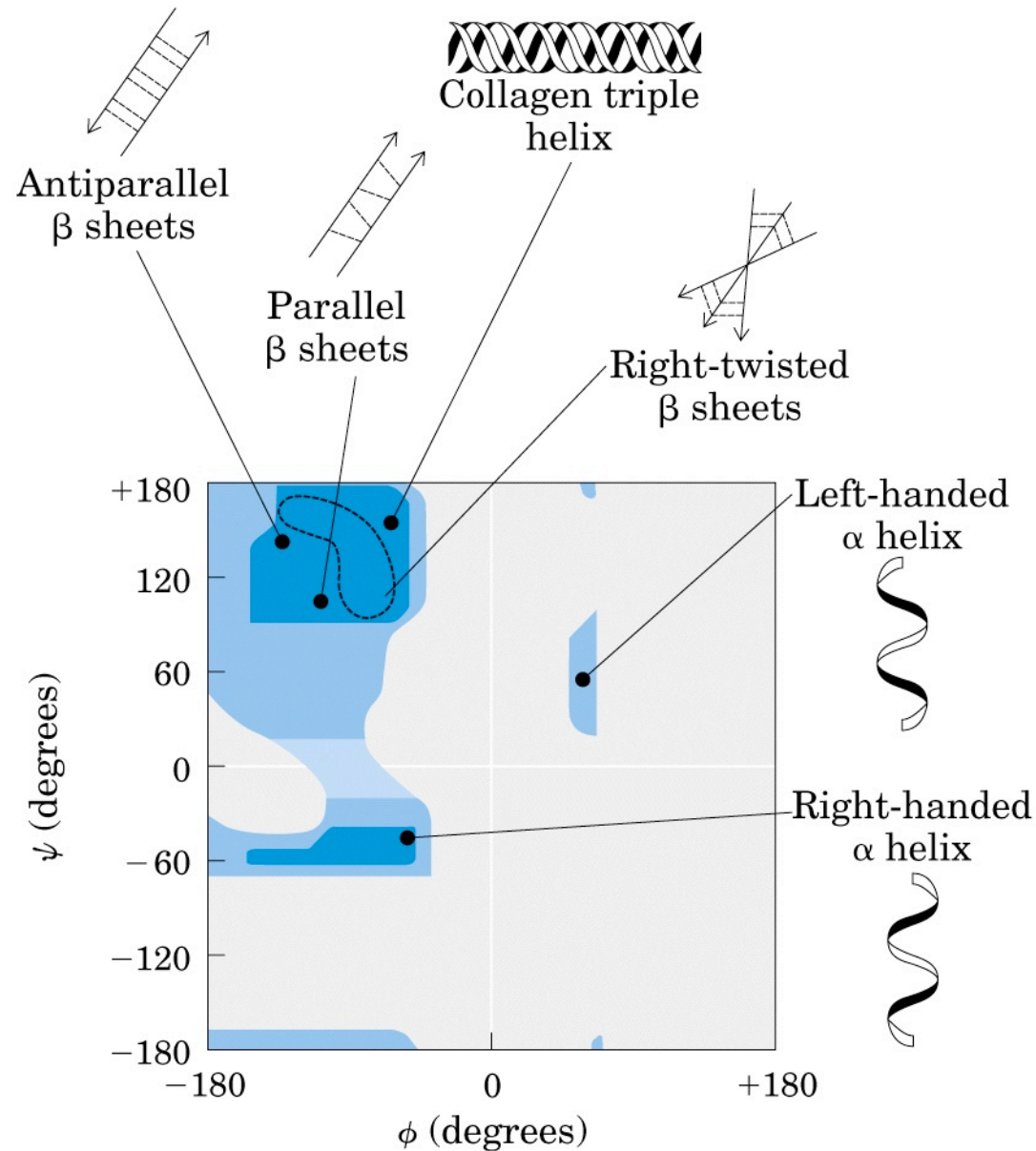


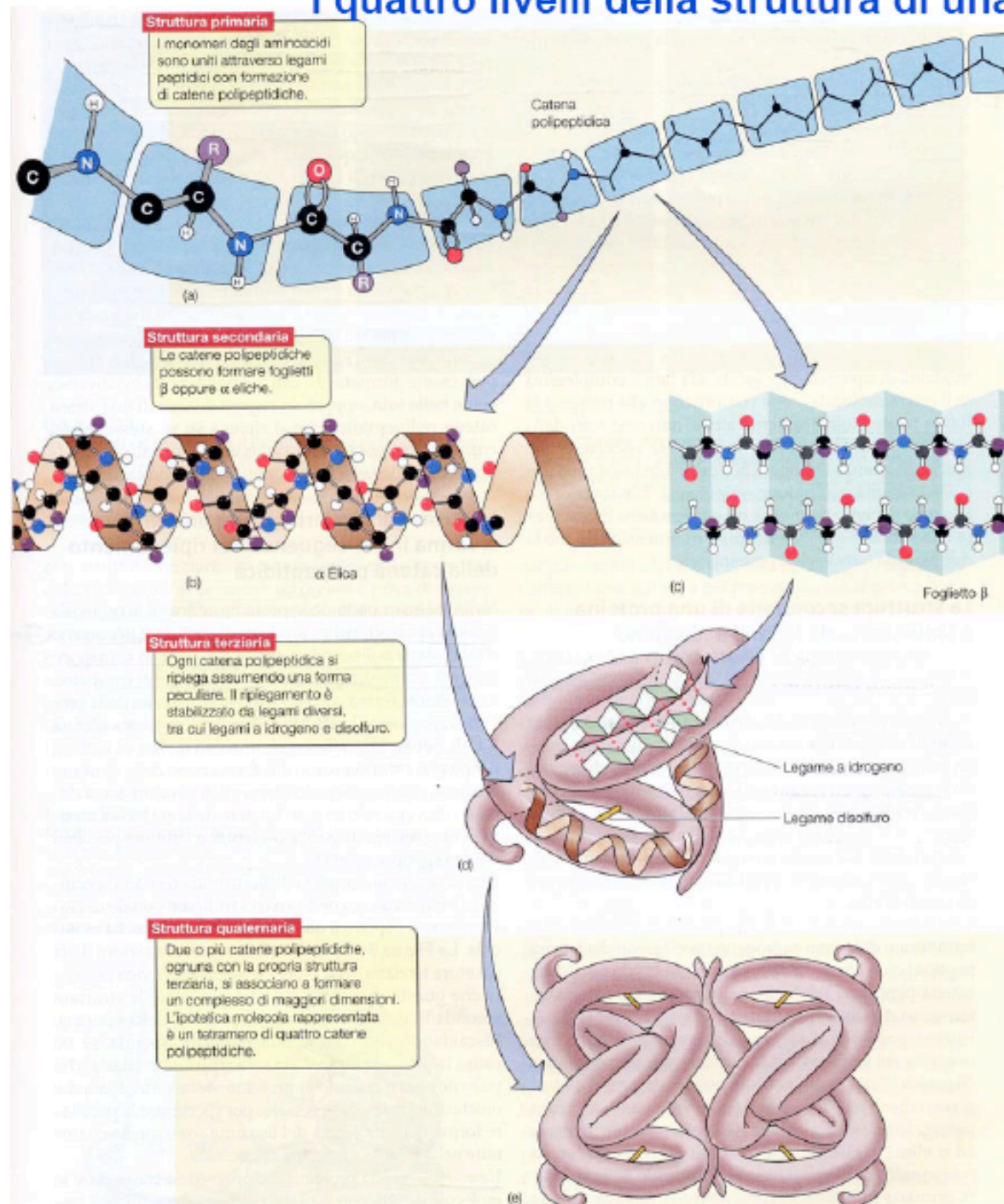
Distribuzione delle strutture secondarie nel Diagramma di Ramachandran



(a)

STRUTTURA TERZIARIA DELLE PROTEINE

I quattro livelli della struttura di una proteina



La **struttura primaria** descrive la sequenza specifica di amminoacidi di una catena polipeptidica.

La **struttura secondaria** descrive la conformazione di una porzione della catena polipeptidica.

La **struttura terziaria** descrive il modo con cui è ripiegata l'intera catena polipeptidica.

Le proteine costituite da più di una catena polipeptidica, hanno una **struttura quaternaria** che descrive il modo con cui le catene sono disposte tra loro nella proteina.

N.B. Le strutture secondaria, terziaria e quaternaria derivano tutte dalla struttura primaria

Denaturazione: perdita della struttura di una proteina.

Il calore ha una azione denaturante.

Es. cottura della carne, cottura dell'albume dell'uovo.

**La STRUTTURA TERZIARIA si riferisce alla
disposizione nello spazio di residui amminoacidici
lontani tra loro nella sequenza lineare**

REGOLE DI RIPIEGAMENTO TERZIARIO:

- Residui **IDROFOBICI** impaccati all'interno della proteina
- Residui **IDROFILICI** rivolti verso il solvente

CONTRIBUTO DI STRUTTURE SUPERSECONDARIE

- foglietti β ritorti o a barilotto
- ripiegamento β
- regioni irregolarmente strutturate o ANSE

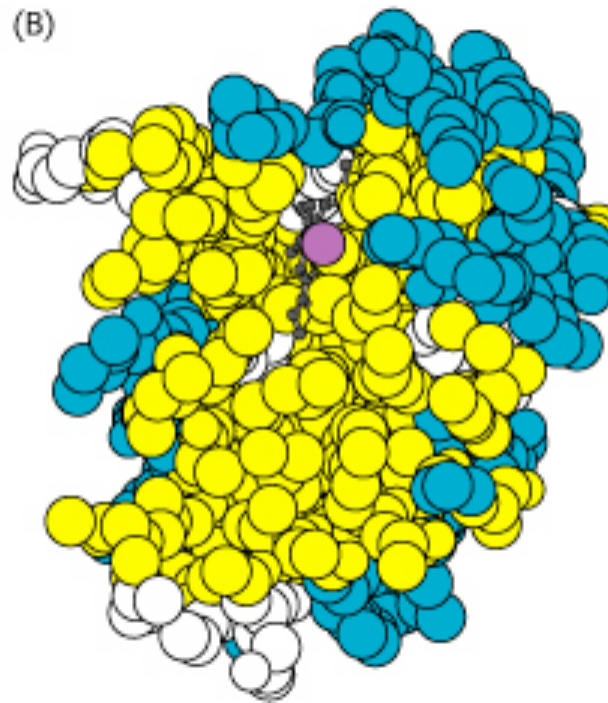
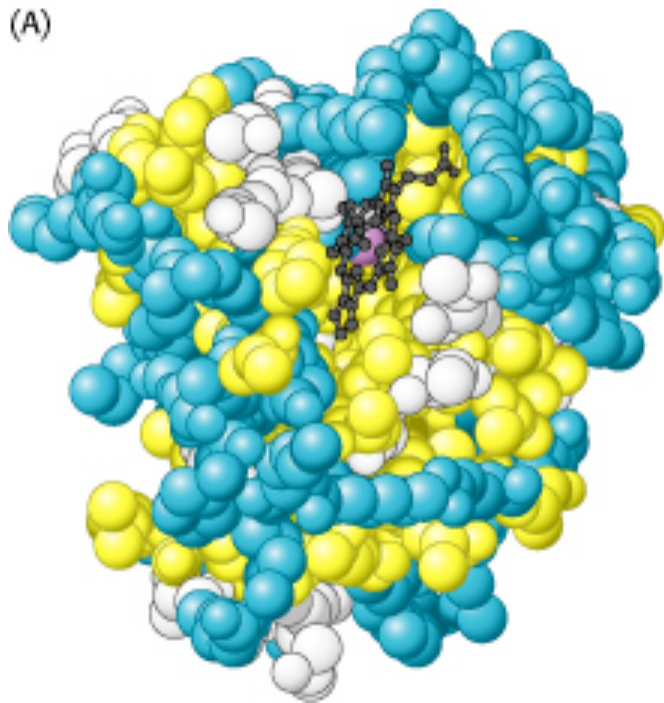
Struttura terziaria: le proteine solubili in acqua si ripiegano in strutture compatte con un nucleo non polare

