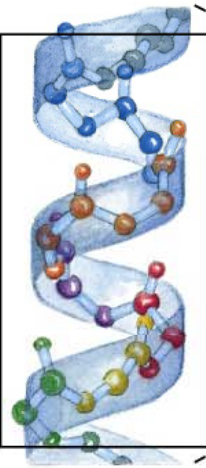


**Primary
structure**



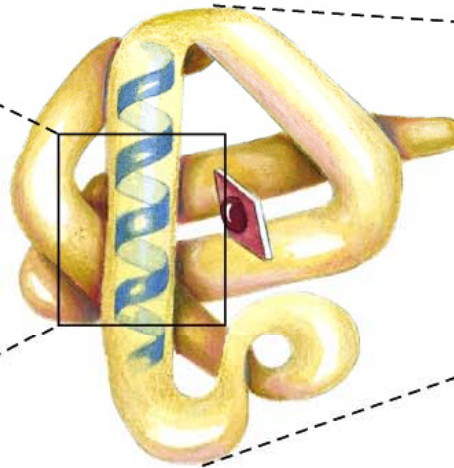
Amino acid residues

**Secondary
structure**



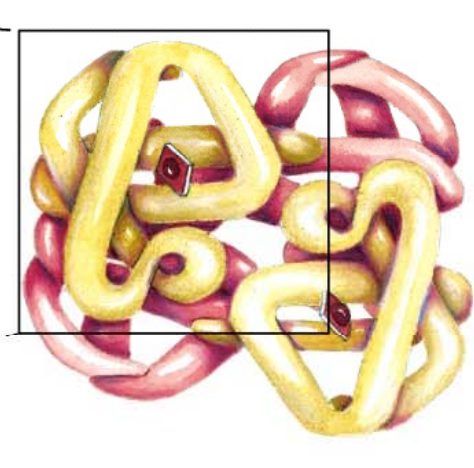
α Helix

**Tertiary
structure**

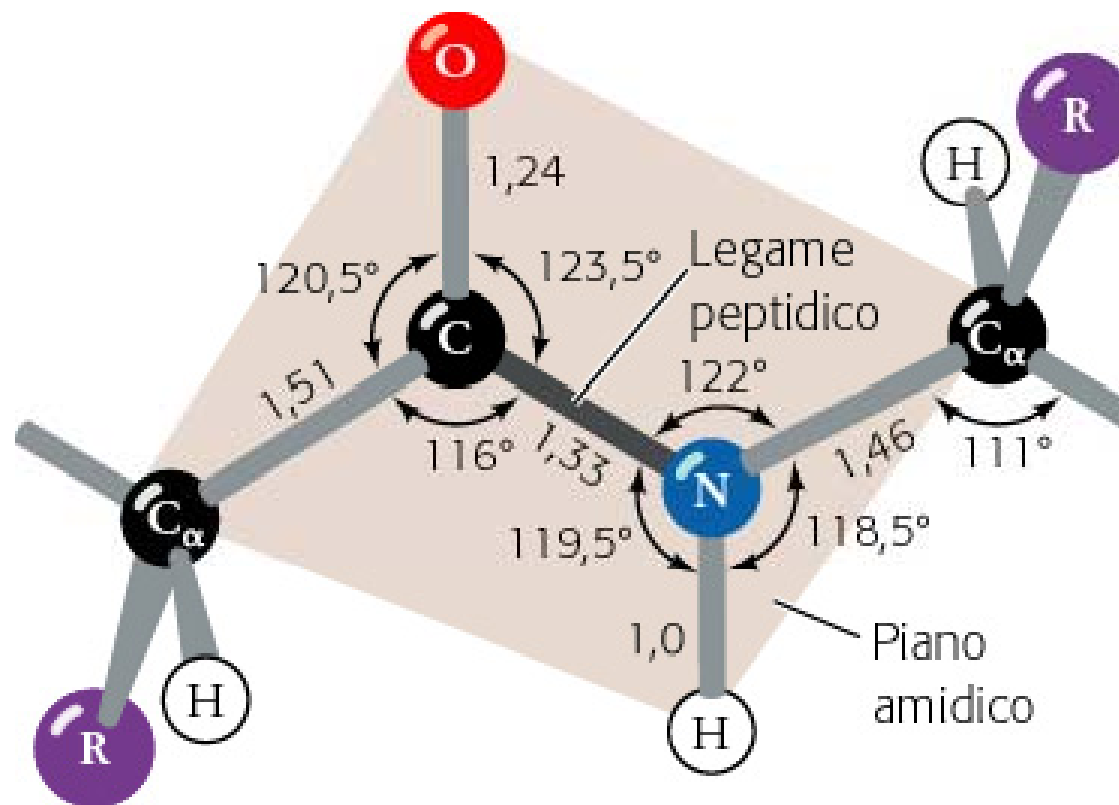


Polypeptide chain

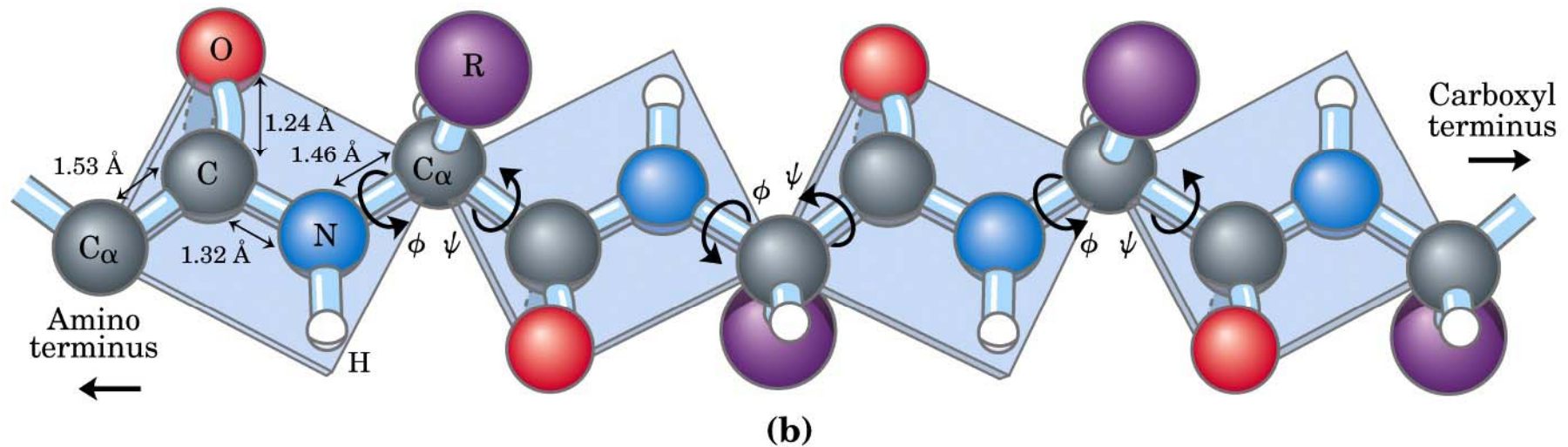
**Quaternary
structure**



Assembled subunits



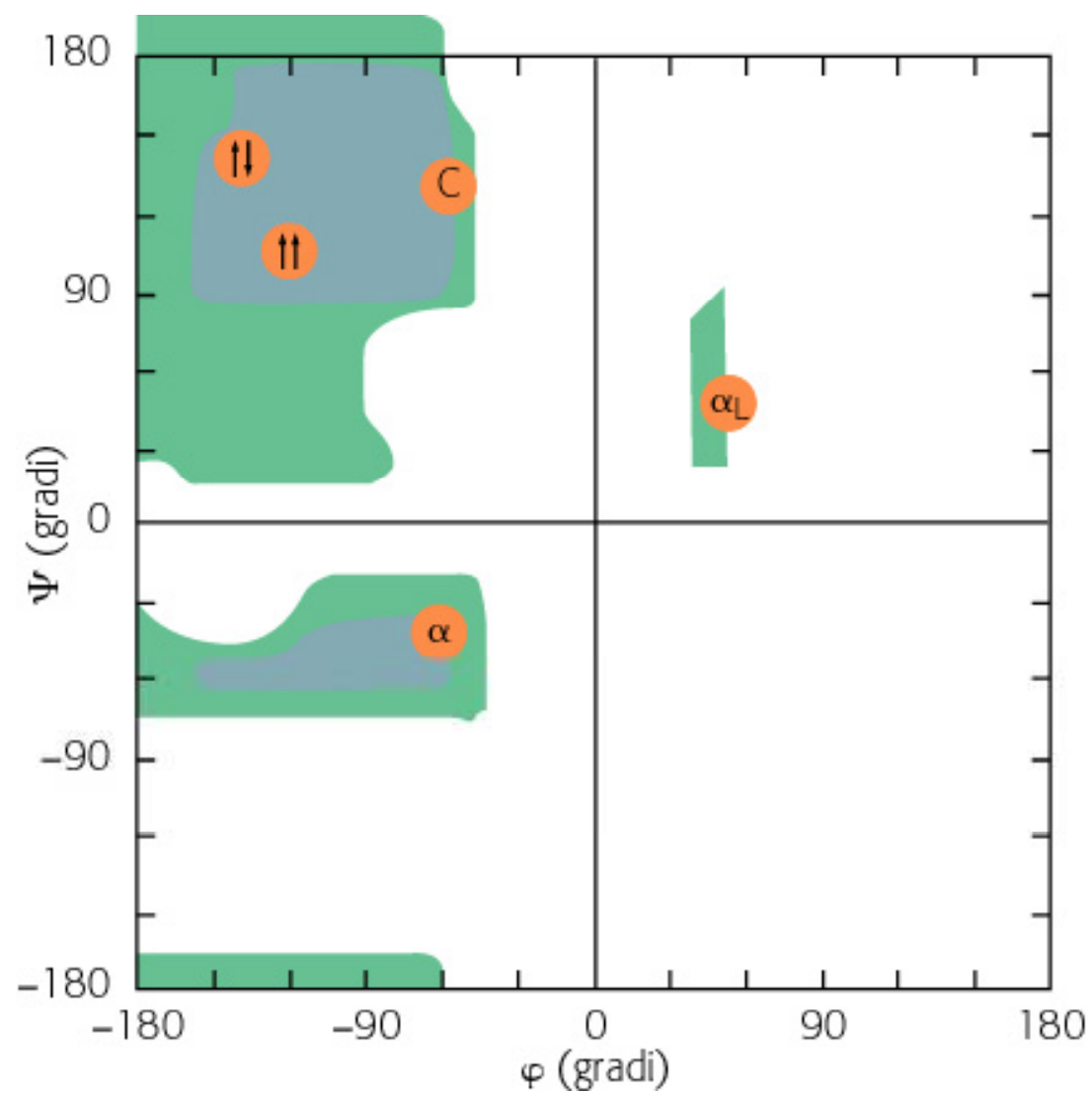
I due carboni alfa sono in **configurazione trans**
(unica possibile eccezione Pro)



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

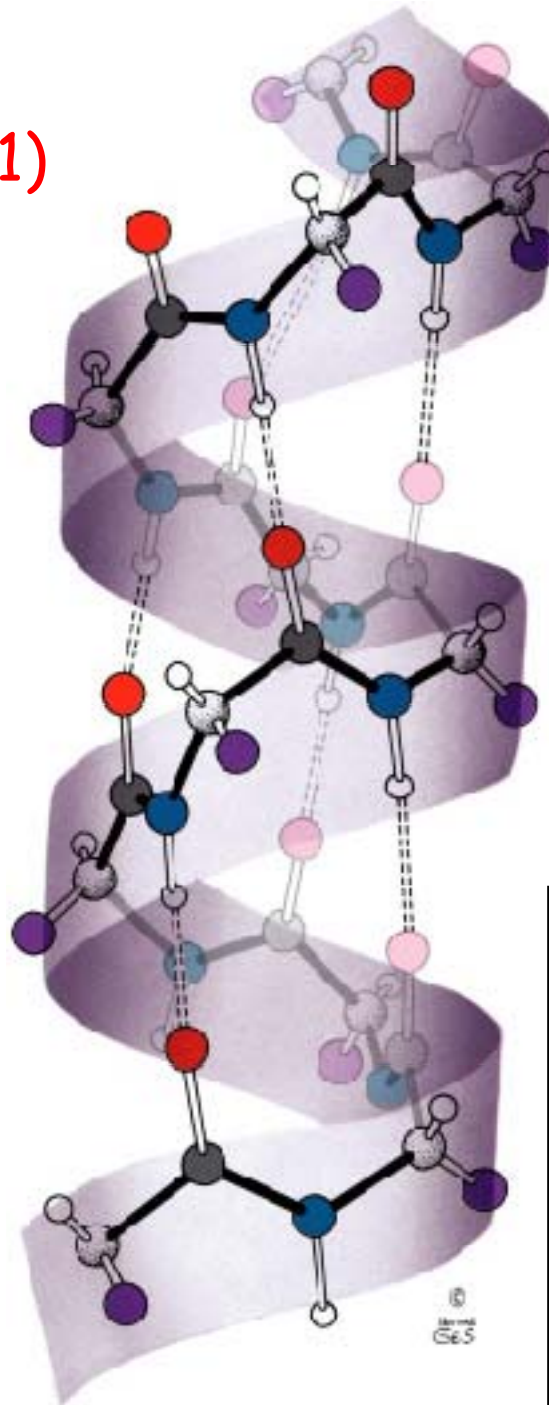


L' α elica (Pauling e Corey 1951)

3,6 residui per giro

Passo di 5,4 Å

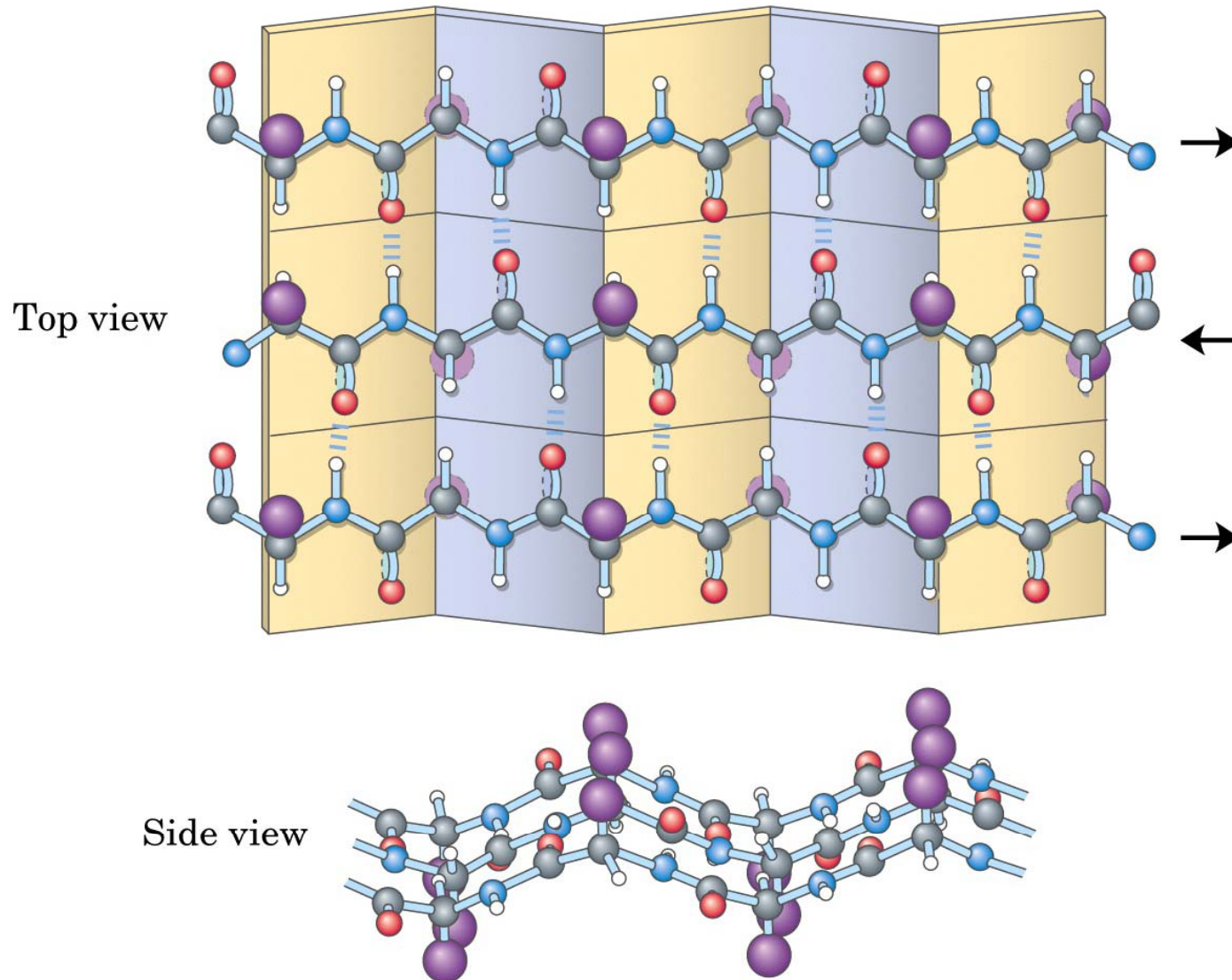
Legame idrogeno
ottimale (2,8 Å)
tra C=O e NH di
quattro residui
successivi



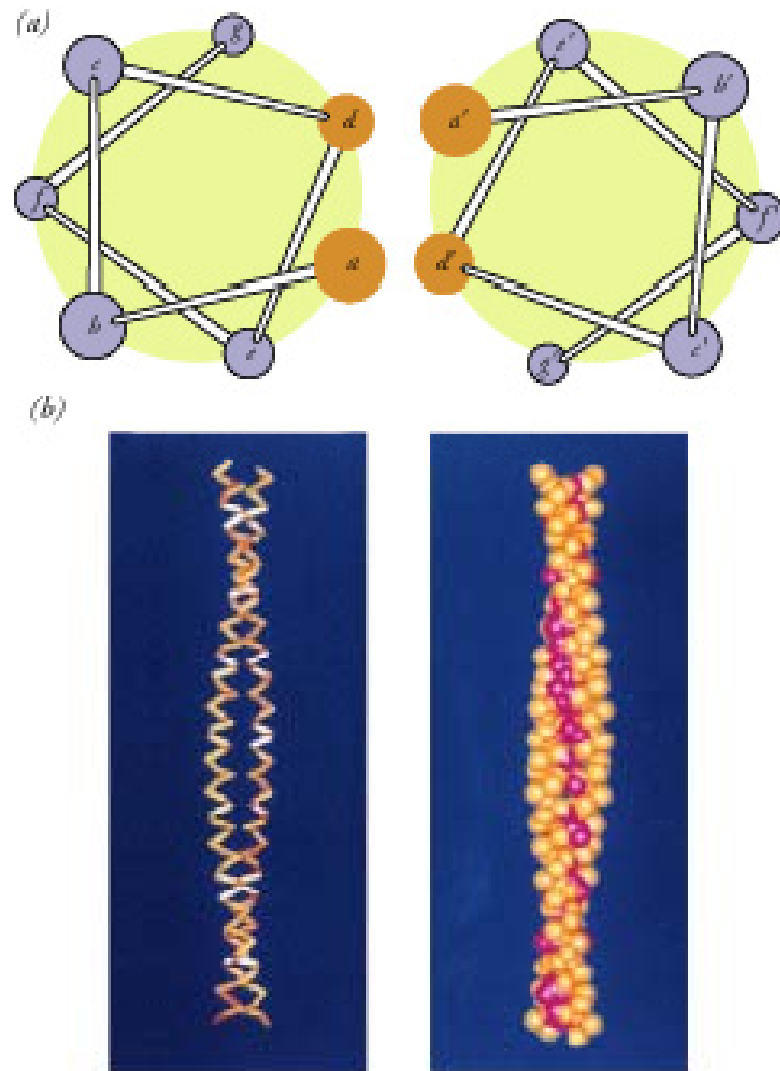
Prolina
Glicina
Residui carichi
consecutivi
Residui ingombranti
Adiacenti
Dipolo elettrico

