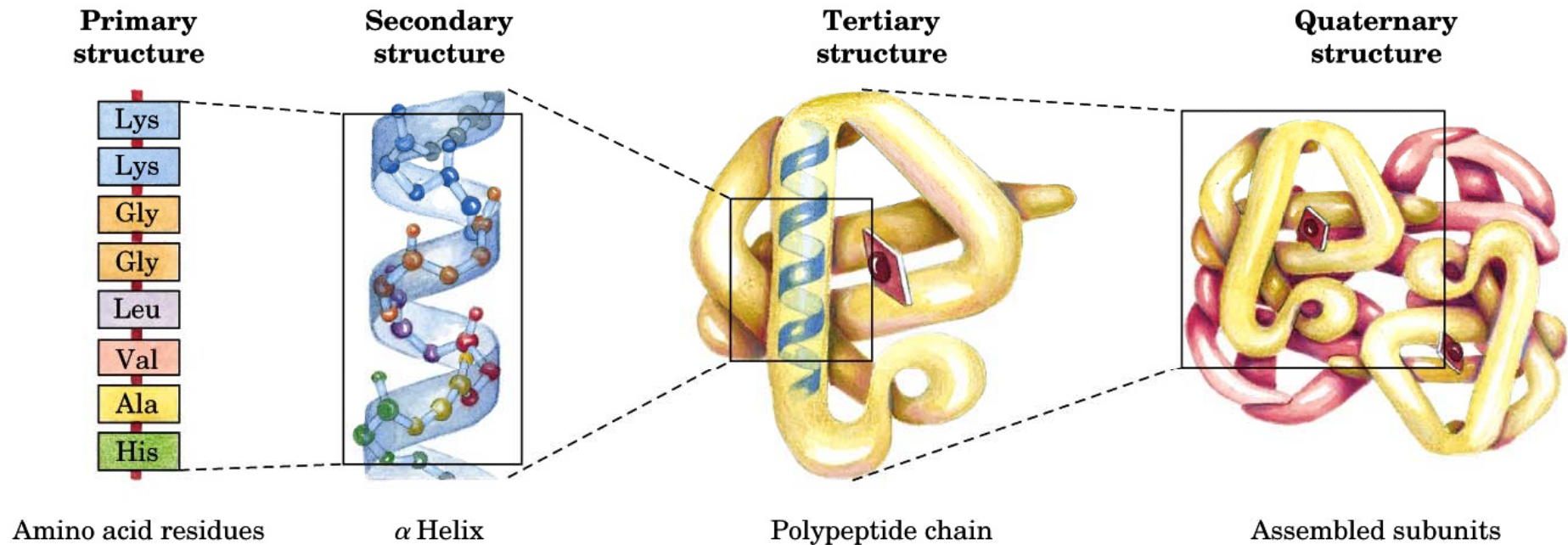
Class	Prosthetic group(s)	Example
Lipoproteins	Lipids	β_1 -Lipoprotein of blood
Glycoproteins	Carbohydrates	Immunoglobulin G
Phosphoproteins	Phosphate groups	Casein of milk
Hemoproteins	Heme (iron porphyrin)	Hemoglobin
Flavoproteins	Flavin nucleotides	Succinate dehydrogenase
Metalloproteins	Iron	Ferritin
	Zinc	Alcohol dehydrogenase
	Calcium	Calmodulin
	Molybdenum	Dinitrogenase
	Copper	Plastocyanin

La struttura delle proteine

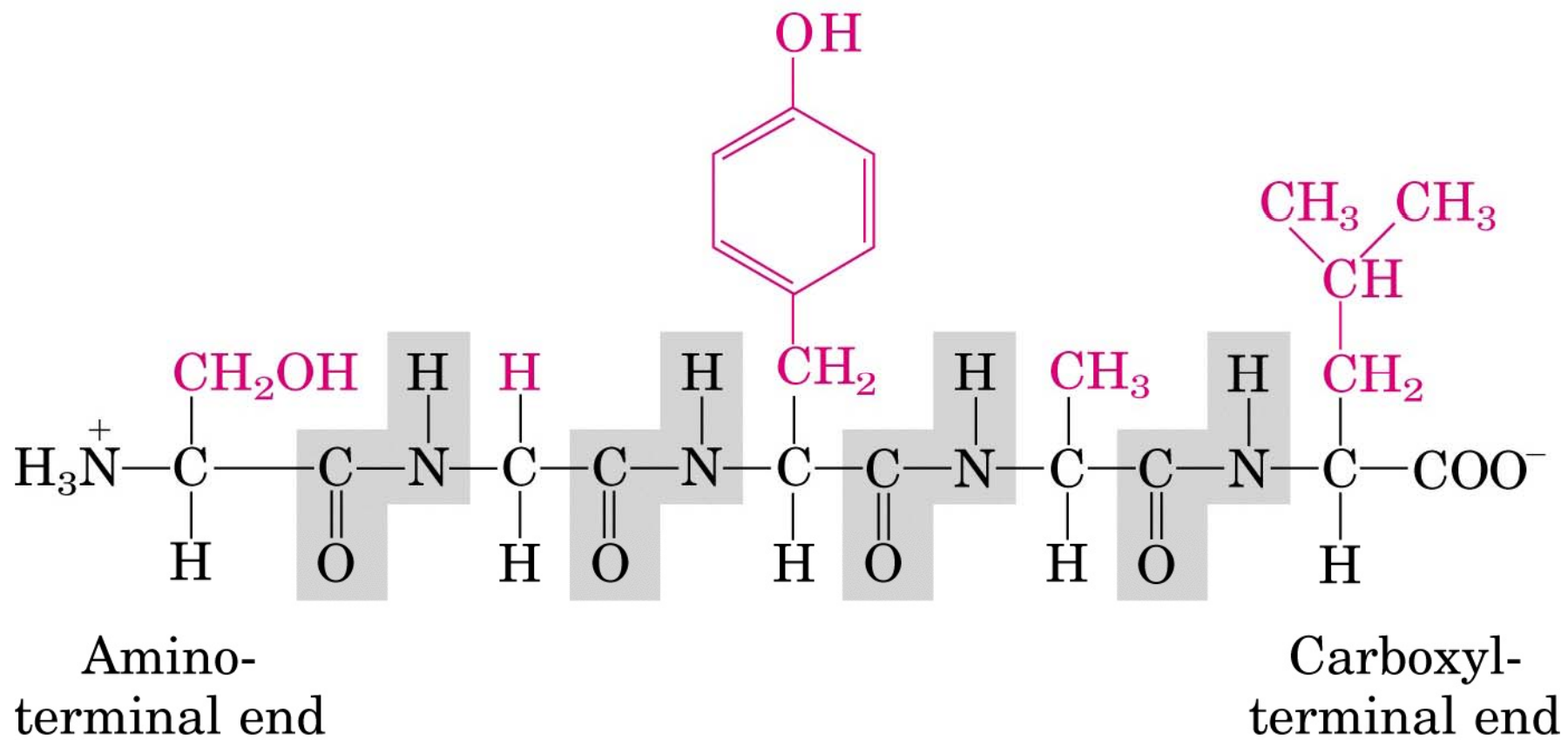
Funzioni delle proteine

- *Strutturali*
- *Contrattili*
- *Trasporto*
- *Riserva*
- *Ormonali*
- *Enzimatiche*
- *protezione*

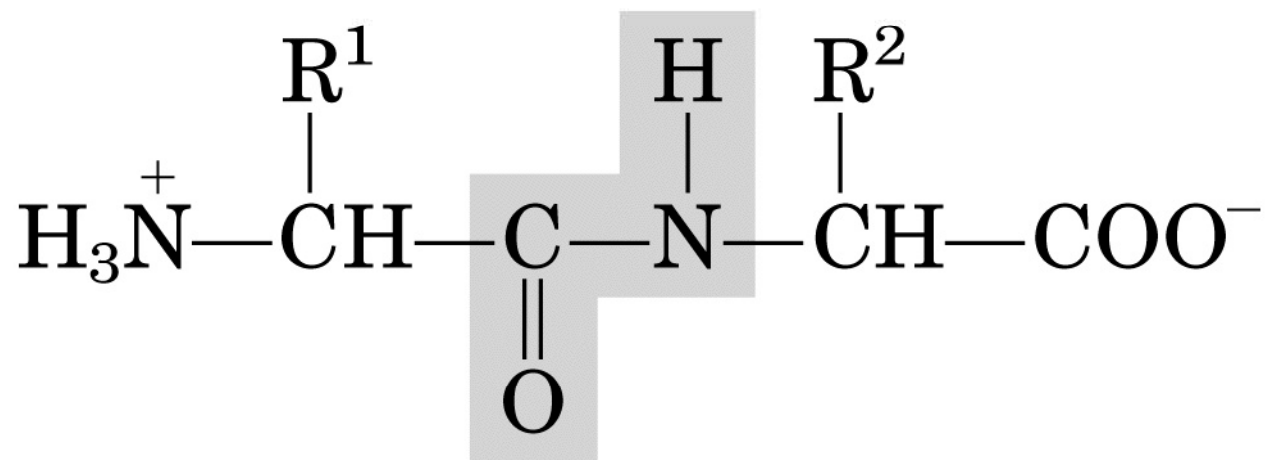
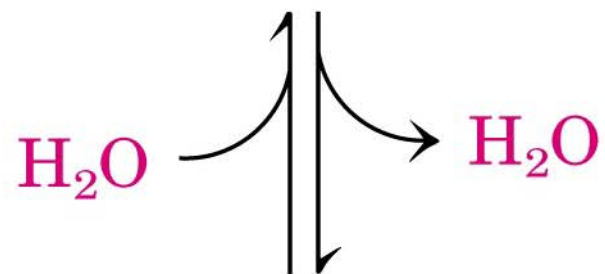
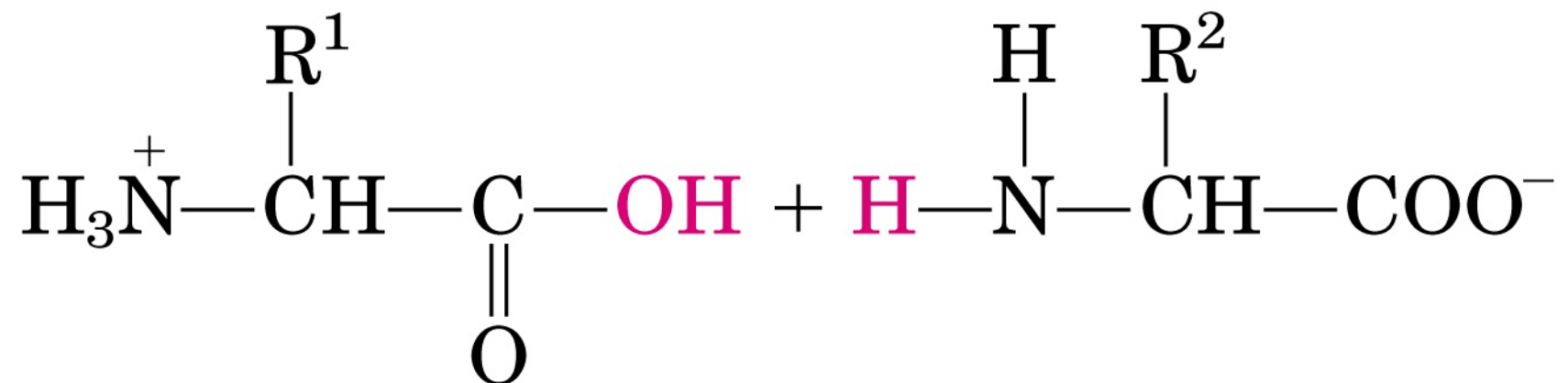
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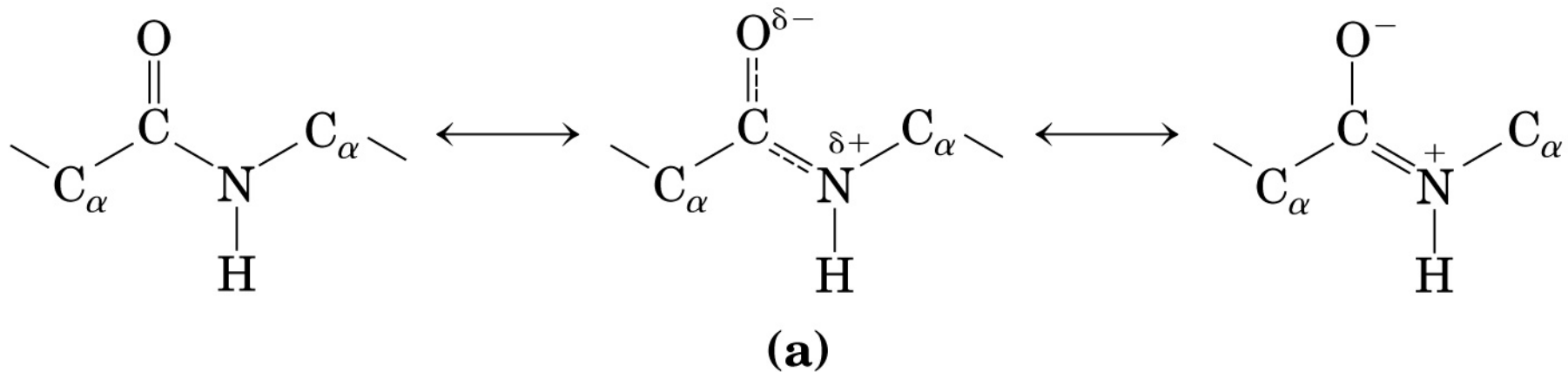
Struttura secondaria: ripiegamento locale della catena polipeptidica con andamento ripetitivo regolare (si considera la disposizione spaziale dello scheletro del polipeptide, senza considerare la disposizione delle catene laterali).



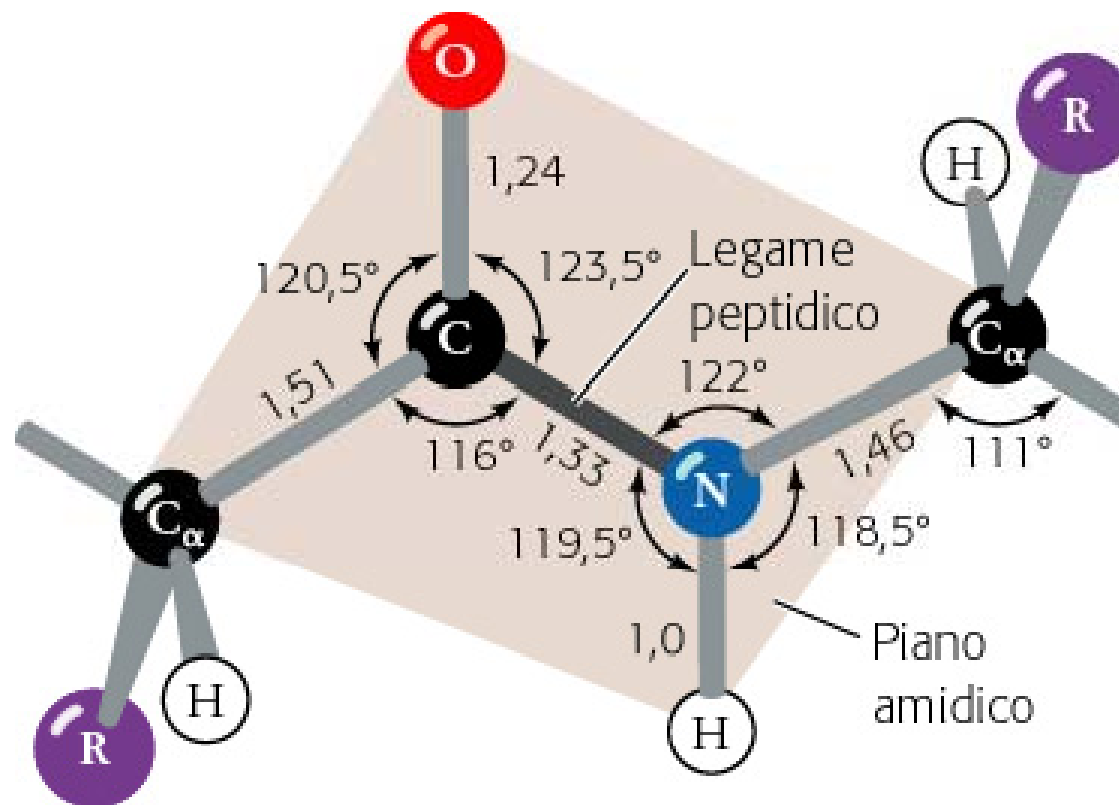
Il legame peptidico



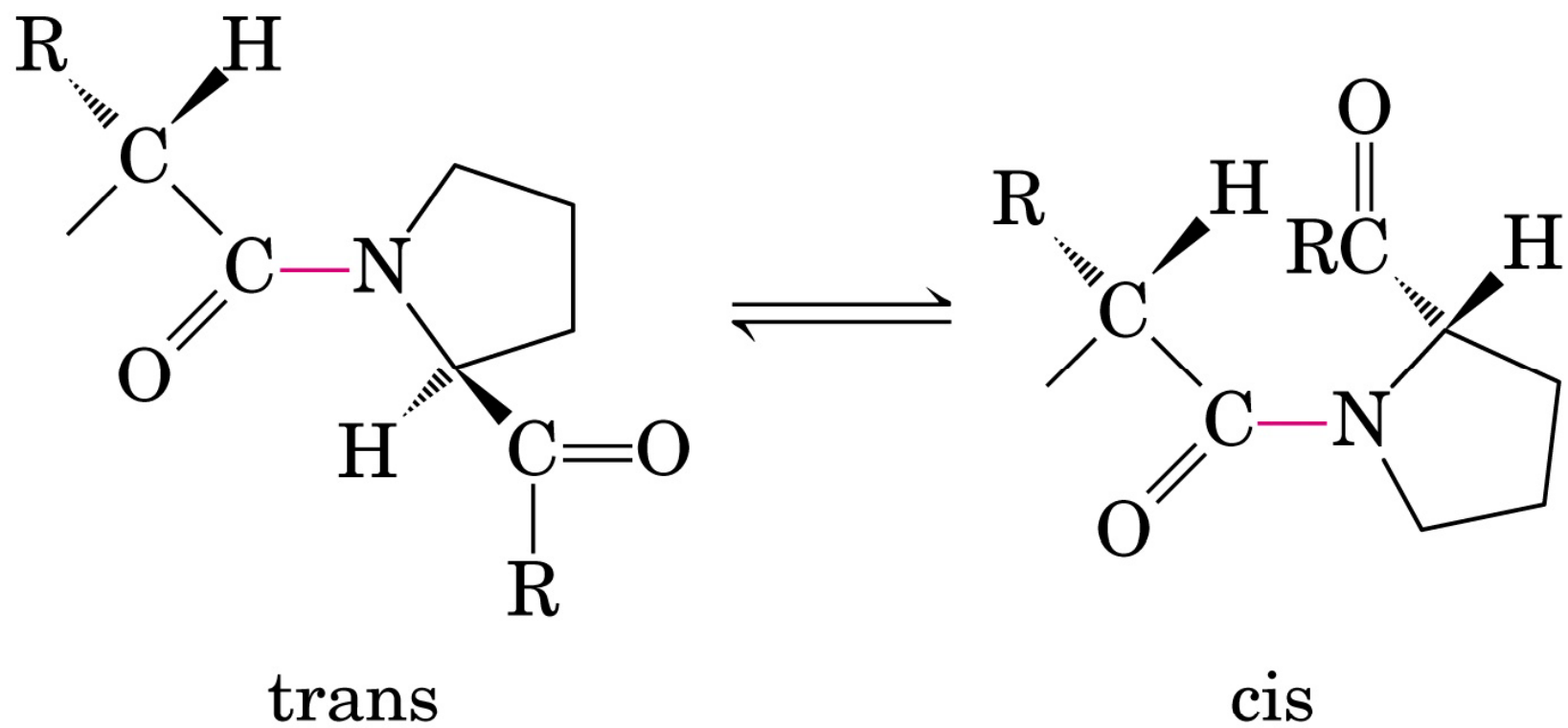
Il gruppo peptidico, come conseguenza delle interazioni di risonanza, è una struttura rigida e planare con le caratteristiche tipiche del doppio legame