Idrofobici: giallo

Polari: blu

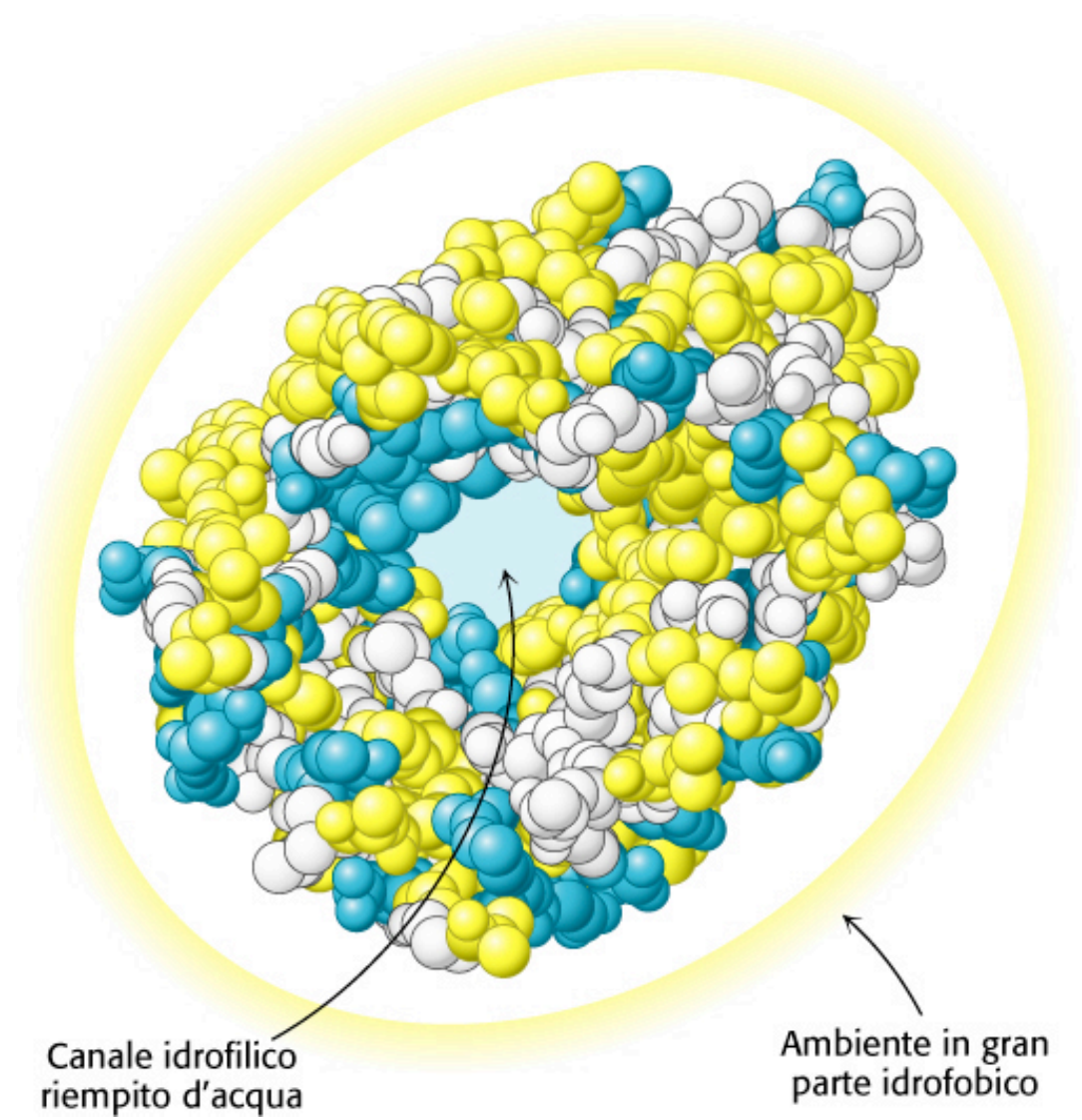
Neutri: bianco

mioglobina

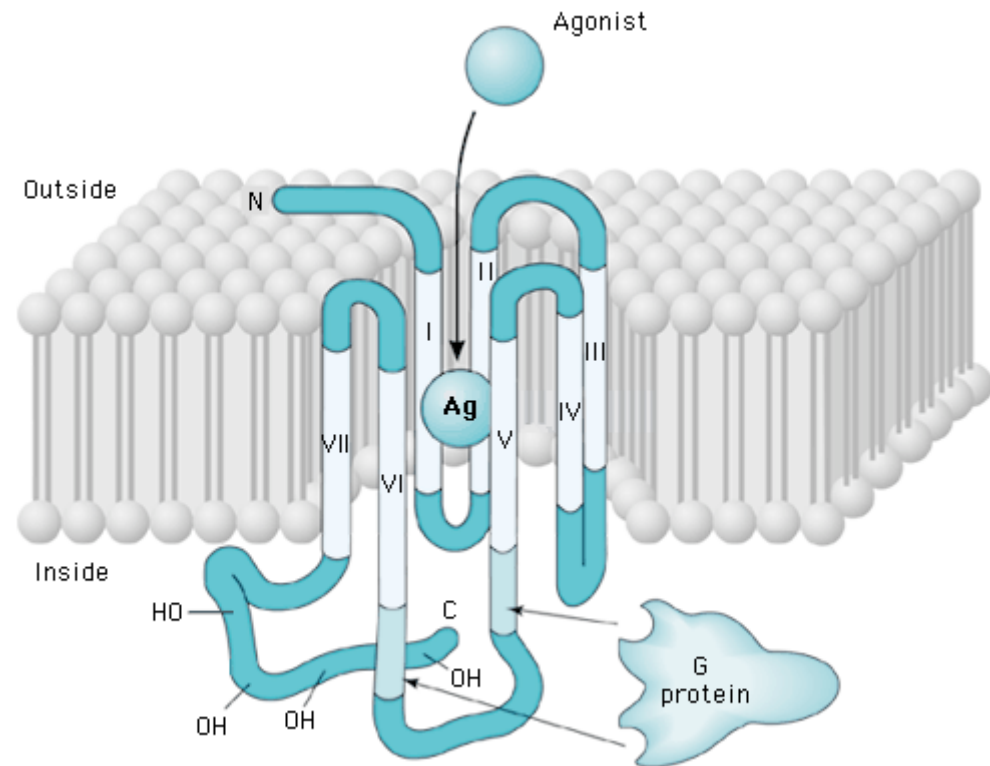
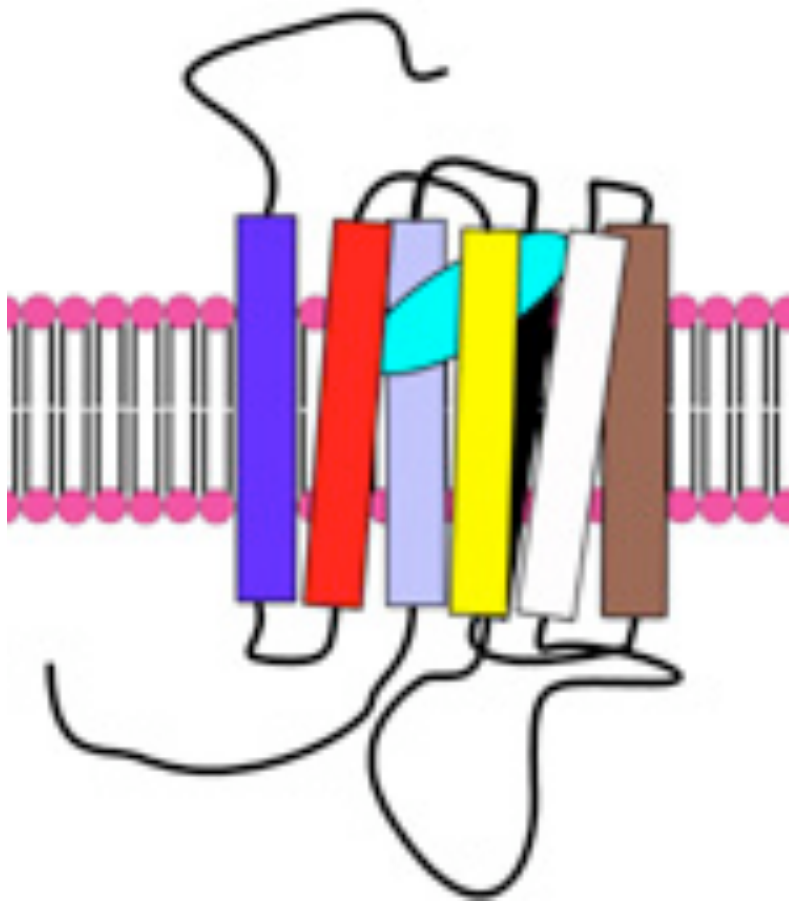


Sezione sagittale

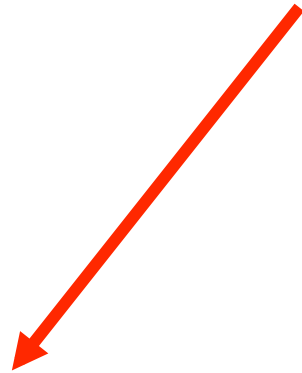
Struttura della porina



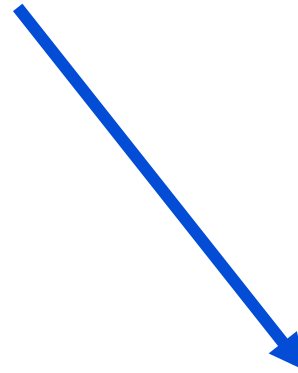
PROTEINE TRANSMEMBRANA: RECETTORI ACCOPPIATI PROTEINE G



CLASSI DI PROTEINE



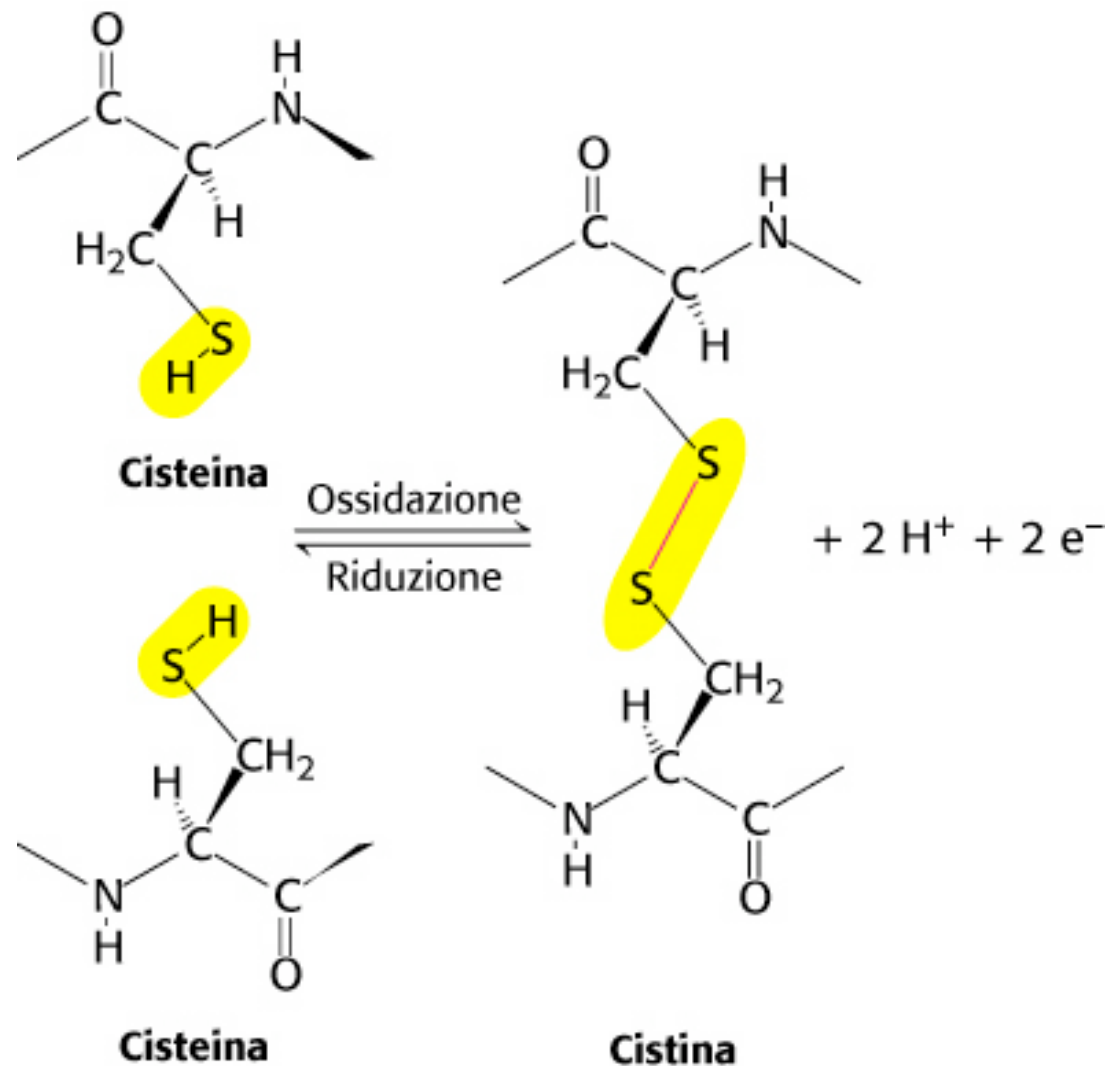
FIBROSE



GLOBULARI

STABILIZZAZIONE DELLA STRUTTURA TERZIARIA

Ponte disolfuro



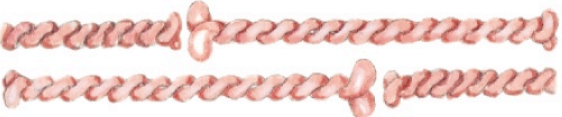
Organizzazione sovramolecolare delle proteine fibrose

Keratin α helix — 

Le SINGOLE CATENE sono superavvolte a coppie e formano tra di loro numerosi ponti disolfuro

Two-chain coiled coil — 

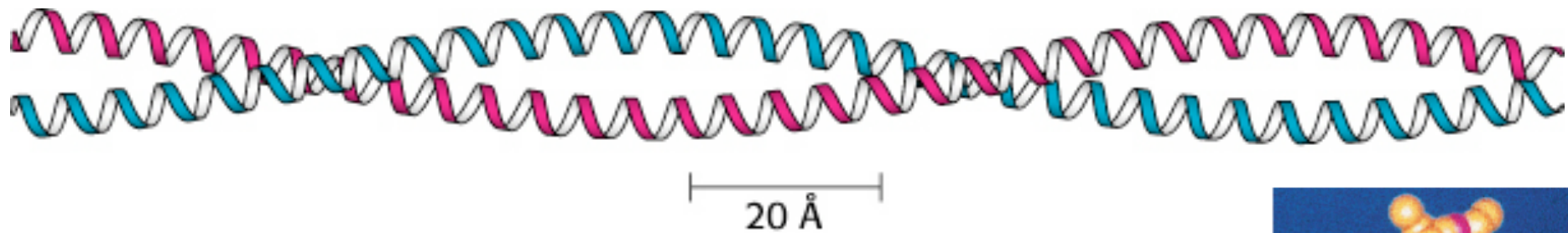
Le MOLECOLE di cheratina si appaiano lateralmente e testa-coda formando protofilamenti

Protofilament {  } 20–30 Å

Protofilamenti e protofibrille sono a loro volta stabilizzati da -S-S-

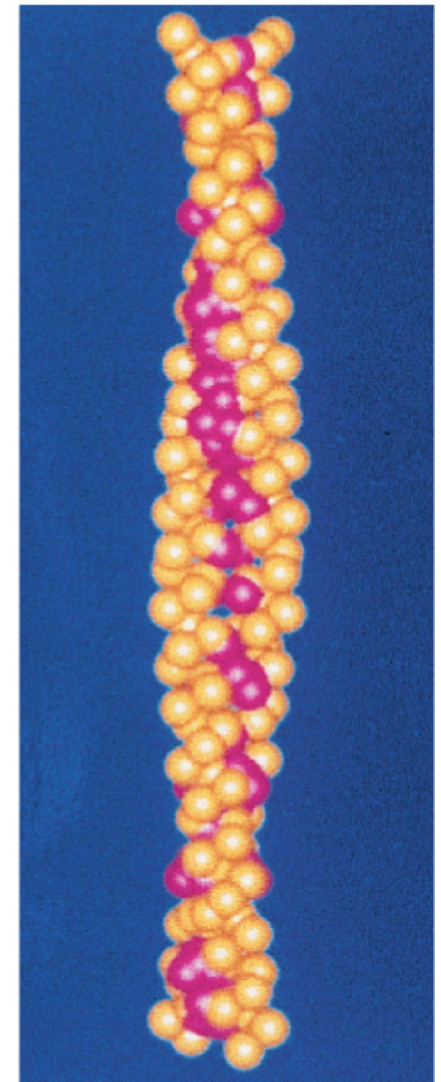
Protofibril {  } 40–50 Å

(a)



Cheratina dei capelli e delle unghie è una proteina fibrosa

Alfa elica con una particolarità...le distanze interatomiche
non rispettano i canoni di una classica alfa elica !!!!