La conformazione beta delle catene polipeptidiche Pauling e Corey 1951

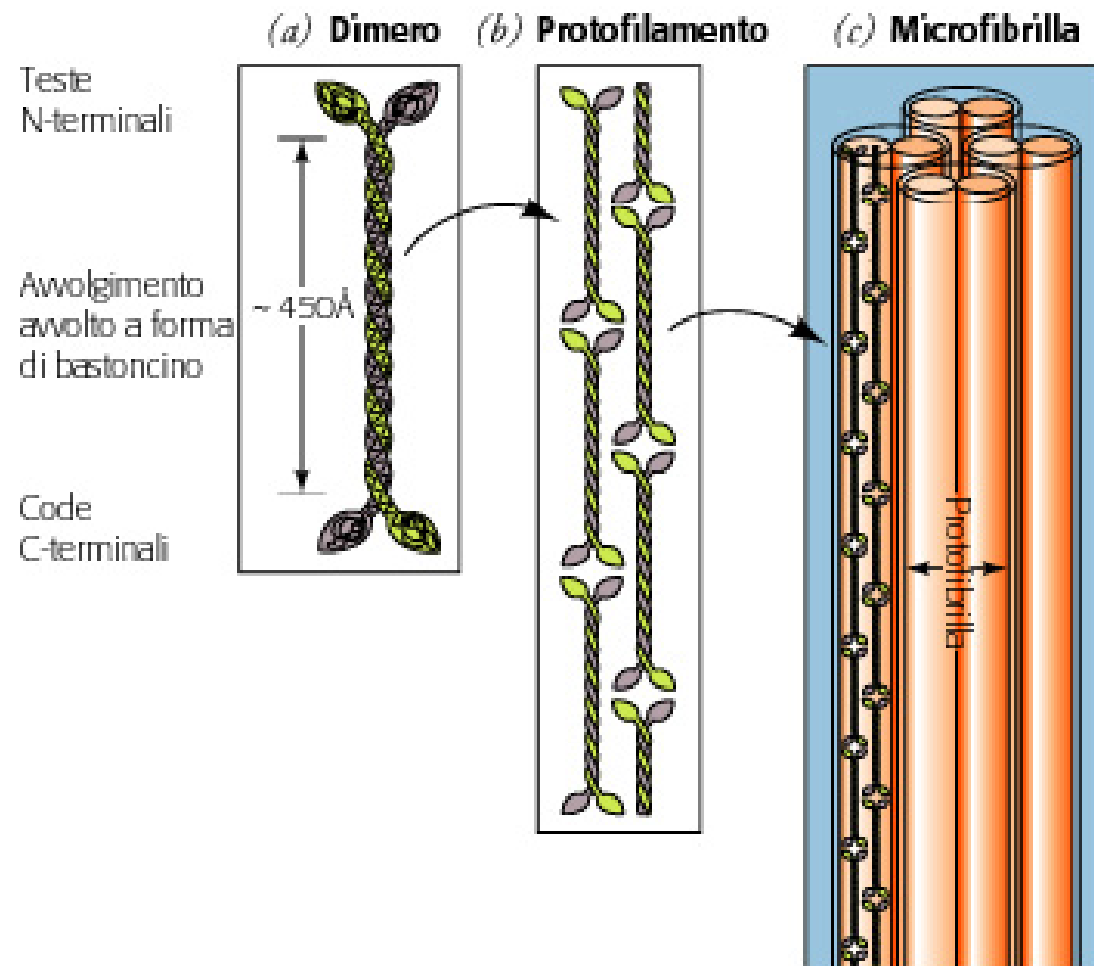
(a) Antiparallel

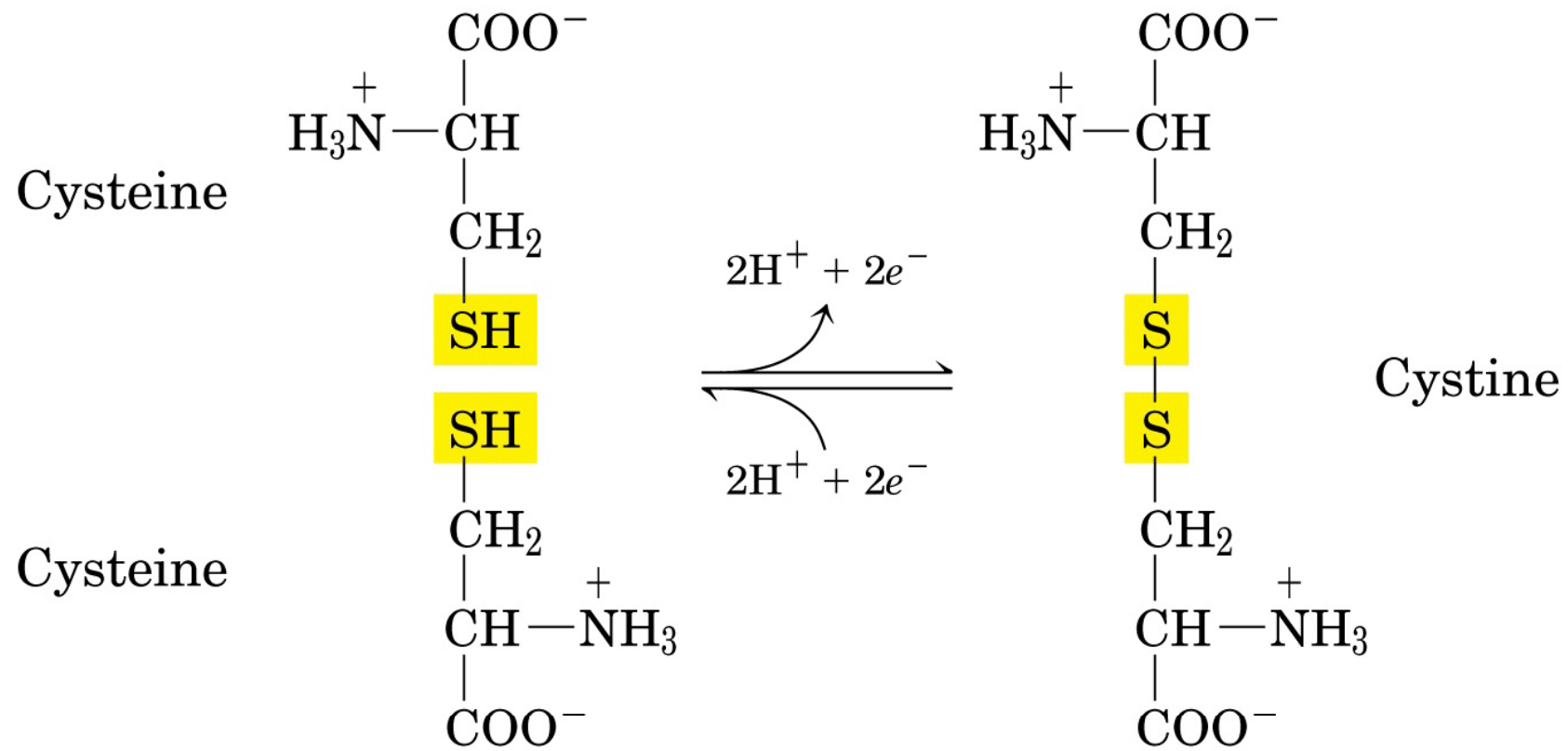


Avvolgimento dell' α -cheratina

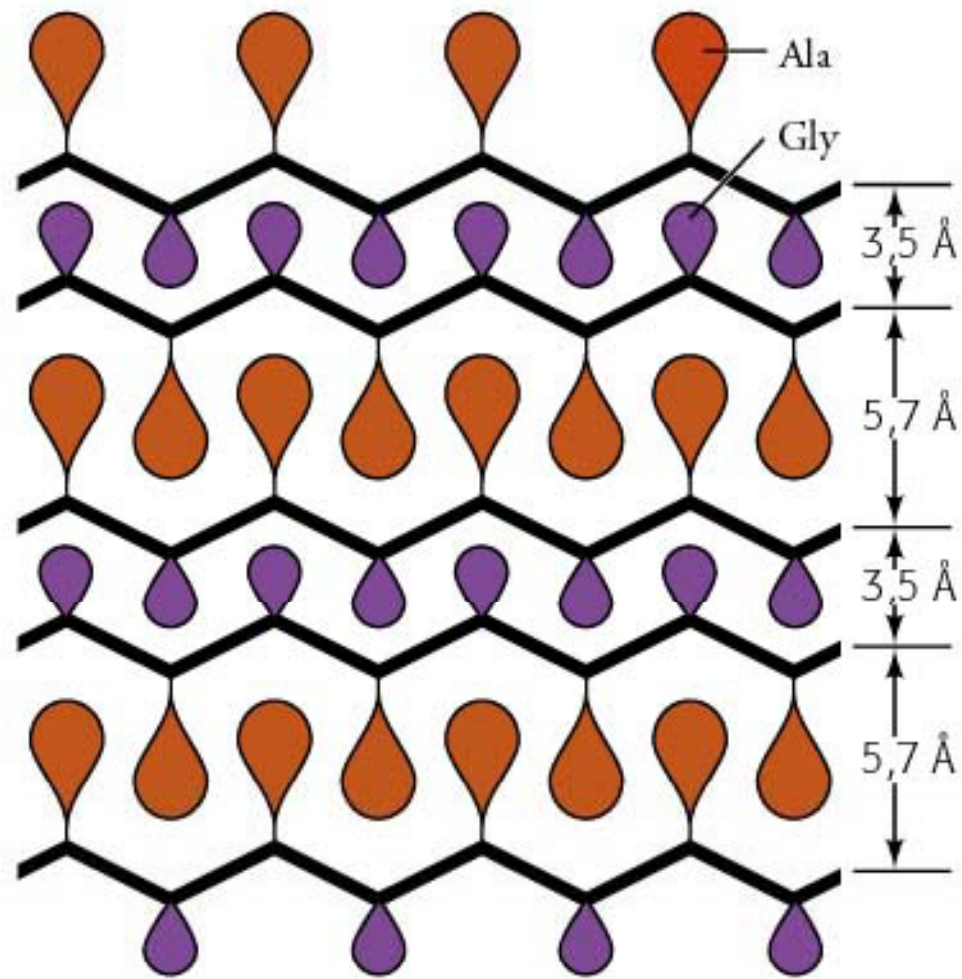


Diversi livelli di organizzazione della cheratina





La fibroina della seta



La tripla elica del collageno

Vari tipi di catene

Conformazione elicoidale sinistrorsa con tre residui circa per giro

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

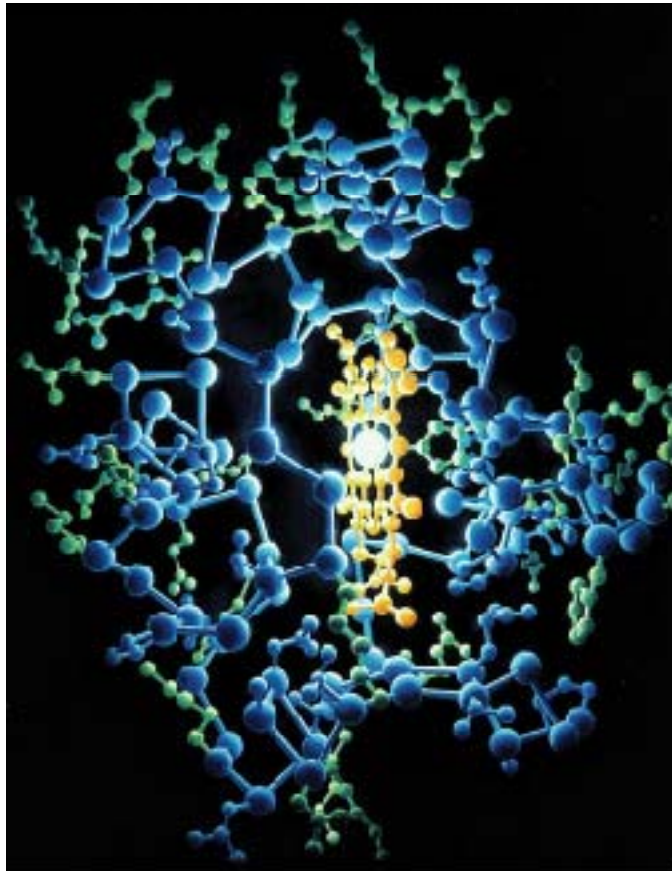


Gly-X-Y

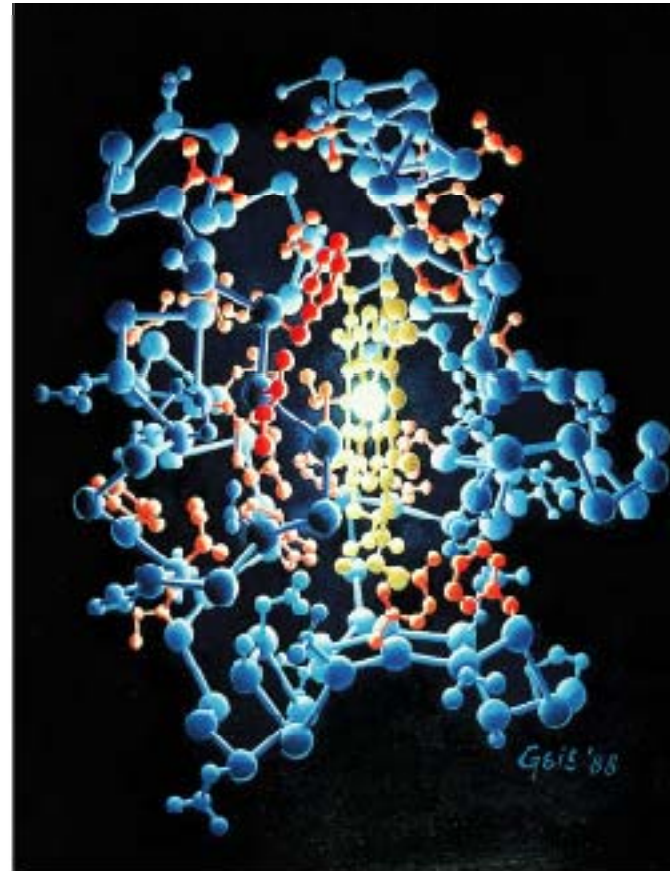
X-Pro
Y-HyPro

Prolil idrossilasi
Vitamina C

Distribuzione delle catene laterali

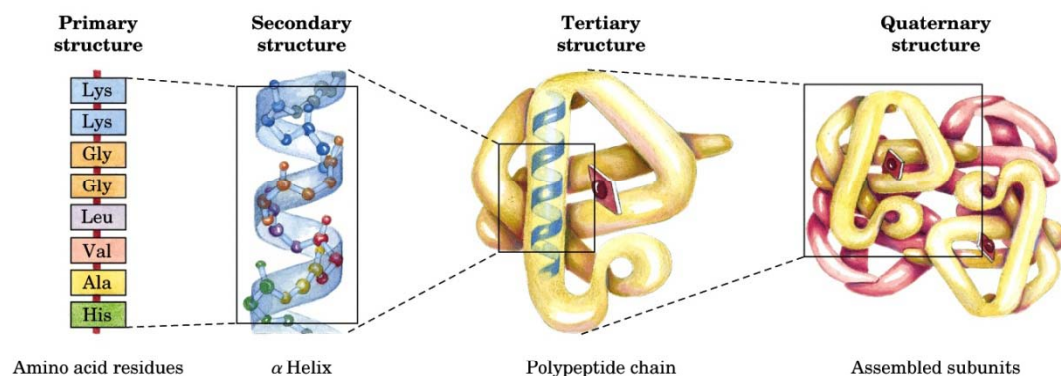


(a)



(b)

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**

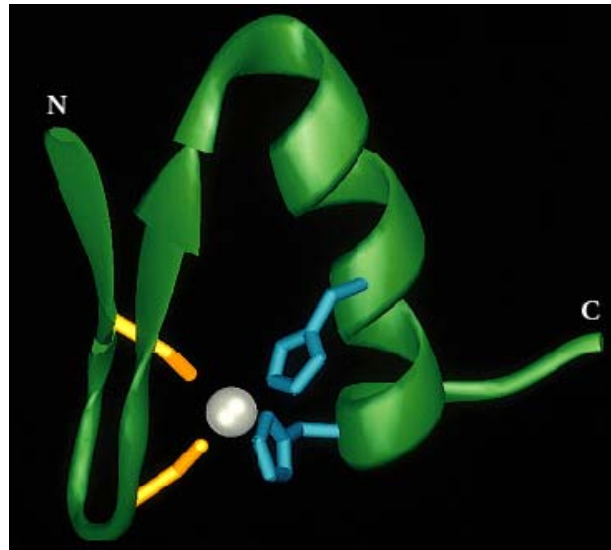
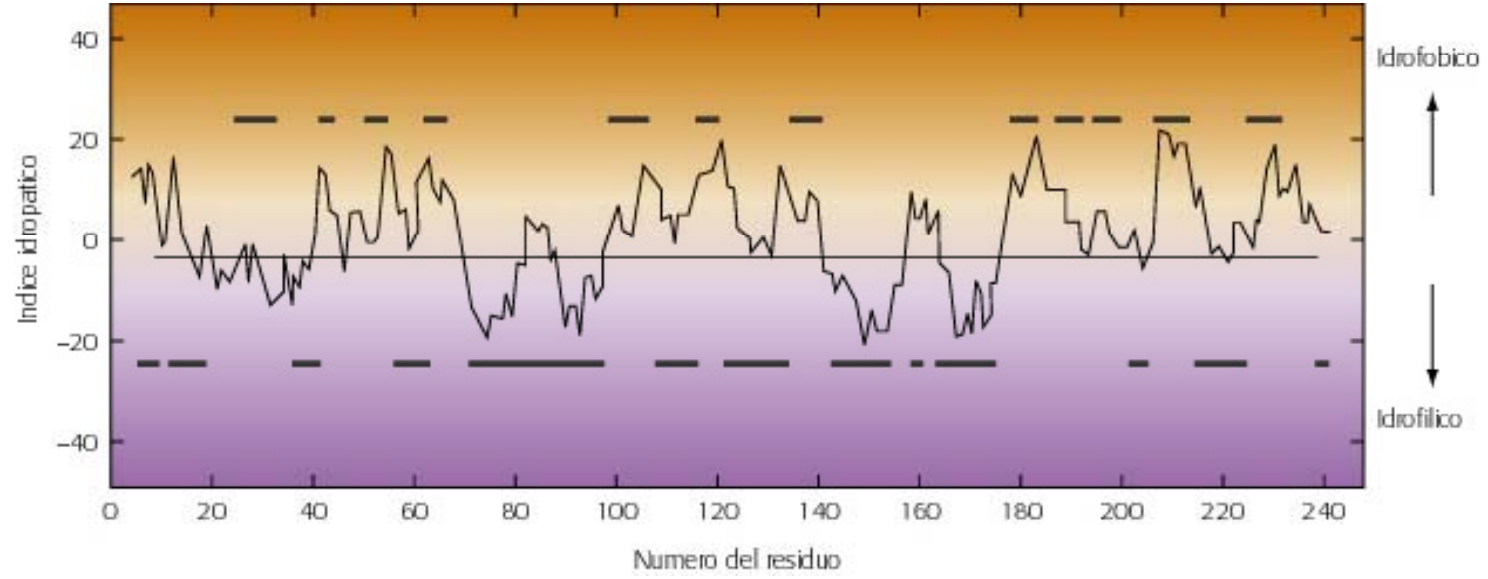
table 5–1