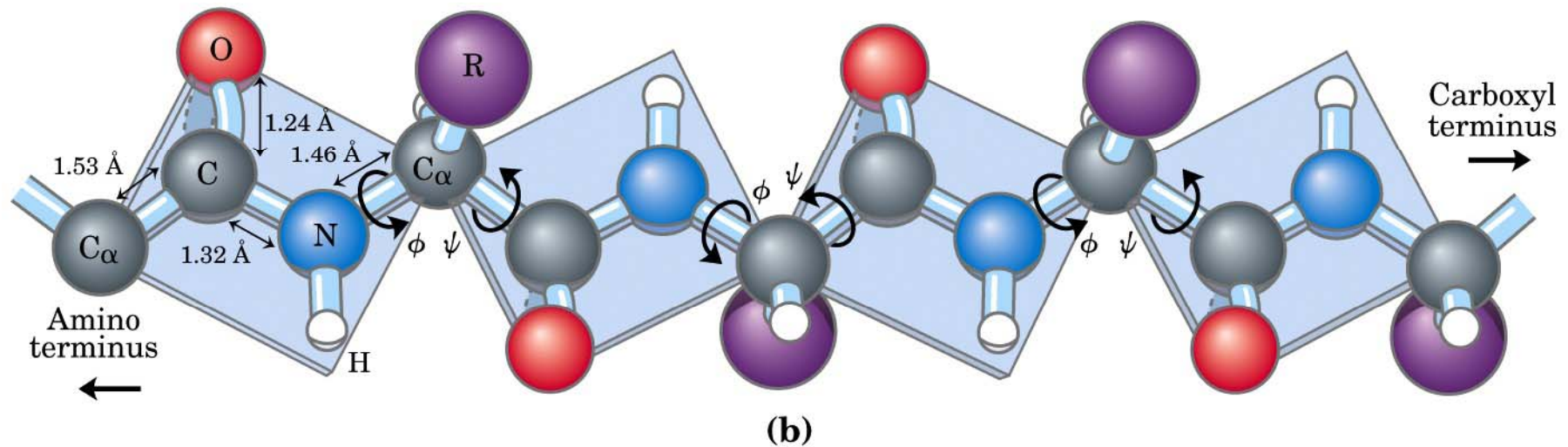
Il legame C-N è circa 0.13 Å più corto del legame N-C_α;
mentre il il legame C=O è circa 0.02 più lungo di quello delle aldeidi
o dei chetoni.



I due carboni alfa sono in **configurazione** trans
(unica possibile eccezione Pro)

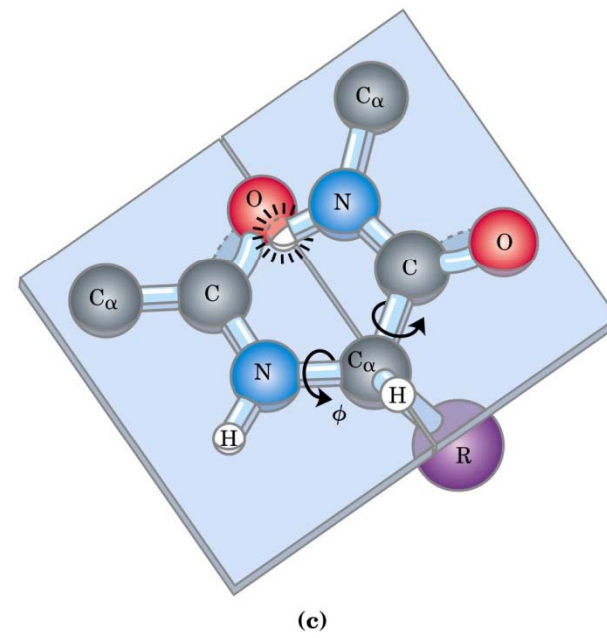
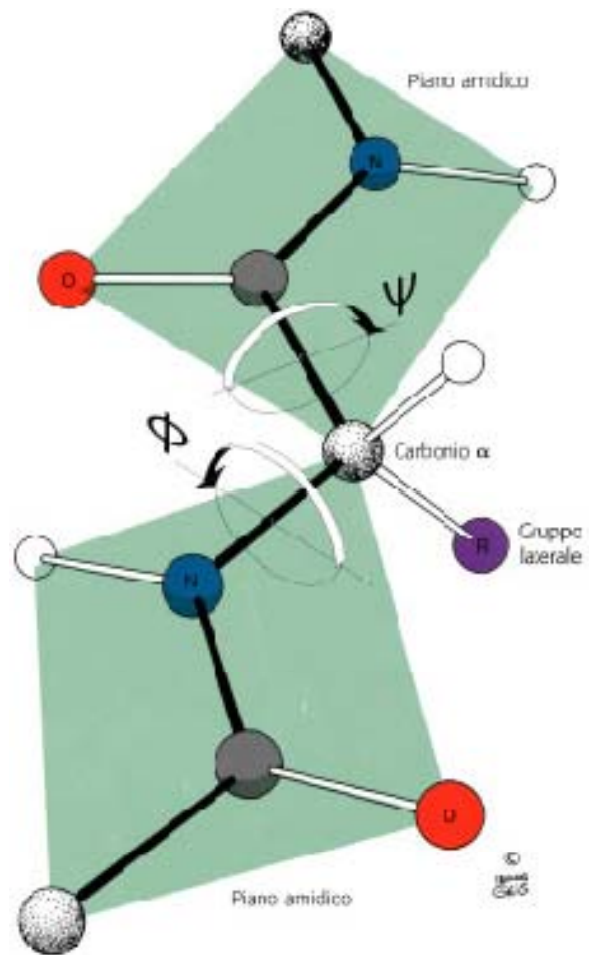


Proline isomers
(b)

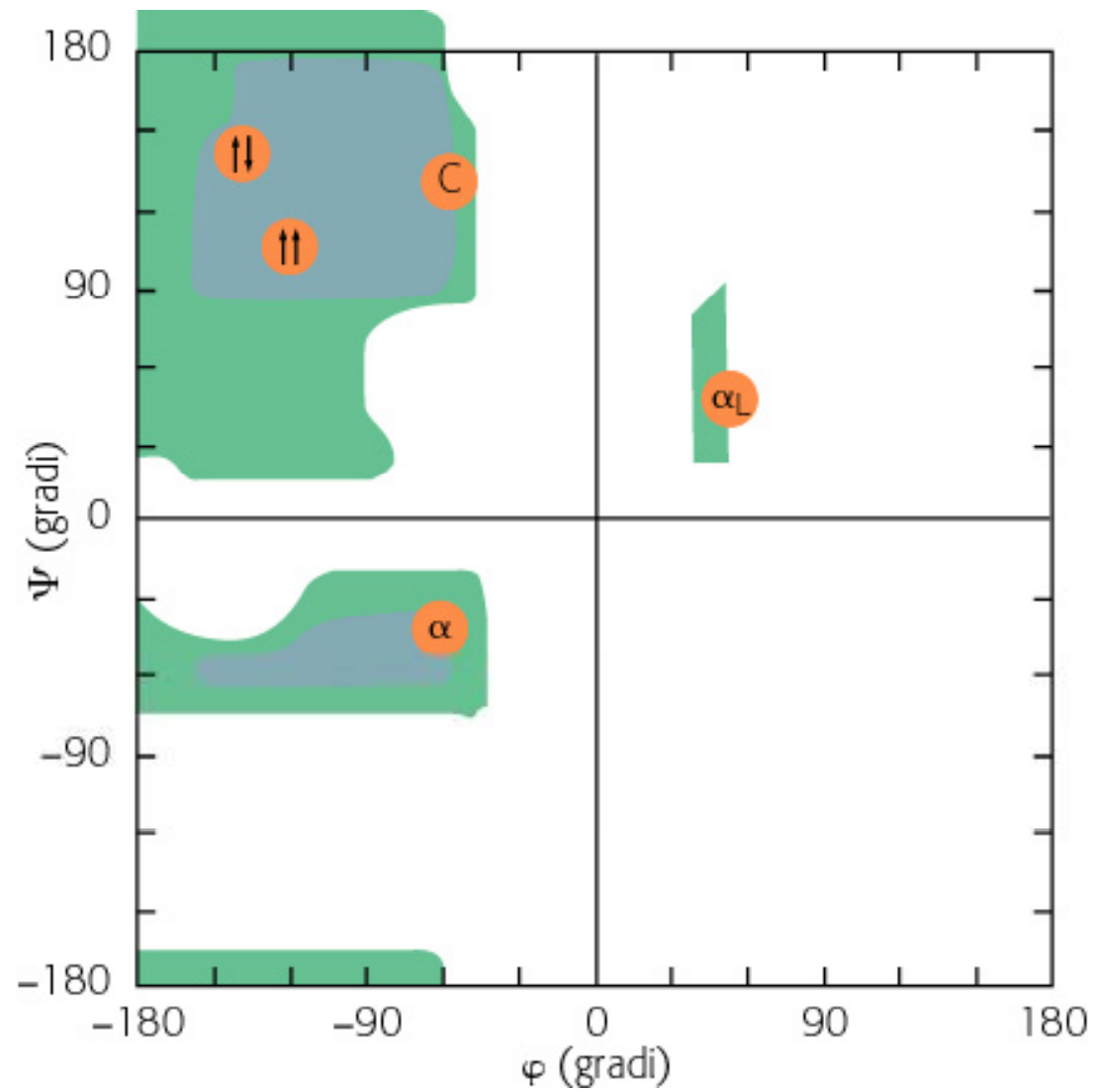


Per convenzione gli angoli di torsione ϕ (N-C α) e ψ (C α -C) sono uguali a 180°
 Quando il polipeptide è nella conformazione completamente estesa

In linea di principio gli angoli ϕ e ψ possono assumere qualunque valore compreso tra -180° e $+180^\circ$, ma molti di questi valori sono impediti per problemi di interferenza sterica tra gli atomi dello scheletro polipeptidico e quelli della catena laterale



Il grafico di Ramachandran



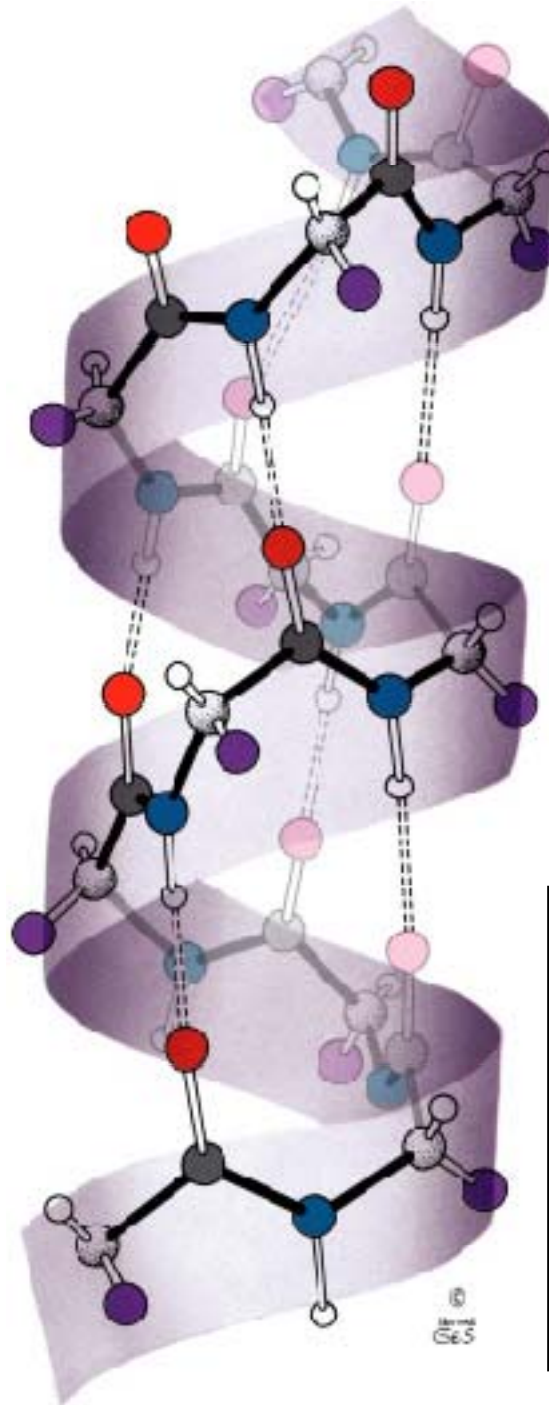
L' α elica

(Pauling e Corey 1951)

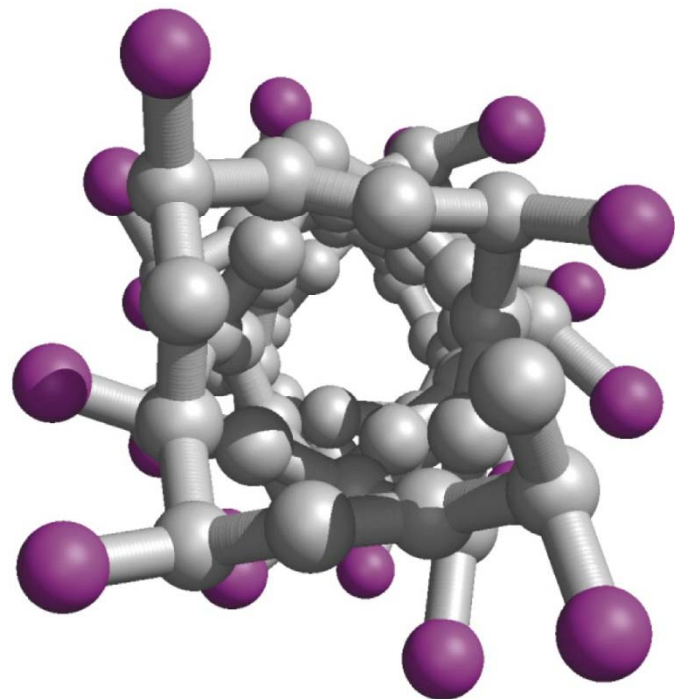
3,6 residui per giro

Passo di 5,4 Å

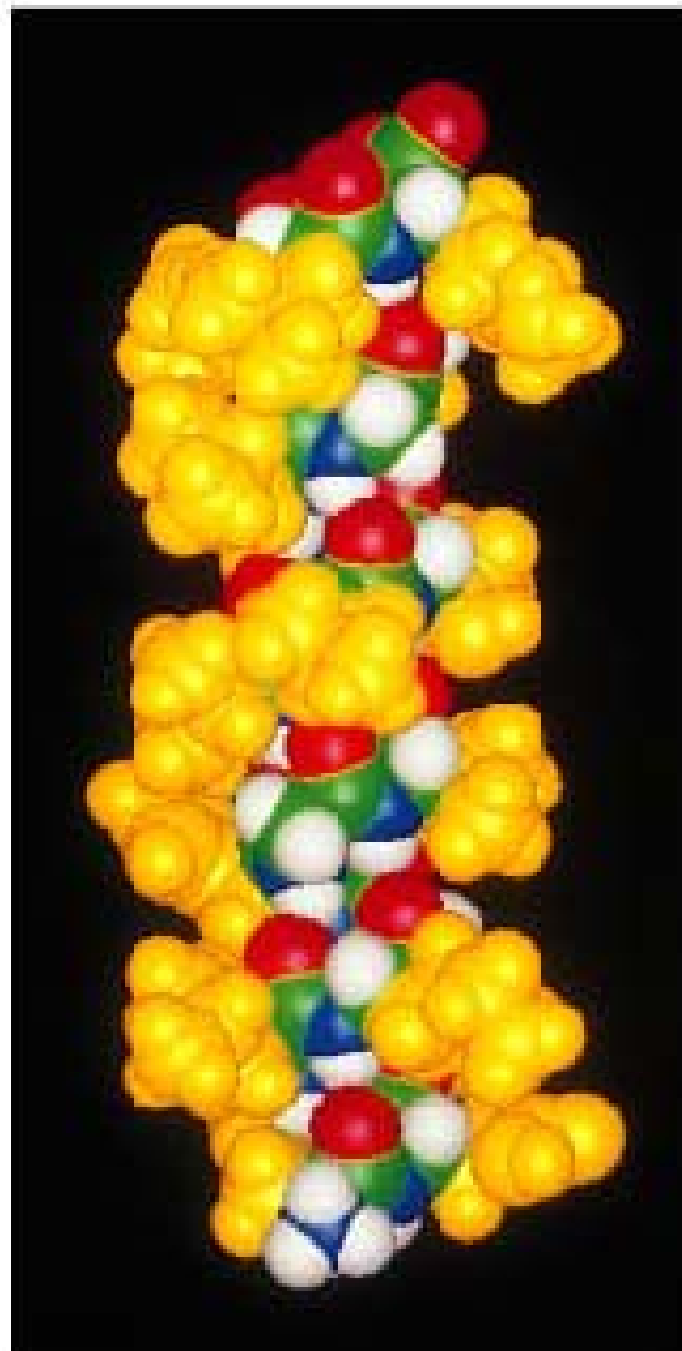
Legame idrogeno
ottimale (2,8 Å)
tra C=O e NH di
quattro residui
successivi

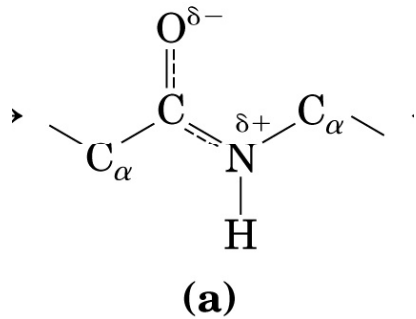


Prolina
Glicina
Residui carichi
consecutivi
Residui ingombranti
Adiacenti
Dipolo elettrico

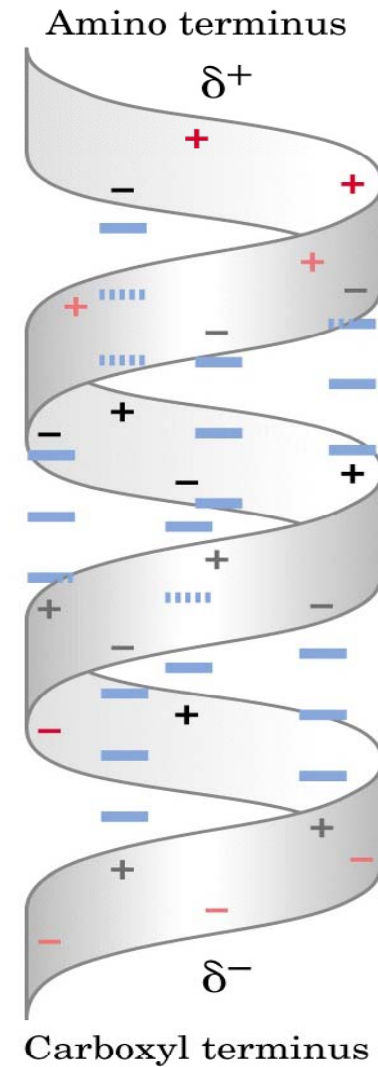


(c)