α elica
della cheratina



Avvolgimento
avvolto
a due catene

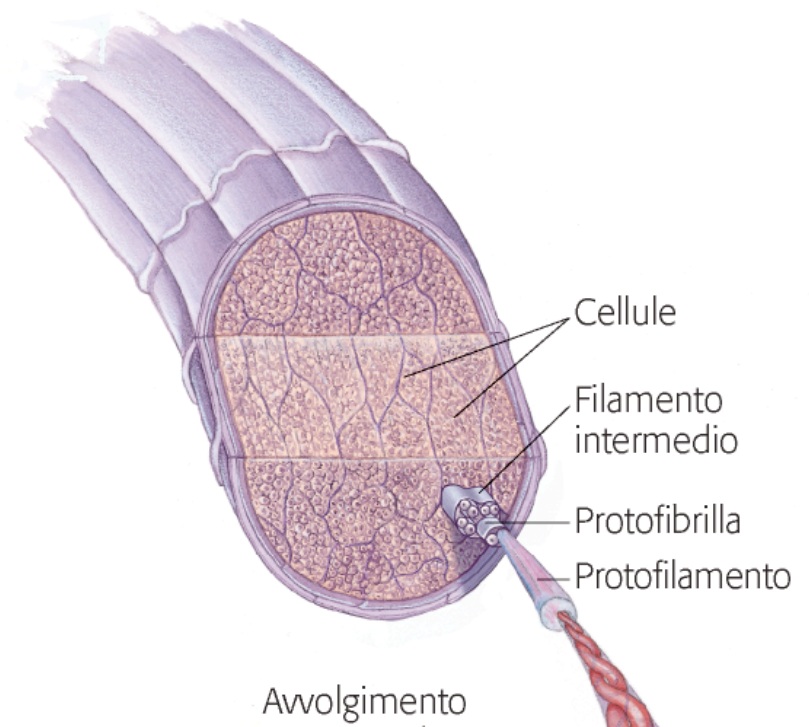


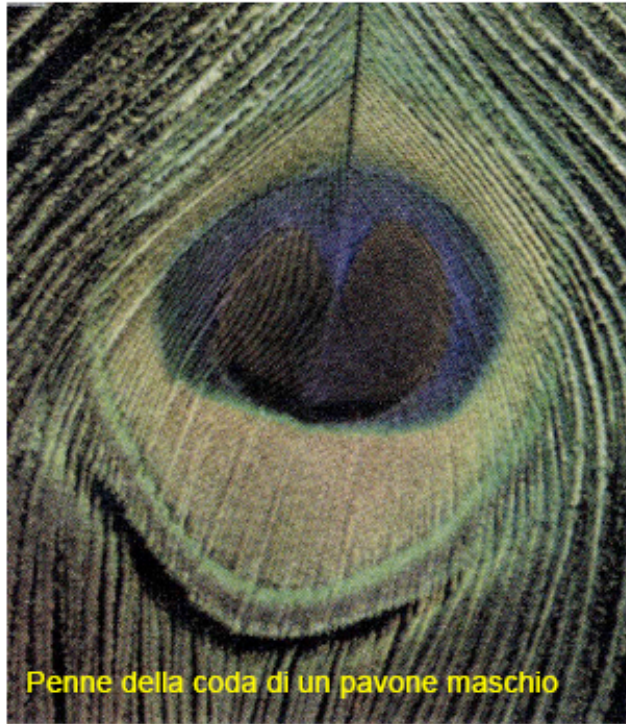
450 Å

Protofilamento {  20-30 Å

Protofibrilla {  40-50 Å

(a)





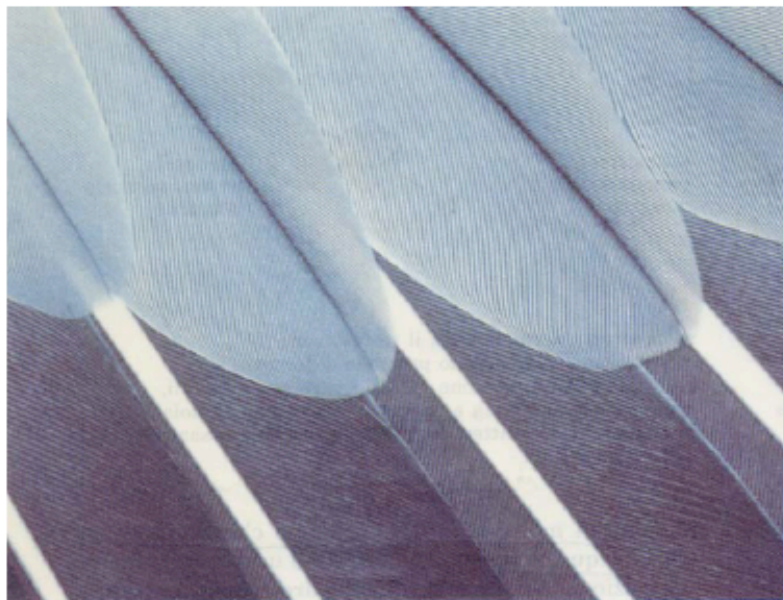
Penne della coda di un pavone maschio

CHERATINA

proteina
strutturale



Corno di rinoceronte



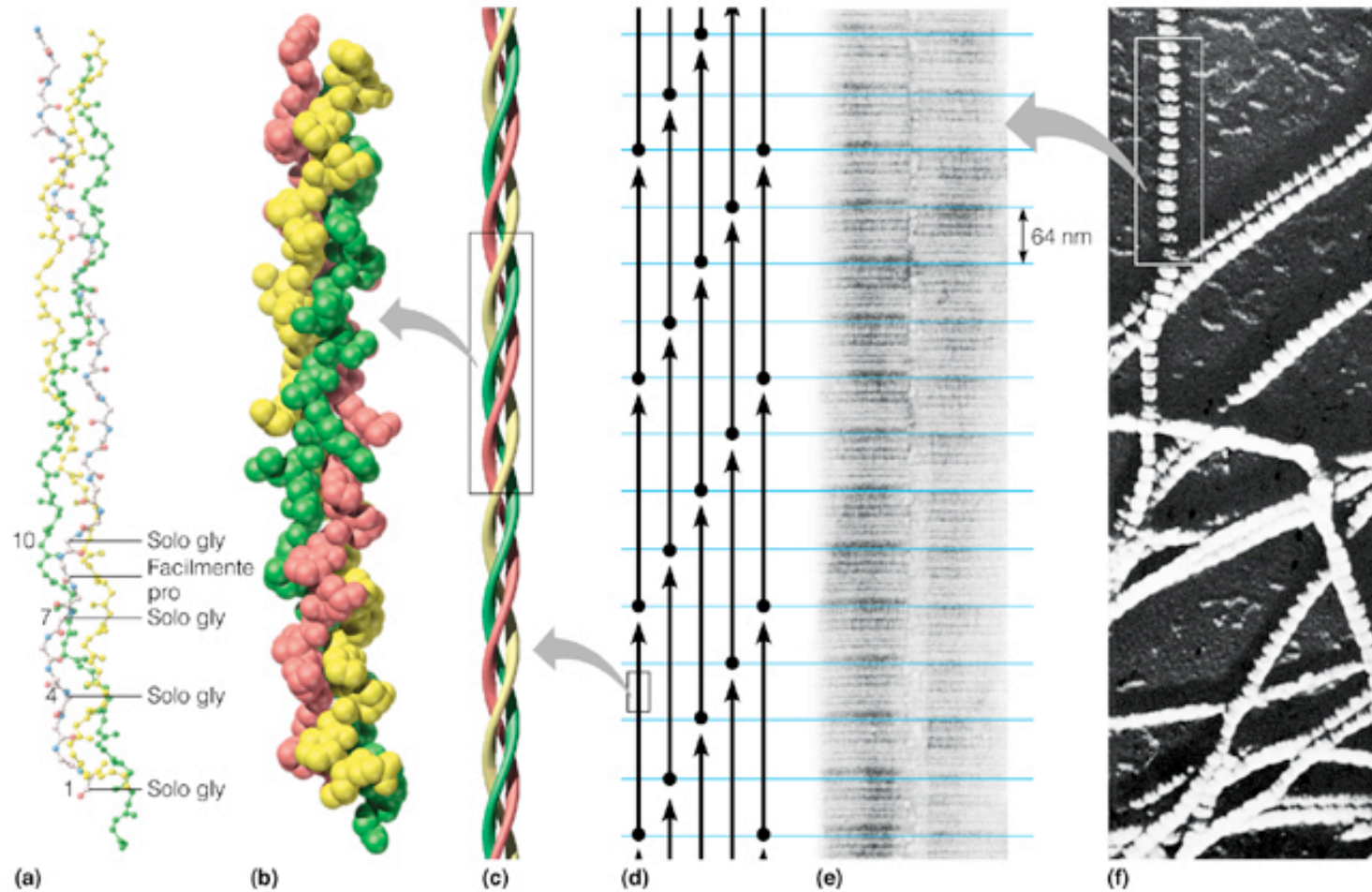
La cheratina, una proteina fibrosa con struttura secondaria, è la principale componente di lana, unghie, penne, capelli, corna.

SETA – costituita da una proteina strutturale



Un filamento di cattura è costituito da una fibra di seta strettamente avvolta, ricoperta di un liquido appiccicoso. Un impatto sul filamento causa lo svolgimento della fibra e lo stiramento del filamento. Quando la forza cessa, la tensione superficiale causa la formazione di grumi dal liquido e quindi il riavvolgimento della fibra.

COLLAGENE la più abbondante proteina dei mammiferi



3000*15A



MOLECOLA COLLAGENE (Procollagene)

3 CATENE con andamento SINISTRORSO

NON ALFA ELICHE!

SUPERAVVOLTE con andamento DESTORSO

IL COLLAGENE HA UNA SEQUENZA MOLTO PARTICOLARE

GLY-X-Y

31

-Gly-Pro-Met-Gly-Pro-Ser-Gly-Pro-Arg-

22

-Gly-Leu-Hyp-Gly-Pro-Hyp-Gly-Ala-Hyp-

31

-Gly-Pro-Gln-Gly-Phe-Gln-Gly-Pro-Hyp-

40

-Gly-Glu-Hyp-Gly-Glu-Hyp-Gly-Ala-Ser-

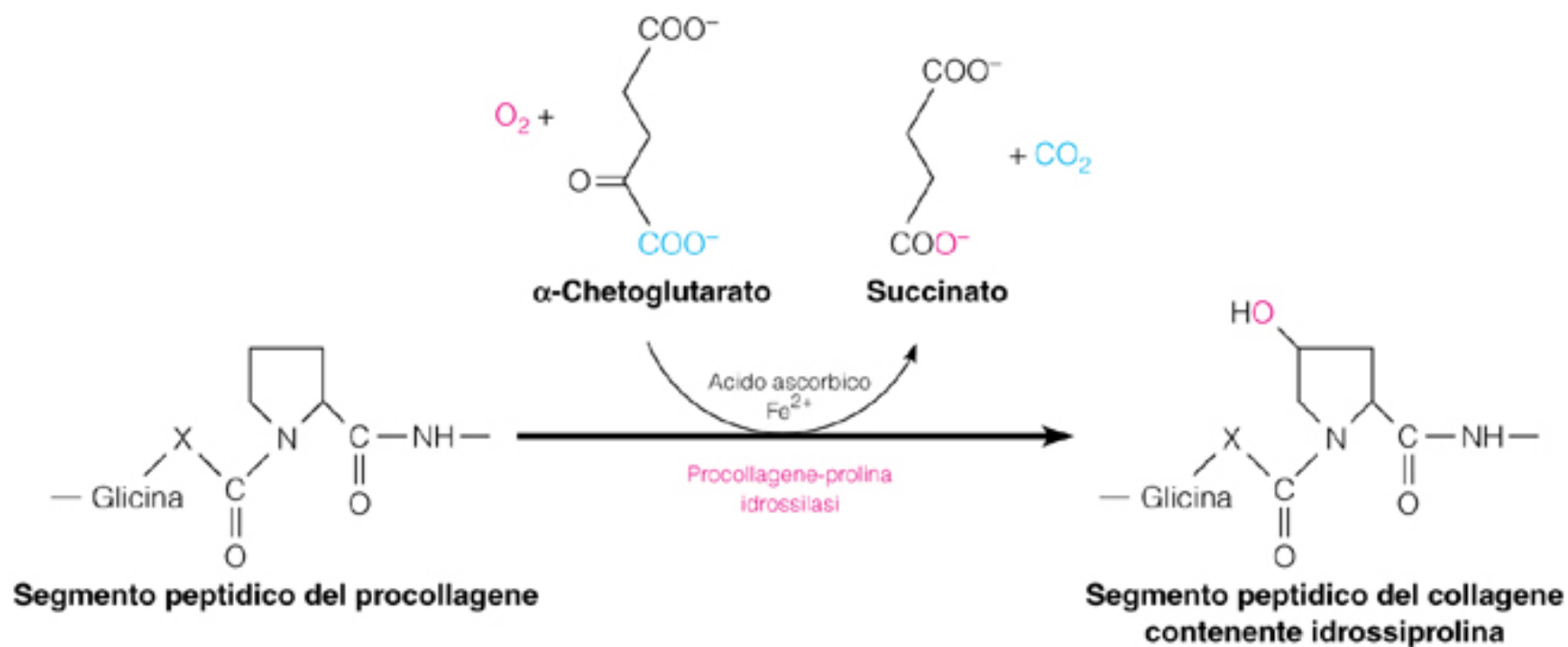
49

-Gly-Pro-Met-Gly-Pro-Arg-Gly-Pro-Hyp-

58

-Gly-Pro-Hyp-Gly-Lys-Asn-Gly-Asp-Asp-

Idrossilazione dei residui di idrossiprolina



Temperatura di fusione (dissociazione)