Properties and Conventions Associated with the Standard Amino Acids

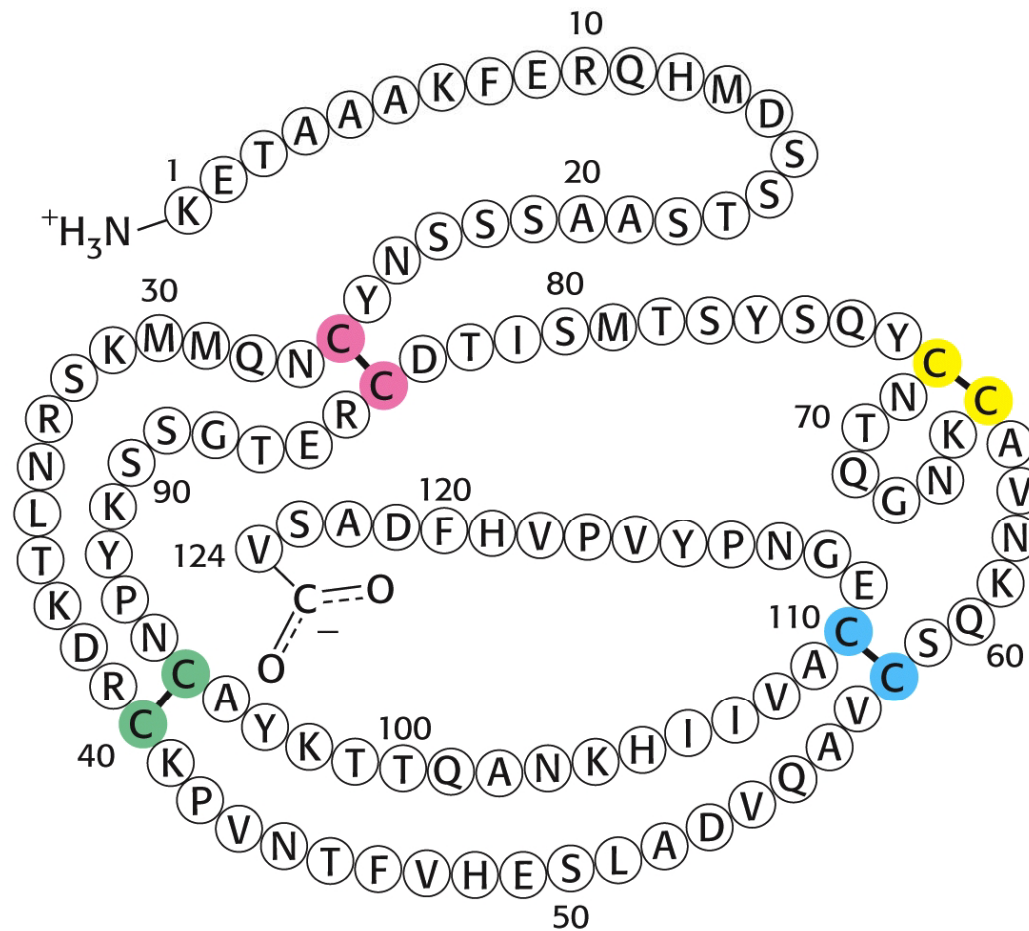
Amino acid	Abbreviated names		M_r	pK_a values			pI	Hydropathy index*	Occurrence in proteins (%)
				pK_1 (—COOH)	pK_2 (—NH ₃ ⁺)	pK_R (R group)			
Nonpolar, aliphatic R groups									
Glycine	Gly	G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala	A	89	2.34	9.69		6.01	1.8	7.8
Valine	Val	V	117	2.32	9.62		5.97	4.2	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.

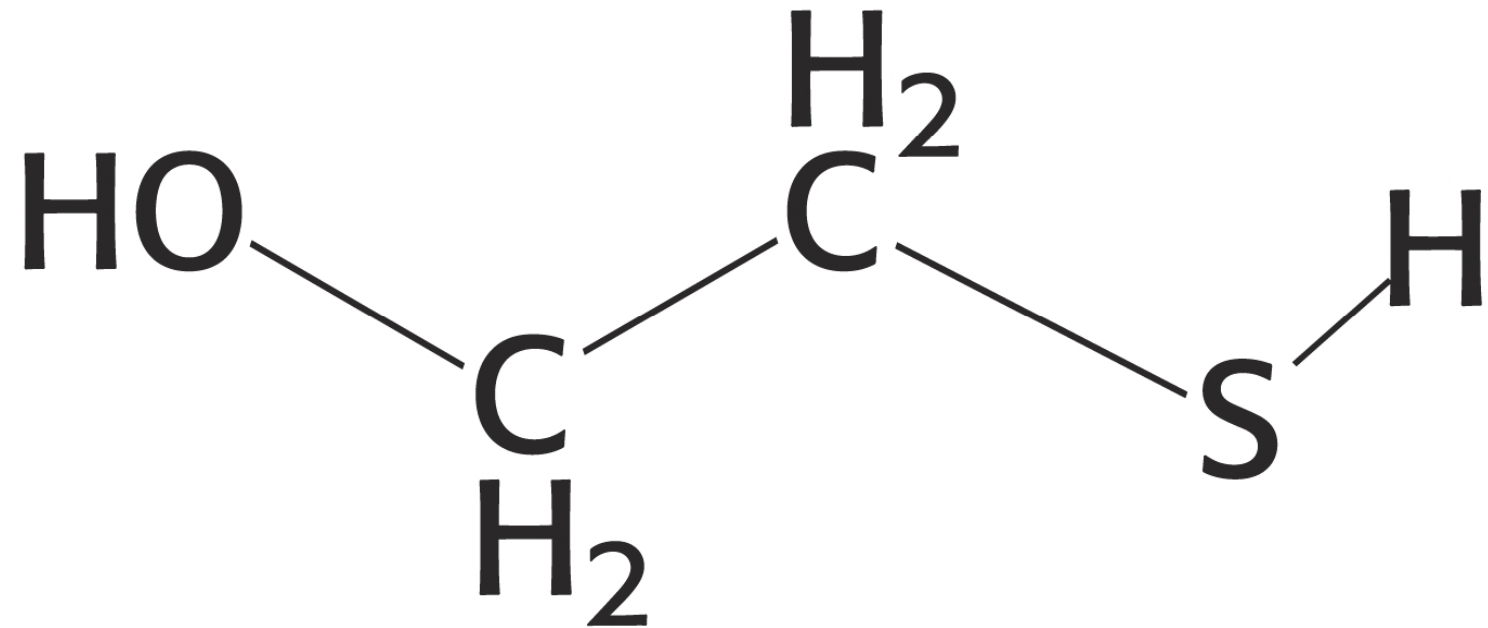
†Average occurrence in over 1150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed) Plenum Press, NY, pp. 599–623.



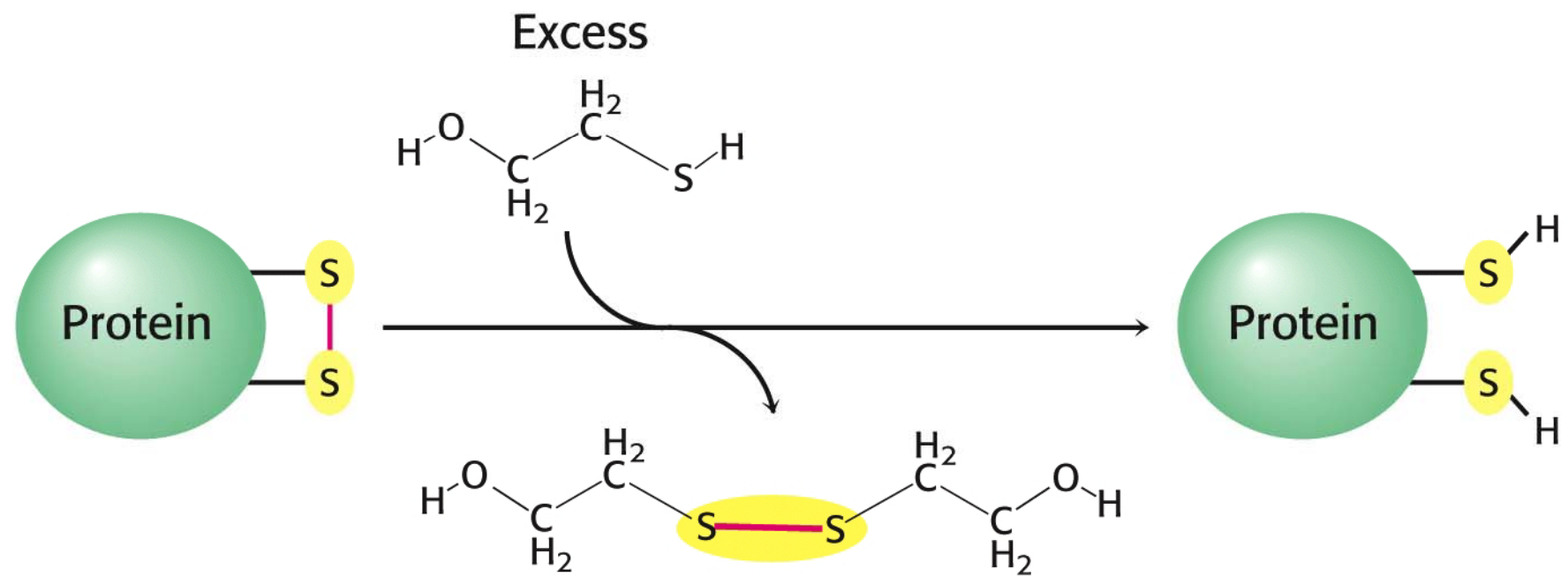
Denaturazione e rinaturazione delle proteine