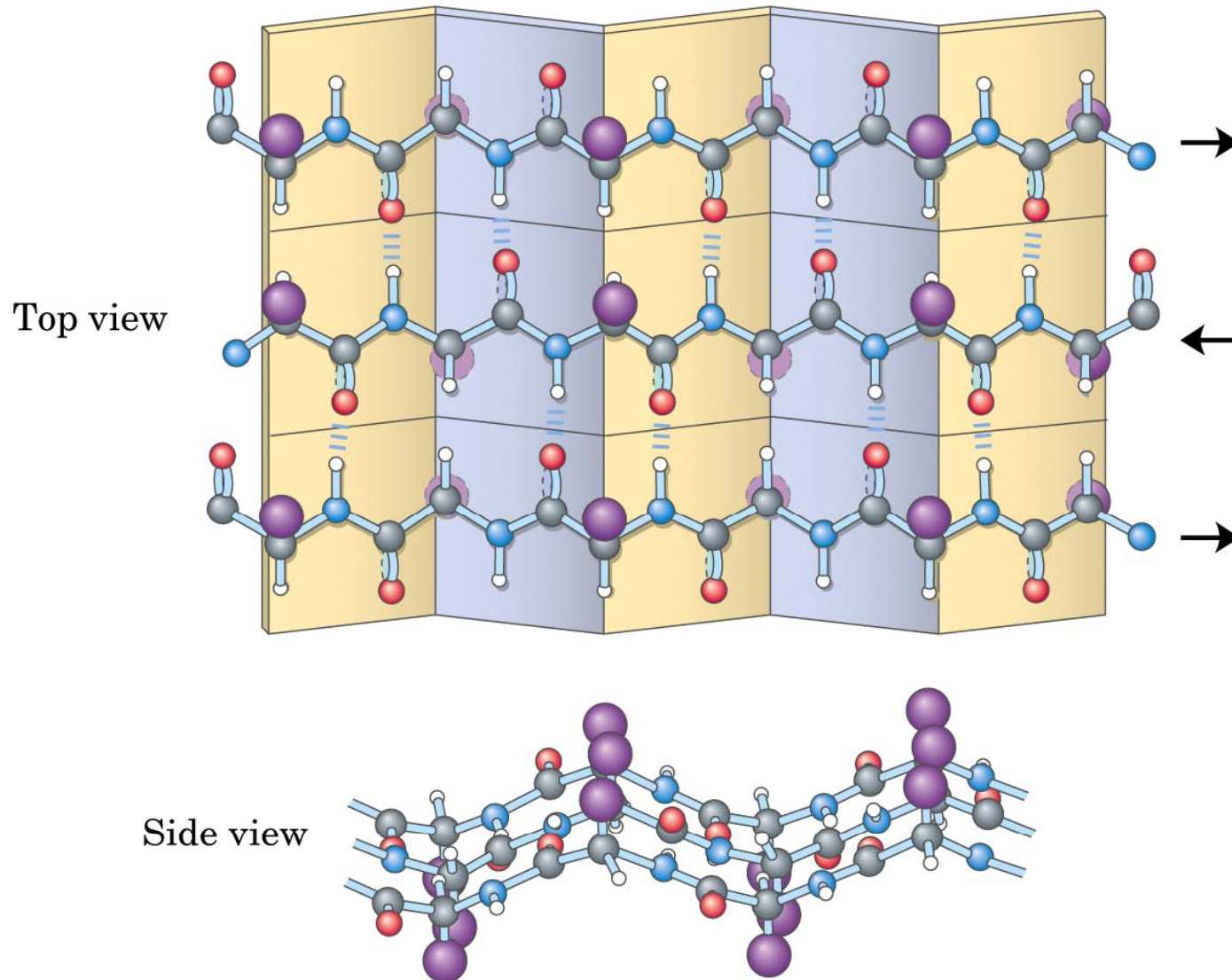
Il dipolo elettrico di
un legame peptidico
viene trasmesso lungo
l'elica mediante i
legami idrogeno
intercatena,
generando un dipolo
complessivo dell'elica



La conformazione beta delle catene polipeptidiche

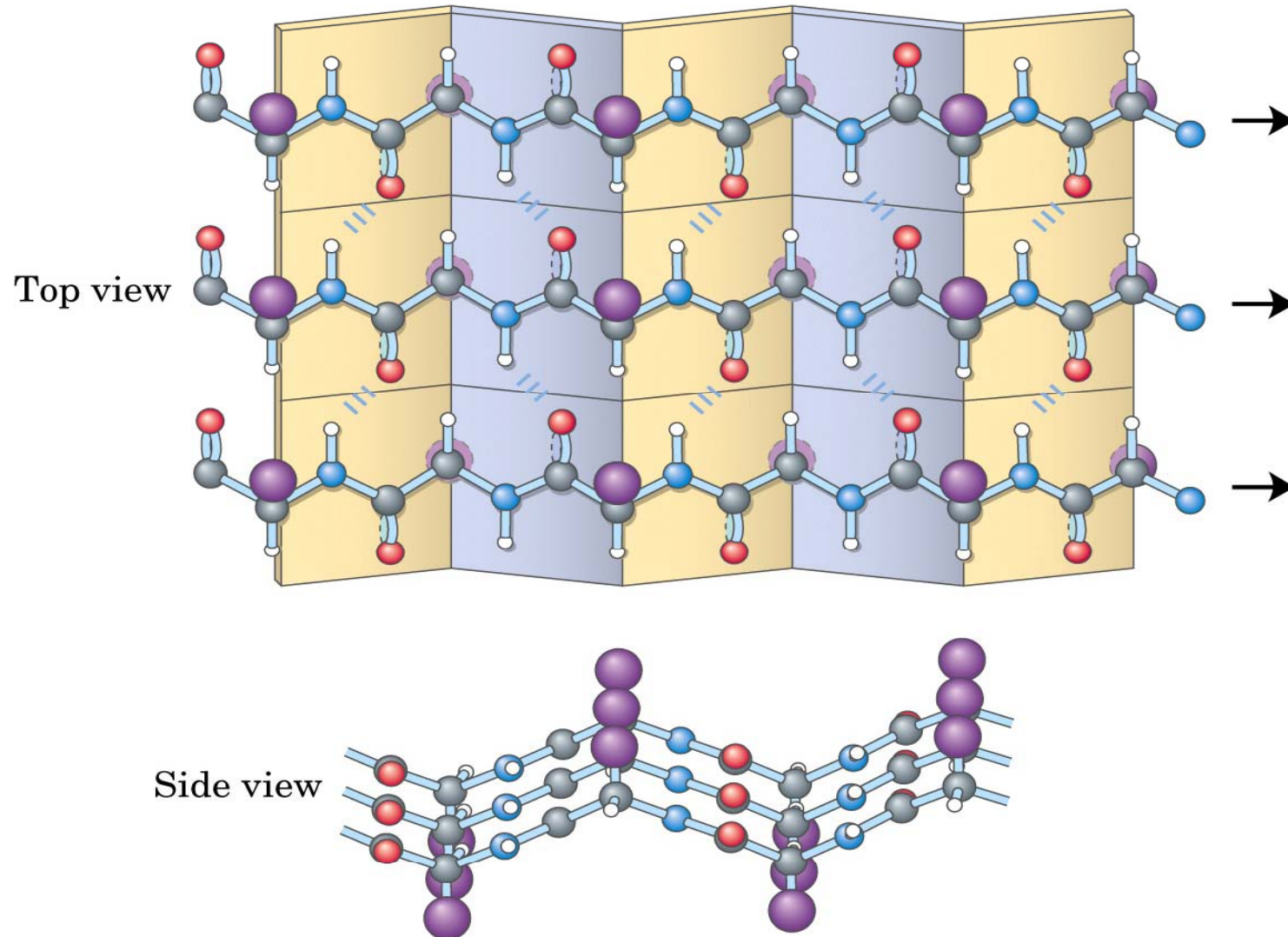
Pauling e Corey 1951

(a) Antiparallel

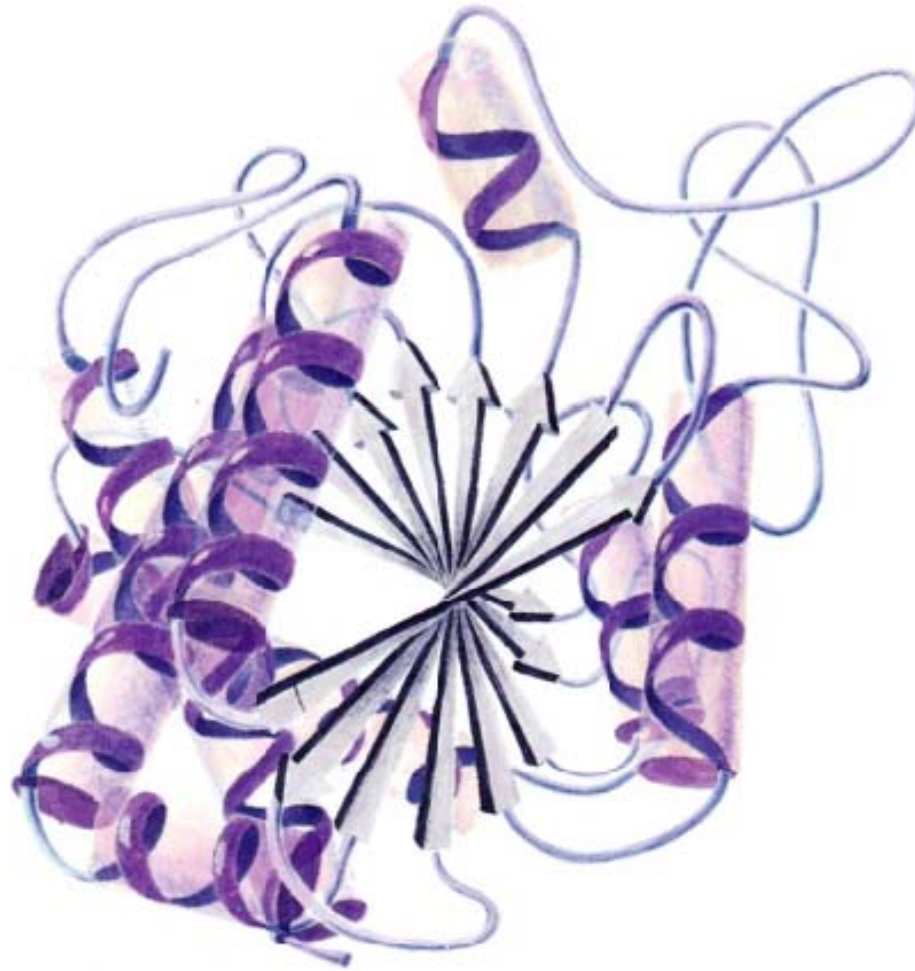


La conformazione beta delle catene polipeptidiche

(b) Parallel



Rappresentazione schematica della carbossipeptidasi A



Connessioni tra catene adiacenti nei foglietti β

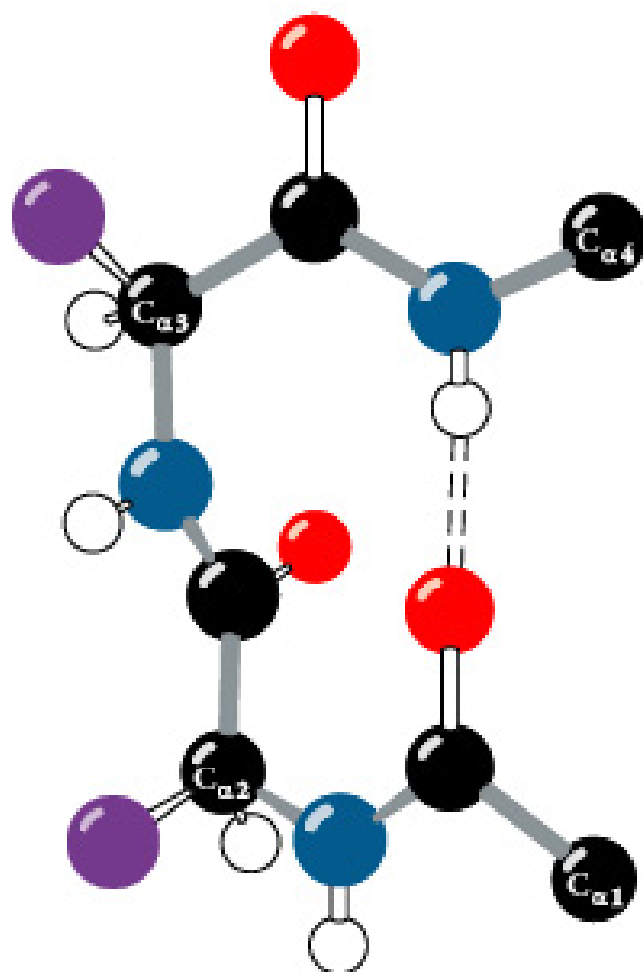
(a)



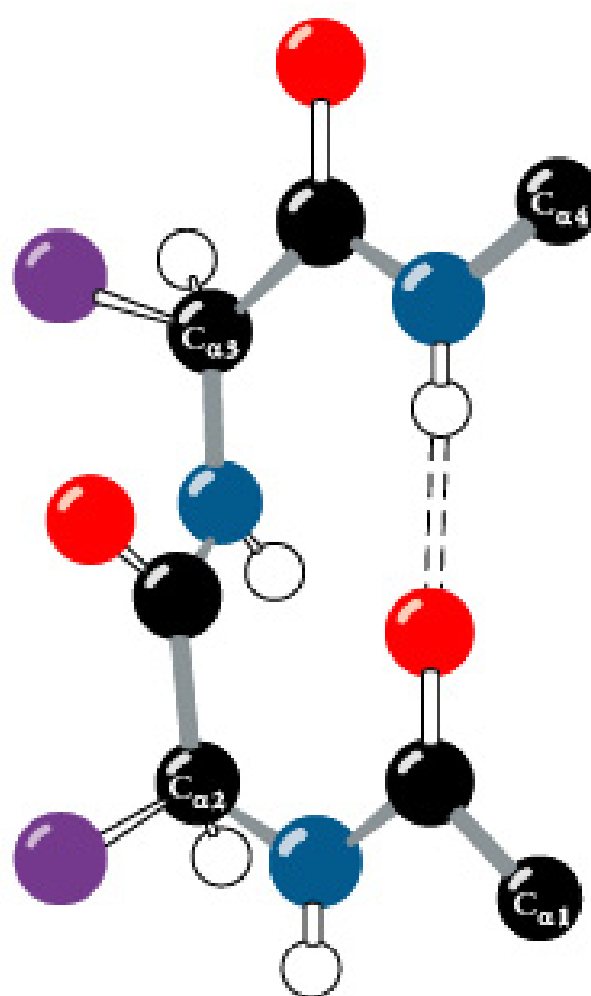
(b)

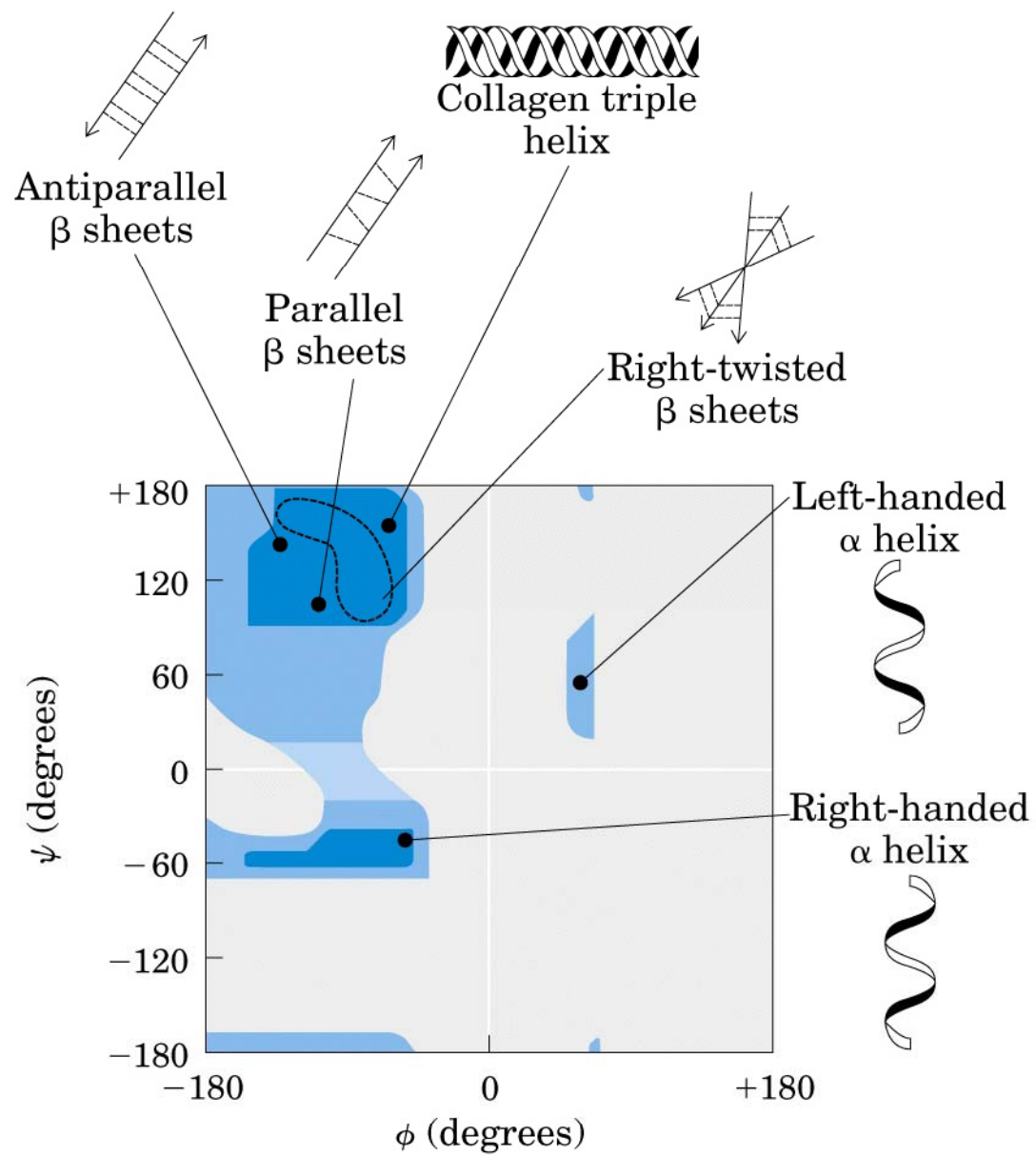


(a) Ripiegamento Tipo I



(b) Ripiegamento Tipo II





(a)