(GLY-PRO-PRO)₁₀ 41⁰C

(GLY-PRO-HYP)₁₀ 69⁰C

SCORBUTO deriva dalla mancata idrossilazione della prolina

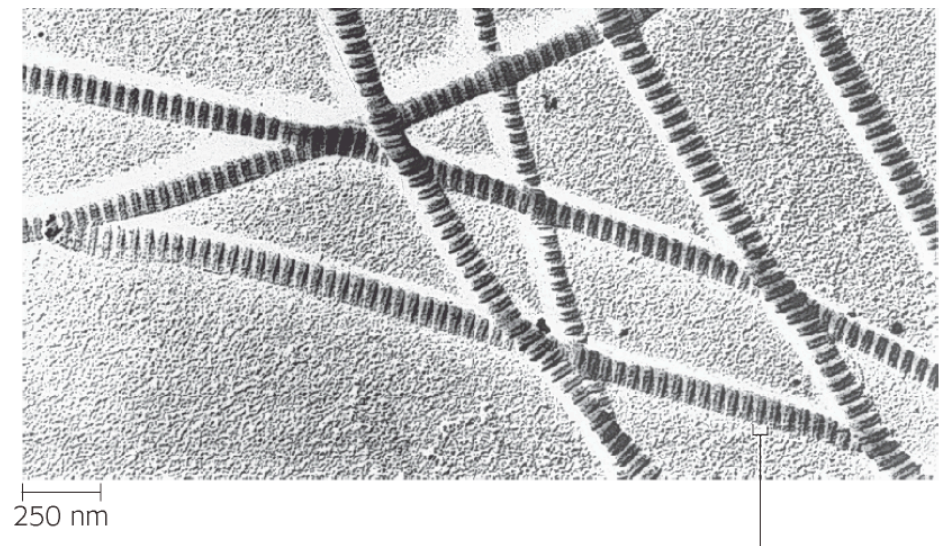
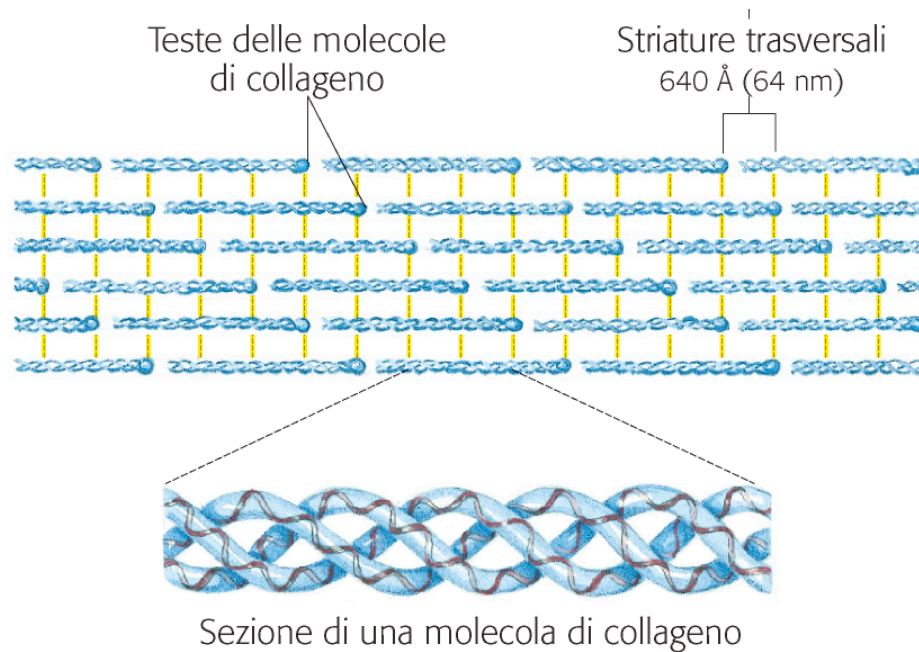


Indebolimento delle fibre

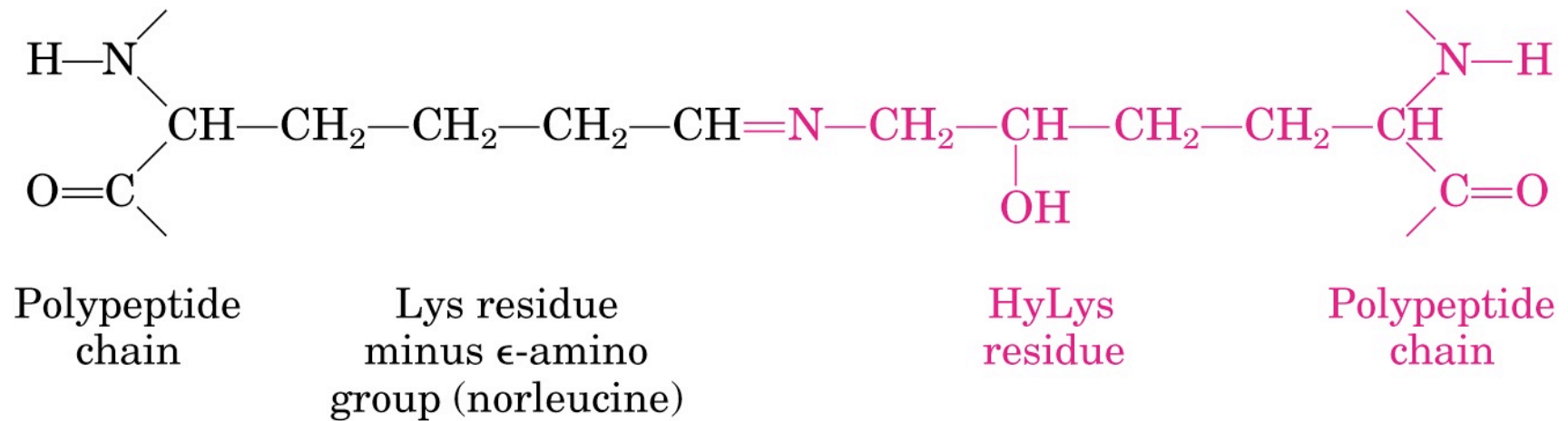


Lesioni della pelle, delle gengive e dei vasi sanguigni

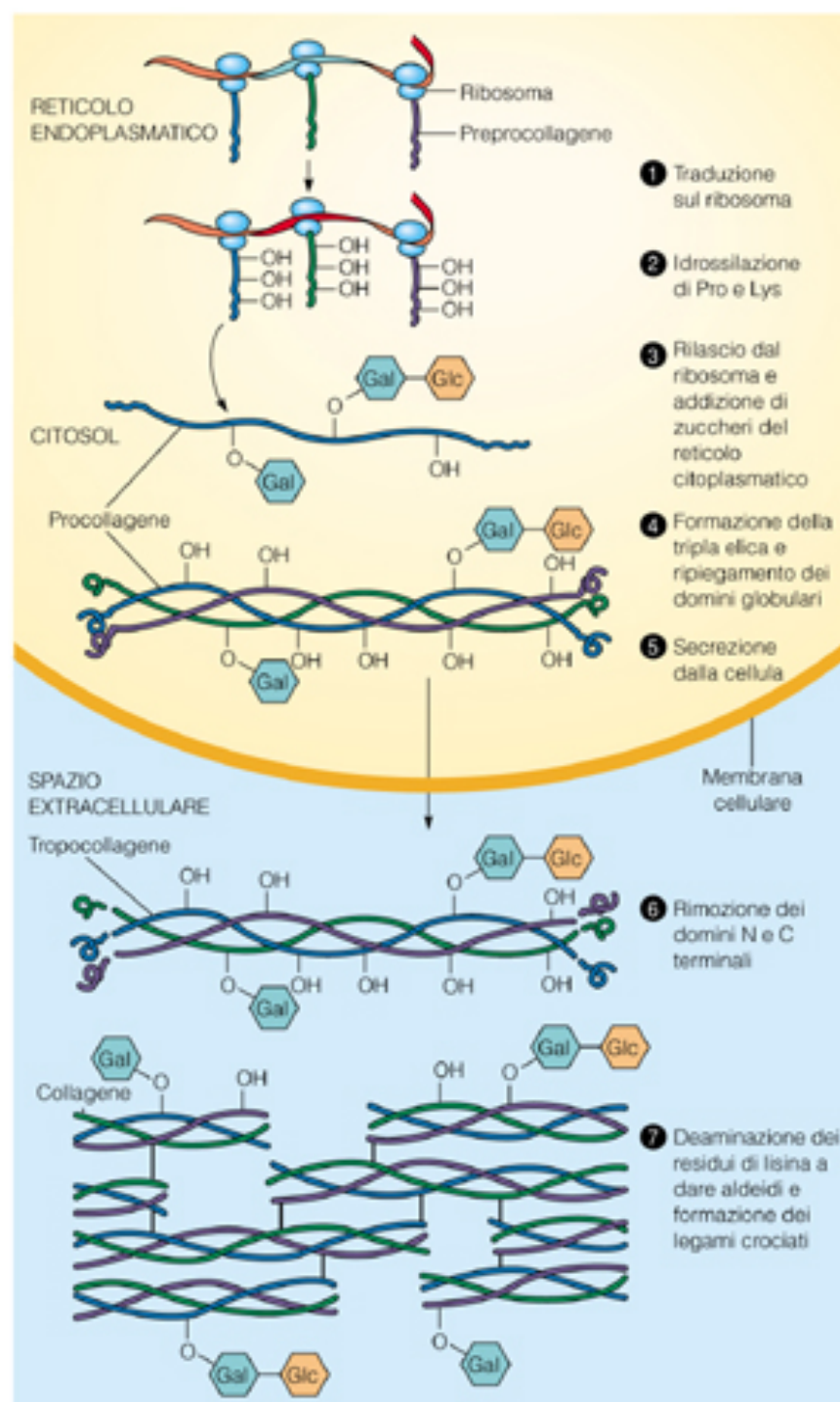
Come interagiscono le molecole di collagene per formare fibrille o fasci?



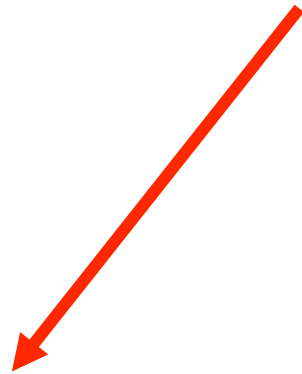
**Legami crociati
tra residui di Lys, HyLys o di His di catene diverse**



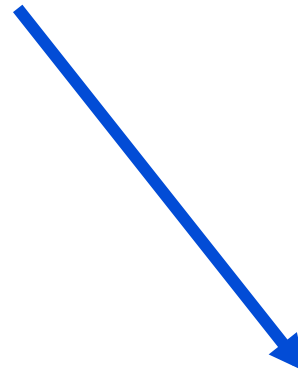
Dehydrohydroxylysinonorleucine



CLASSI DI PROTEINE



FIBROSE



GLOBULARI

PROTEINE GLOBULARI

contengono:

strutture secondarie

Strutture super-secondarie (motivi)

Dominii

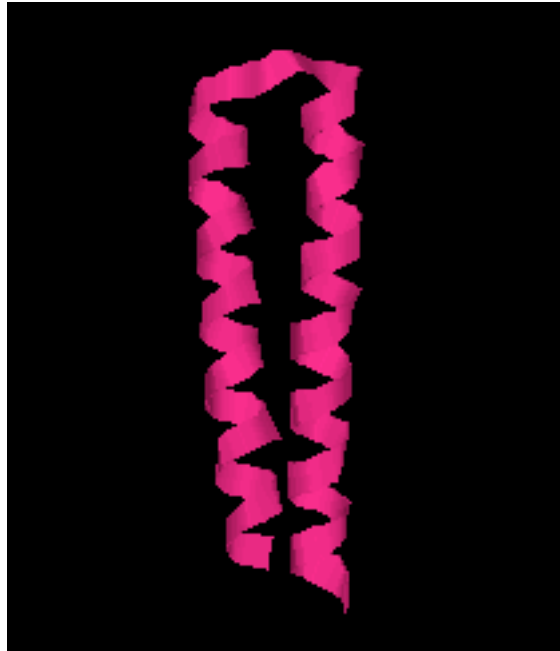
Conformazione β
 $2000 \times 5 \text{ \AA}$