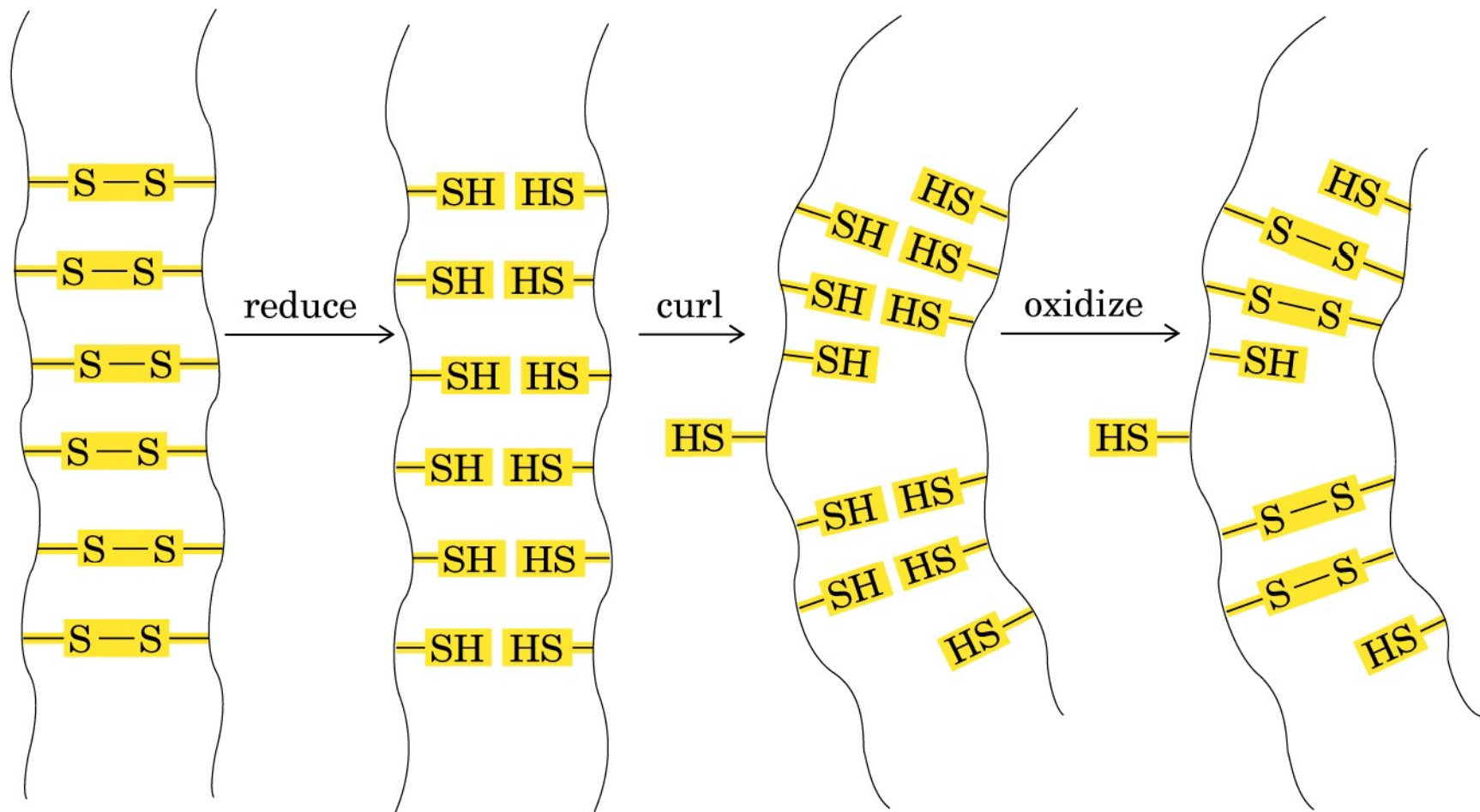


I legami disolfuro possono essere rotti da agenti riducenti

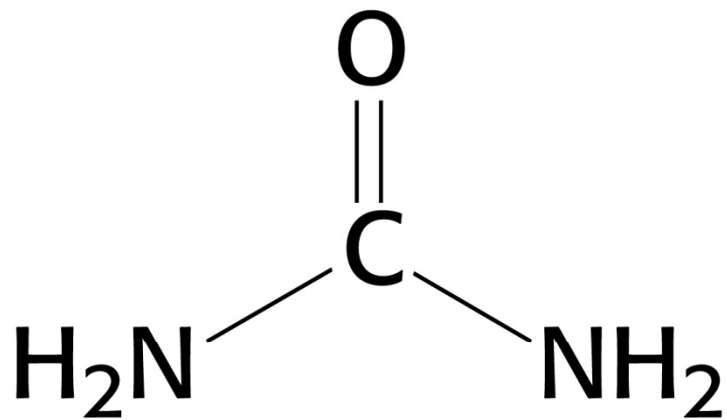


β-Mercaptoethanol

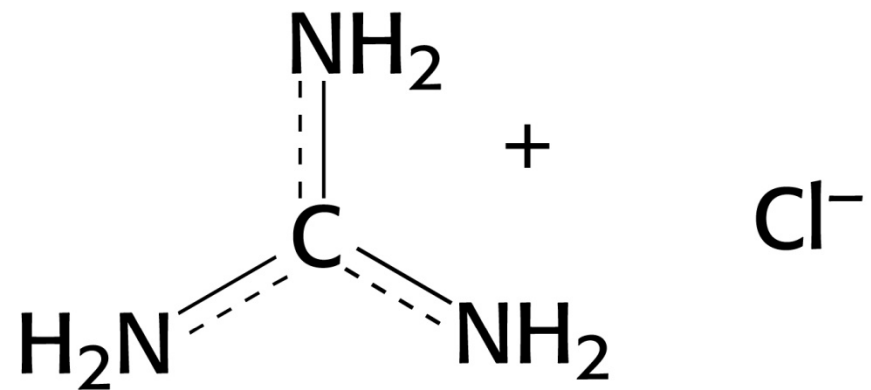




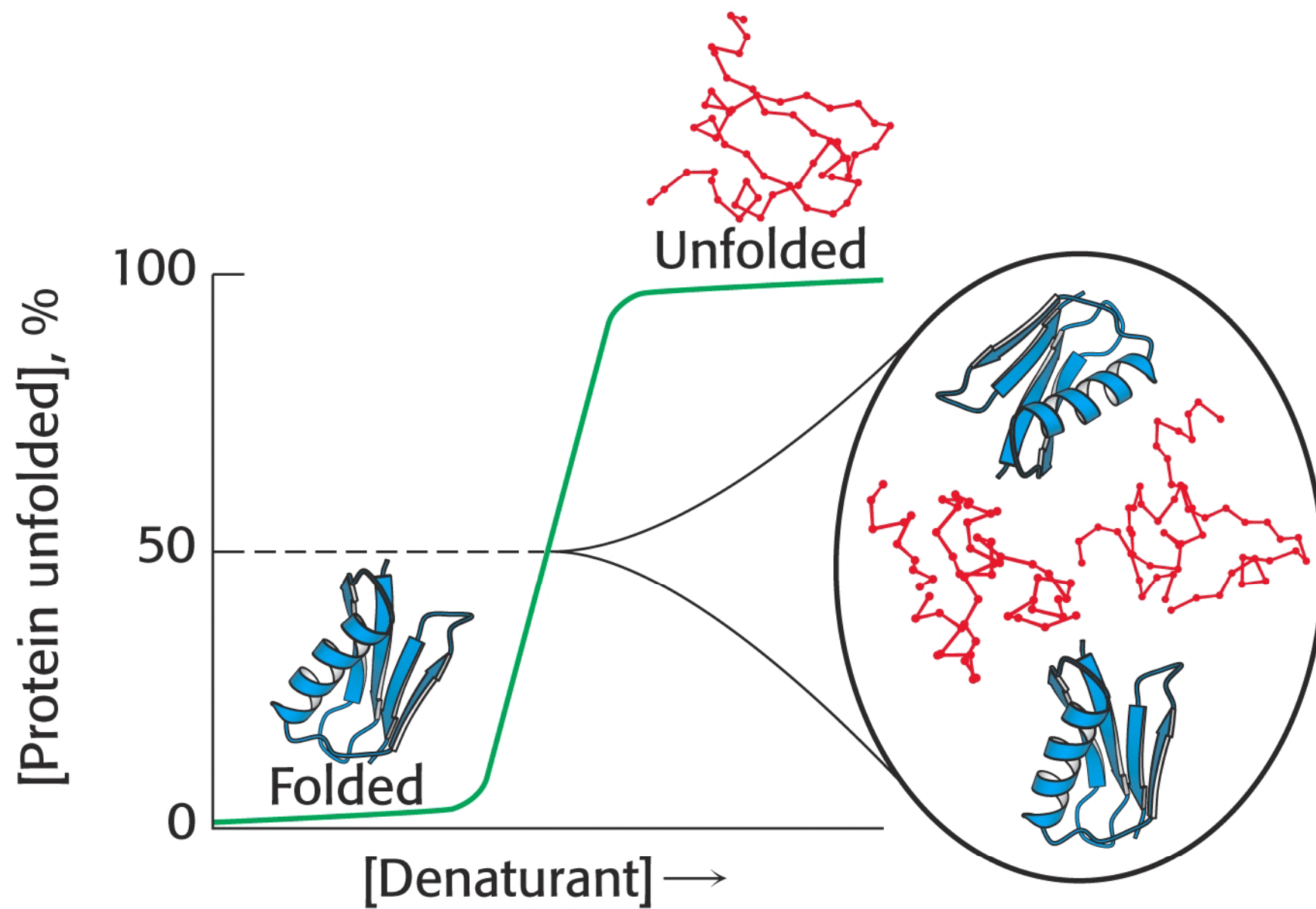
Gli agenti caotropici

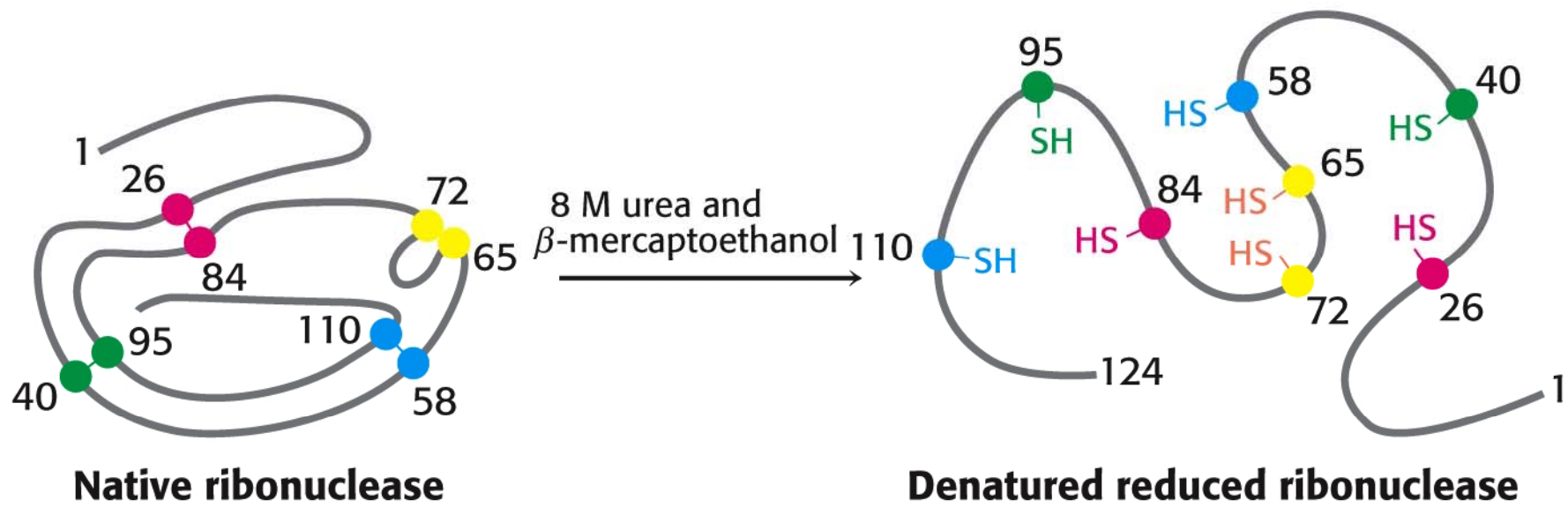


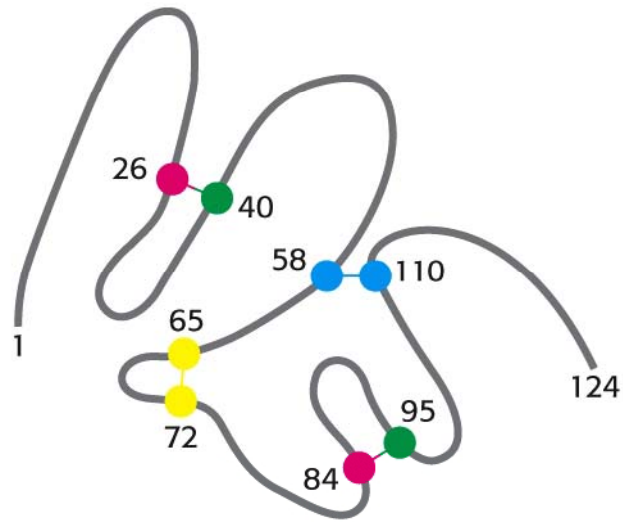
Urea



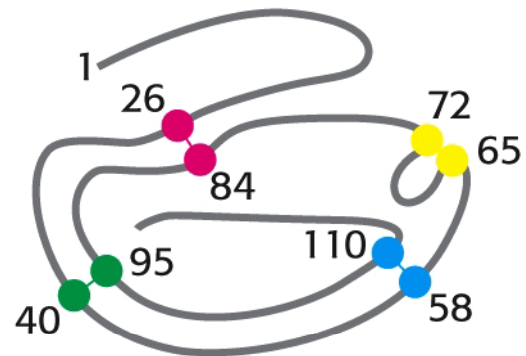
Guanidinium chloride







Trace of
 β -mercaptoethanol

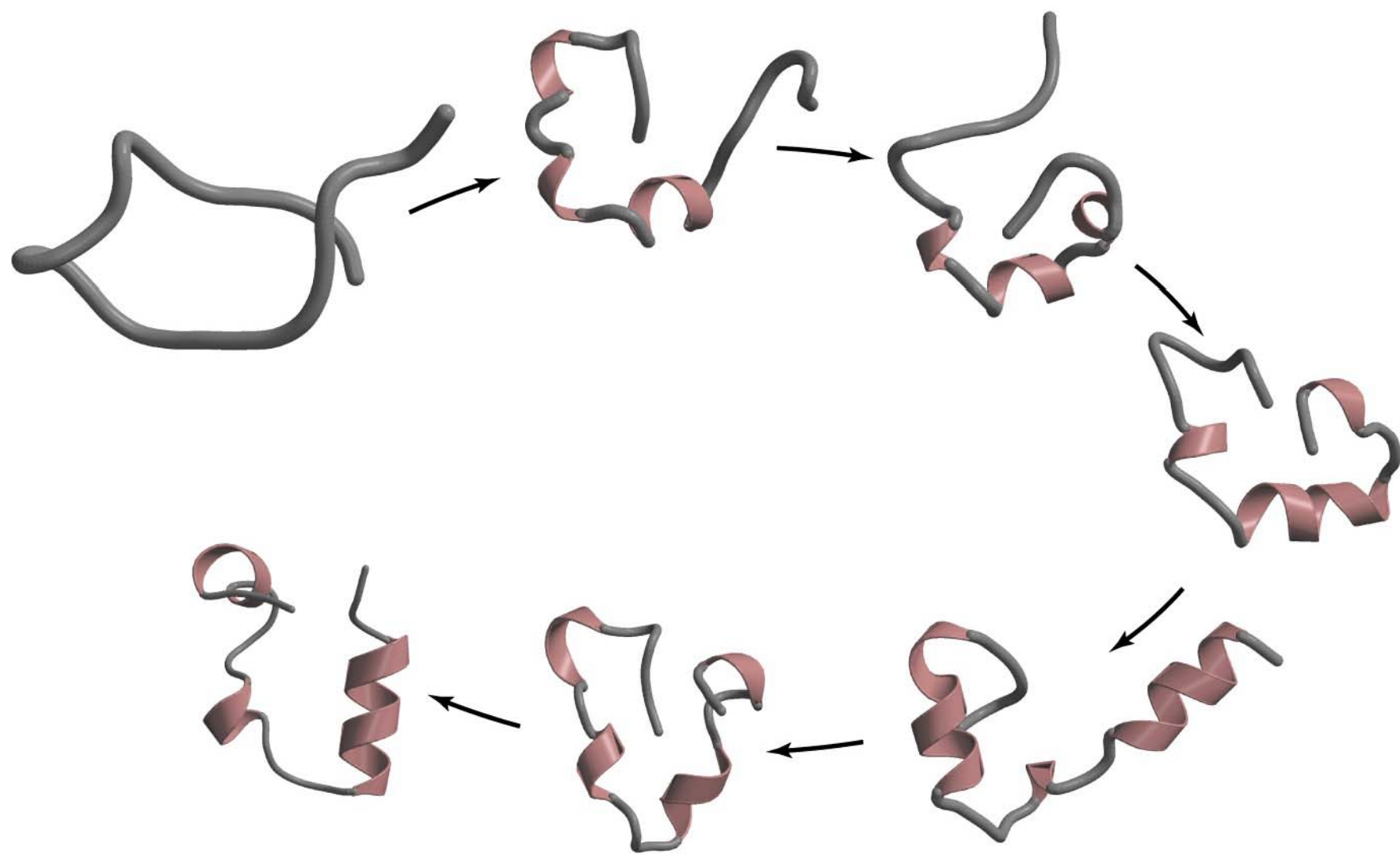


Native ribonuclease

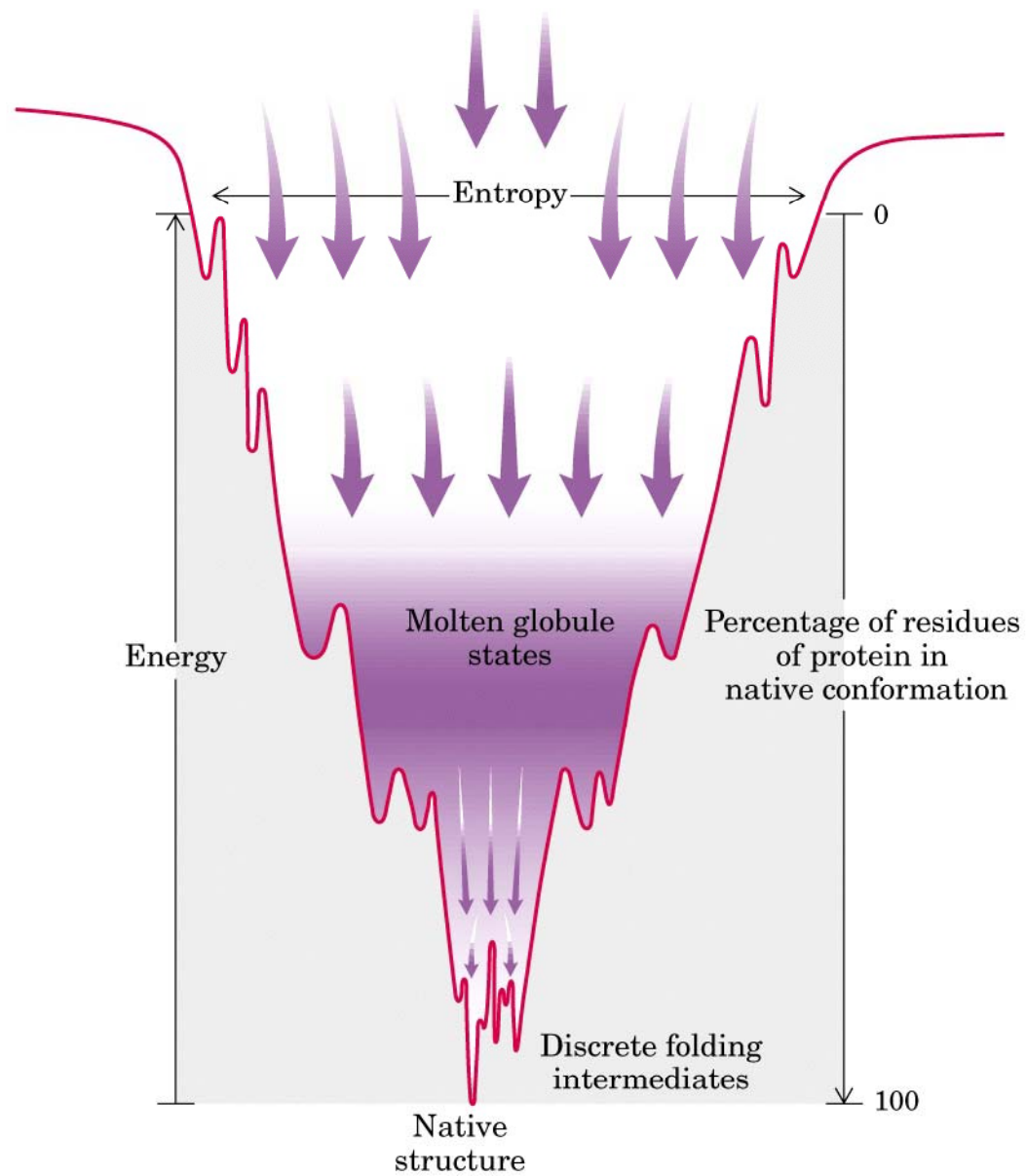
Il paradosso di Levinthal

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^{87} anni per testare tutte le conformazioni possibili alla ricerca della migliore

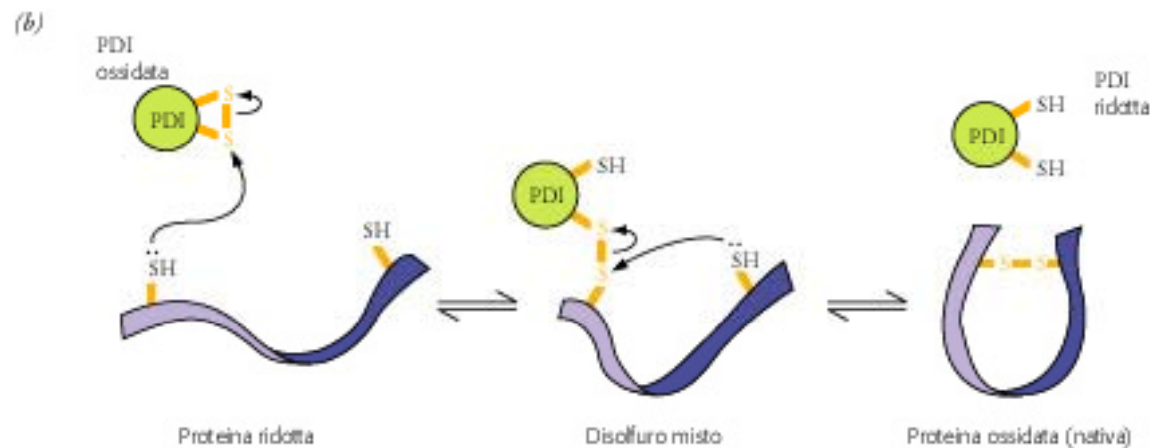
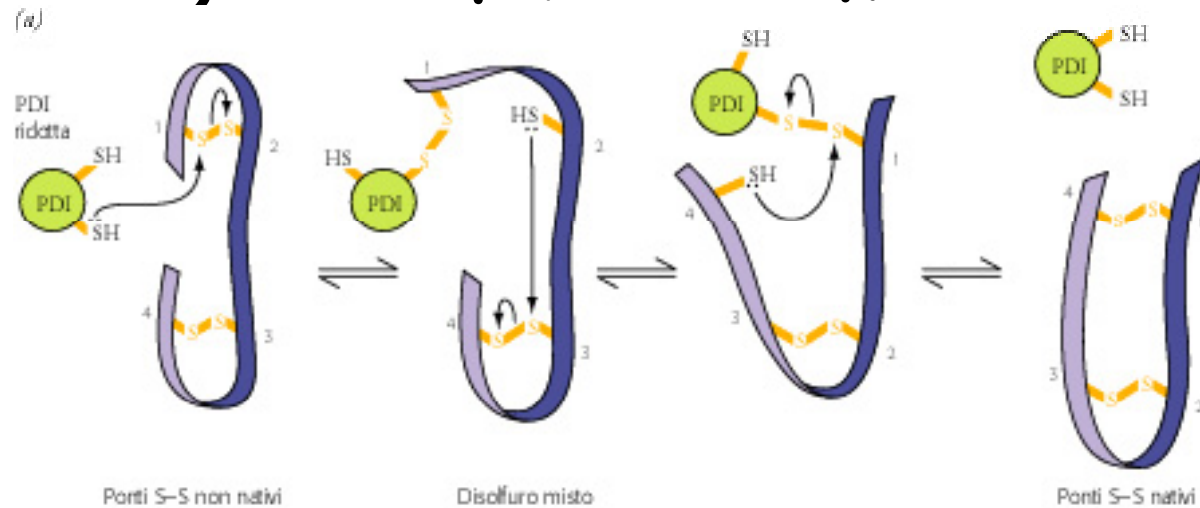