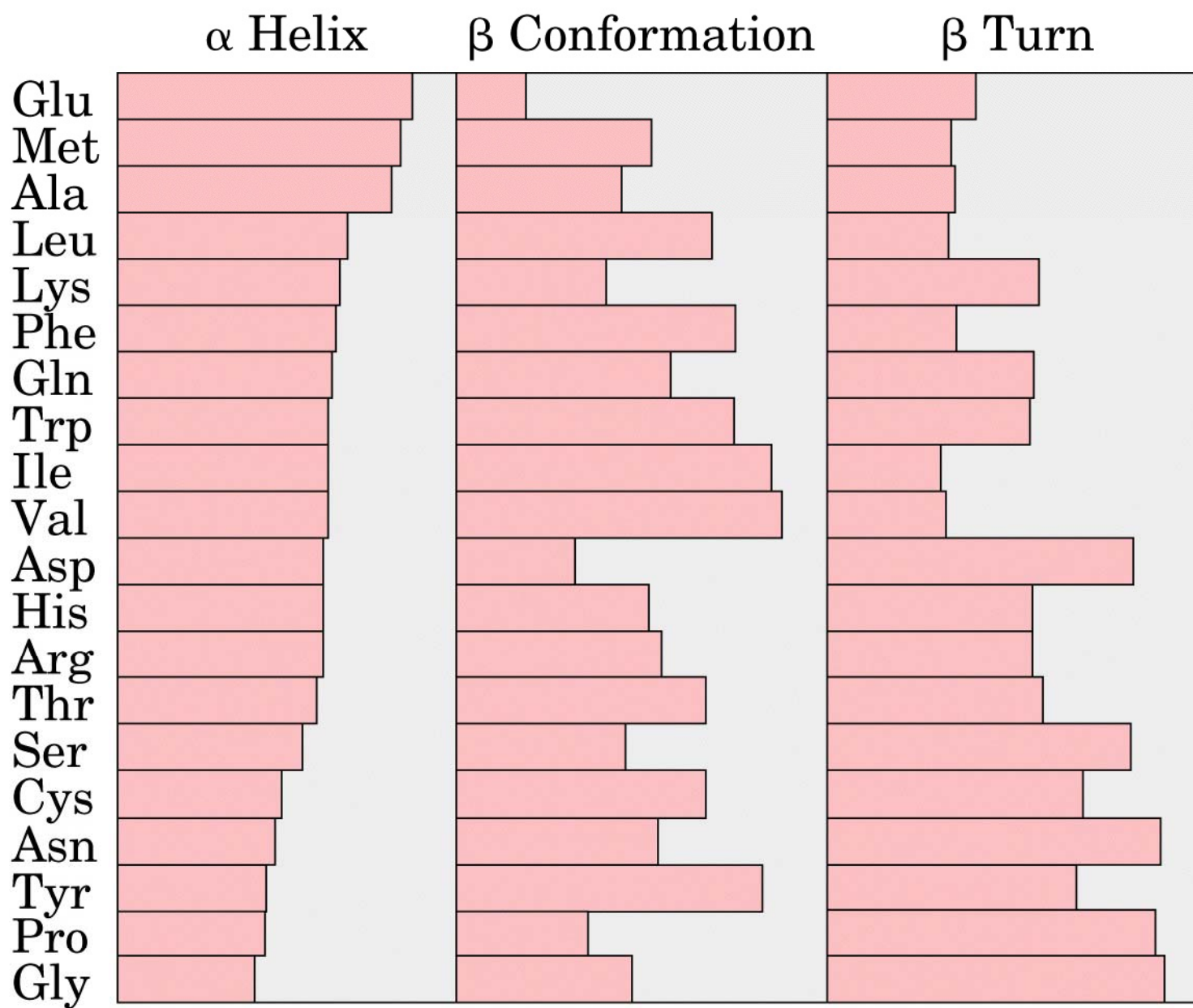


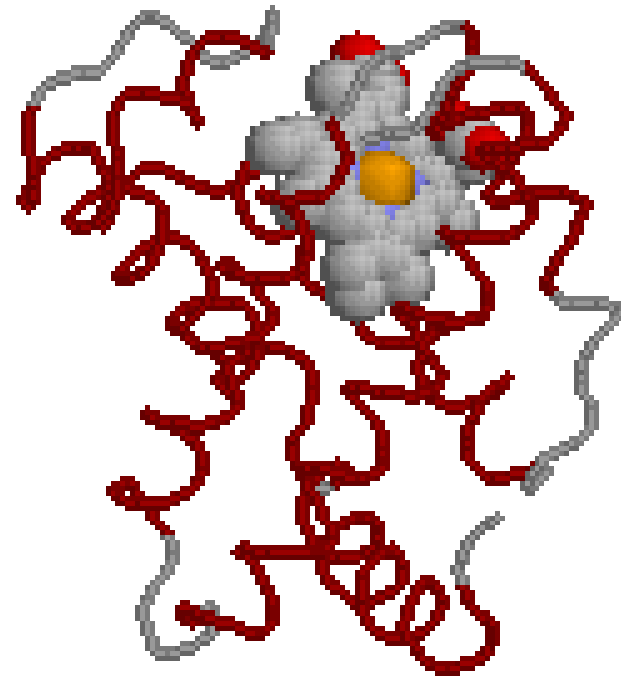
TABLE 3.3 Relative frequencies of amino acid residues in secondary structures

Amino acid	α helix	β sheet	Turn
Ala	1.29	0.90	0.78
Cys	1.11	0.74	0.80
Leu	1.30	1.02	0.59
Met	1.47	0.97	0.39
Glu	1.44	0.75	1.00
Gln	1.27	0.80	0.97
His	1.22	1.08	0.69
Lys	1.23	0.77	0.96
Val	0.91	1.49	0.47
Ile	0.97	1.45	0.51
Phe	1.07	1.32	0.58
Tyr	0.72	1.25	1.05
Trp	0.99	1.14	0.75
Thr	0.82	1.21	1.03
Gly	0.56	0.92	1.64
Ser	0.82	0.95	1.33
Asp	1.04	0.72	1.41
Asn	0.90	0.76	1.28
Pro	0.52	0.64	1.91
Arg	0.96	0.99	0.88

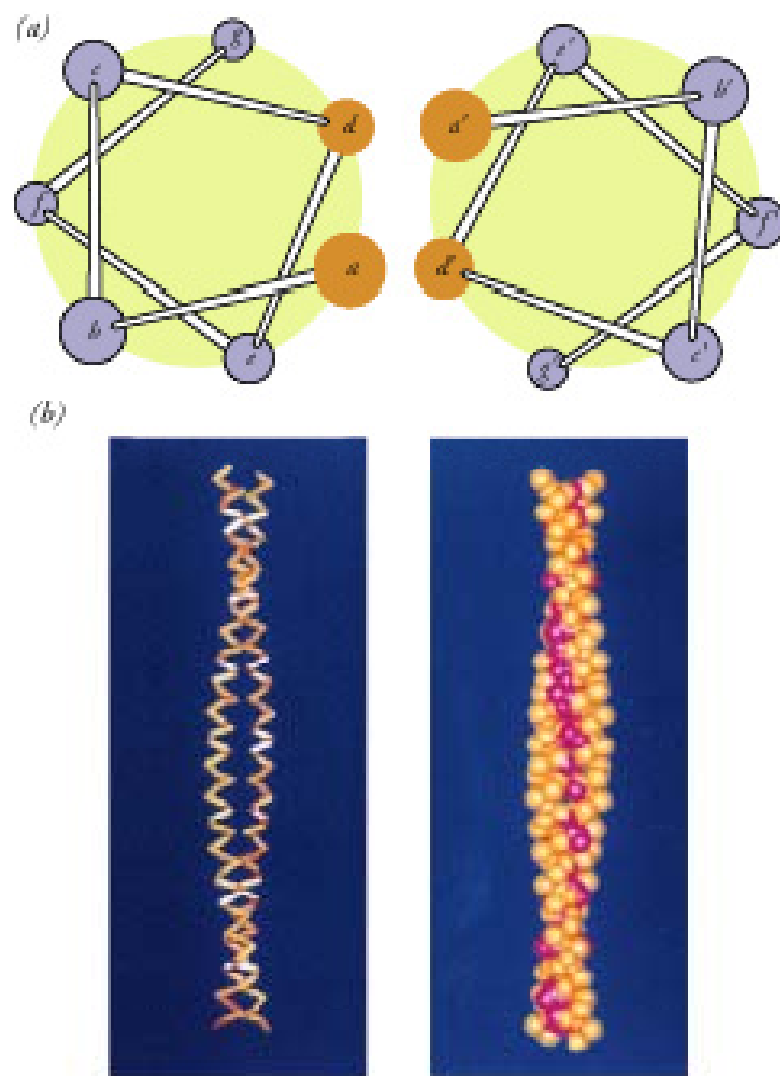
Note: The amino acids are grouped according to their preference for α helices (top group), β sheets (second group), or turns (third group). Arginine shows no significant preference for any of the structures.

After T. E. Creighton, *Proteins: Structures and Molecular Properties*, 2d ed.
(W. H. Freeman and Company, 1992), p. 256.

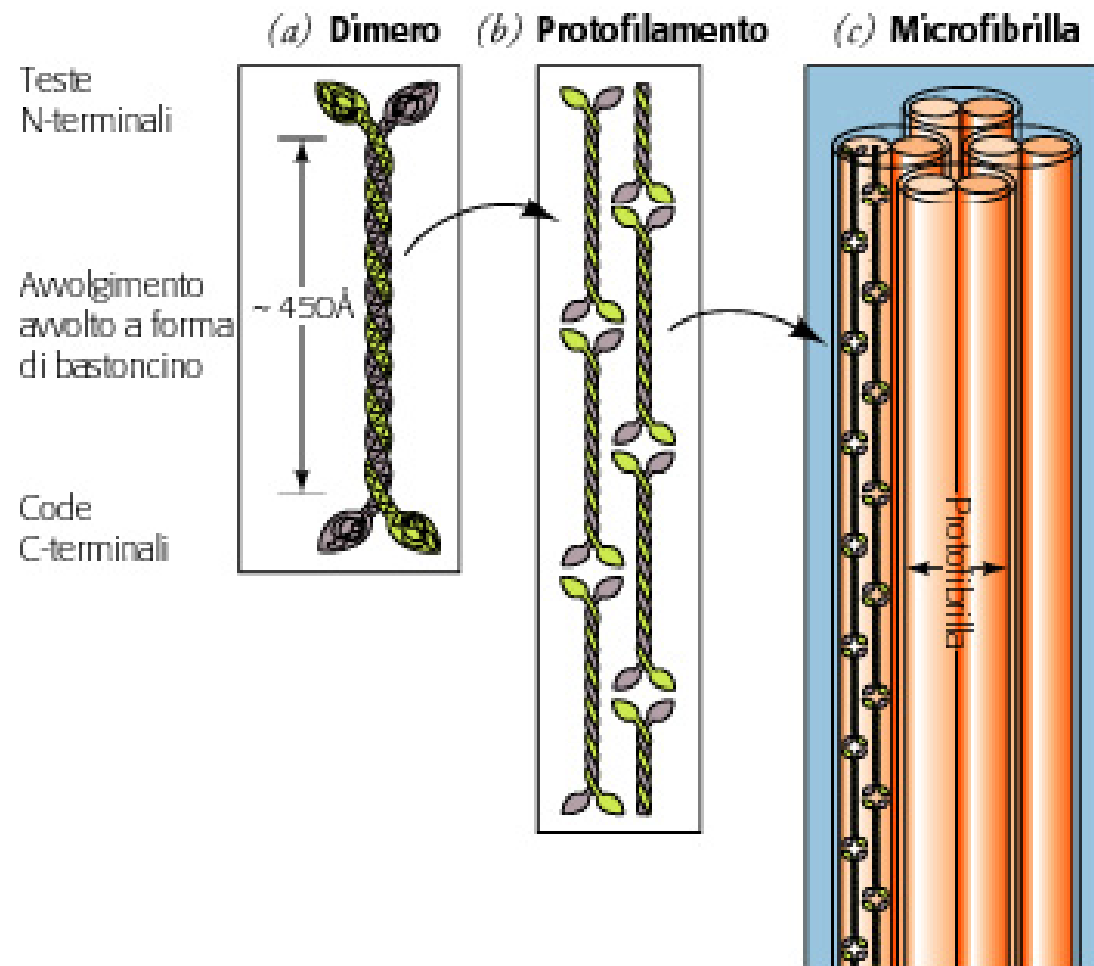
La struttura terziaria e quaternaria delle proteine