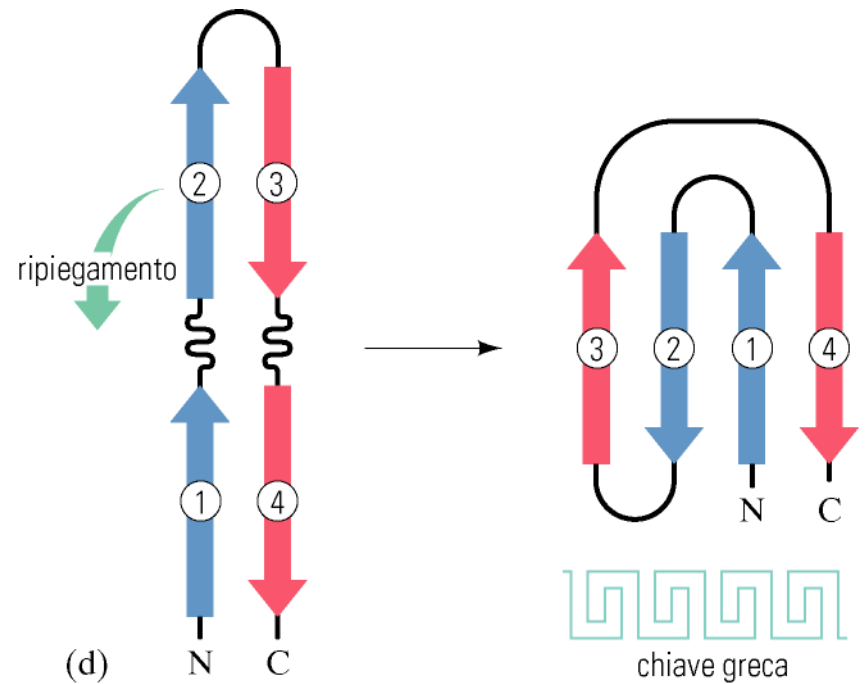
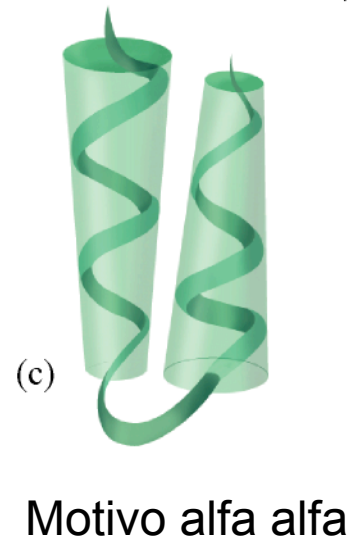
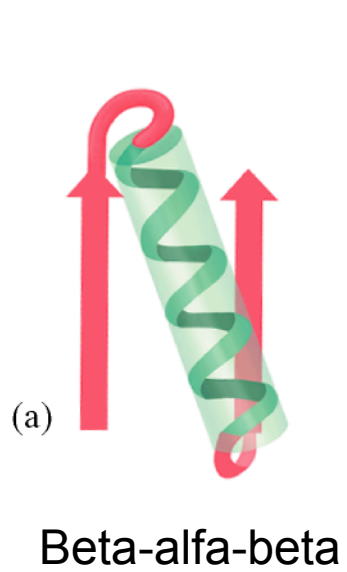
Dimensioni ipotetiche e reali
di Albumina

α elica
 $900 \times 11 \text{ \AA}$

Forma globulare nativa
 $100 \times 60 \text{ \AA}$

STRUTTURE SUPERSECONDARIE

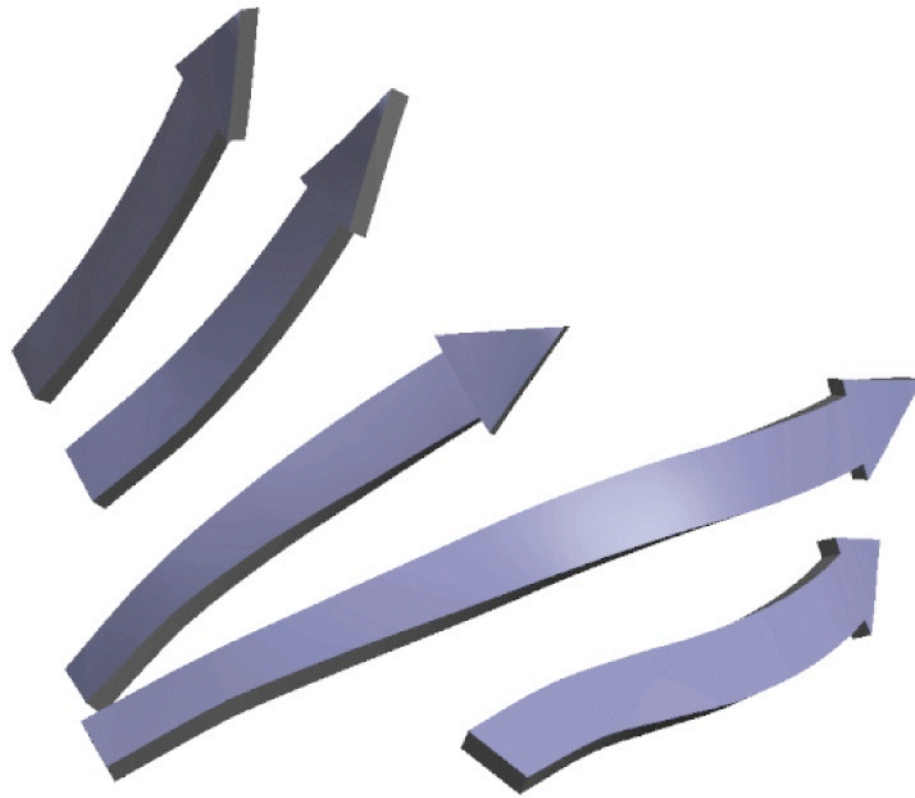




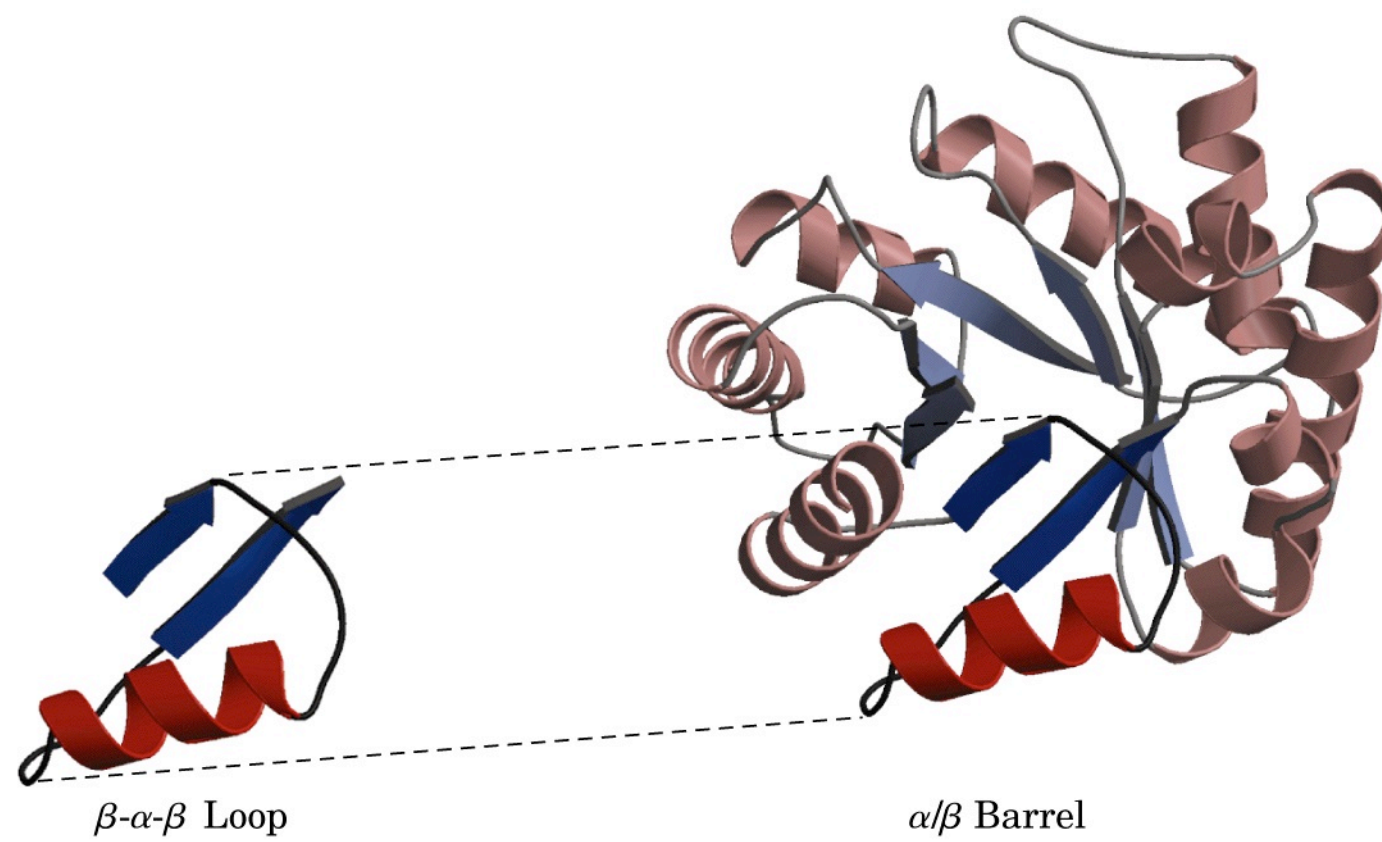
Motivo a chiave greca



(d) β Barrel



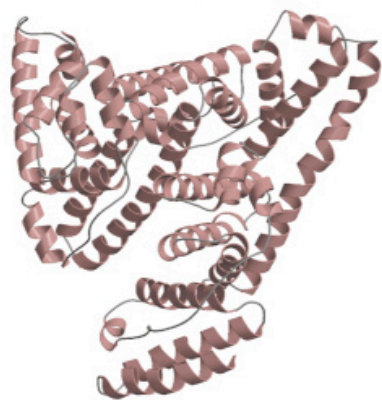
Twisted β sheet



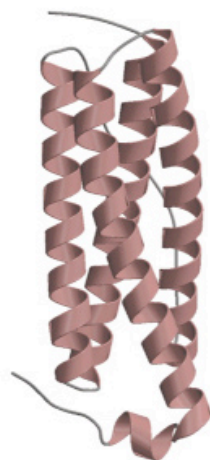
DOMINI PROTEICI

**Sequenze amminoacidiche con una struttura terziaria
ben definita nella sequenza della proteina totale e
funzione specifica**

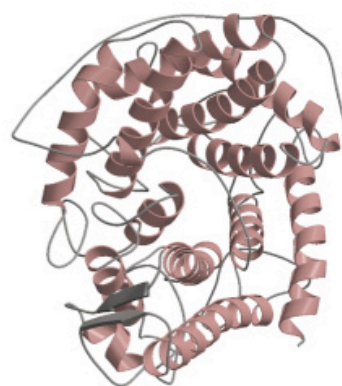
All α



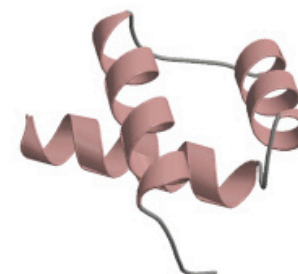
1ao6
 Serum albumin
 Serum albumin
 Serum albumin
 Serum albumin
 Human (*Homo sapiens*)



1bcf
 Ferritin-like
 Ferritin-like
 Ferritin
 Bacterioferritin (cytochrome b_1)
Escherichia coli



1gai
 α/α toroid
 Glycosyltransferases of the
 superhelical fold
 Glucoamylase
 Glucoamylase
Aspergillus awamori, variant x100



1enh
 DNA-binding 3-helical bundle
 Homeodomain-like
 Homeodomain
engrailed Homeodomain
Drosophila melanogaster

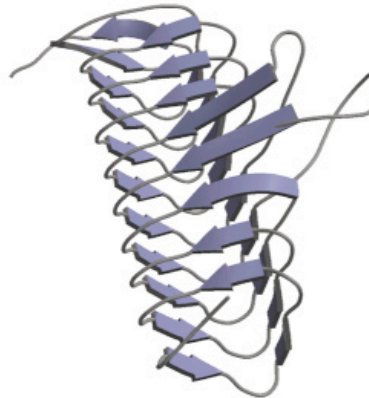
Key

PDB identifier
 Fold
 Superfamily
 Family
 Protein
 Species

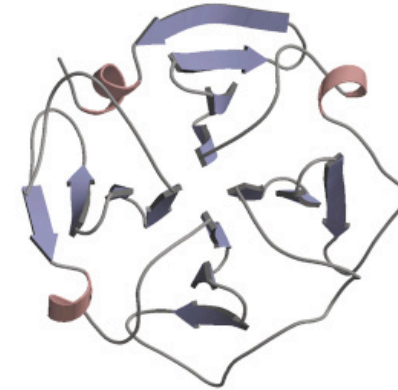
All β



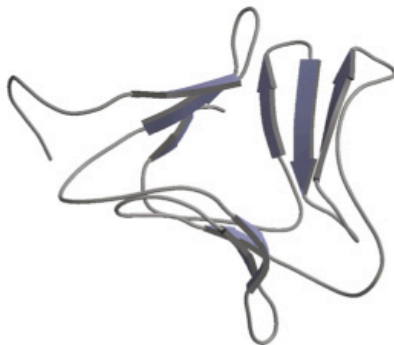
- 1hoe
- α -Amylase inhibitor
- α -Amylase inhibitor
- α -Amylase inhibitor
- HOE-467A
- Streptomyces tendae* 4158



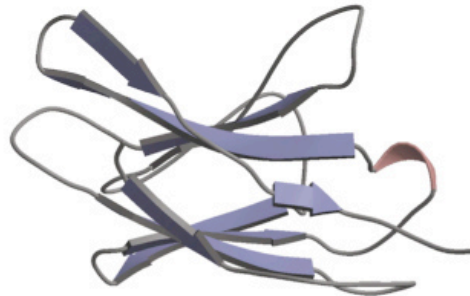
- 1lxa
- Single-stranded left-handed β helix
- Trimeric LpxA-like enzymes
- UDP *N*-acetylglucosamine acyltransferase
- UDP *N*-acetylglucosamine acyltransferase
- Escherichia coli*



- 1pex
- Four-bladed β propeller
- Hemopexin-like domain
- Hemopexin-like domain
- Collagenase-3 (MMP-13), carboxyl-terminal domain
- Human (*Homo sapiens*)



- 1jpc
- β -Prism II
- α -D-Mannose-specific plant lectins
- α -D-Mannose-specific plant lectins
- Lectin (agglutinin)
- Snowdrop (*Galanthus nivalis*)

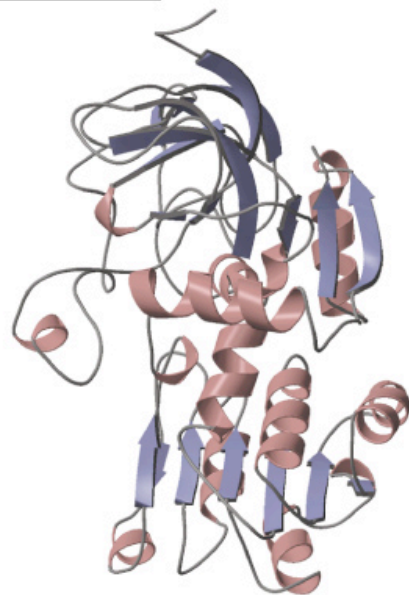


- 1cd8
- Immunoglobulin-like β sandwich
- Immunoglobulin
- Antibody variable domain-like
- CD8
- Human (*Homo sapiens*)