Beginning of helix formation and collapse

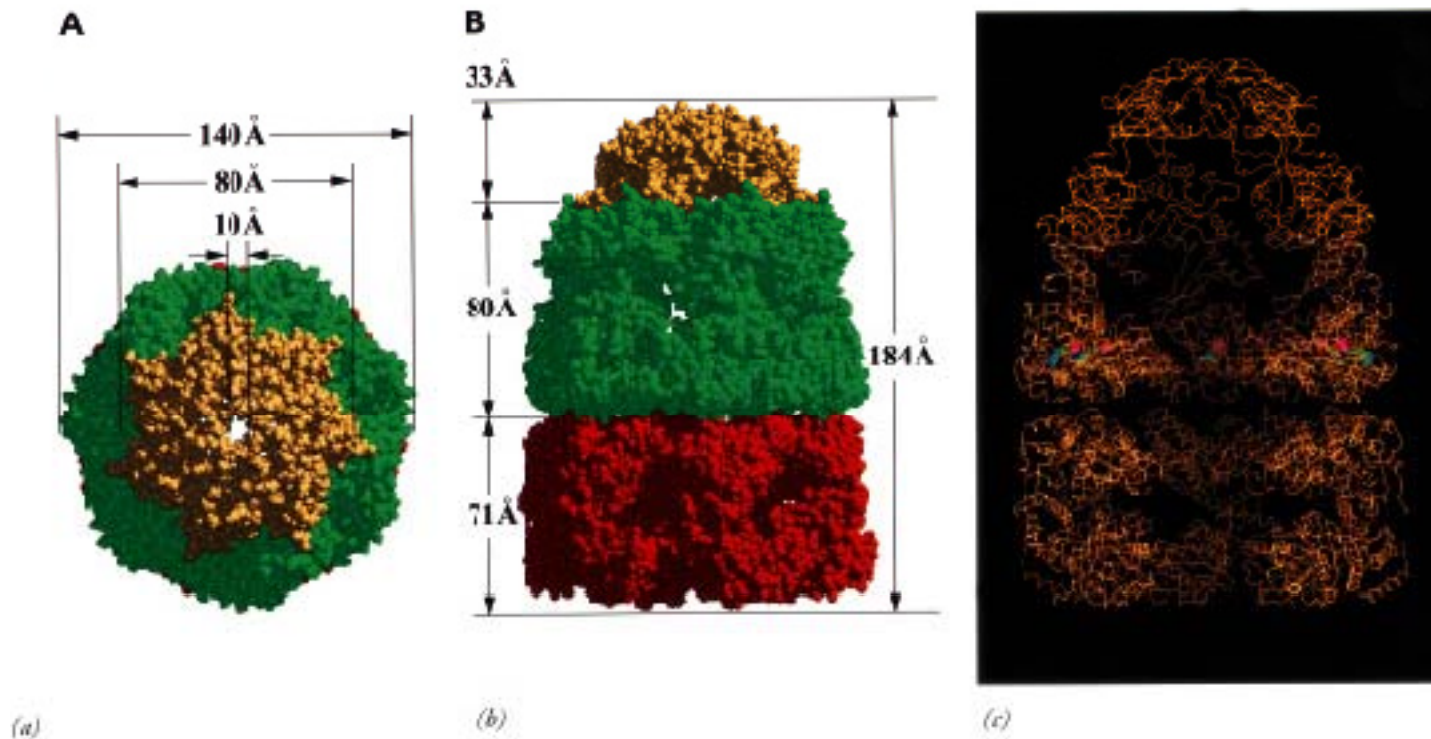


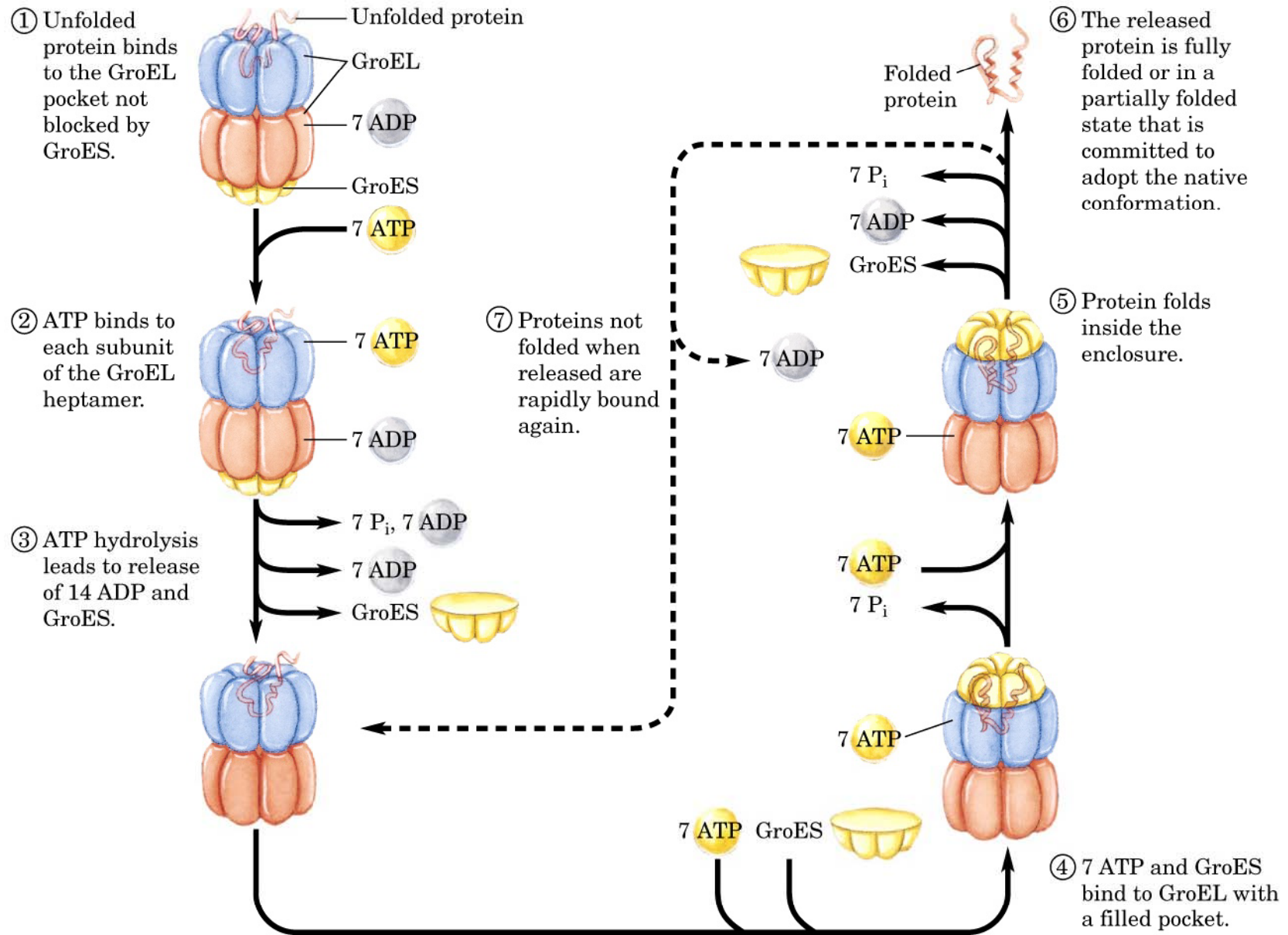
I chaperoni molecolari

a) disolfuro isomerasi



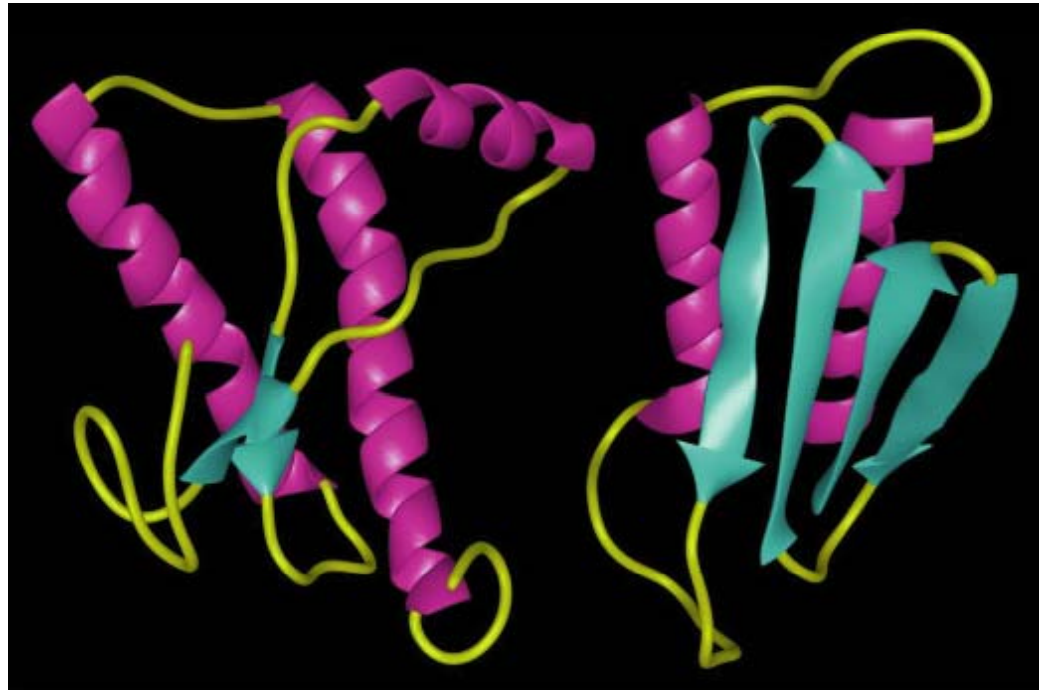
Il complesso chaperoninico GroEL-GroES



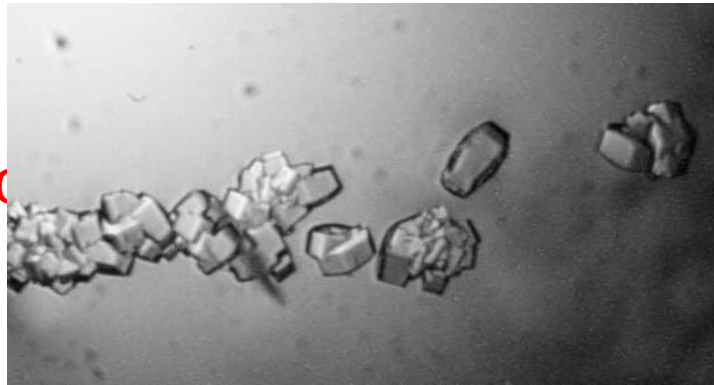


(a)

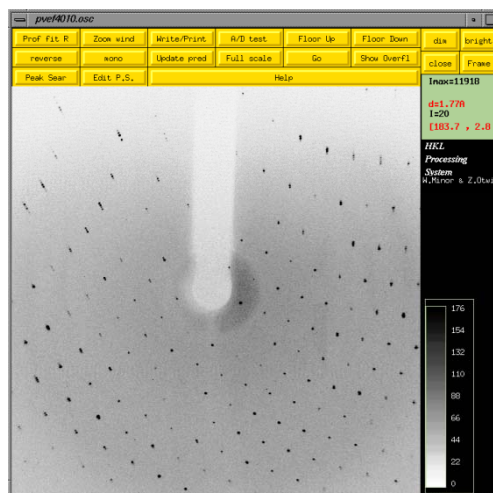
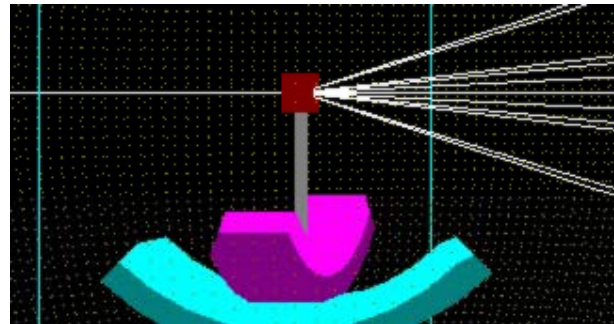
Alcune patologie sono legate ad
un errato ripiegamento delle
proteine



Un cristallo proteico



È posto sotto una sorgente di raggi X

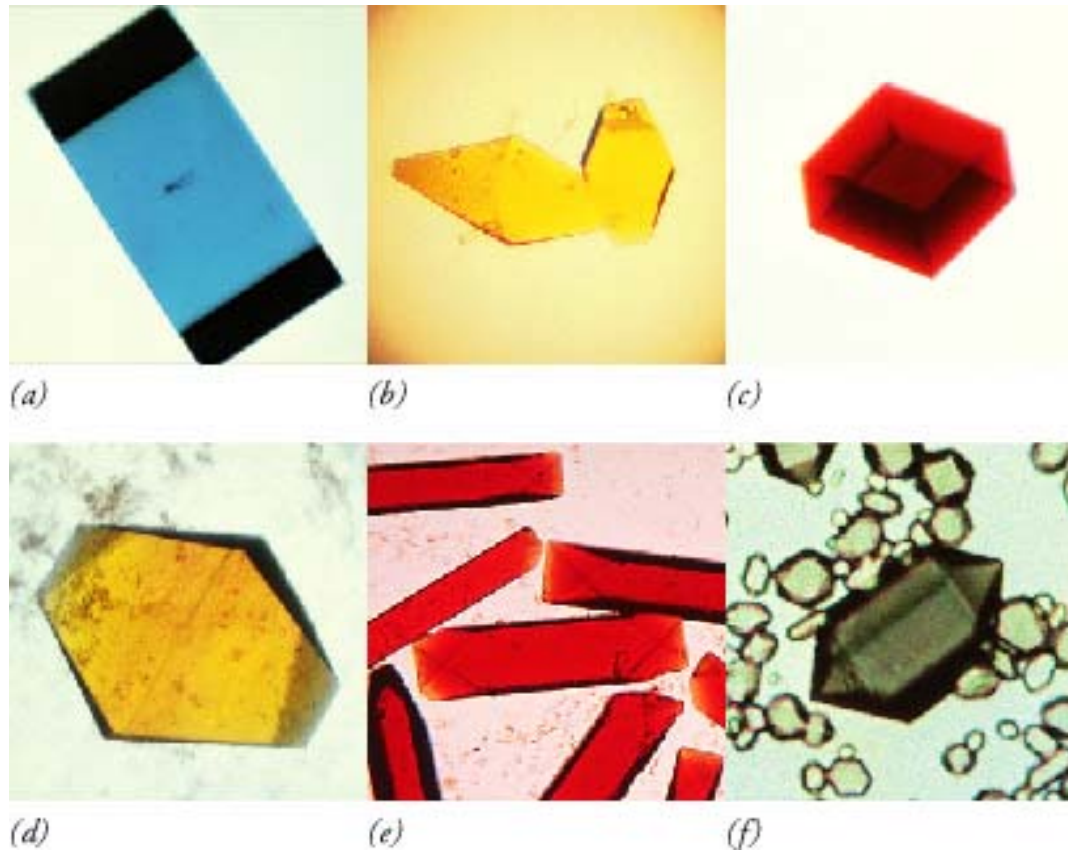


I raggi X sono diffratti dalle
Nuvole elettroniche
Intorno agli atomi



da questi dati si può dedurre
la struttura atomica

I cristalli si ottengono per precipitazione lenta della molecola
Da una soluzione, in condizioni che non dovrebbero alterare la struttura



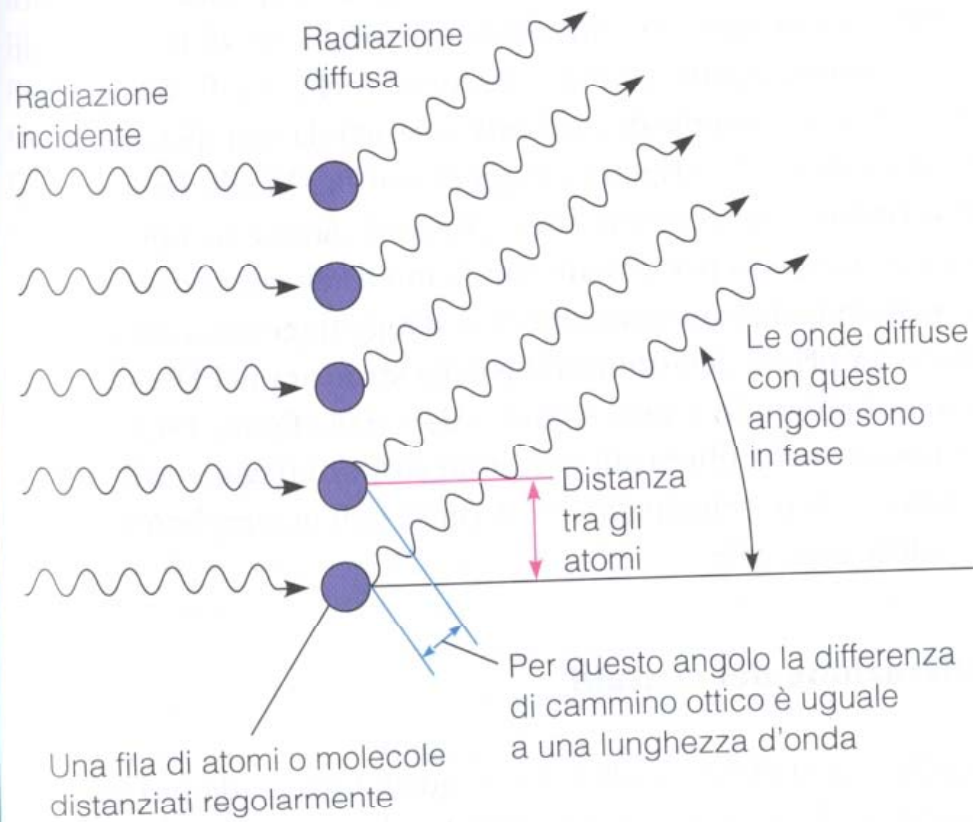
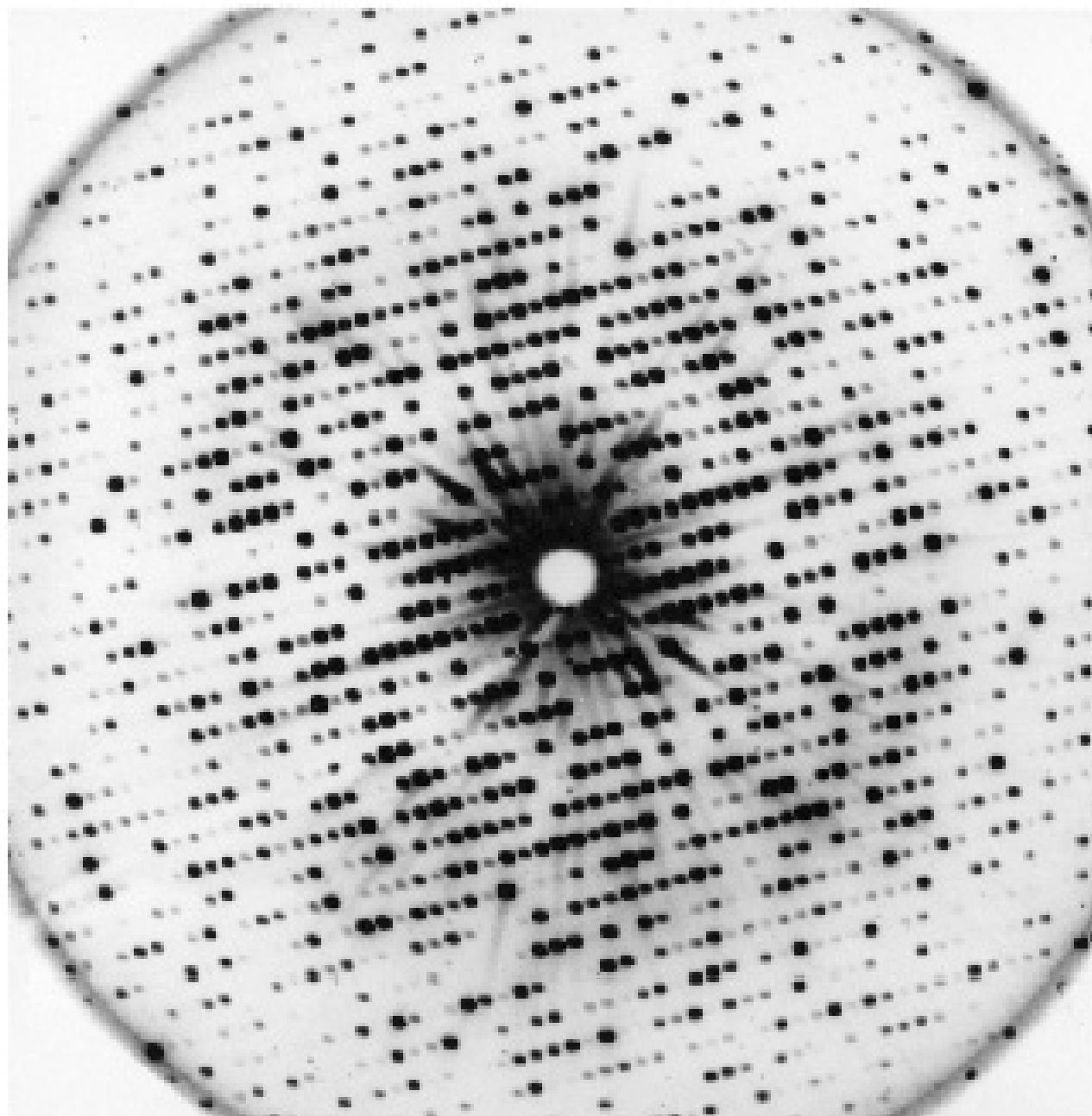


FIGURA 4B.1

Diffrazione di una struttura molto semplice: una fila di atomi o di molecole.