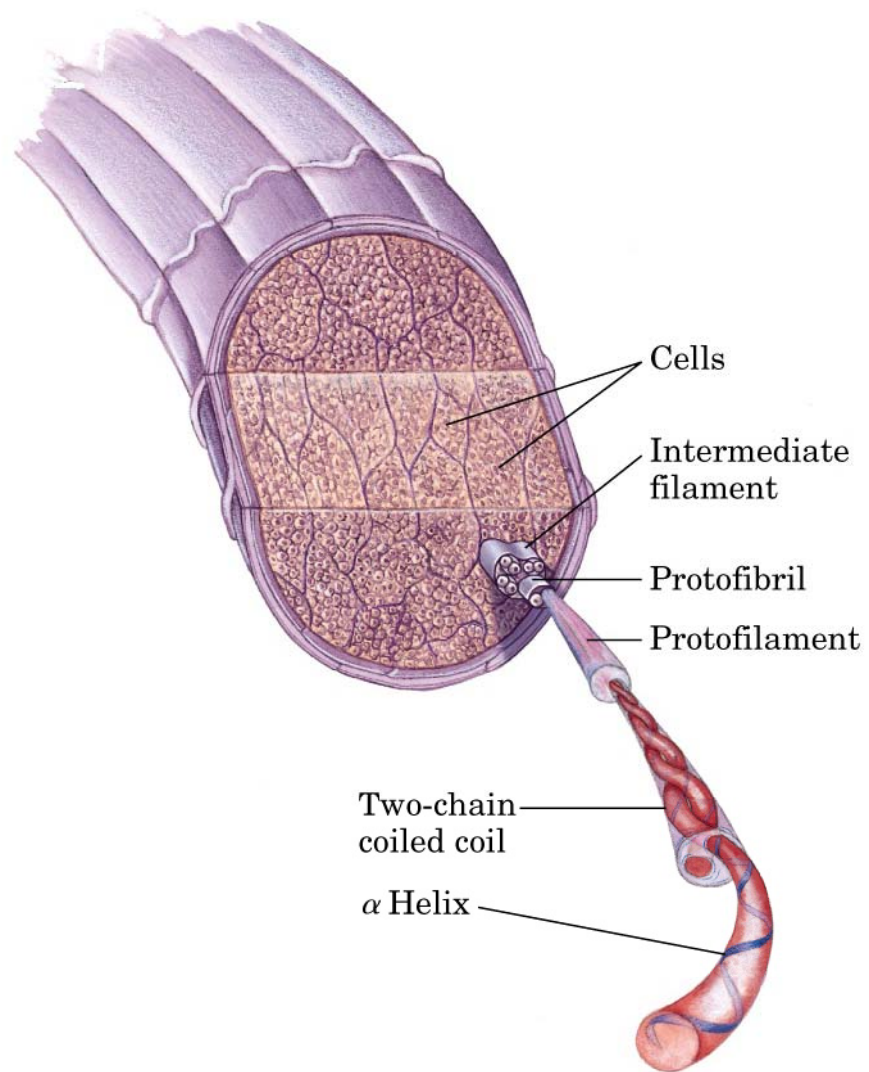


Avvolgimento dell' α -cheratina

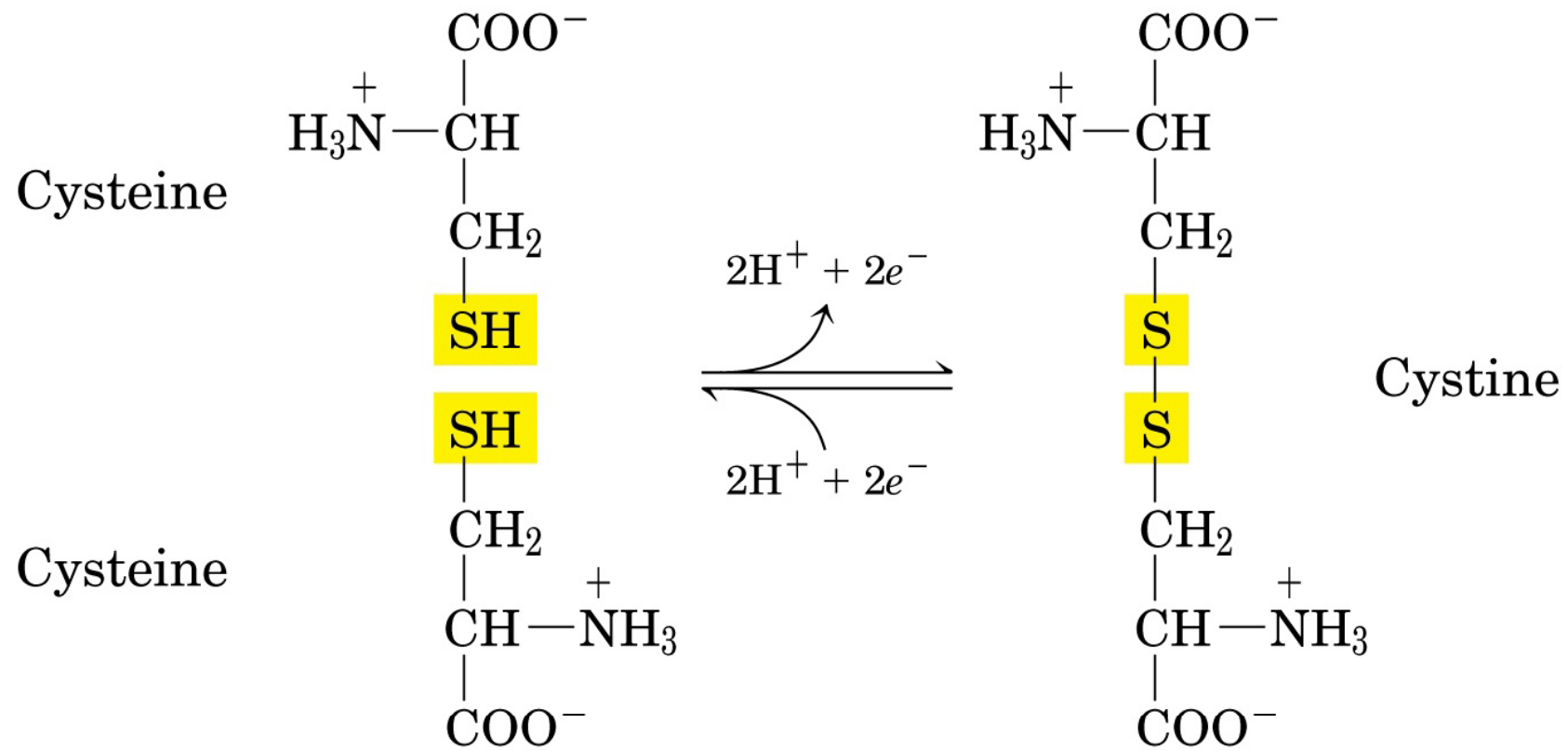


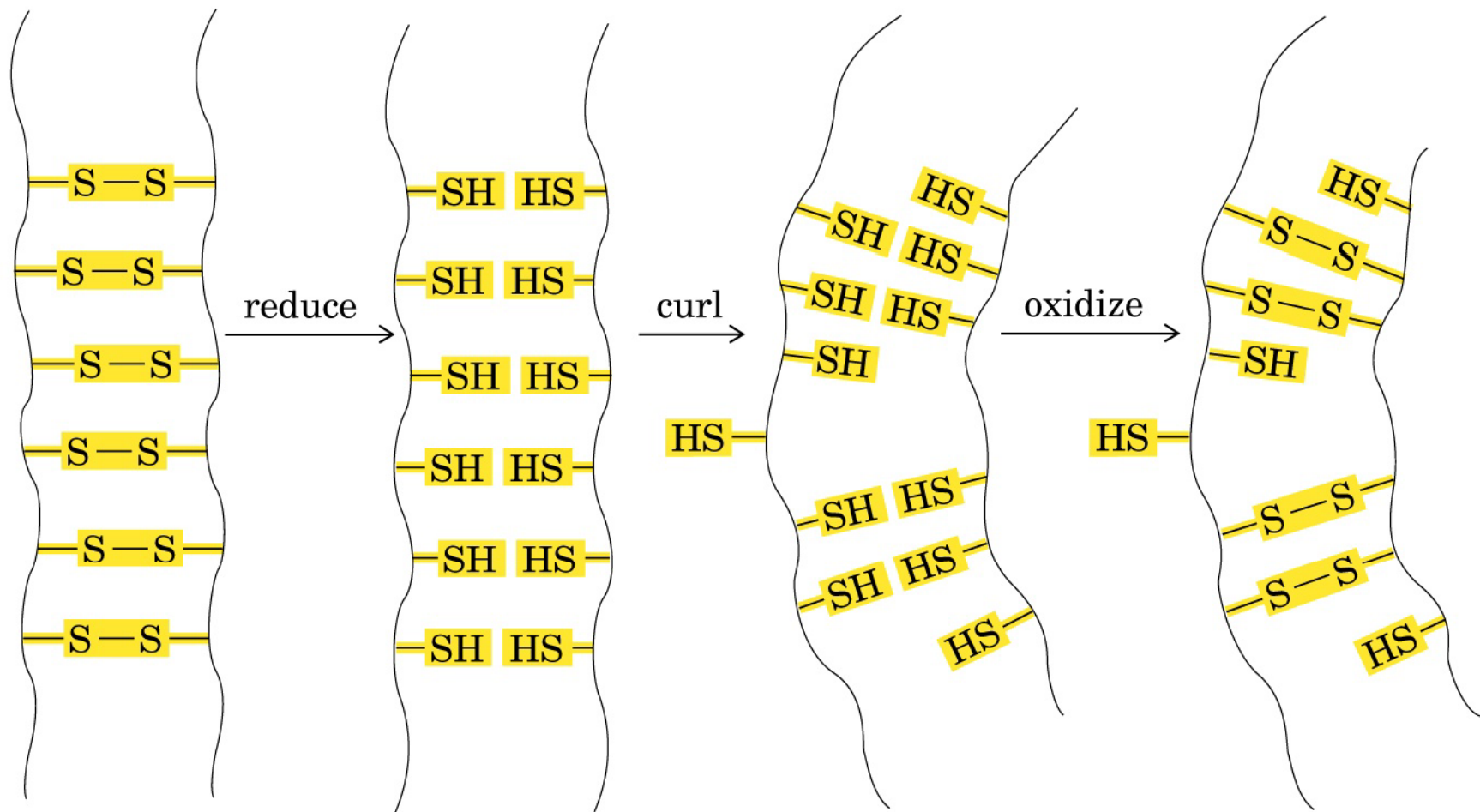
Diversi livelli di organizzazione della cheratina

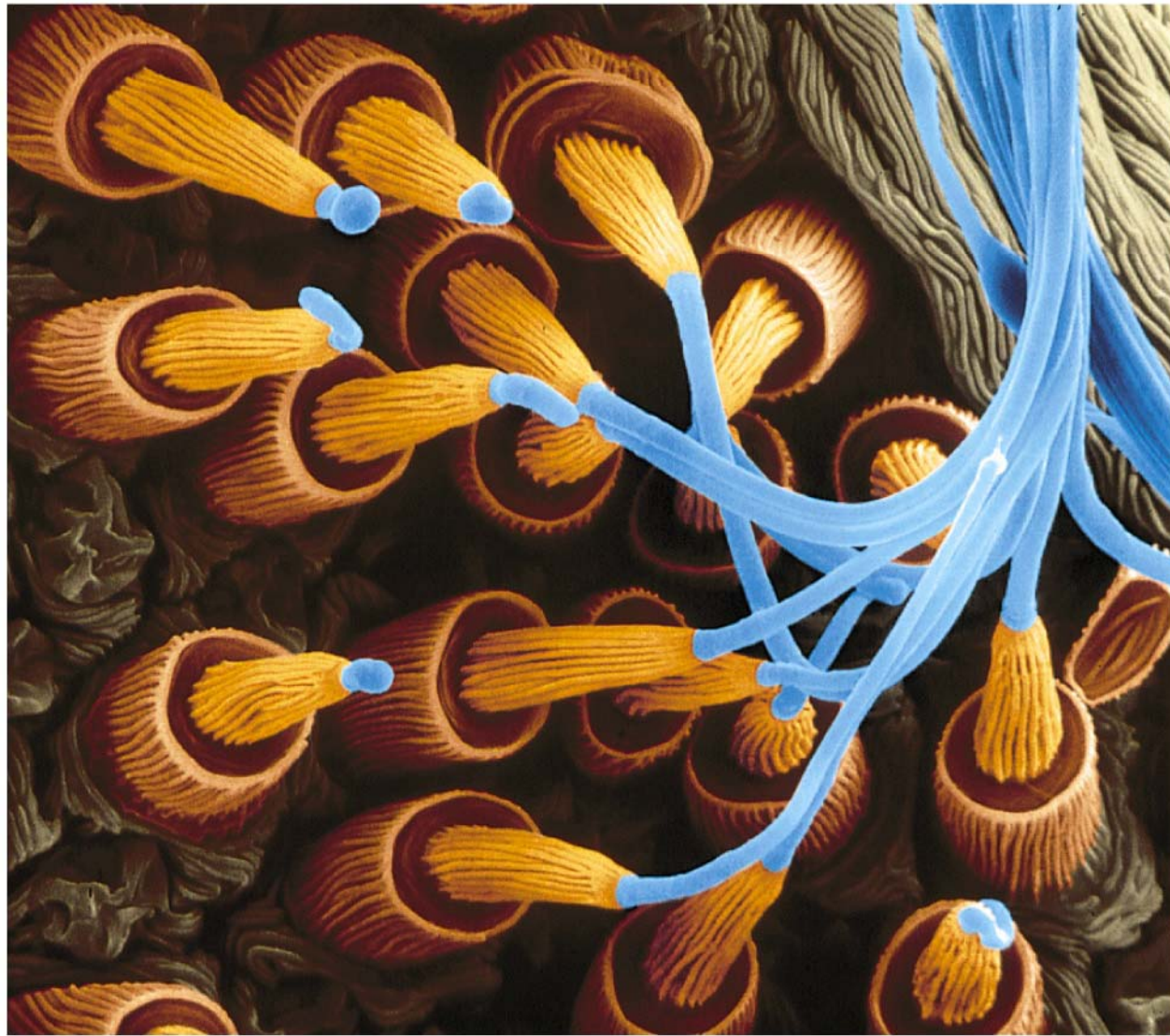




Cross section of a hair
(b)



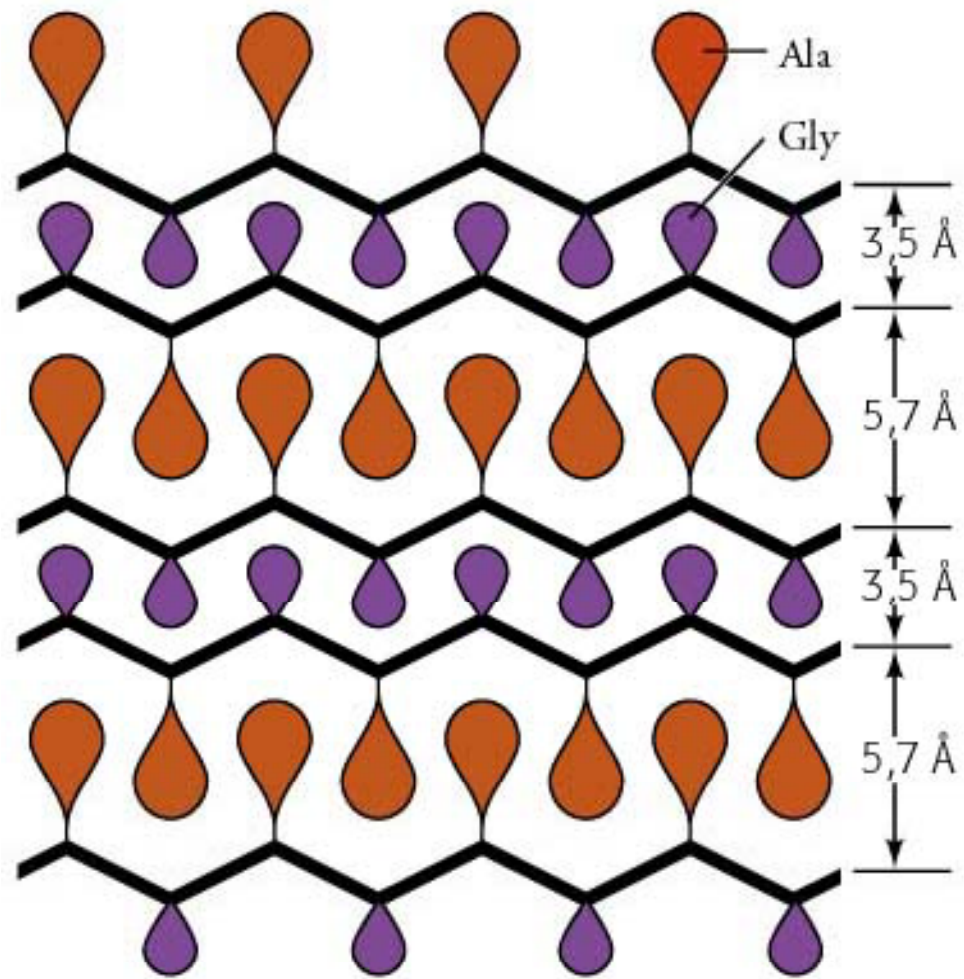




70 μm

(b)

La fibroina della seta



La tripla elica del collagene

Vari tipi di catene

Conformazione elicoidale
sinistrorsa con tre residui
circa per giro

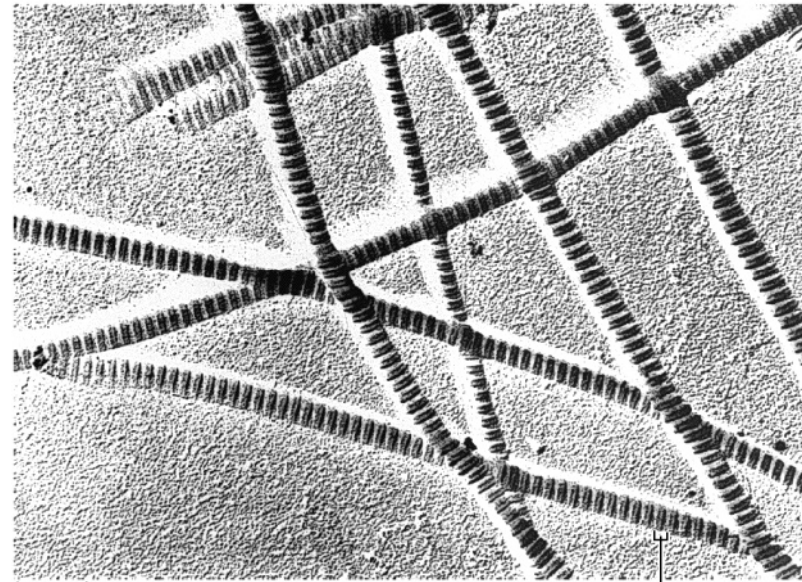
Tre catene si avvolgono
l'una sull'altra con
andamento destrorso



Gly-X-Y

X-Pro
Y-HyPro

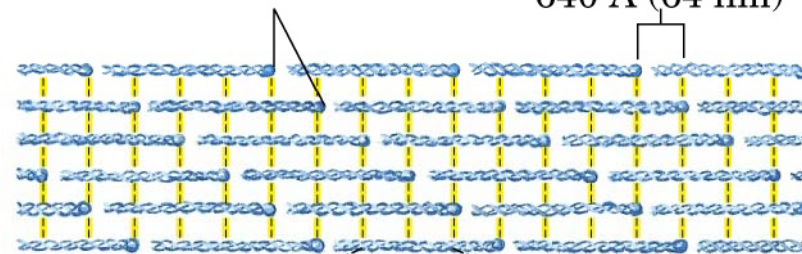
Prolil idrossilasi
Vitamina C



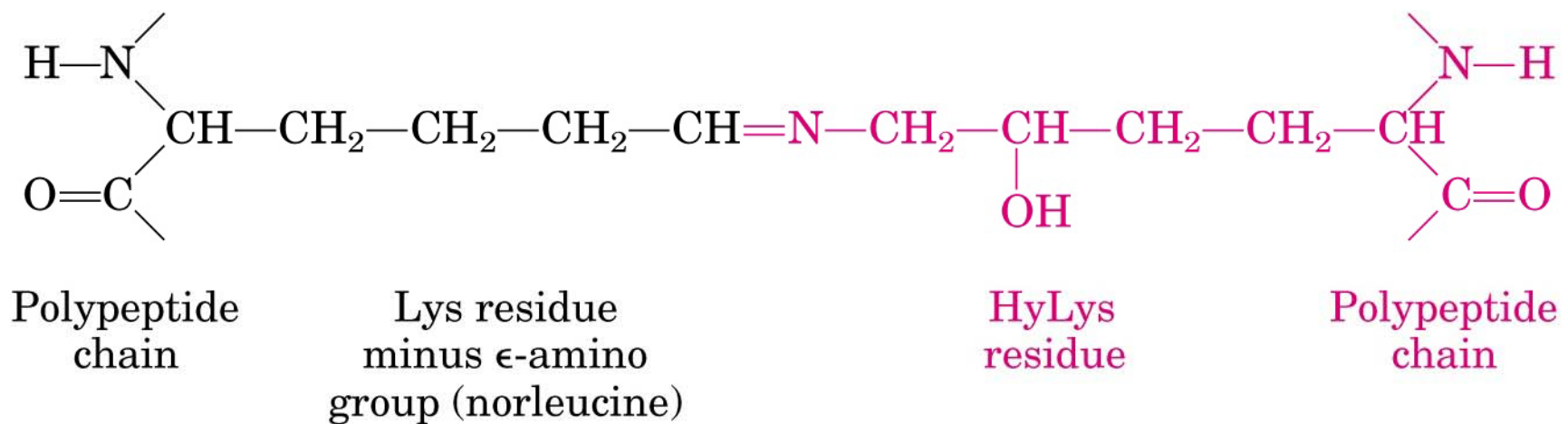
250
nm

Heads of collagen
molecules

Cross-striations
640 Å (64 nm)

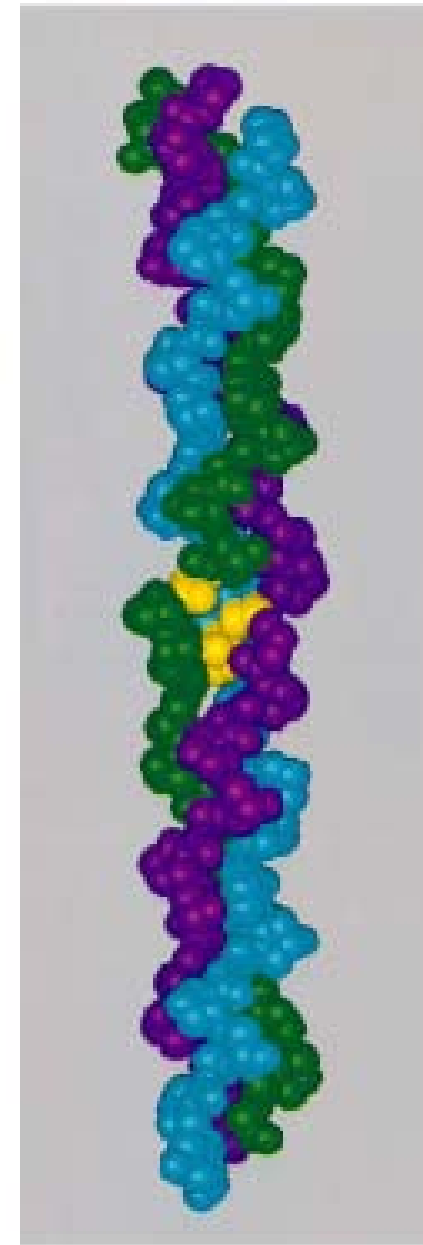
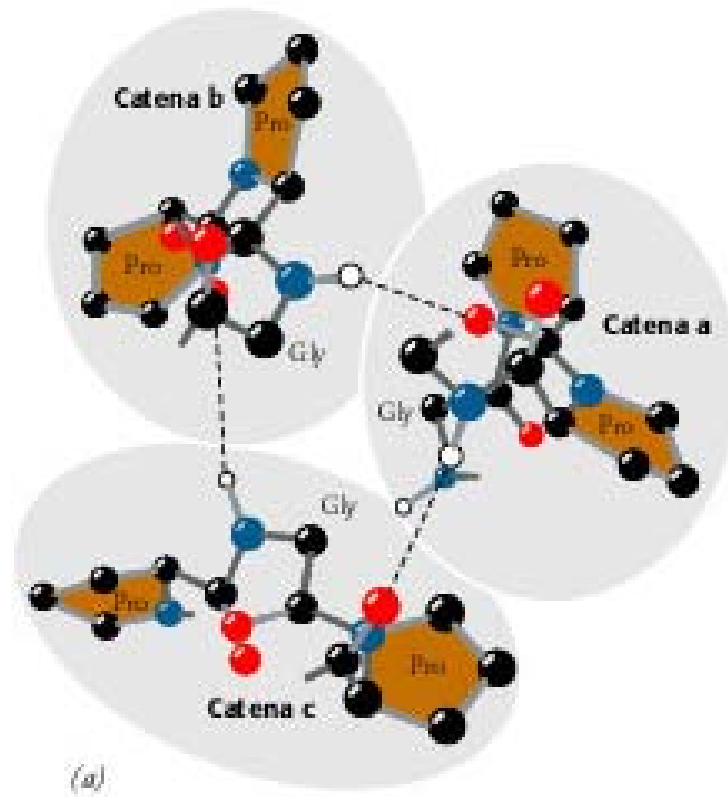


Section of collagen
molecule



Dehydrohydroxylysinonorleucine

Interazioni molecolari nel collagene



(b)