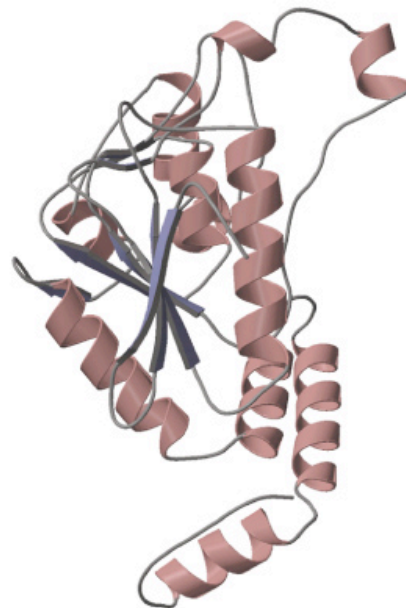
Key

- PDB identifier
- Fold
- Superfamily
- Family
- Protein
- Species

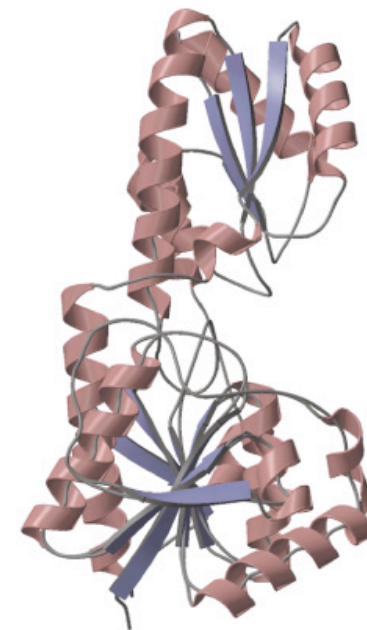
α/β



- 1deh
- NAD(P)-binding Rossmann-fold domains
- NAD(P)-binding Rossmann-fold domains
- Alcohol/glucose dehydrogenases, carboxyl-terminal domain
- Alcohol dehydrogenase
- Human (*Homo sapiens*)



- 1dub
- Crotonase-like
- Crotonase-like
- Crotonase-like
- Enoyl-CoA hydratase
- Rat (*Rattus norvegicus*)

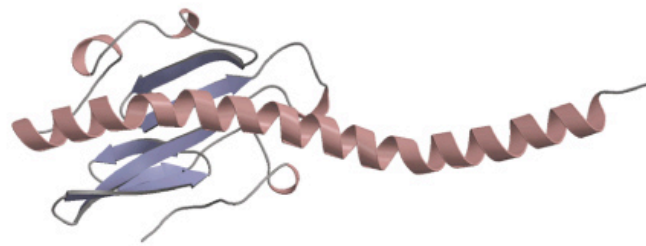


- 1pfk
- Phosphofructokinase
- Phosphofructokinase
- Phosphofructokinase
- Phosphofructokinase
- Escherichia coli*

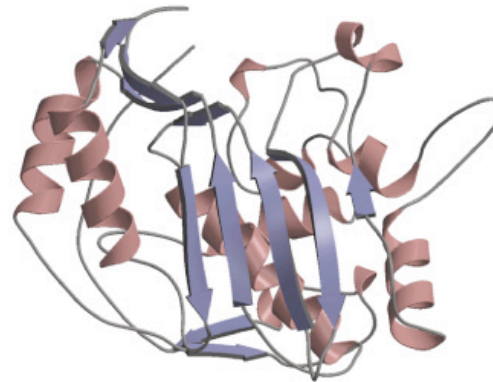
Key

- PDB identifier
- Fold
- Superfamily
- Family
- Protein
- Species

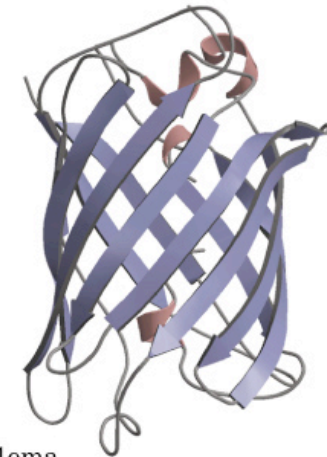
$\alpha + \beta$



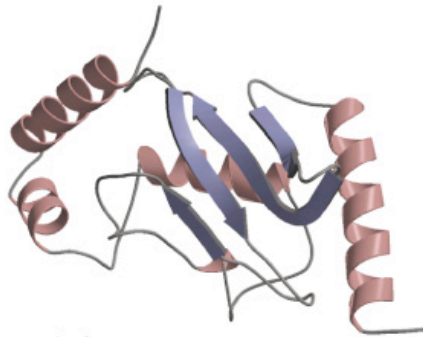
2pil
Pilin
Pilin
Pilin
Pilin
Neisseria gonorrhoeae



1syn
Thymidylate synthase
Thymidylate synthase
Thymidylate synthase
Thymidylate synthase
Escherichia coli



1ema
Green fluorescent protein
Green fluorescent protein
Green fluorescent protein
Green fluorescent protein
Jellyfish (*Aequorea victoria*)



1u9a
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Human (*Homo sapiens*)

Key

PDB identifier
Fold
Superfamily
Family
Protein
Species

TIGHT TURNS (RIPIEGAMENTI “A FORCINA”)

Delta-turn - It is the smallest tight turn which involves only **2** amino acid residues and the intraturn hydrogen bond for a delta-turn is formed between the backbone $\text{NH}(i)$ and the backbone $\text{CO}(i+1)$.

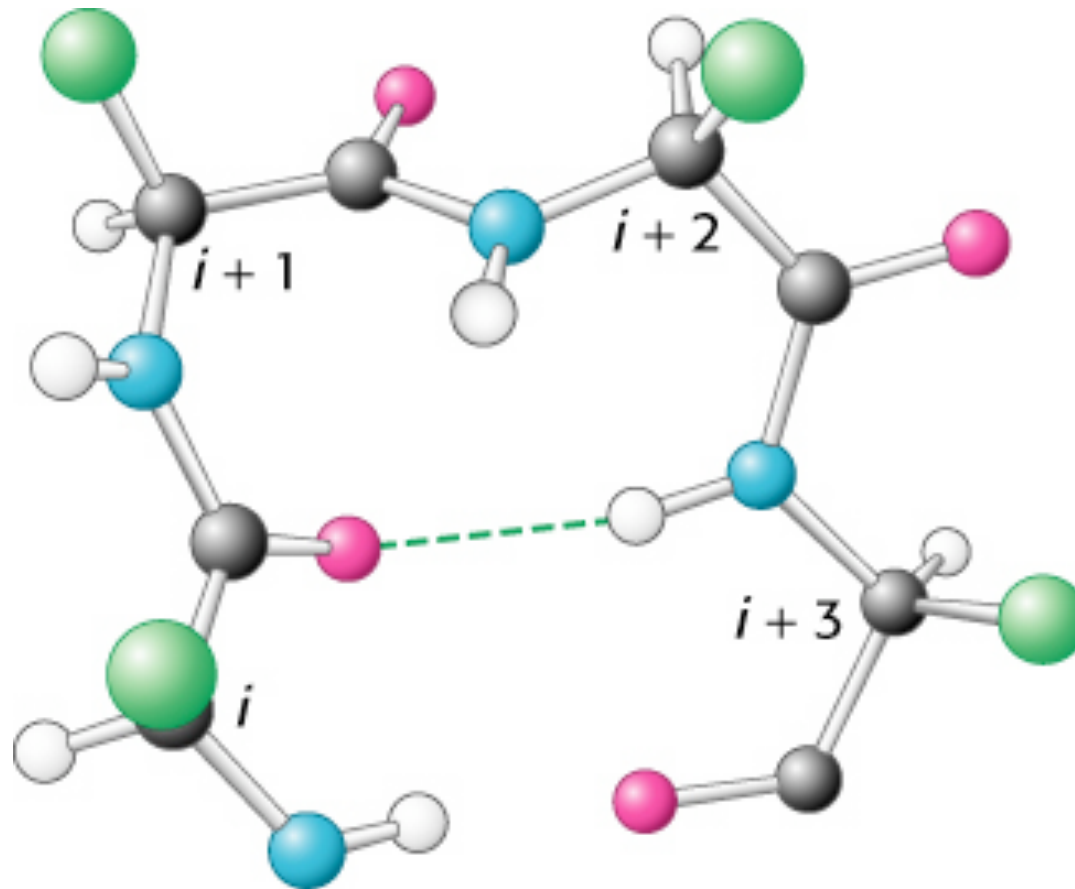
Gamma-turn - It involves three amino acid residues and the intraturn hydrogen bond for a gamma-turn is formed between the backbone $\text{CO}(i)$ and the backbone $\text{NH}(i+2)$.

Beta turn - It involves four amino acid residues and may or may not be stabilized by the intraturn hydrogen bond between the backbone $\text{CO}(i)$ and the backbone $\text{NH}(i+3)$.

Alpha-turn - An alpha-turn involves five amino acid residues where the distance between the $\text{C}\alpha(i)$ and the $\text{C}\alpha(i+4)$ is less than $7\text{\AA}$ and the pentapeptide chain is not in a helical conformation.

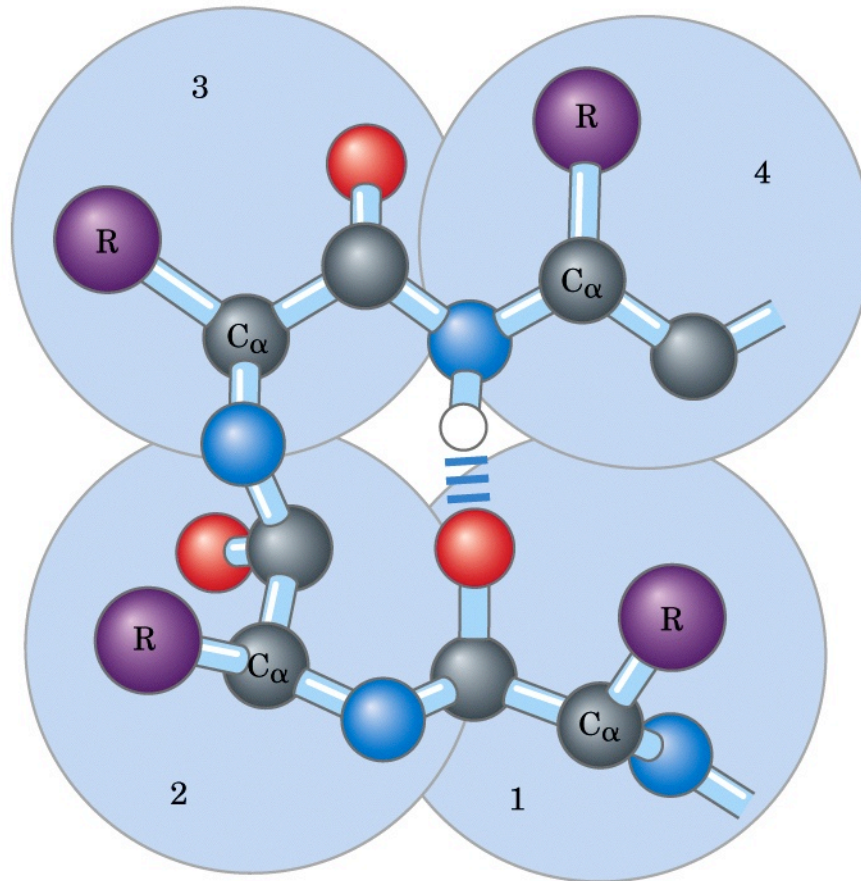
Pi-turn - It is the largest tight turn which involves six amino acid residues.

RIPIEGAMENTO β (4 aa coinvolti)

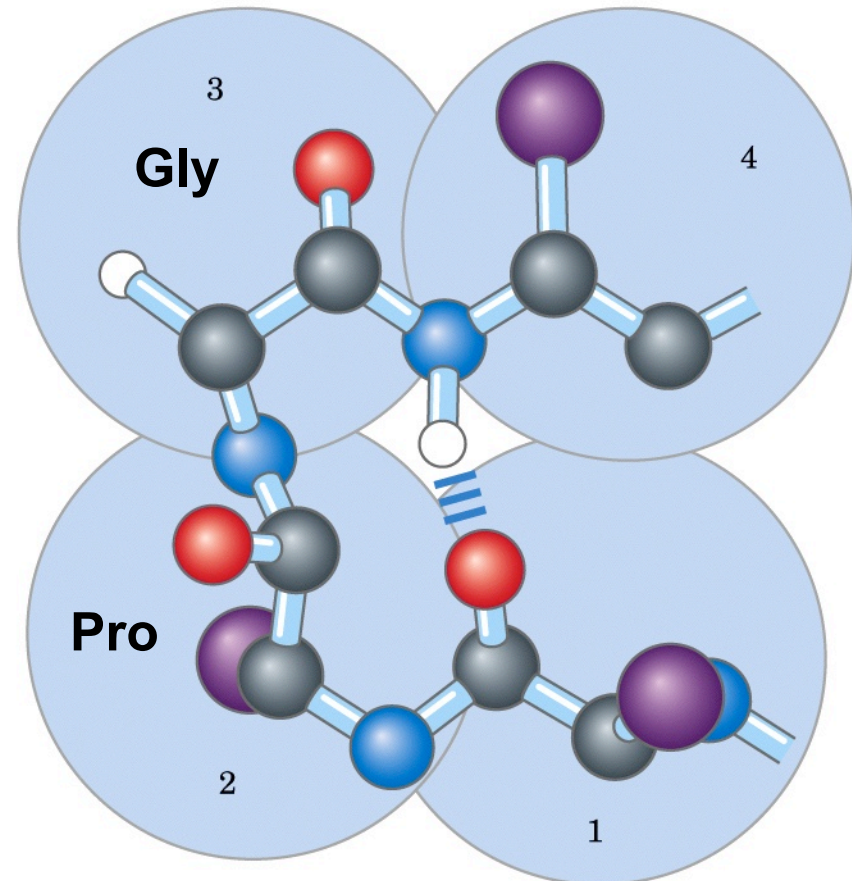


Struttura secondaria: il gruppo C=O del residuo i della catena polipeptidica è unito con legame ad idrogeno al gruppo N-H del residuo $i+3$, stabilizzando la struttura