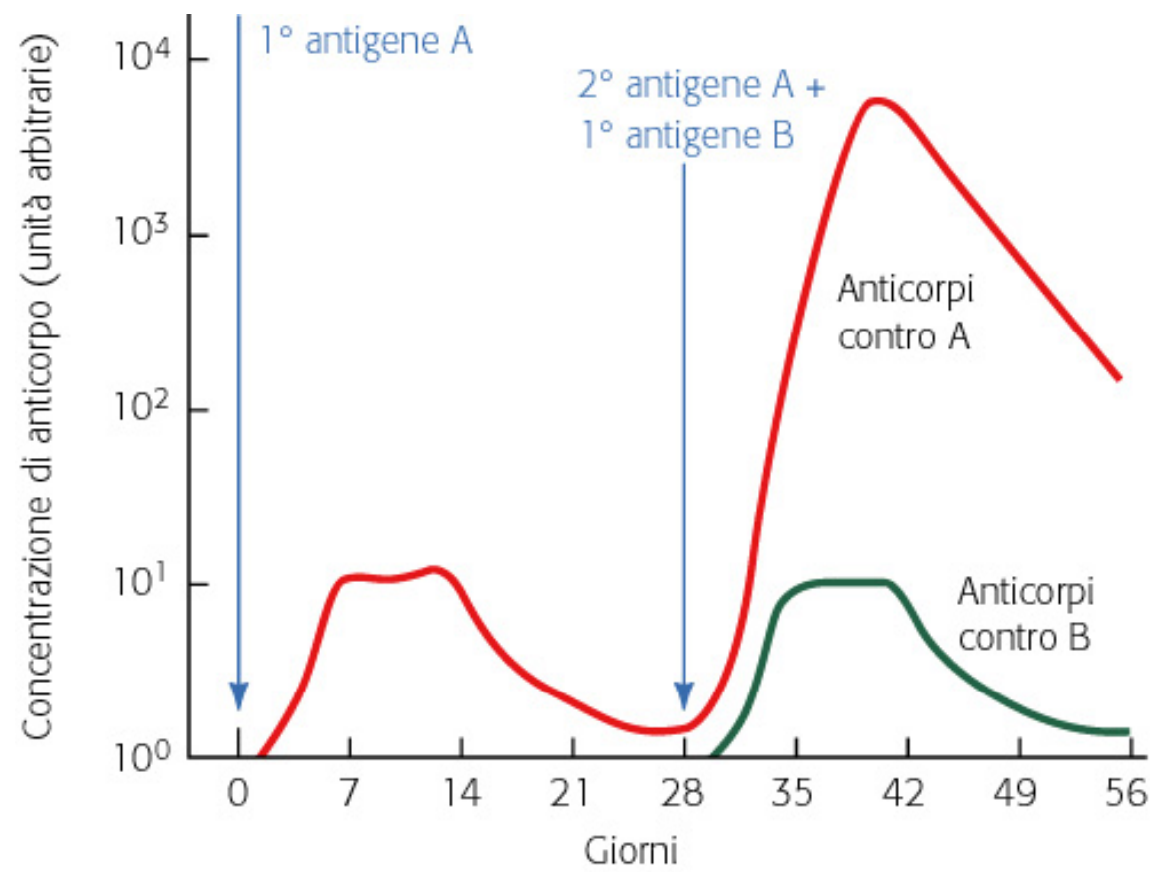
FIGURA 4I
Una sen

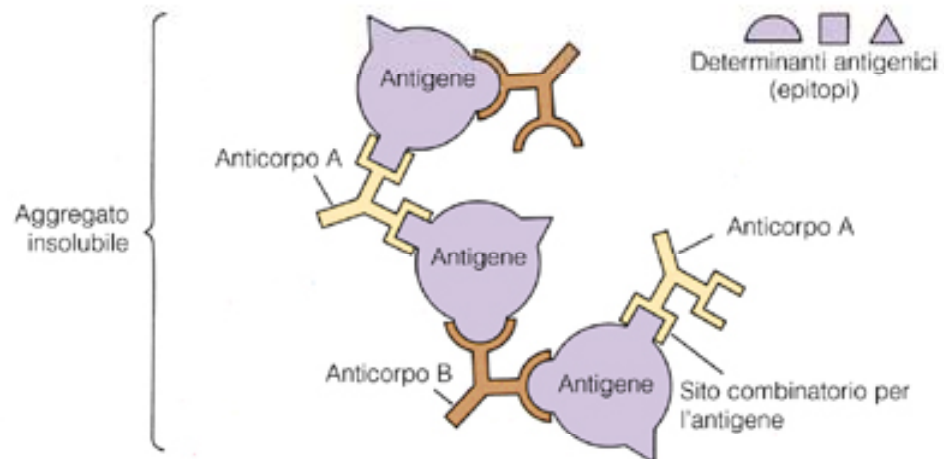




Le proteine sono molecole
flessibili



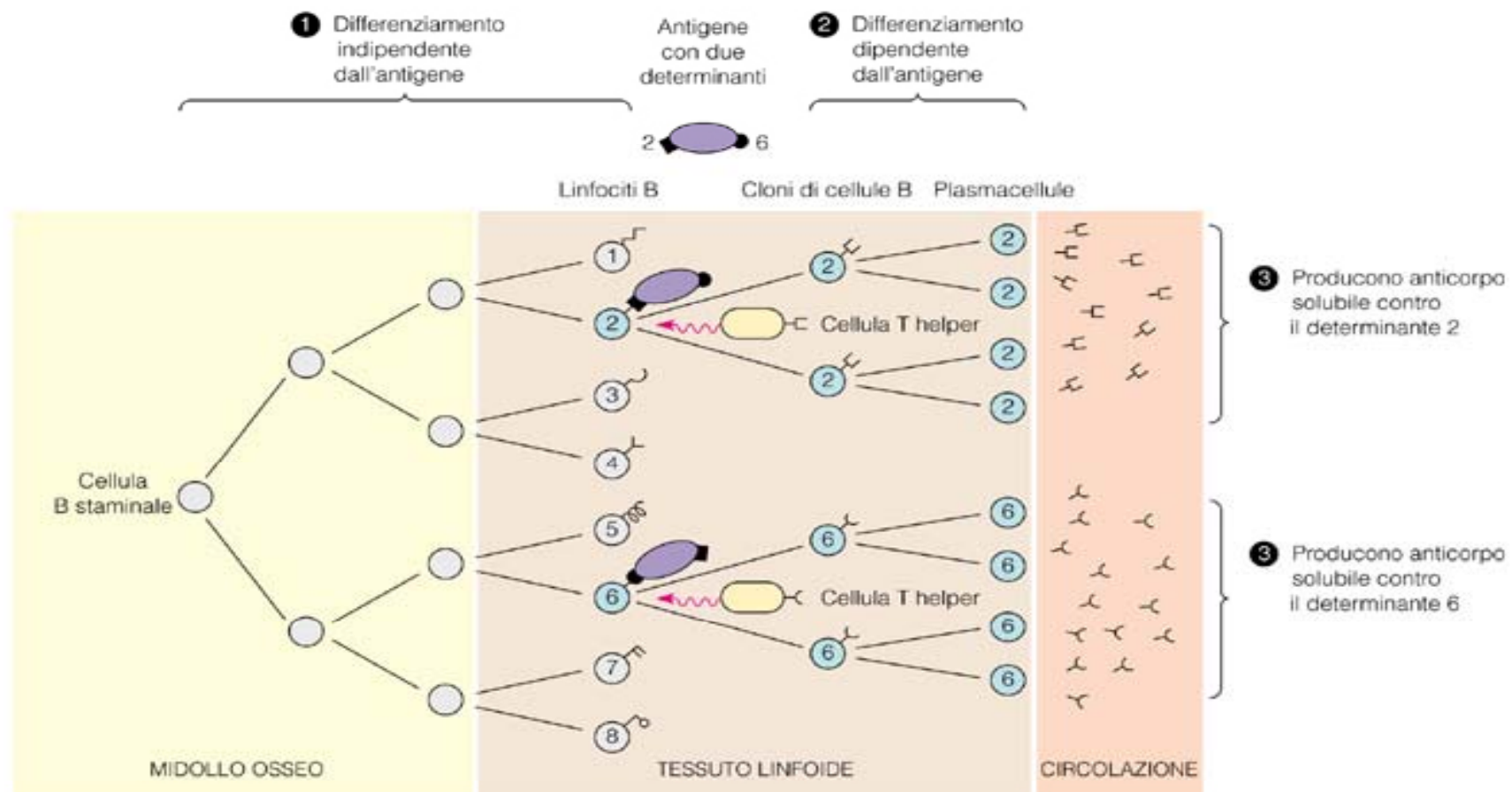


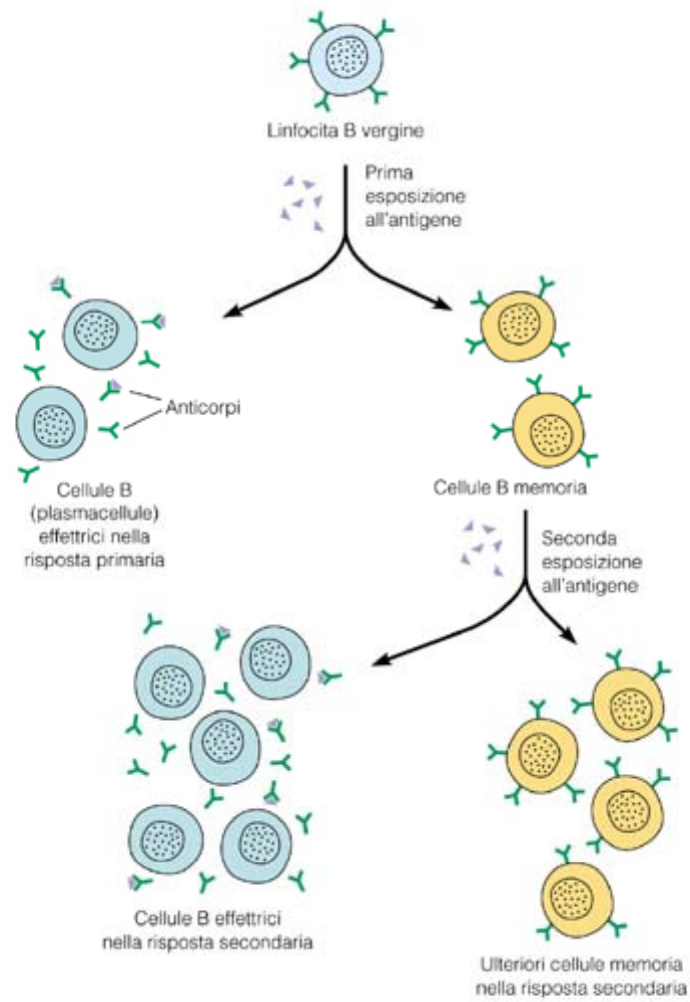


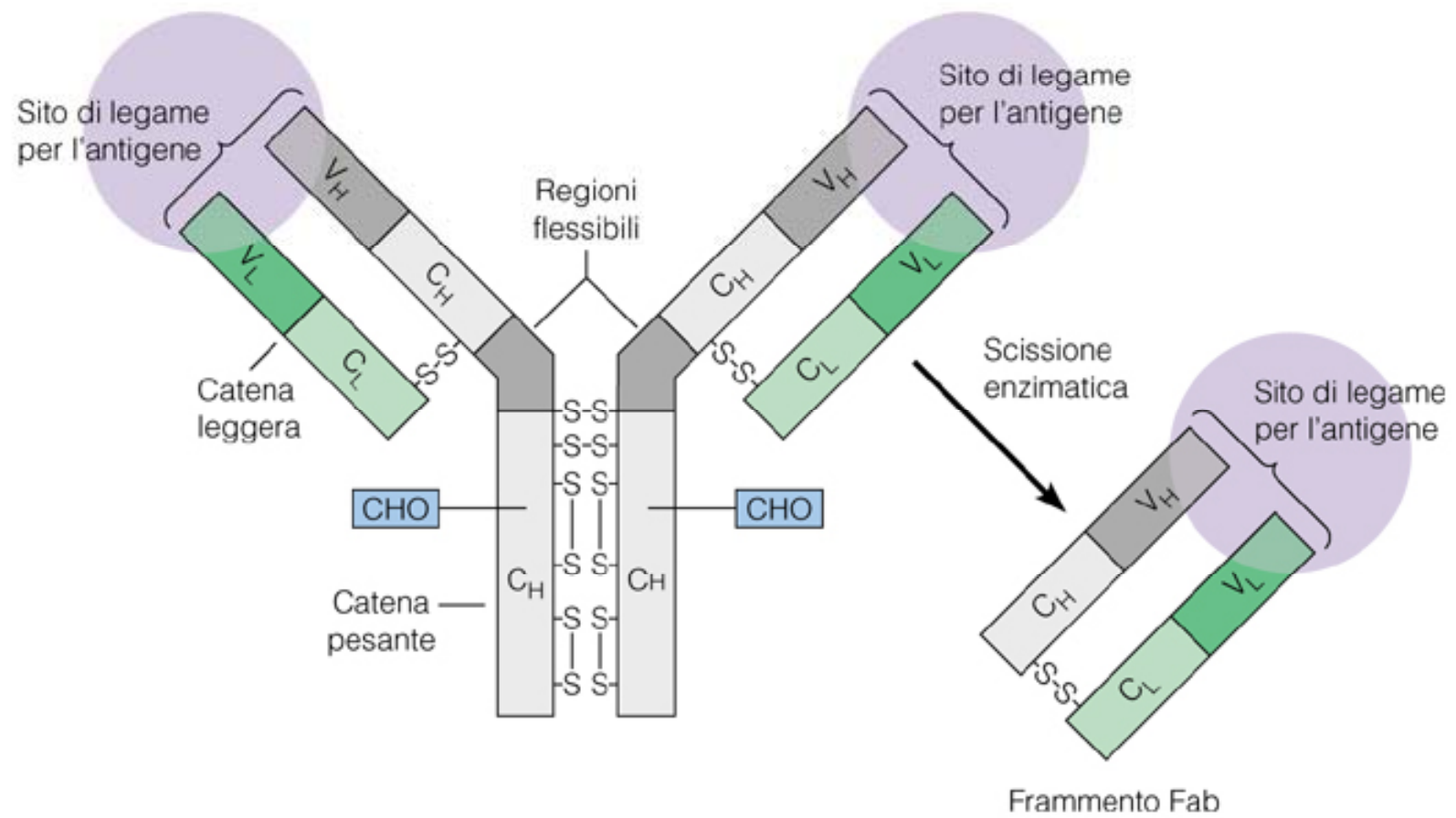
(a) Precipitazione

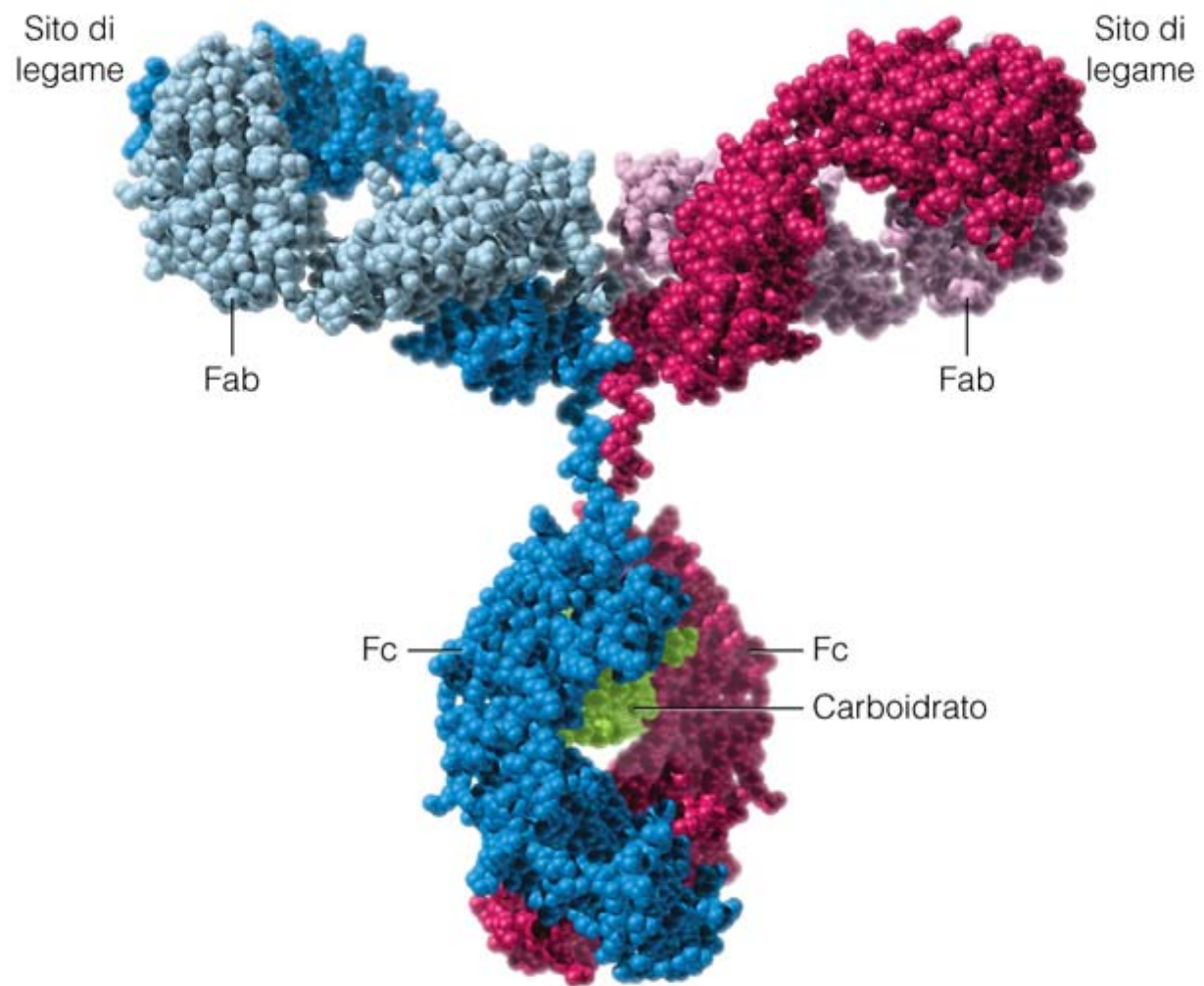


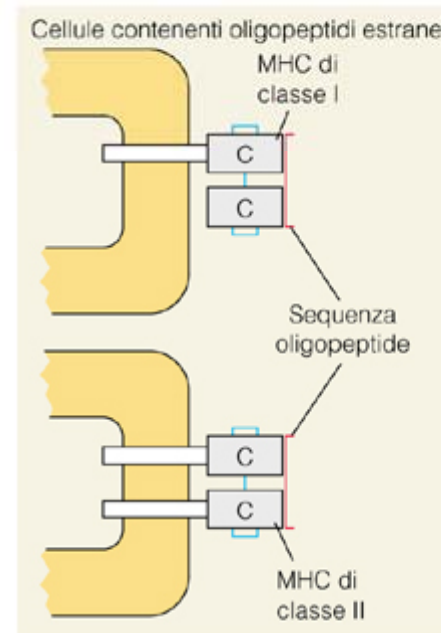
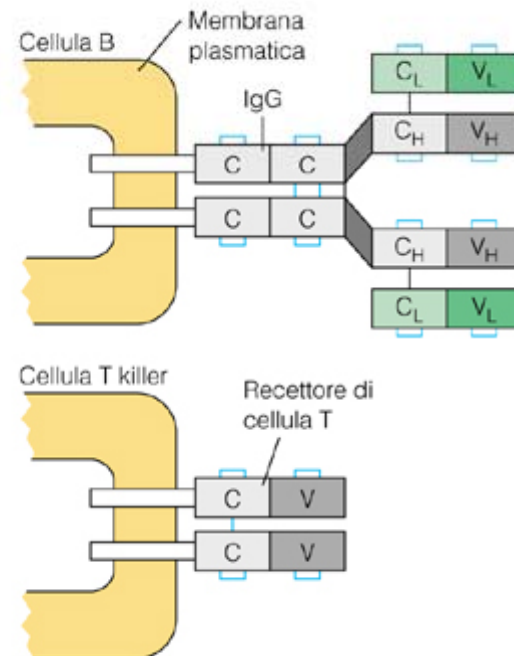
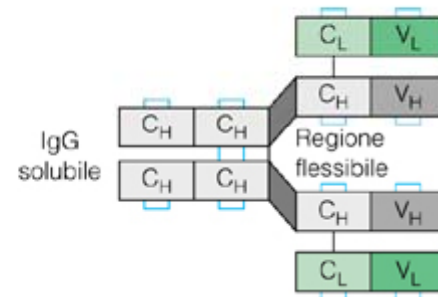
(b) Determinanti antigenici, mioglobina da capodoglio