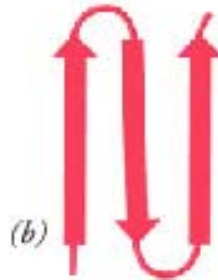
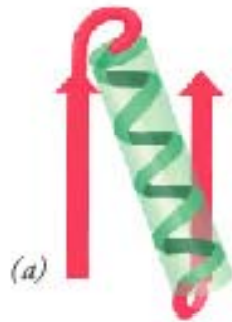
β Conformation
 $2,000 \times 5 \text{ \AA}$

α Helix
 $900 \times 11 \text{ \AA}$

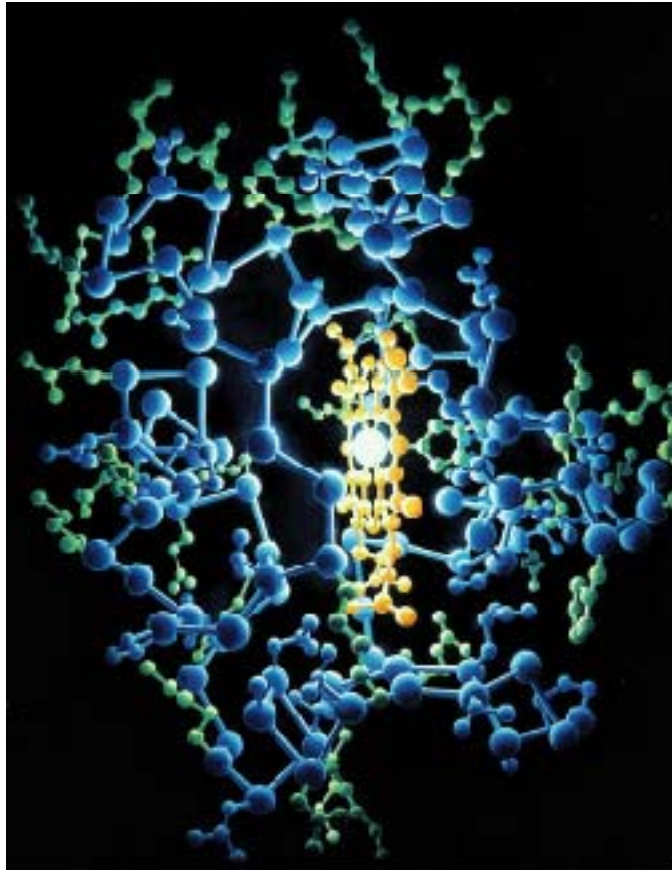
Native globular form
 $130 \times 30 \text{ \AA}$



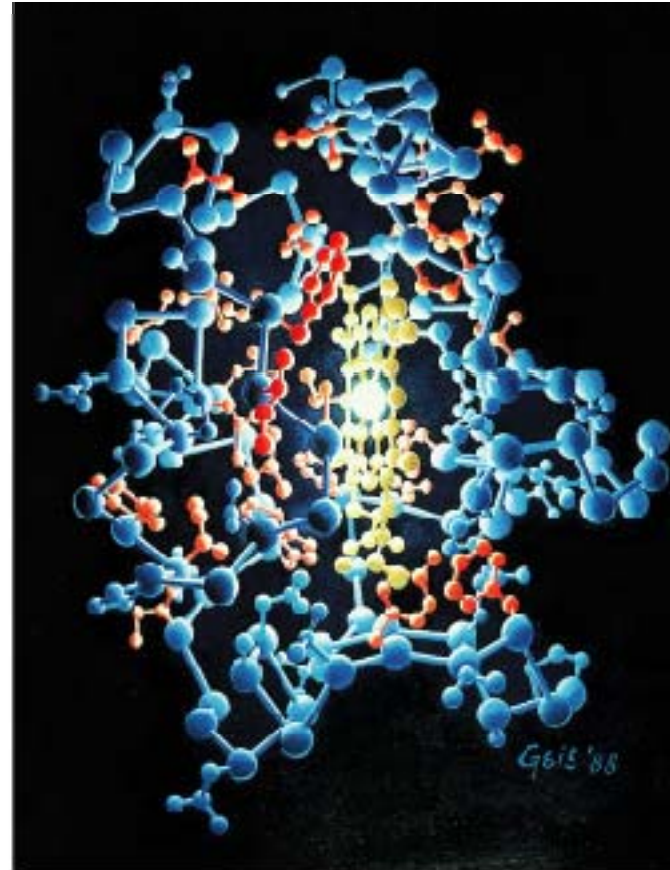
Motivi proteici



Distribuzione delle catene laterali

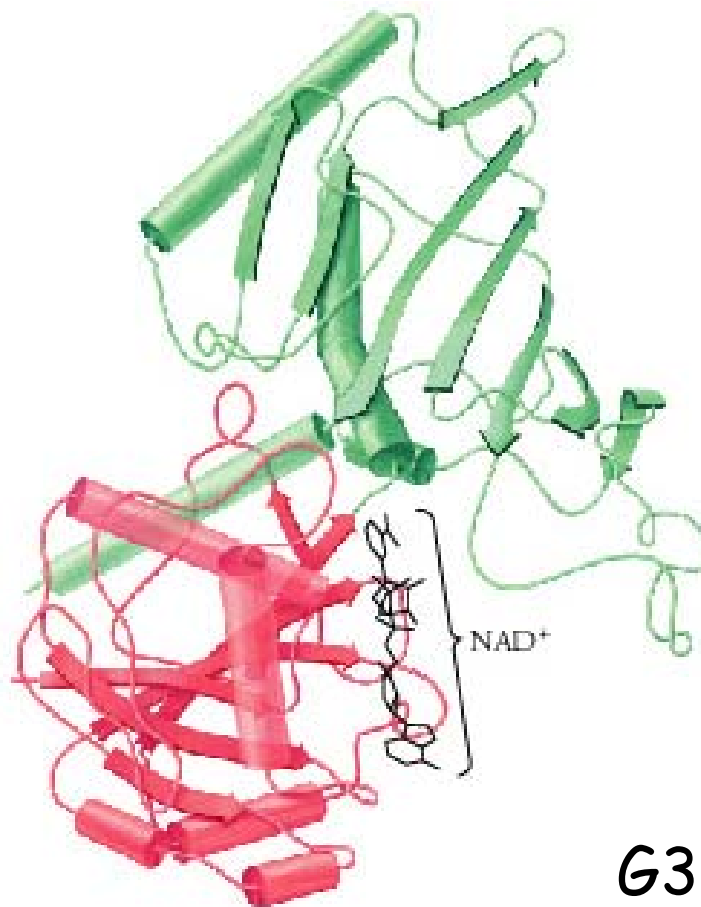


(a)

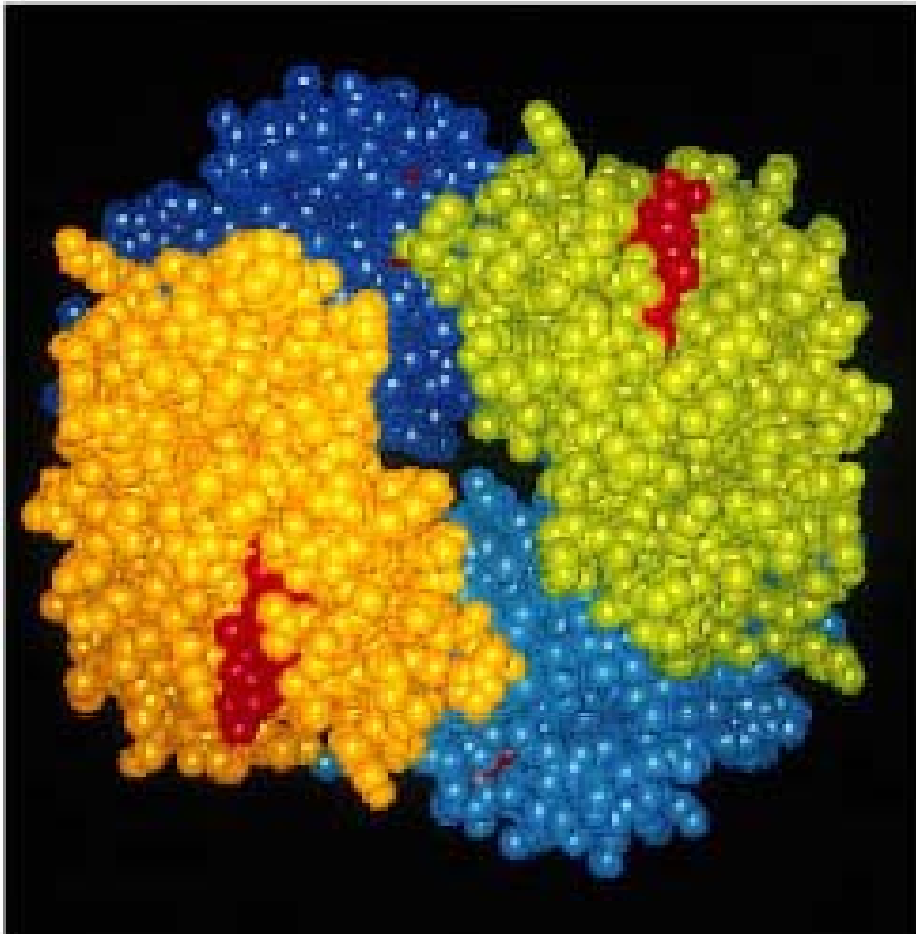


(b)

I domini



La struttura quaternaria ha aspetti funzionali rilevanti



Meno informazione genetica
Maggiore fedeltà di sintesi
Molteplicità dei siti funzionali
Migliore possibilità di regolazione

Simmetria nelle proteine oligomeriche

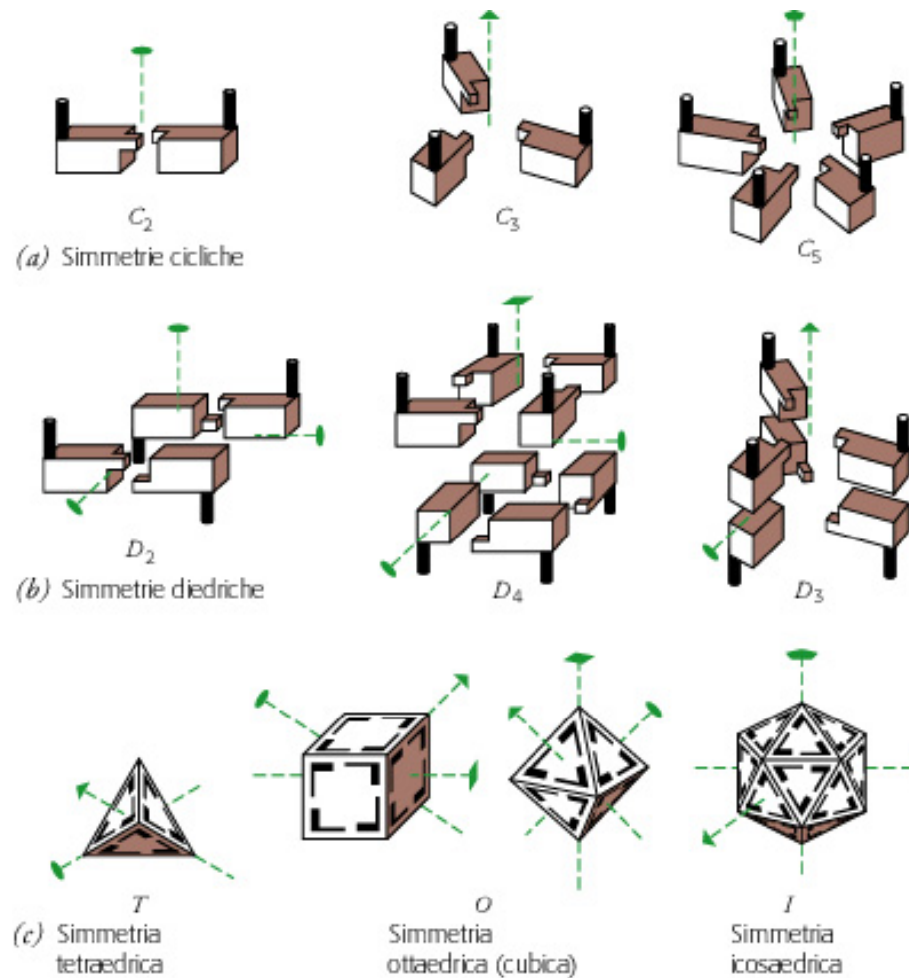


table 5–2

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 (<i>E. coli</i>)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (<i>E. coli</i>)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

Ripiegamento e stabilità delle proteine

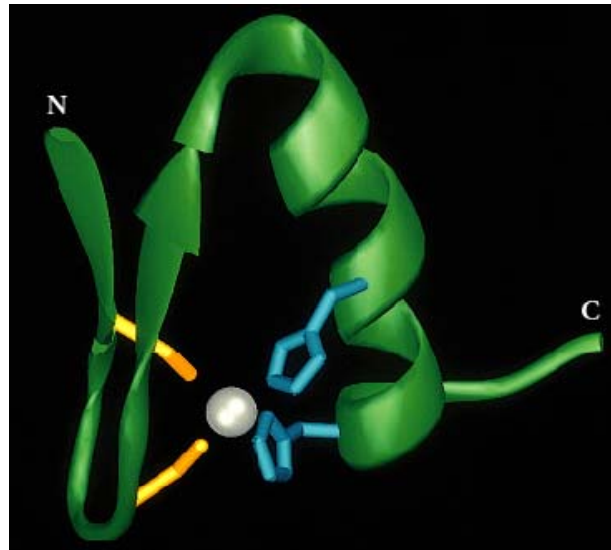
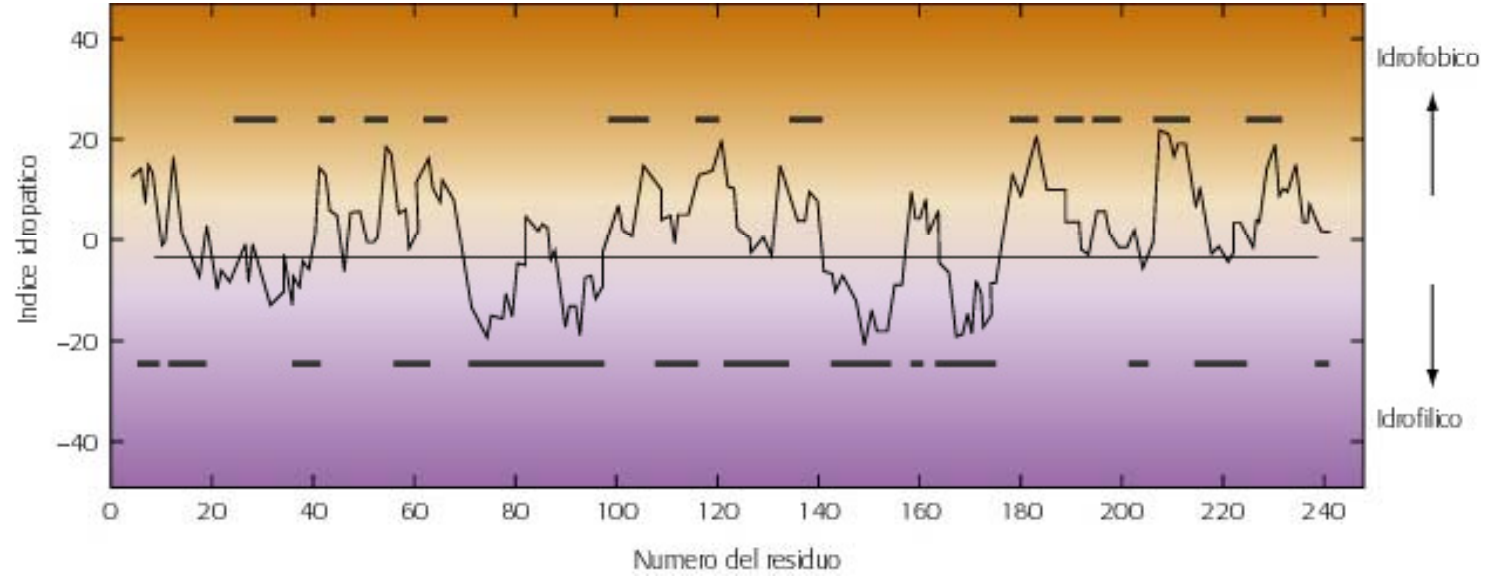
La conformazione nativa di una proteina è quella a cui si associa la sua funzione biologica.

Il termine stabilità può essere definito come la tendenza a mantenere la conformazione nativa

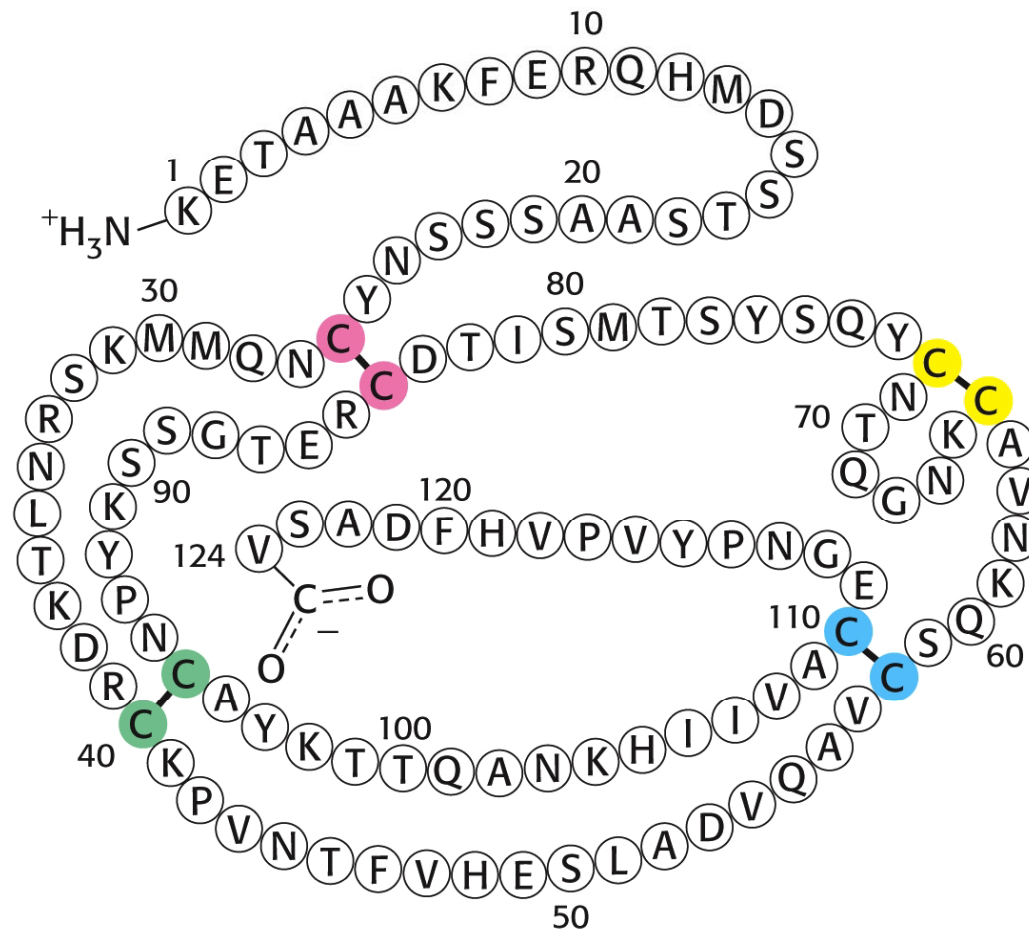
In condizioni fisiologiche le proteine sono solo marginalmente stabili (ΔG compreso tra 15 e 65 kJ/mole)