Ripiegamenti β



Type I

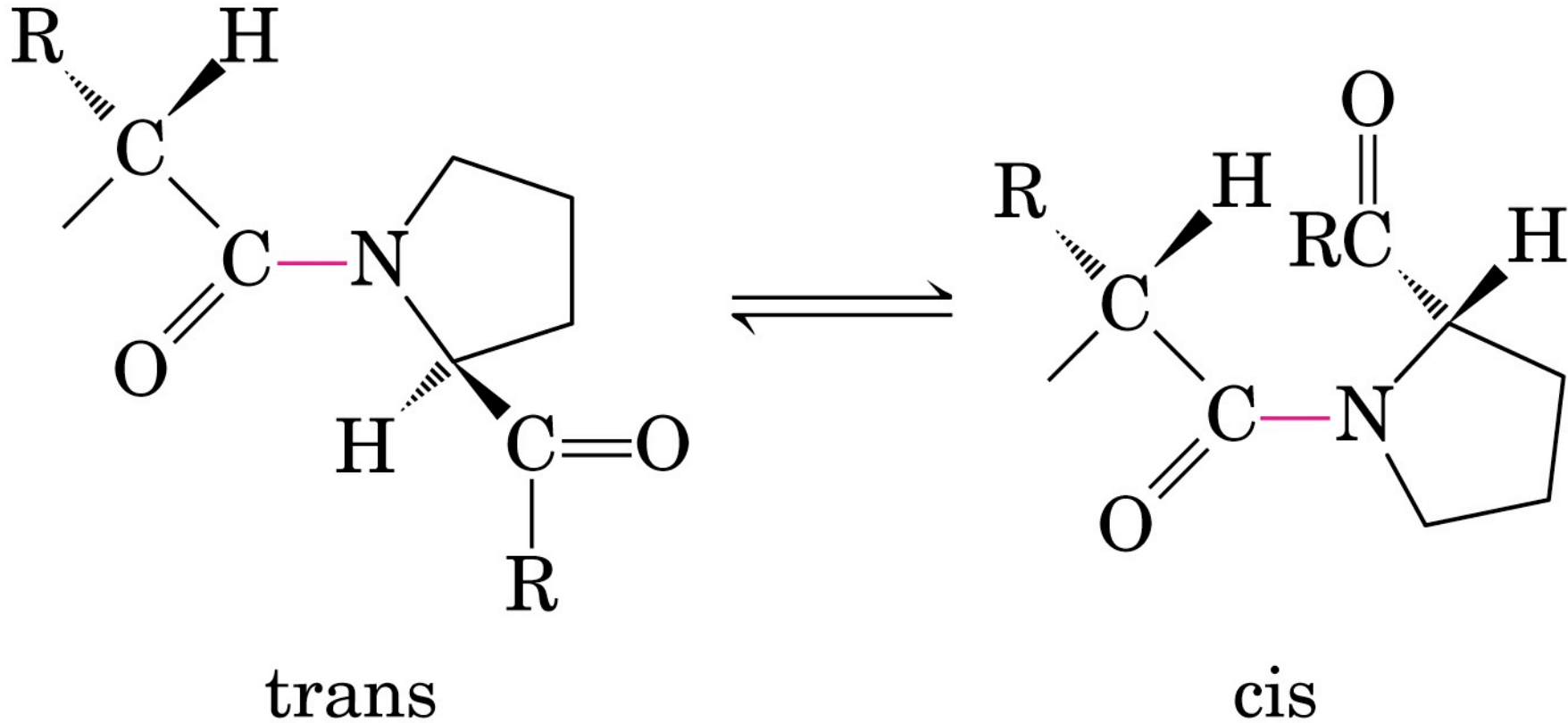


Type II

β Turns
(a)

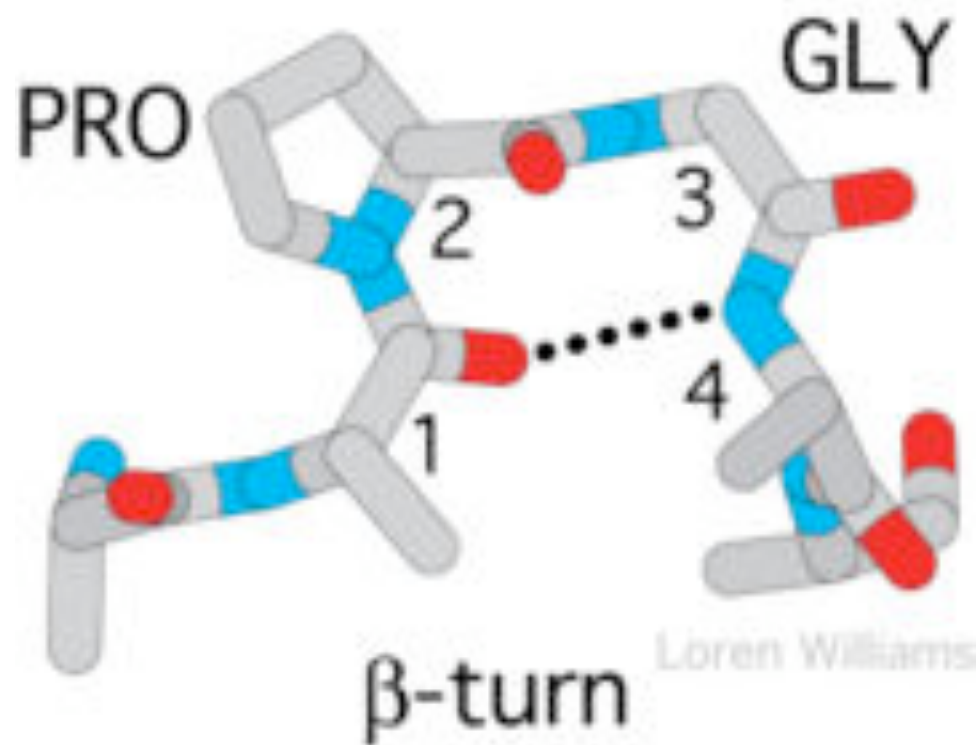
Tipo I : Frequenza doppia rispetto a tipo II

Ripiegamenti β Gly-Pro

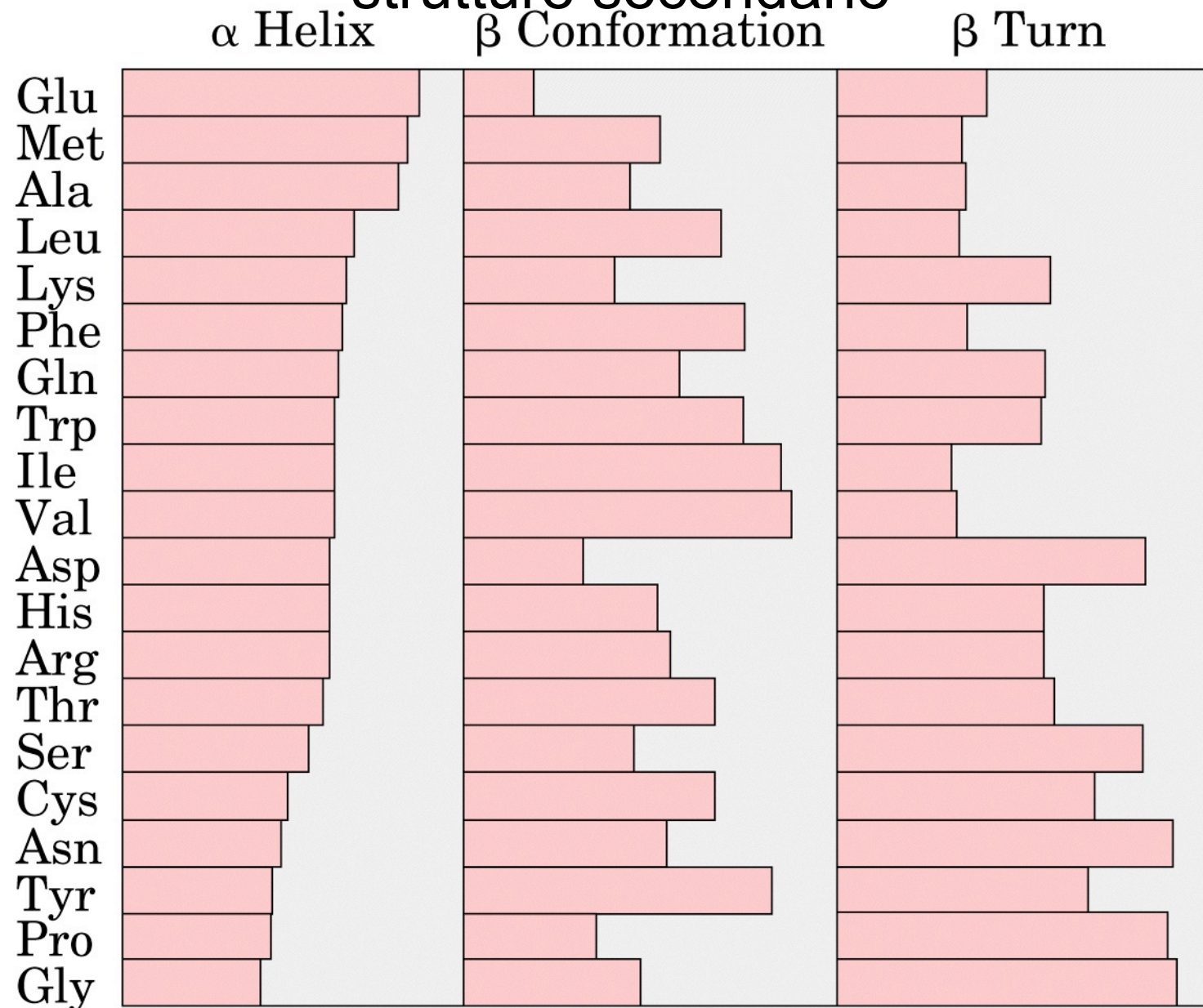


Proline isomers

Beta-turn di tipo II (1x-2-*cis*-Pro-3Gly-4y)

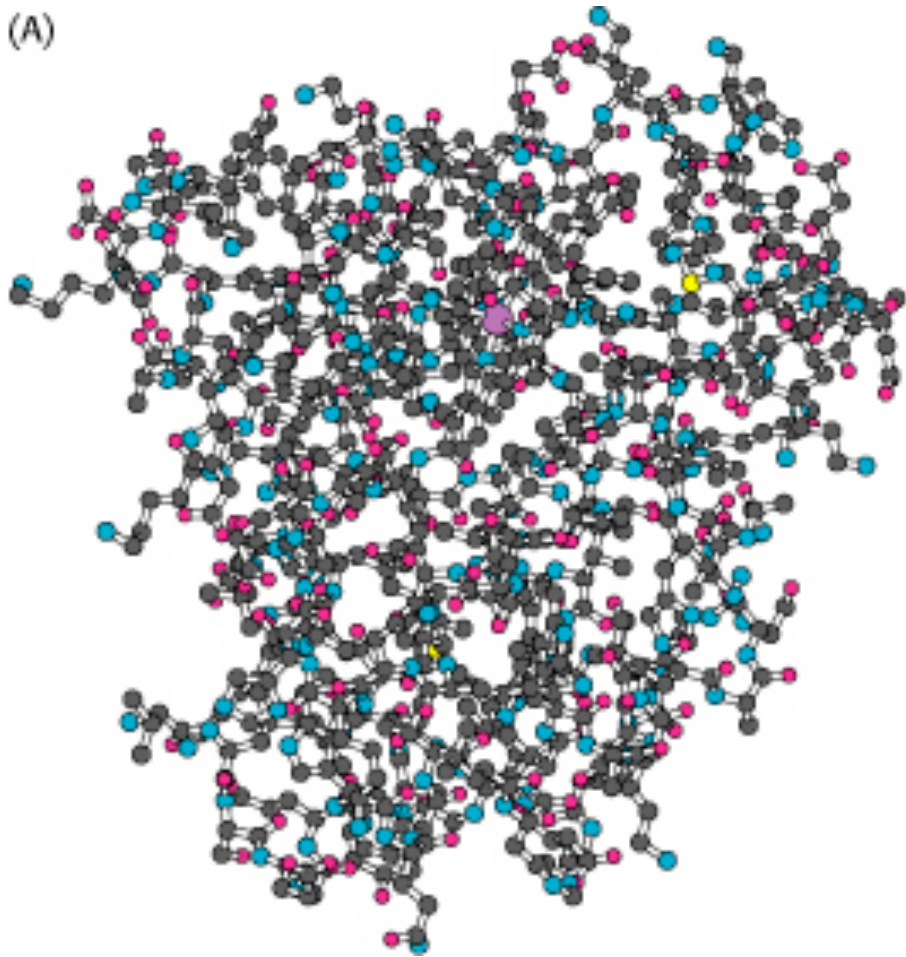


Probabilità relative di presenza degli aa nelle strutture secondarie



struttura della mioglobina

(A)



(B)