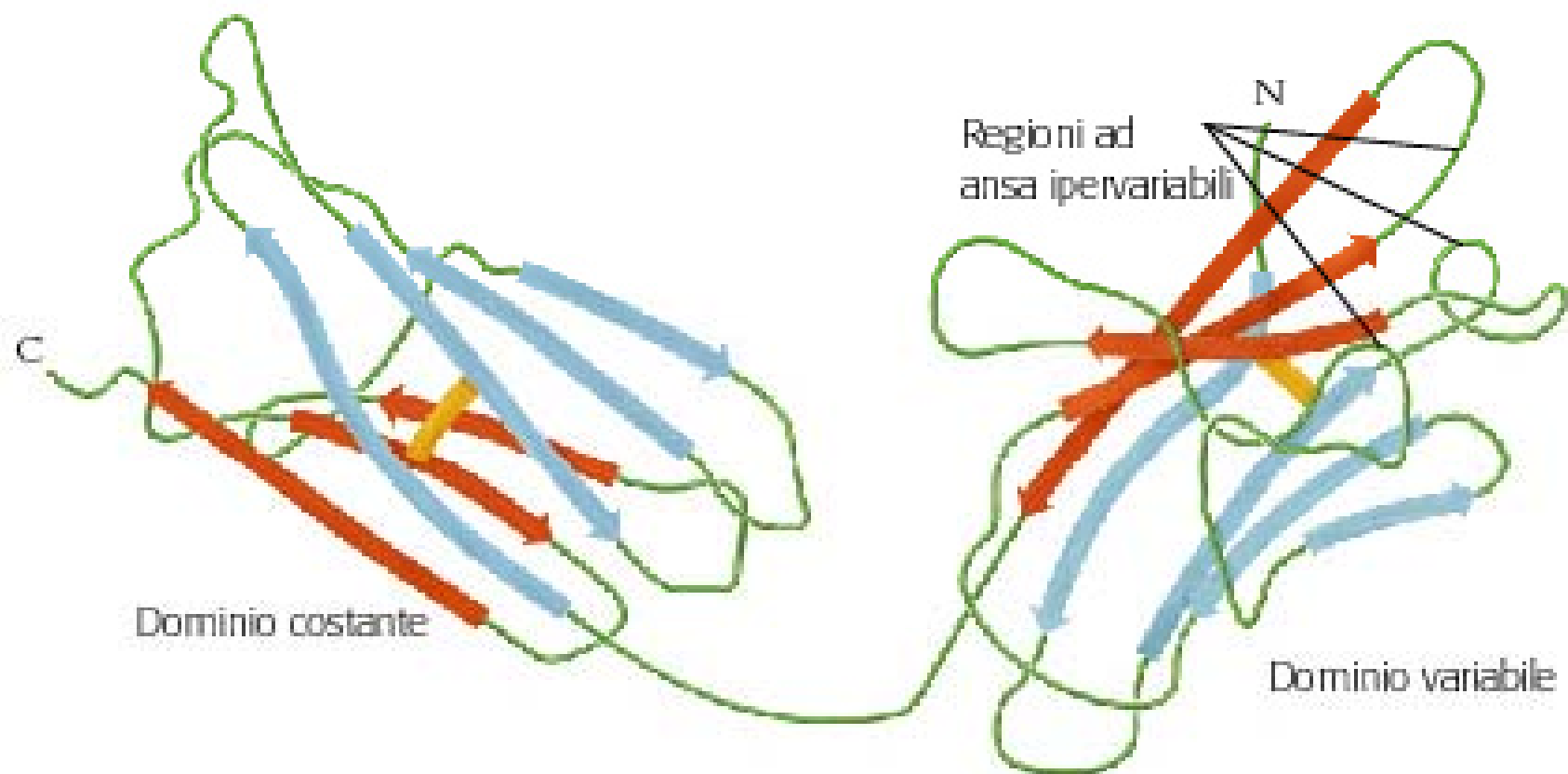


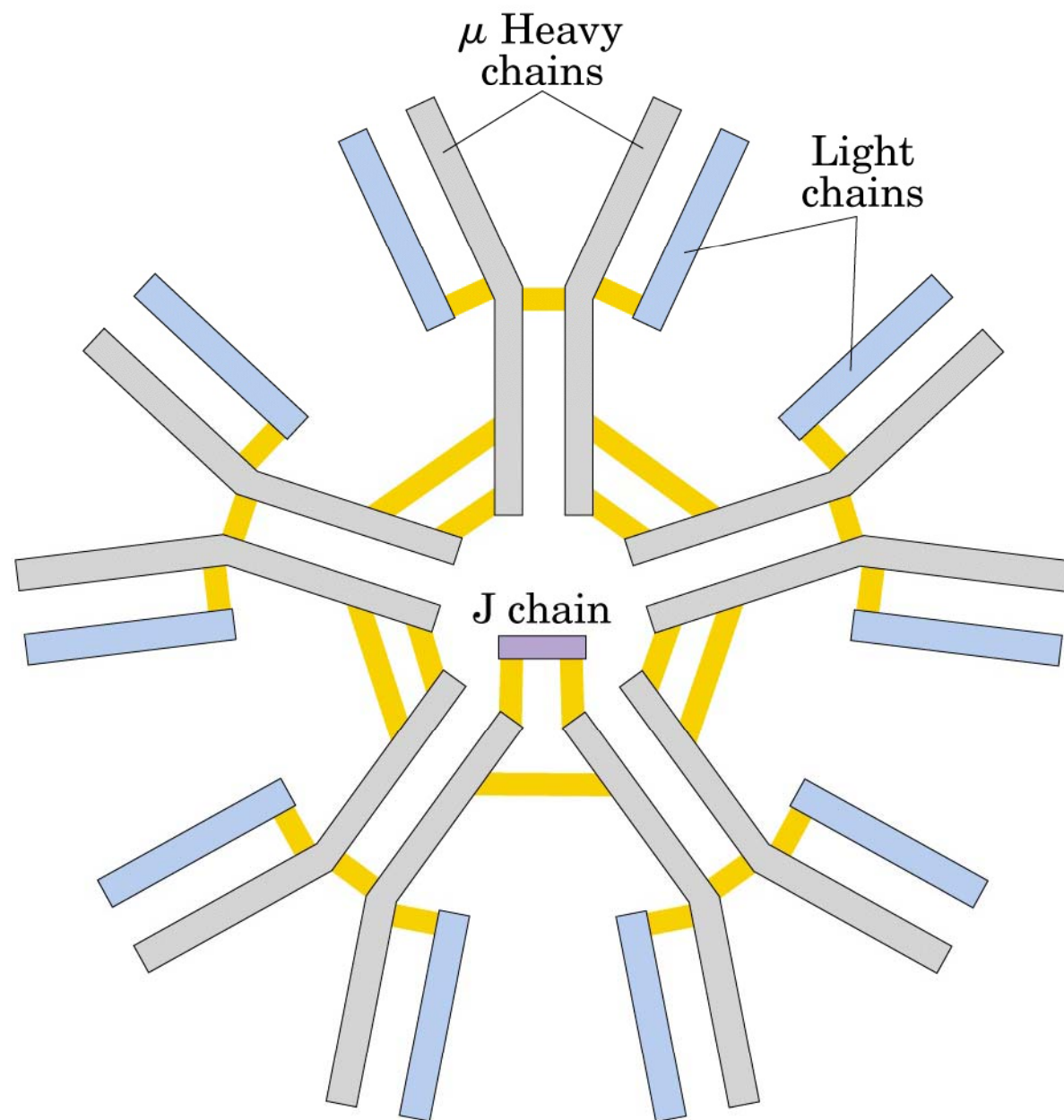


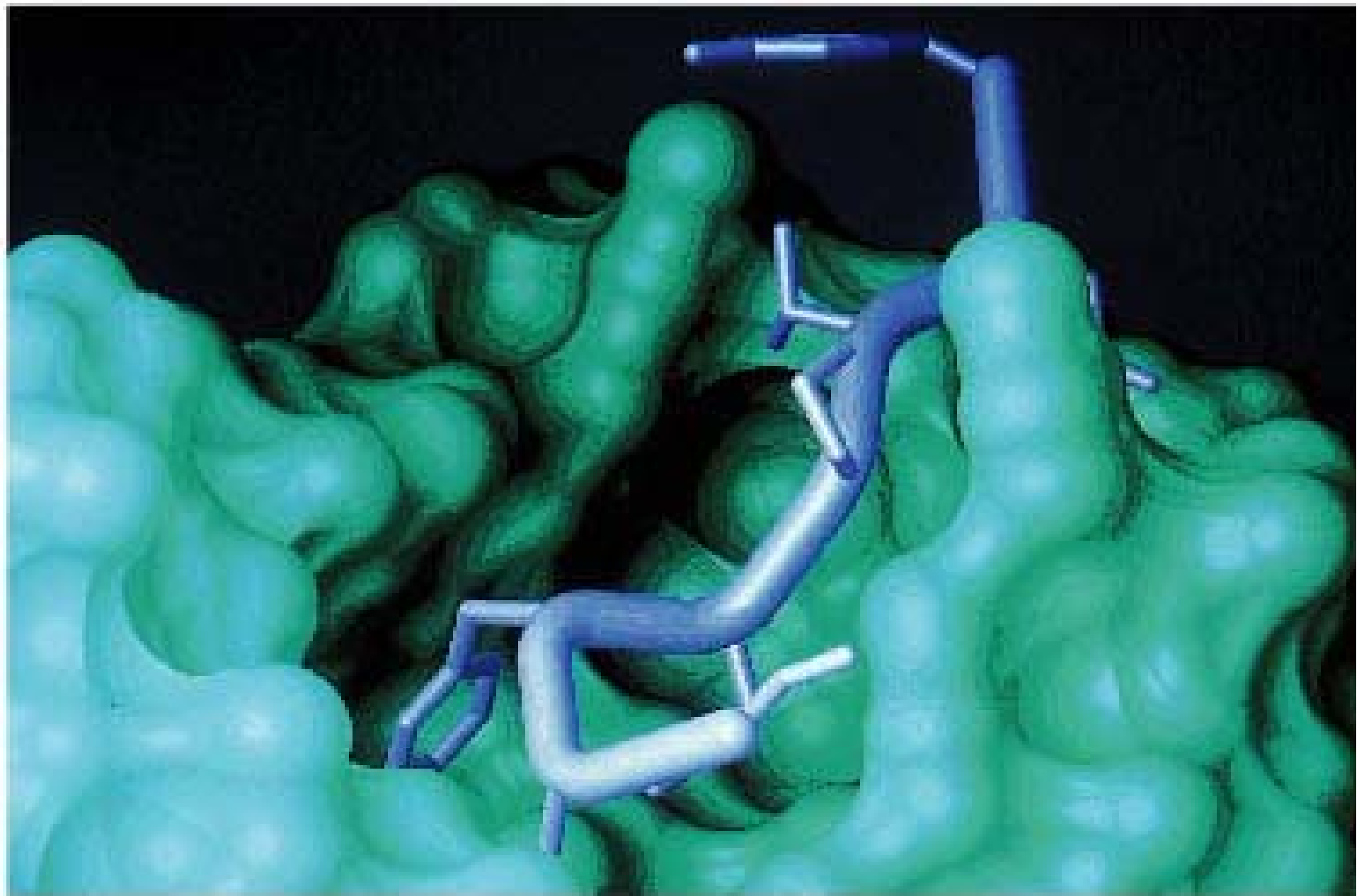


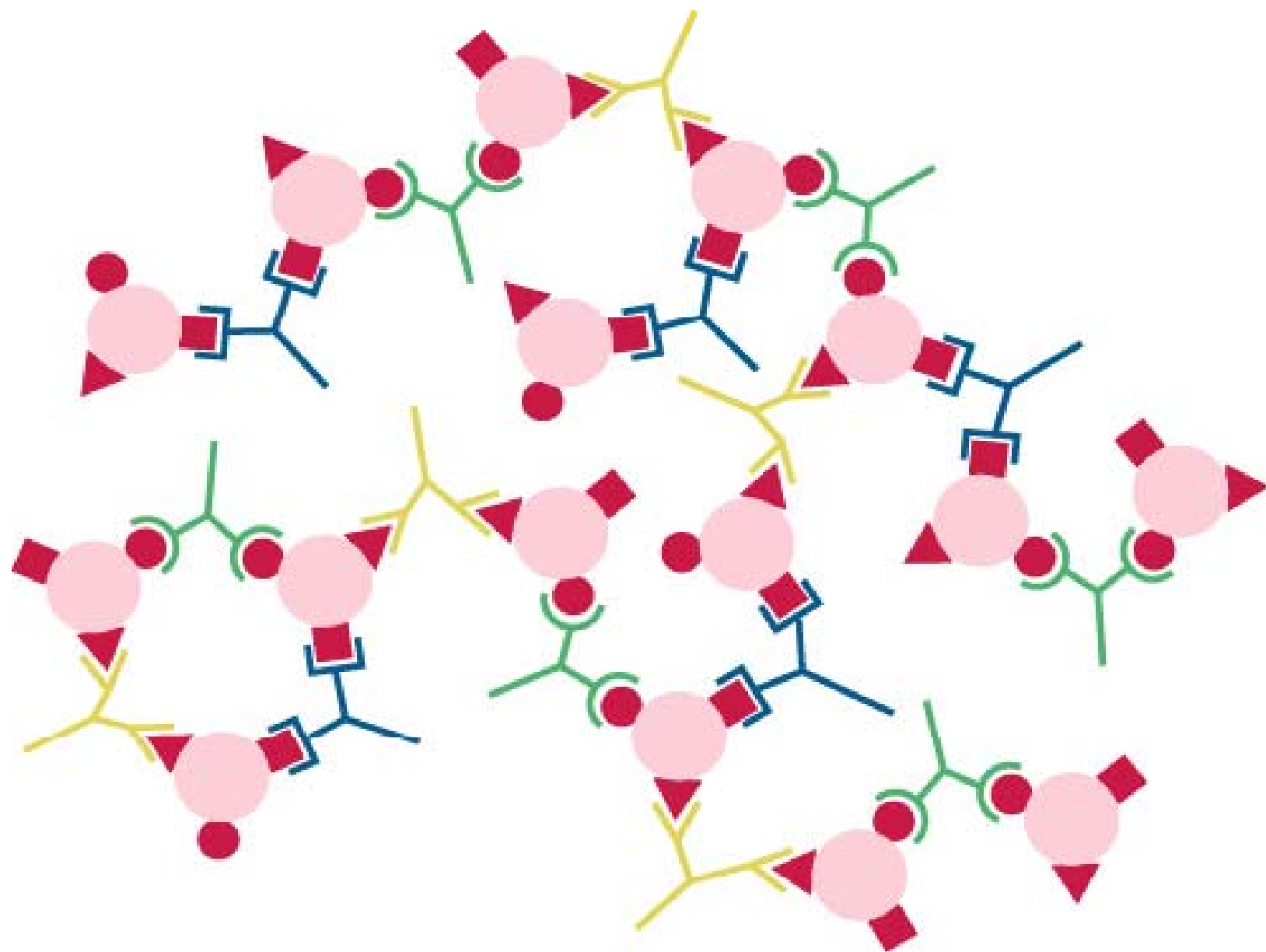


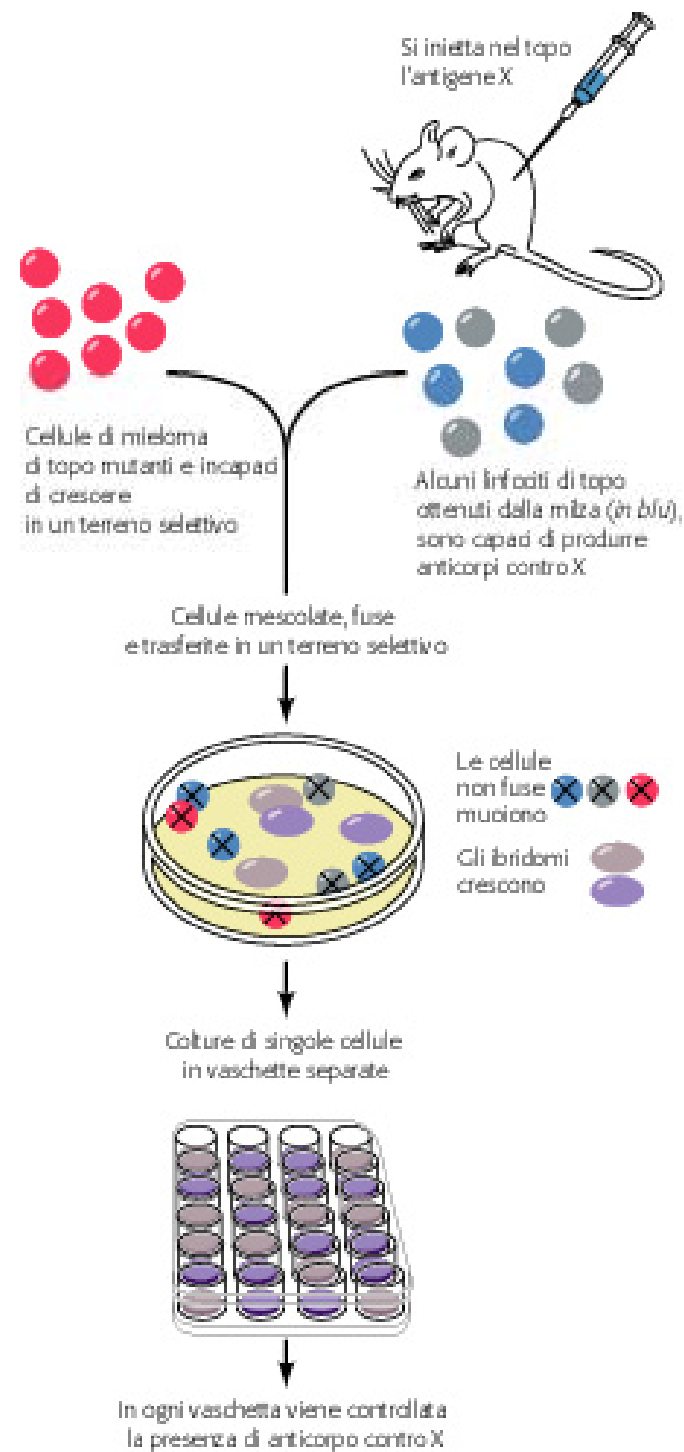


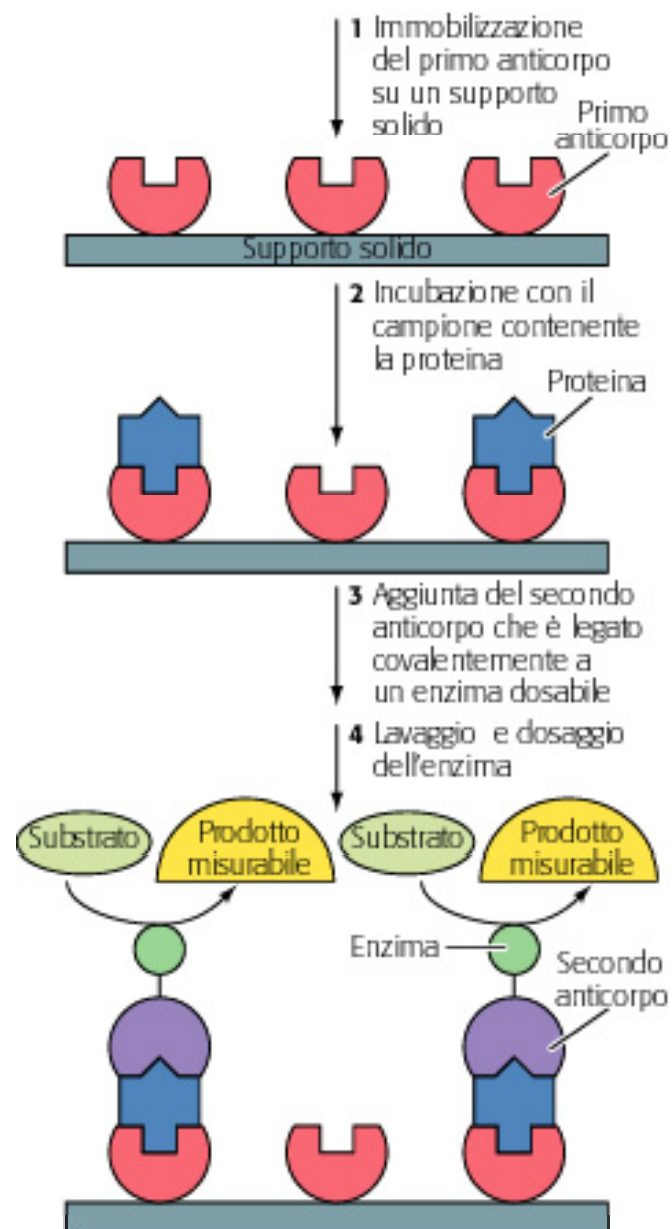


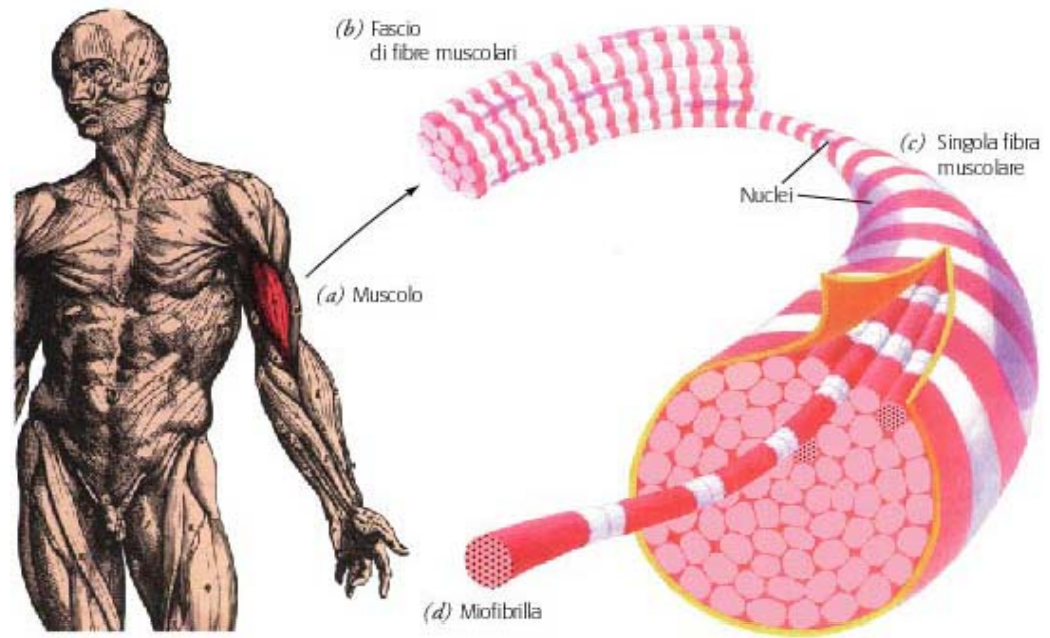
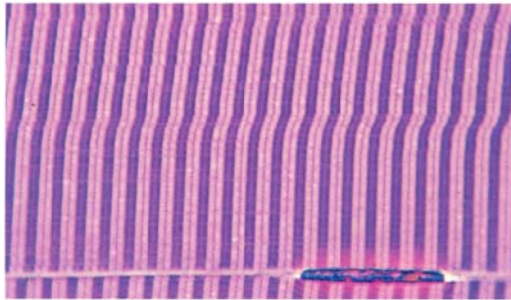