Forze che stabilizzano le proteine

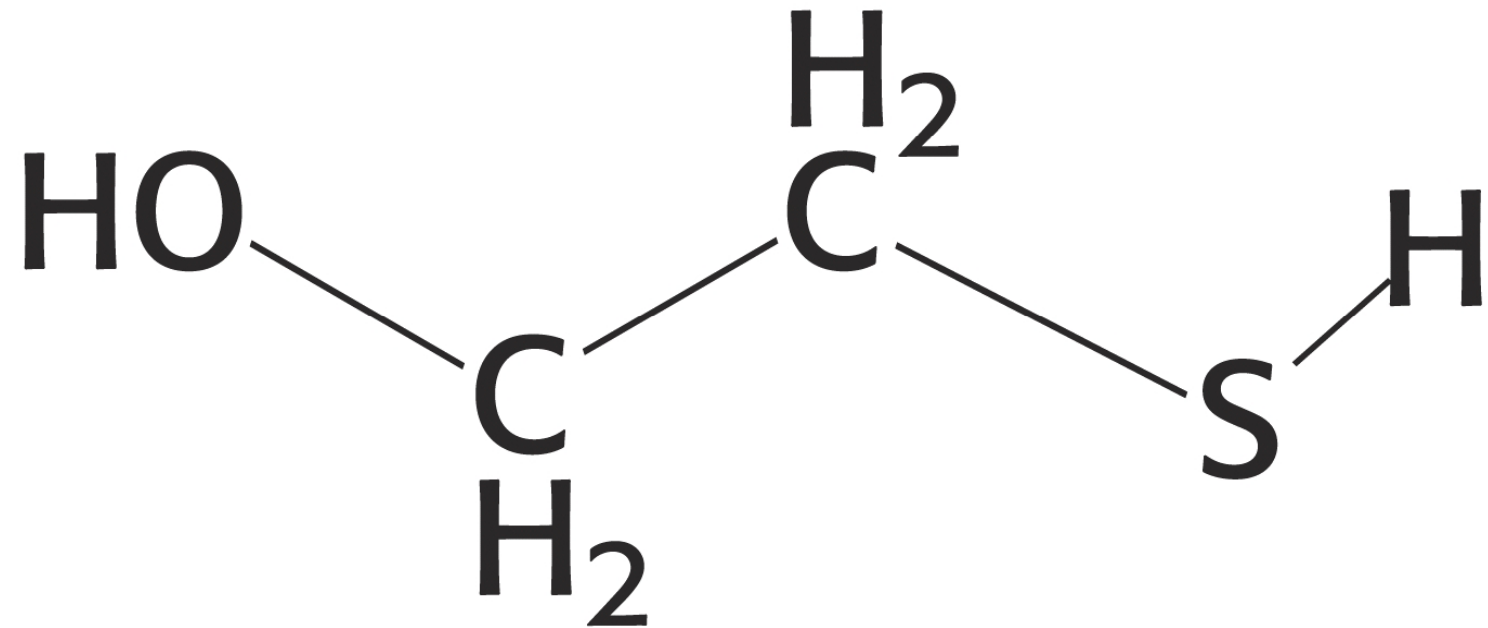
- **L'effetto idrofobico** tendenza delle sostanze non polari a minimizzare il contatto con l'acqua
- **Interazioni elettrostatiche**
- **Legami chimici trasversali**



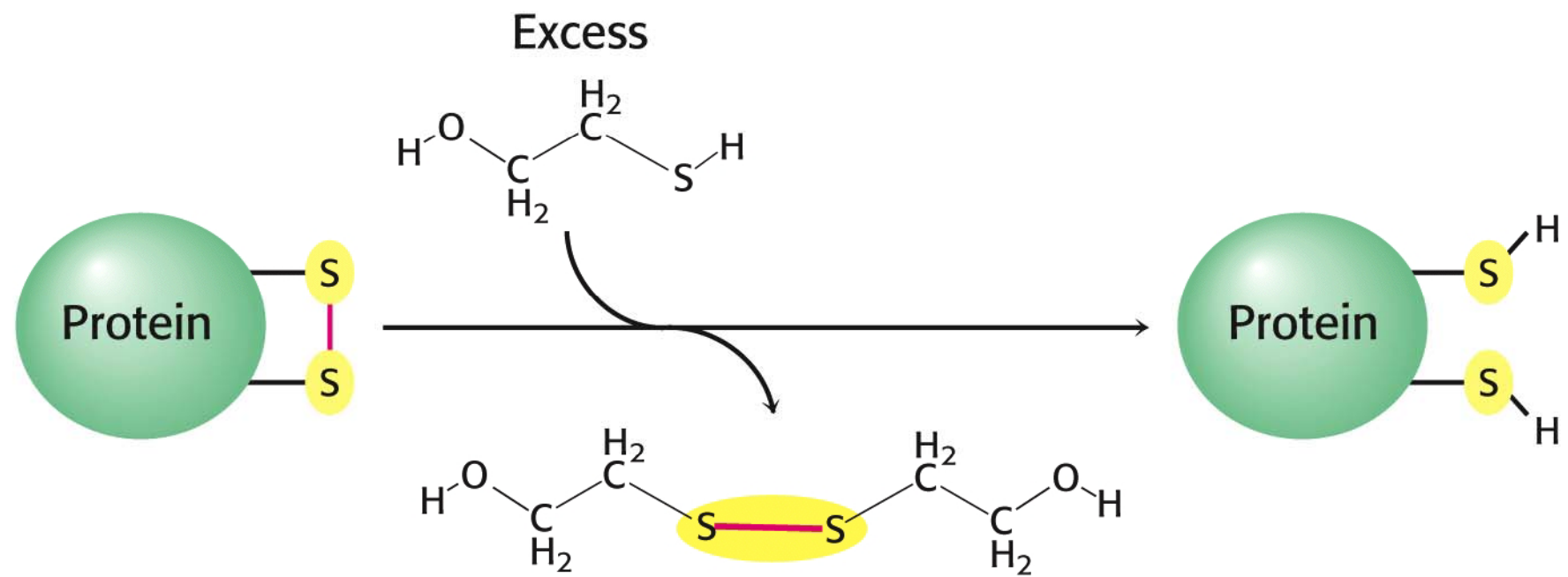
Denaturazione e rinaturazione delle proteine



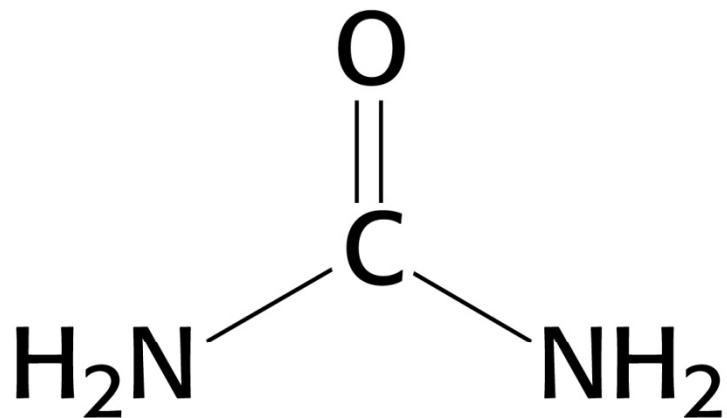
I legami disolfuro possono essere rotti da agenti riducenti