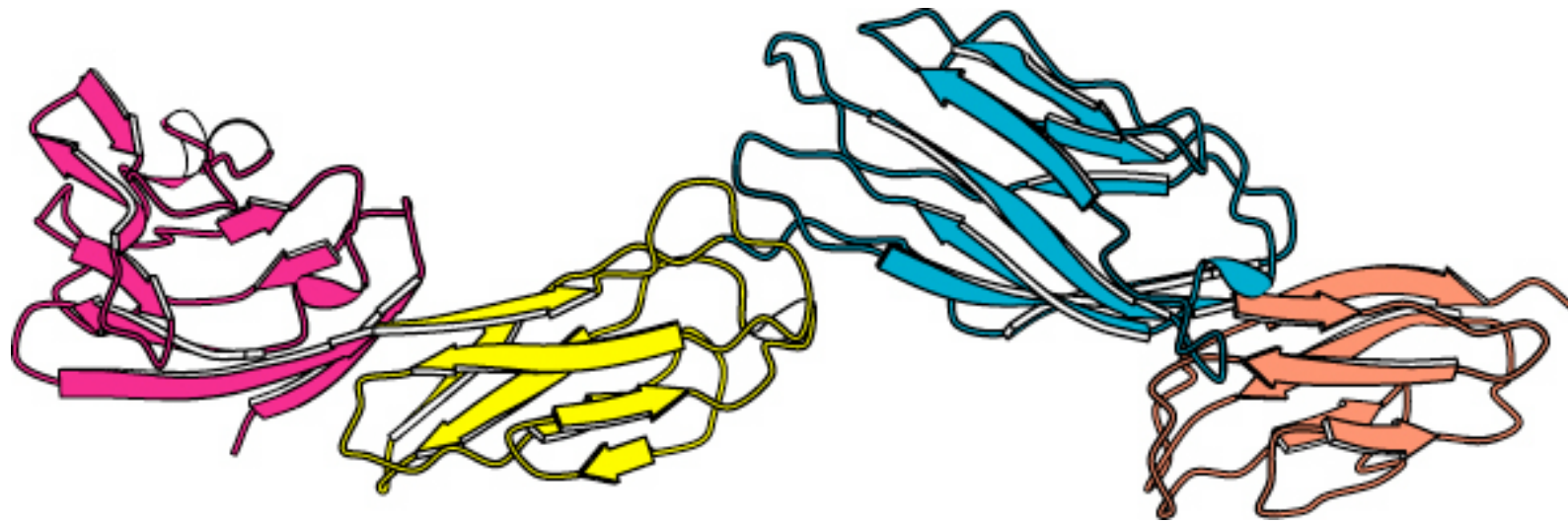


Interno: RESIDUI NON POLARI (Leu, Val, Met, Phe)

Esterno: RESIDUI POLARI E NON POLARI

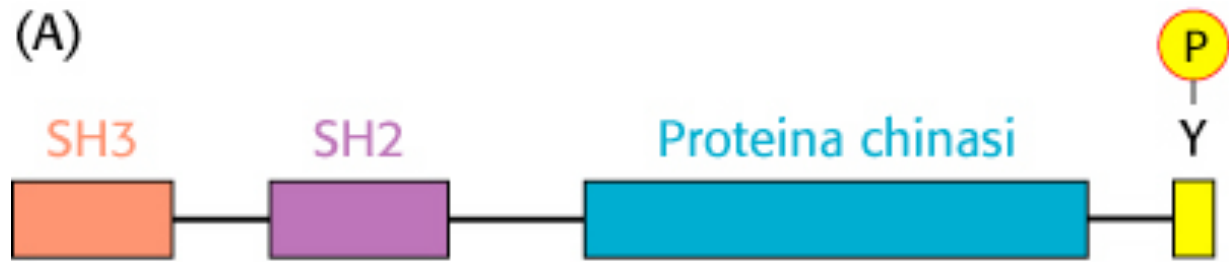
45*25*30

8a

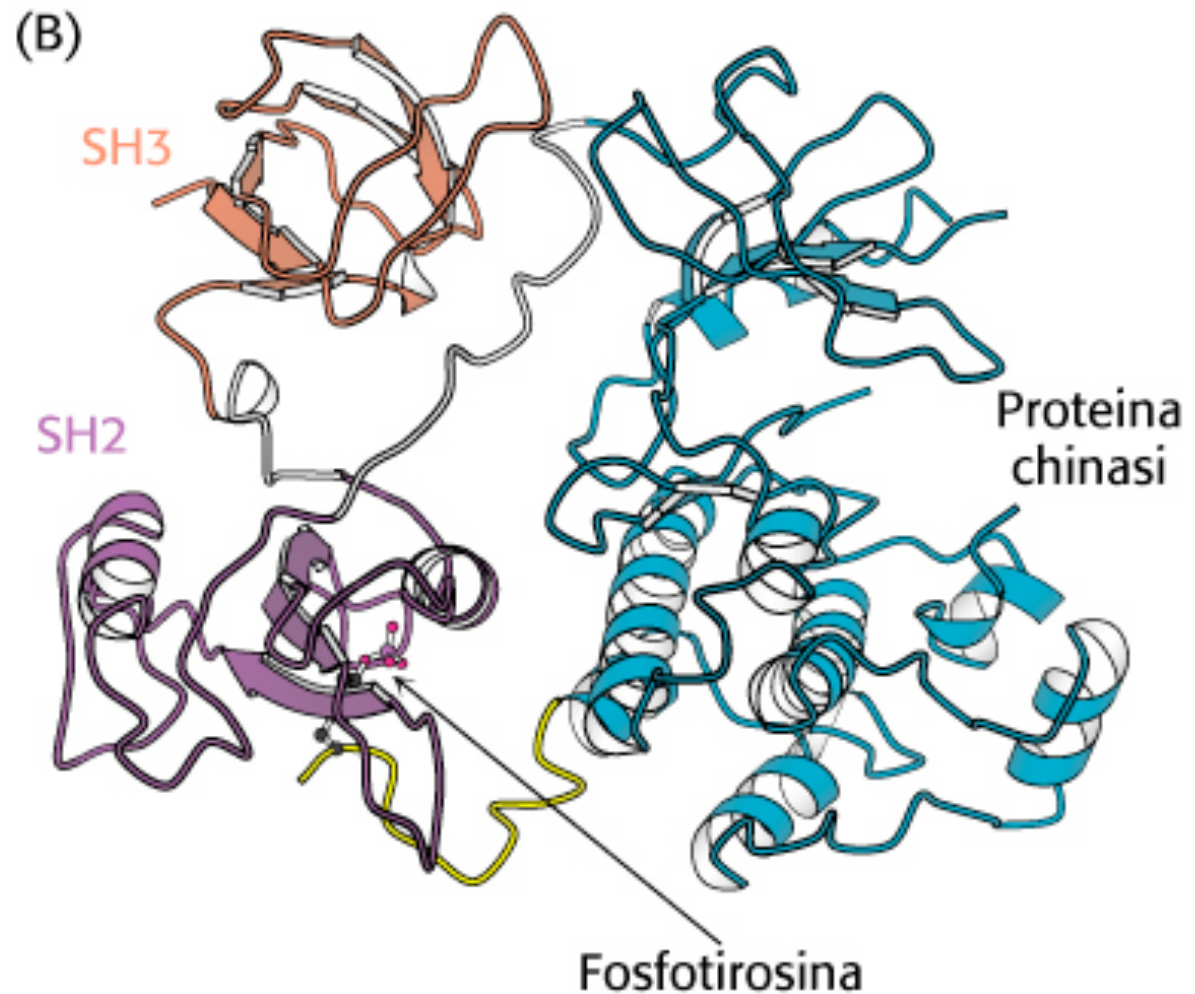


Domini proteici: la struttura di CD4, proteina della superficie di linfociti T, è costituita da 4 domini simili

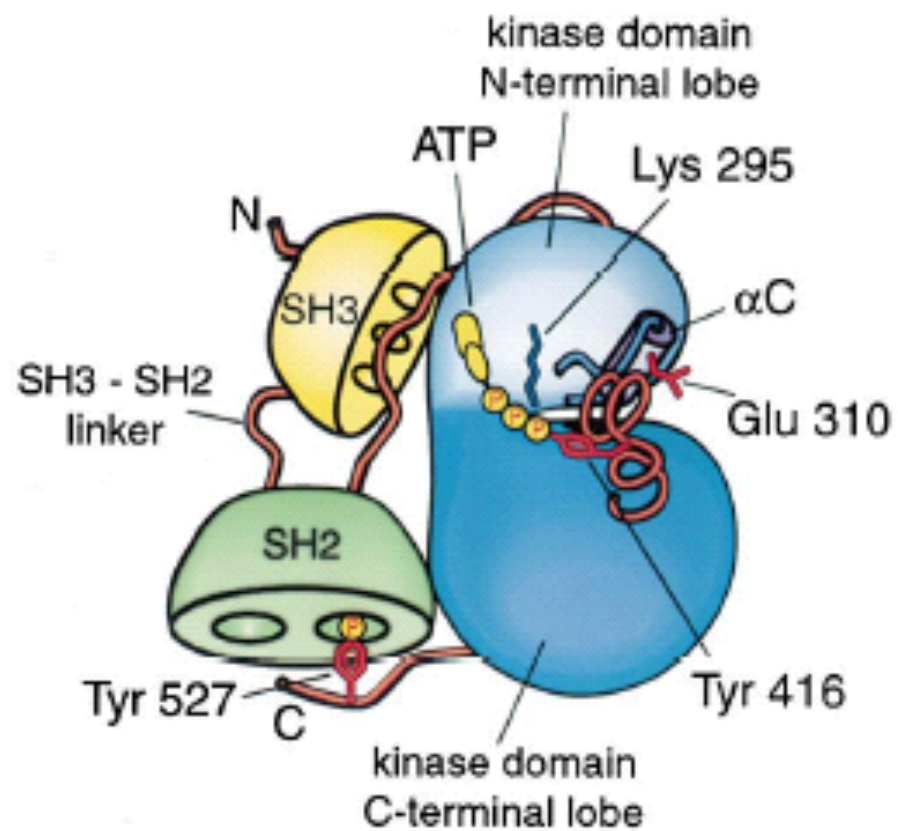
Le proteine sono costituite da domini strutturalmente definiti



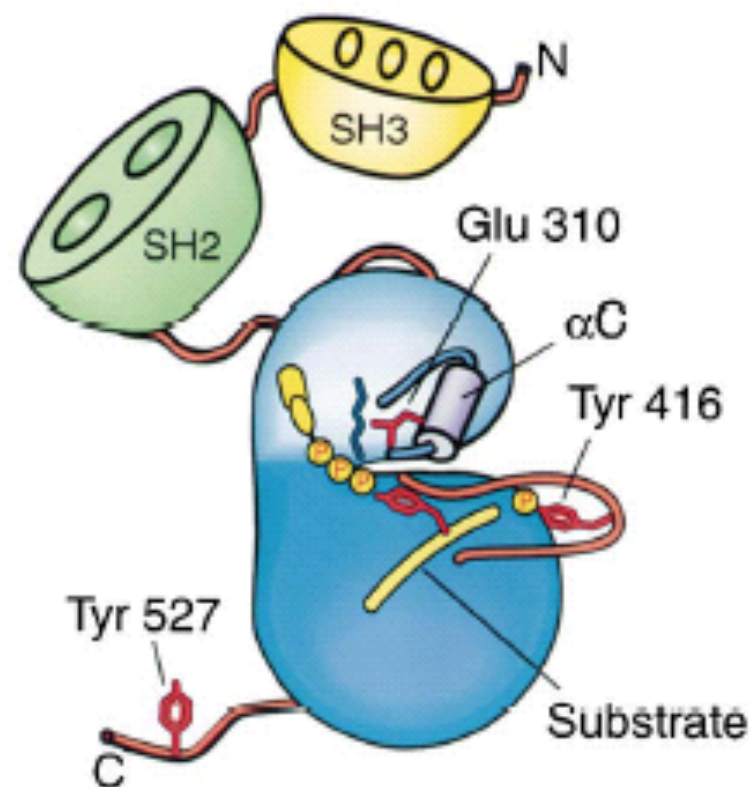
La proteina Src è costituita da 3 domini strutturali diversi

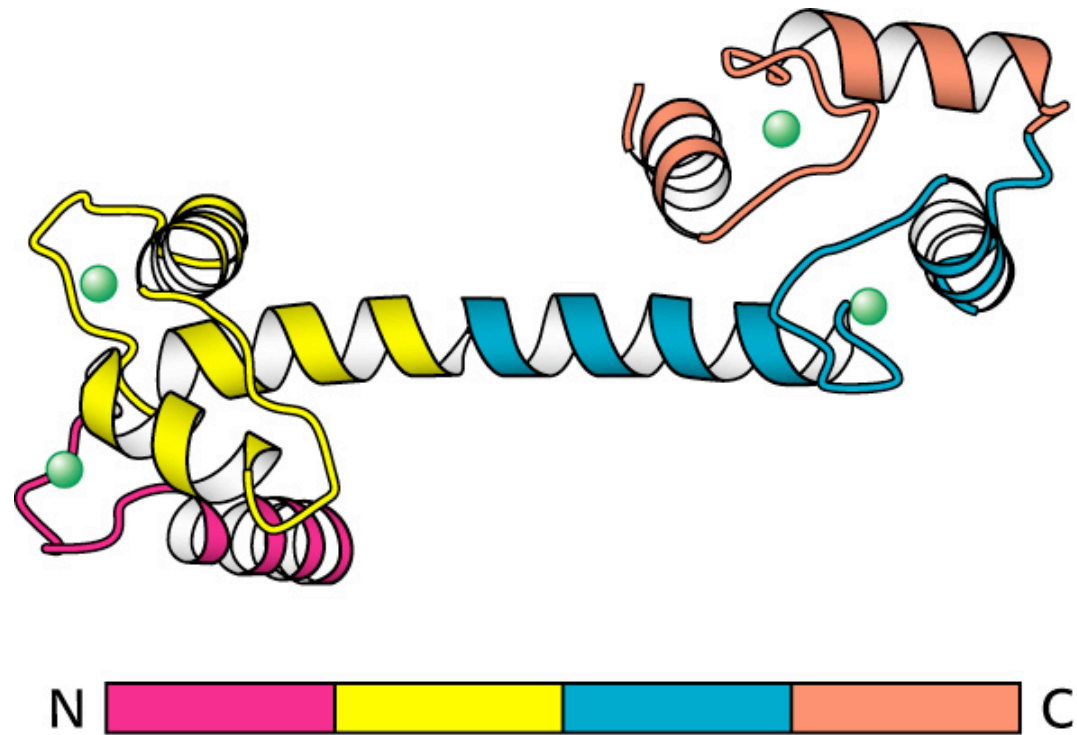


INACTIVE ASSEMBLED



ACTIVE





Struttura della calmodulina (un sensore del calcio) contiene 4 unità simili in una stessa catena polipeptidica