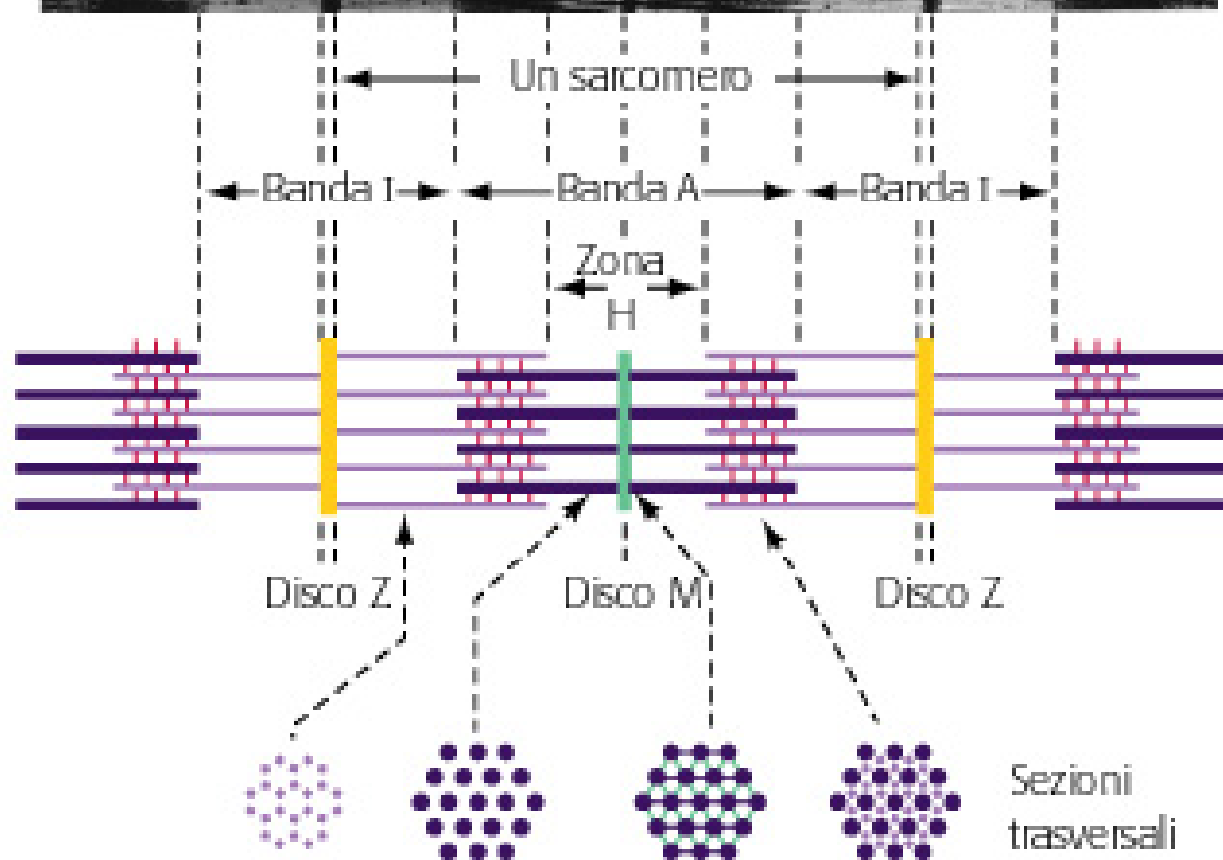
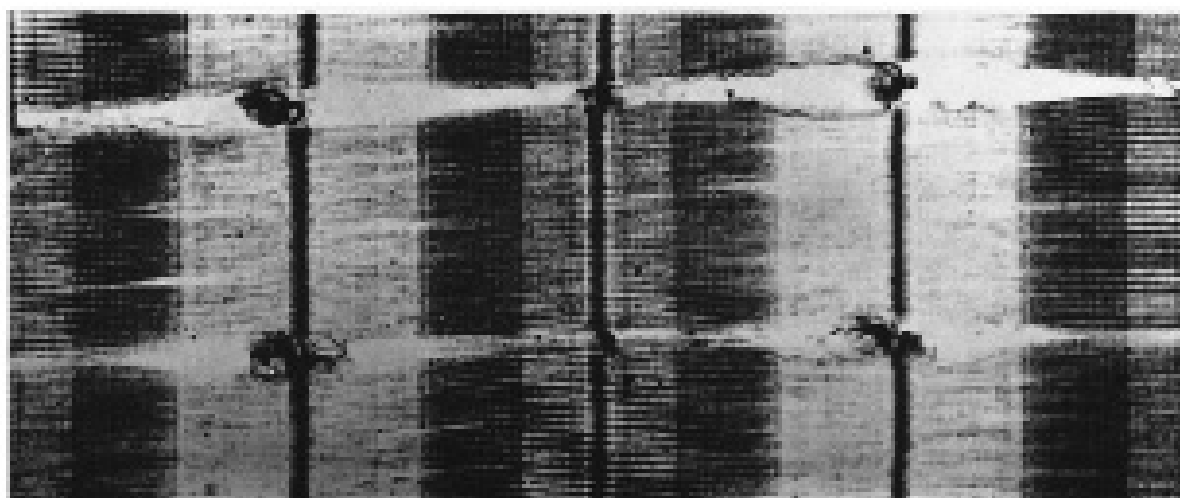


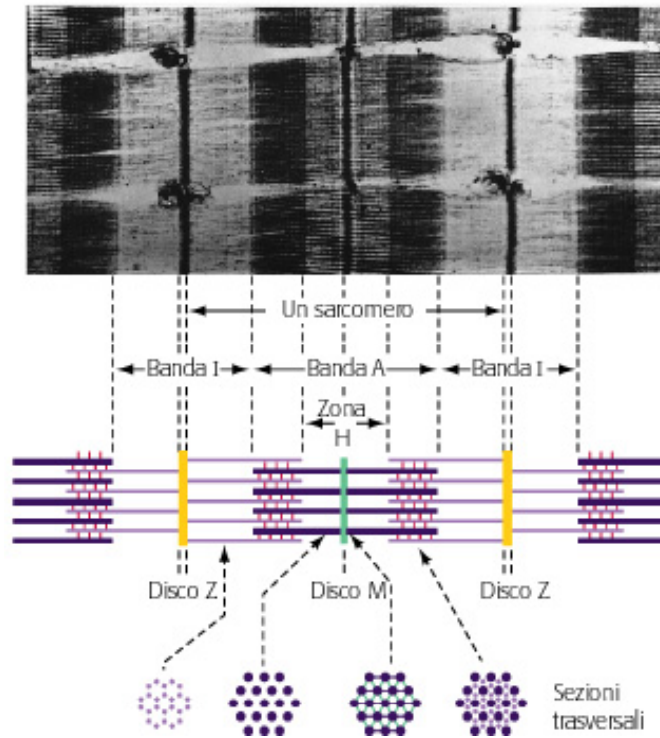




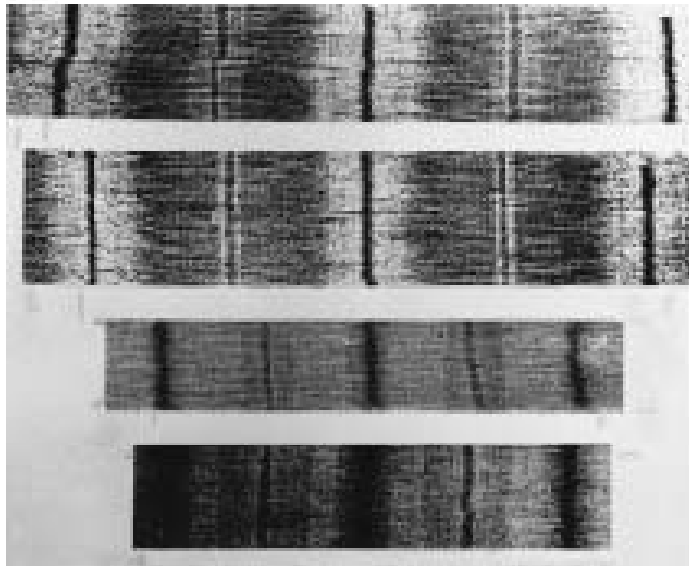




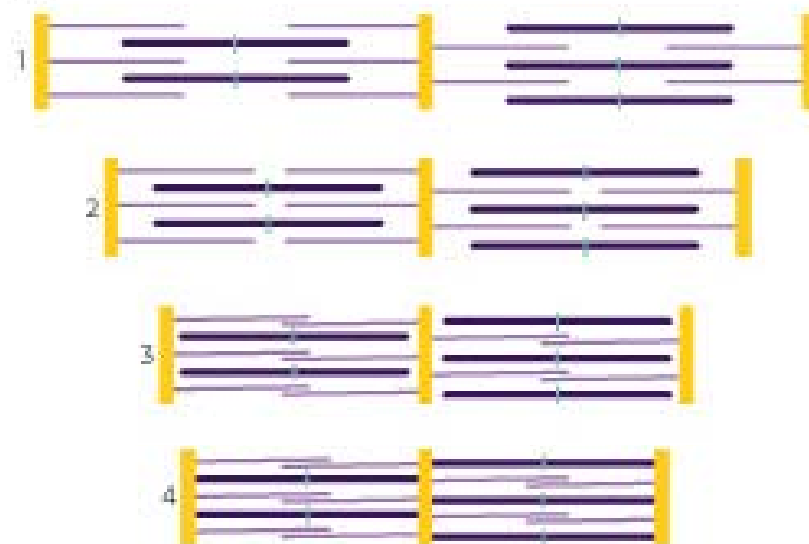


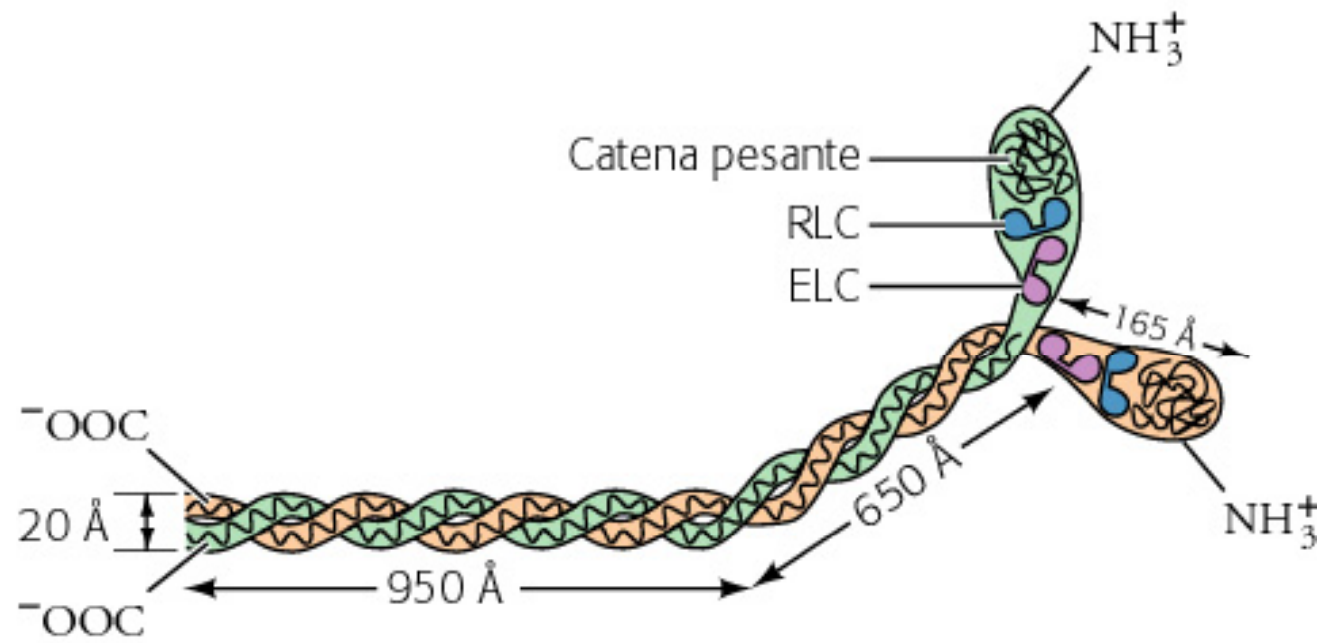


(a)

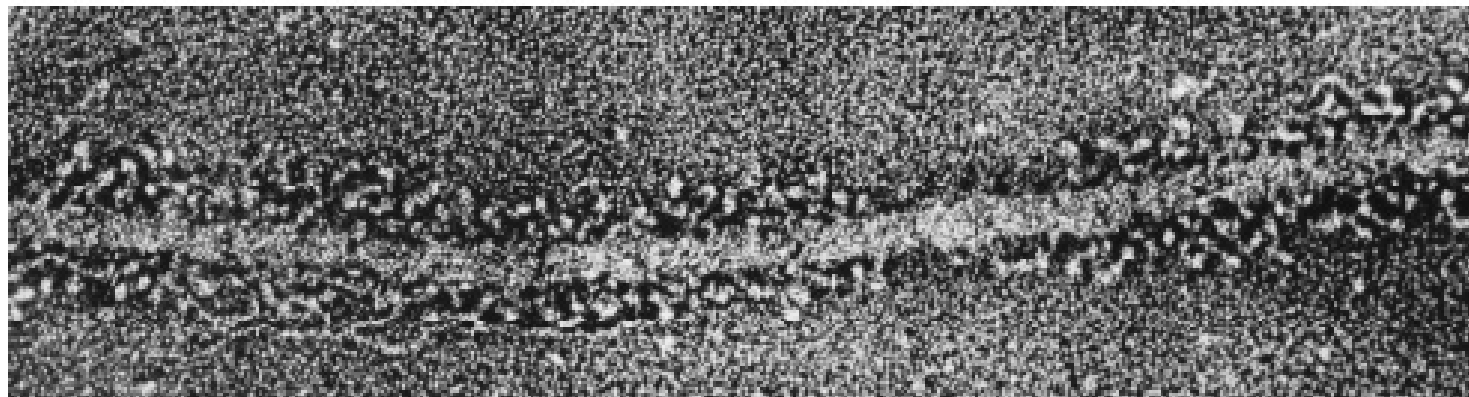


(b)





(a)



(b)