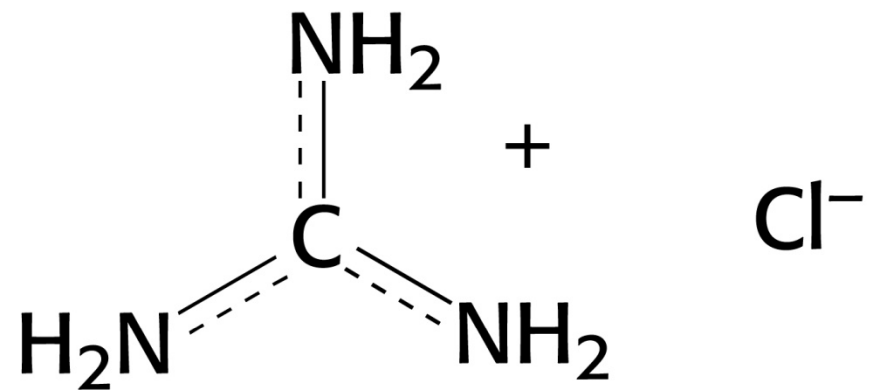
β-Mercaptoethanol



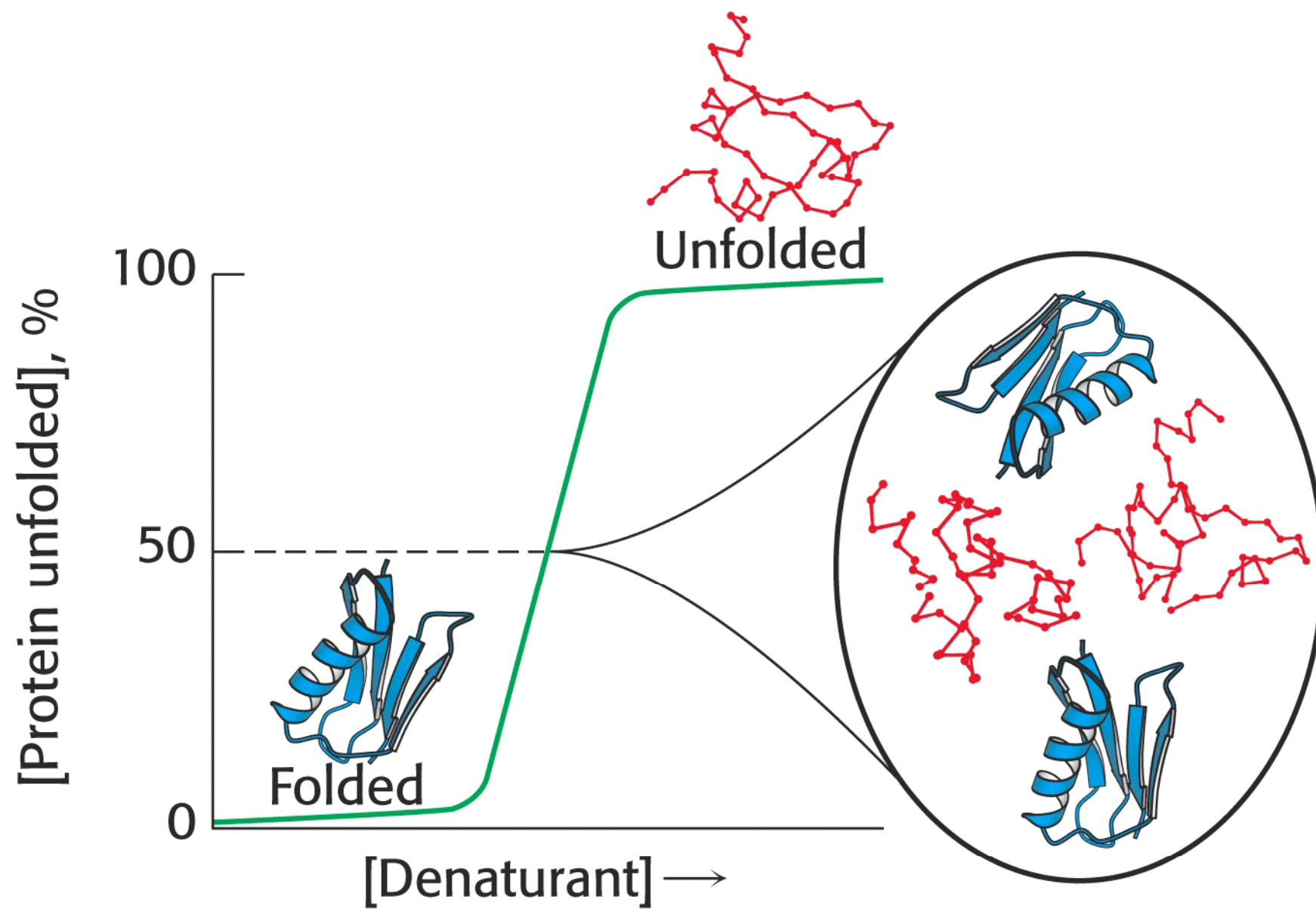
Gli agenti caotropici

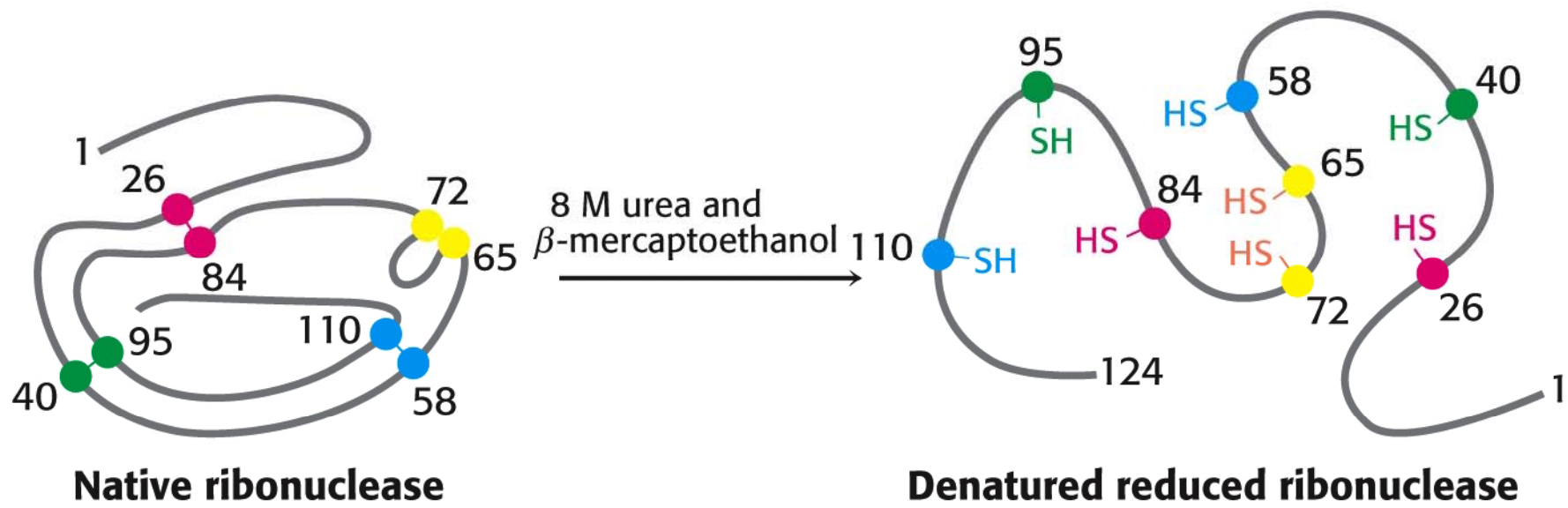


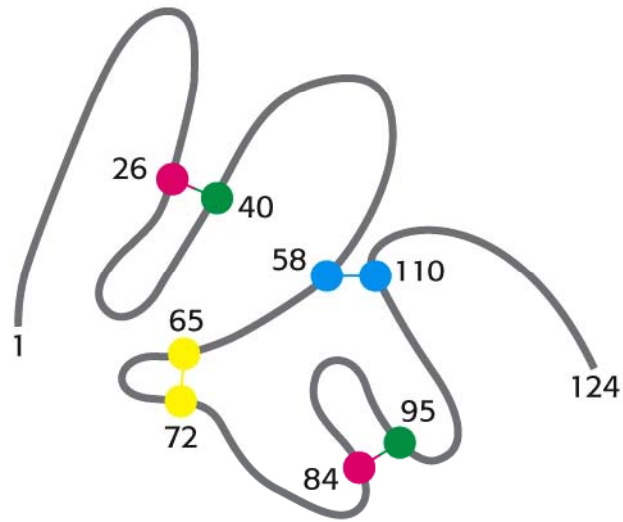
Urea



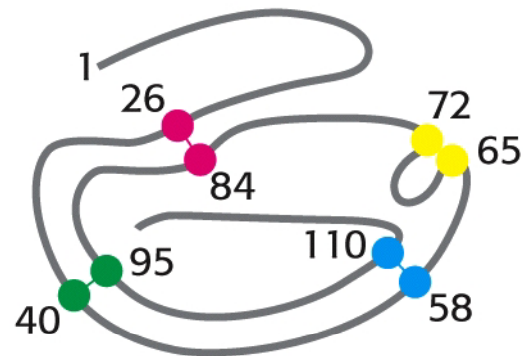
Guanidinium chloride







Trace of
 β -mercaptoethanol

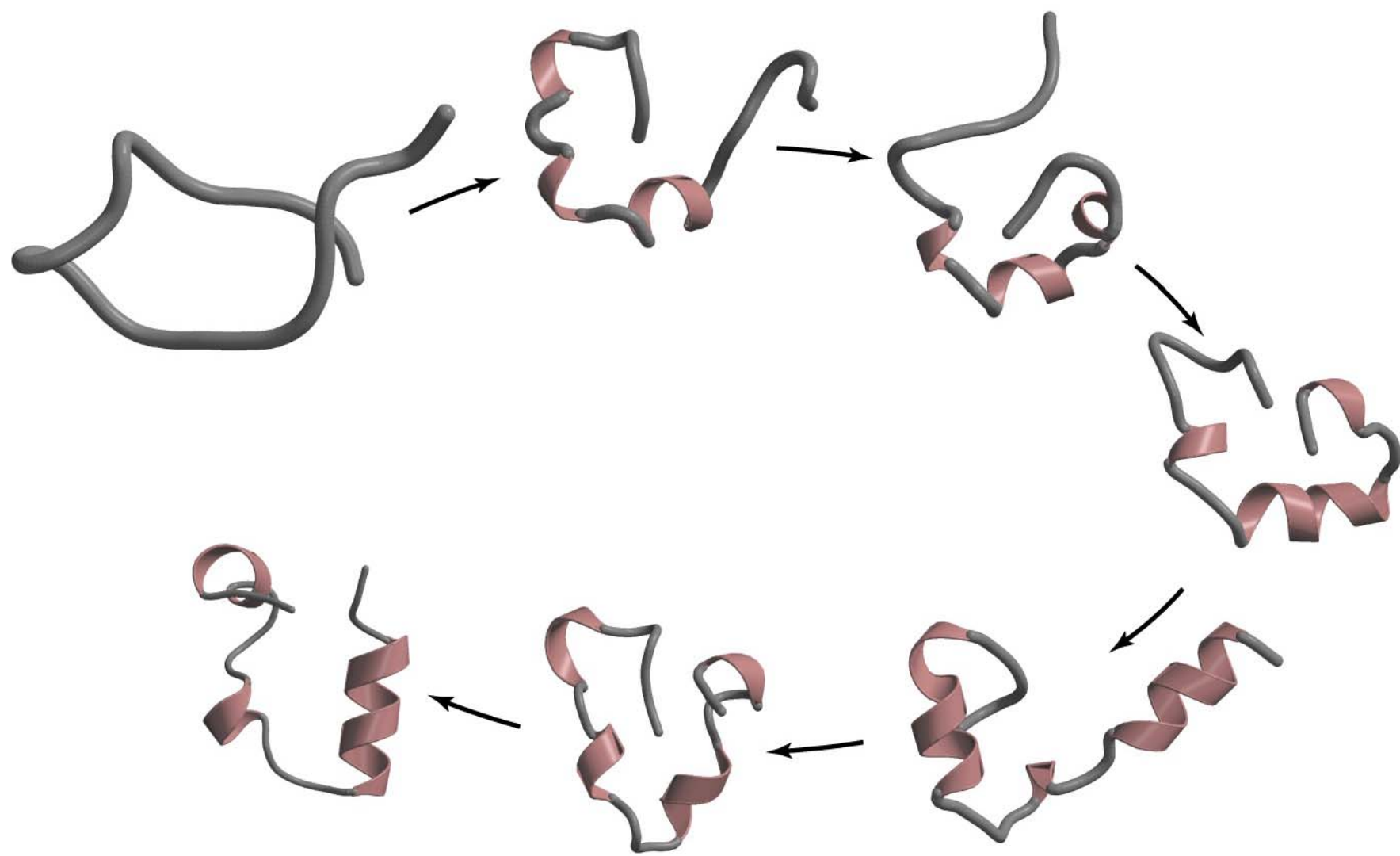


Native ribonuclease

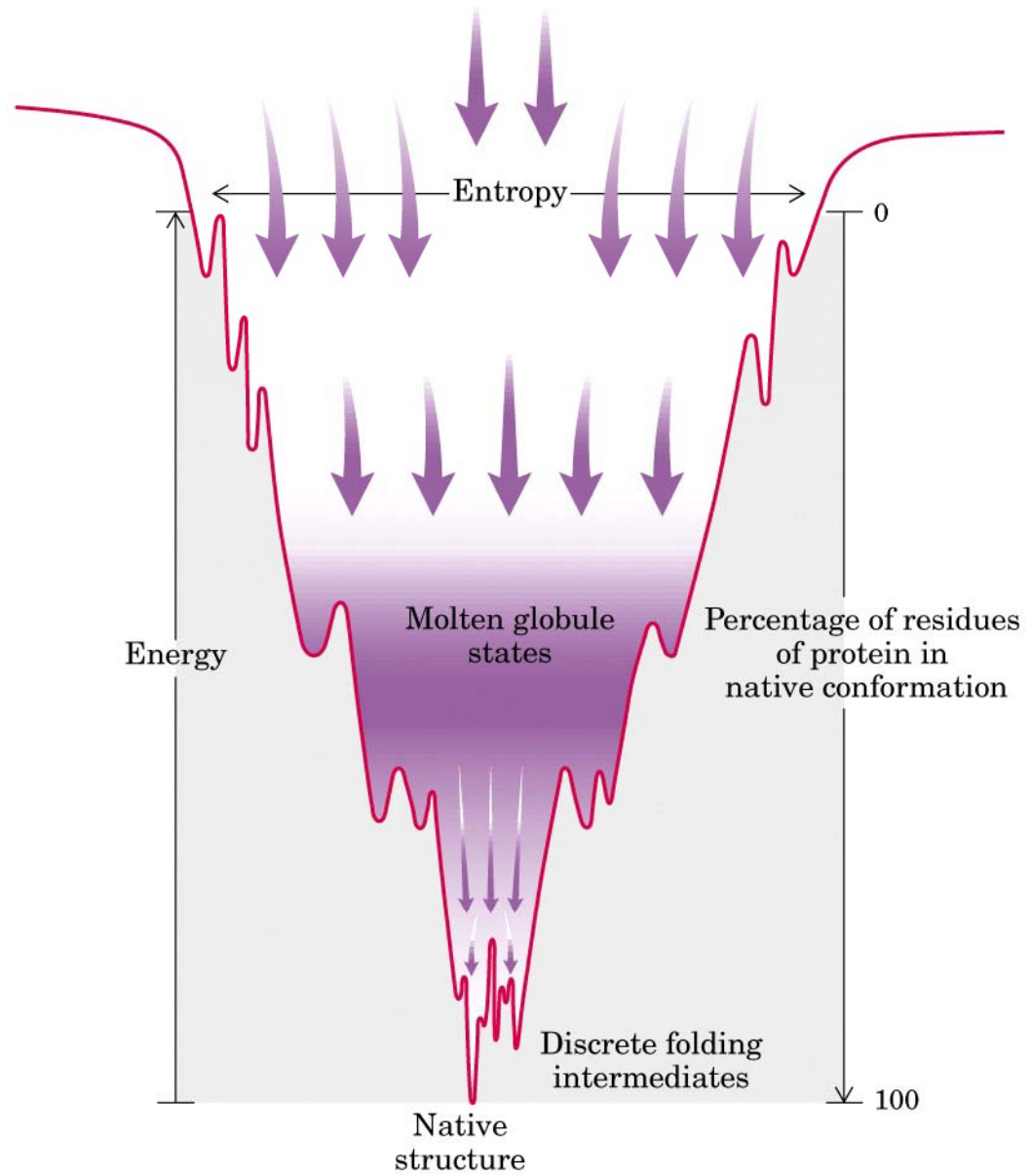
Il paradosso di Levinthal

Come fa una proteina a raggiungere la sua conformazione nativa?

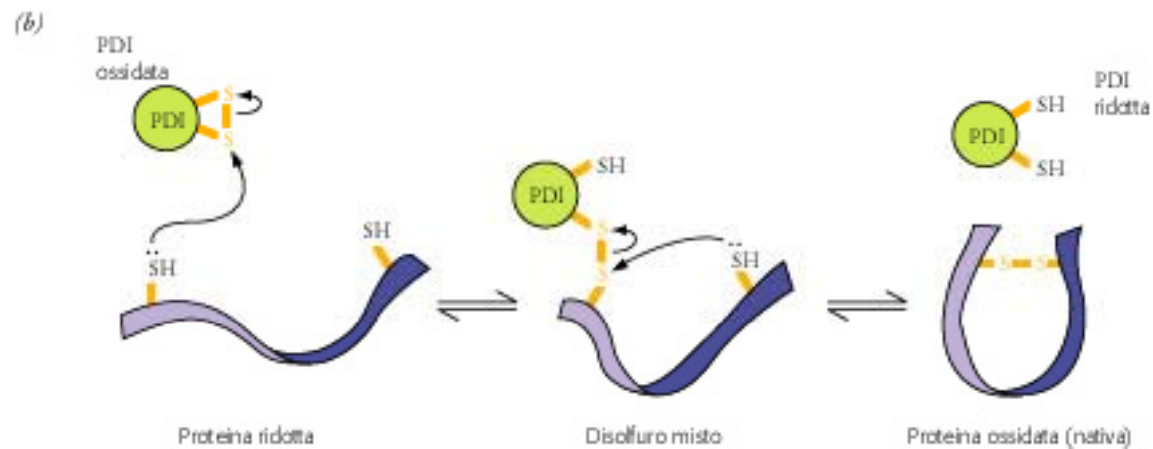
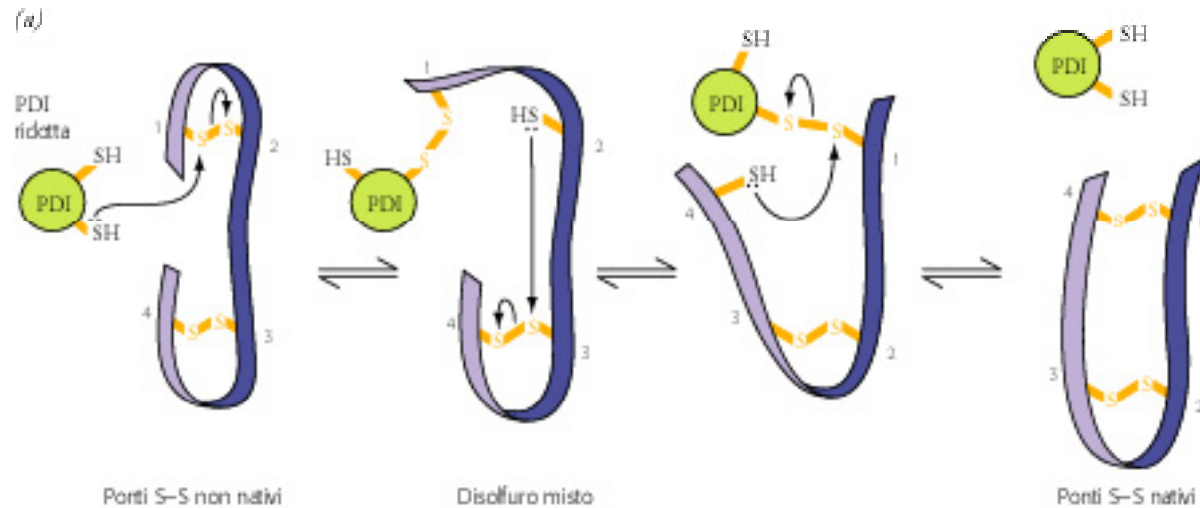
- Proteina di 100 amminoacidi
- supponiamo almeno 10 diverse conformazioni per amminoacido = 10^{100} conformazioni possibili
- se il ripiegamento è casuale e richiede, ad esempio, 10^{-13} sec per sperimentare ciascuna conformazione possibile, ci vorrebbero 10^{77} anni per testare tutte le conformazioni possibili alla ricerca della migliore



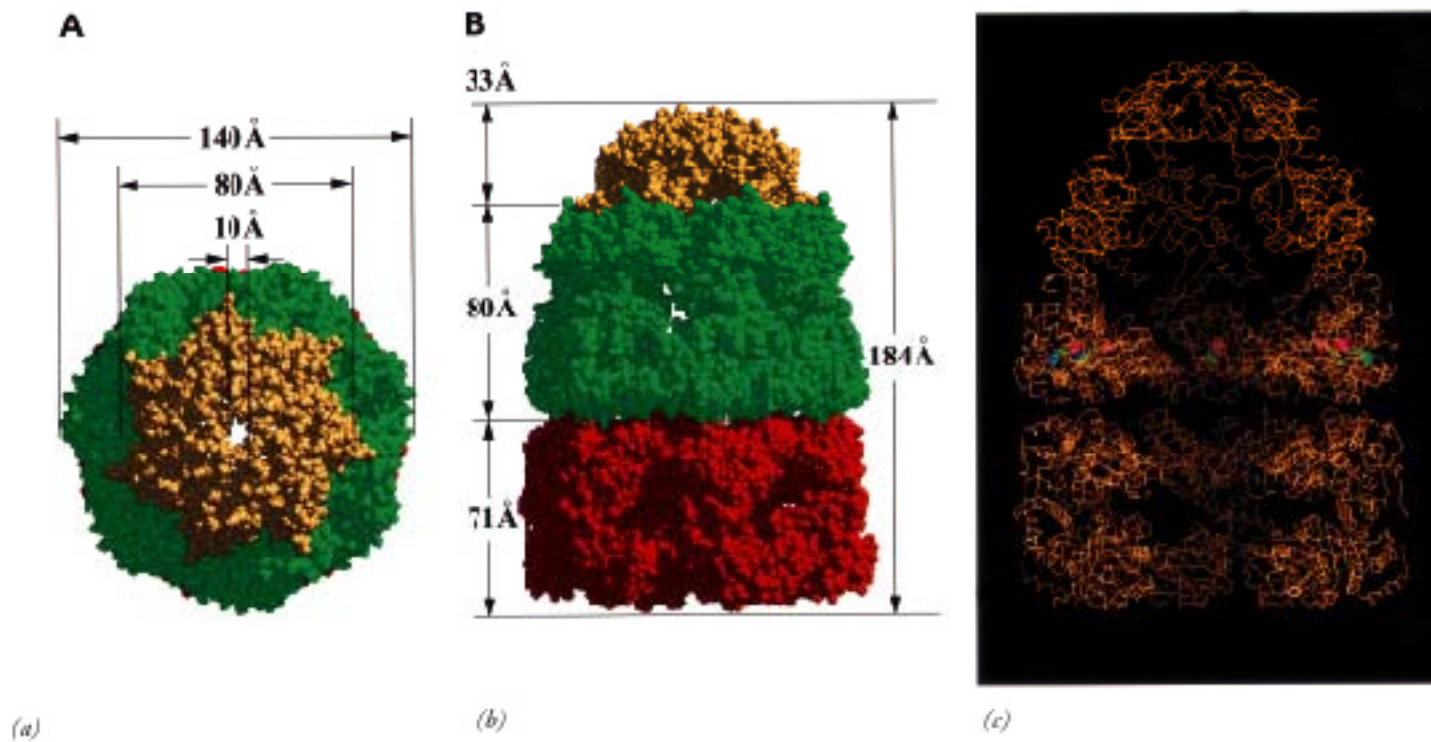
Beginning of helix formation and collapse

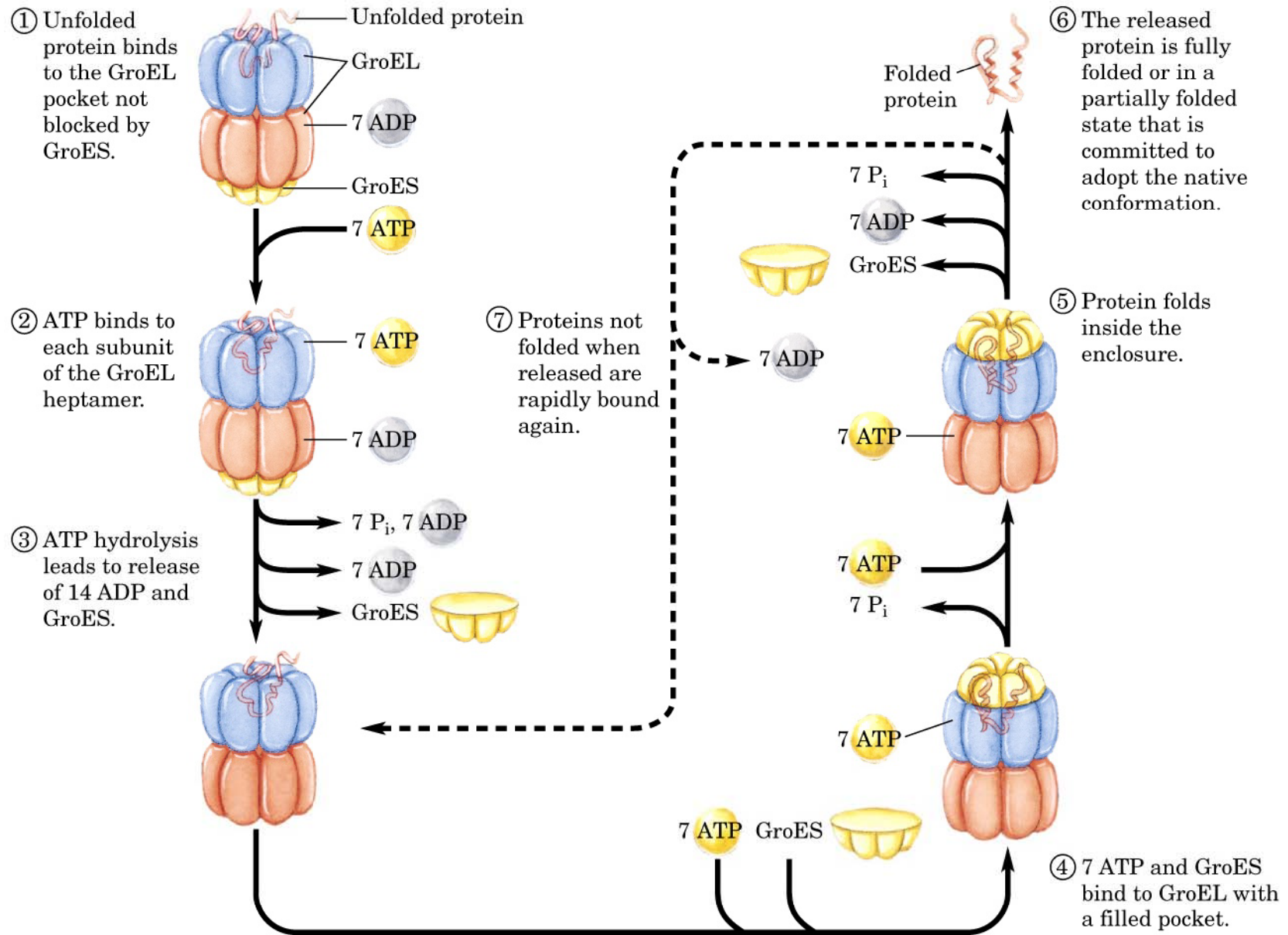


disolfuro isomerasi



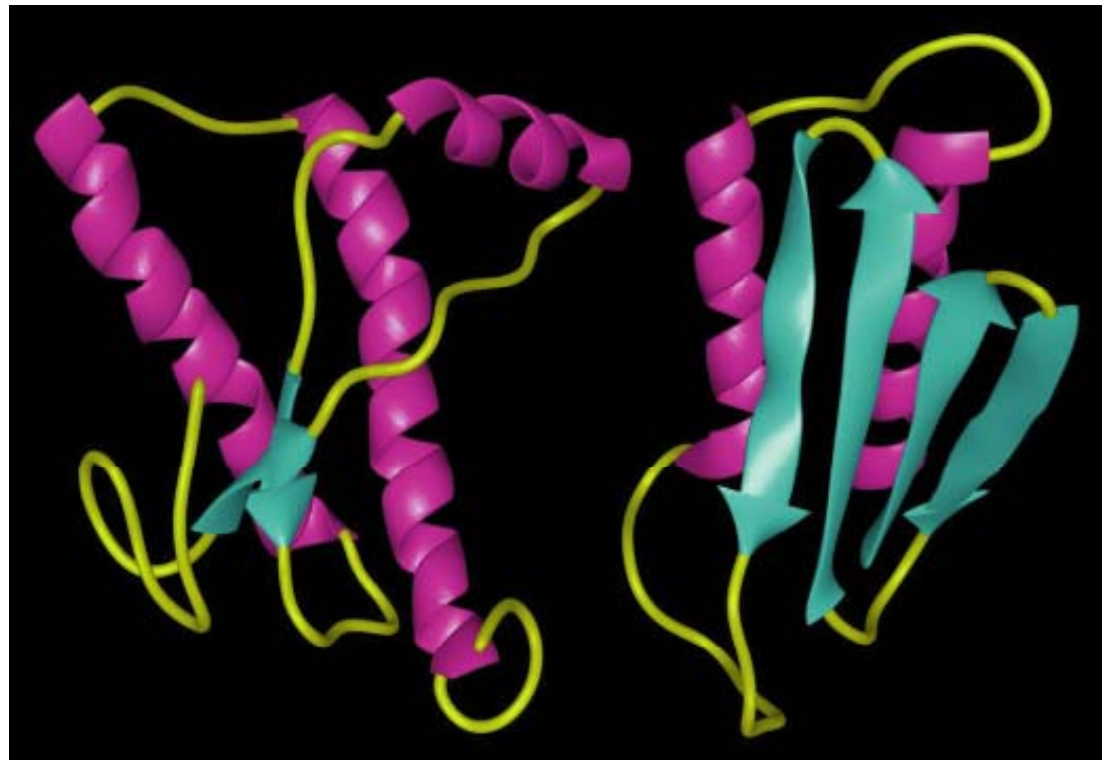
I chaperoni molecolari





(a)

Alcune patologie sono legate ad un errato ripiegamento delle proteine



Le proteine sono molecole flessibili

