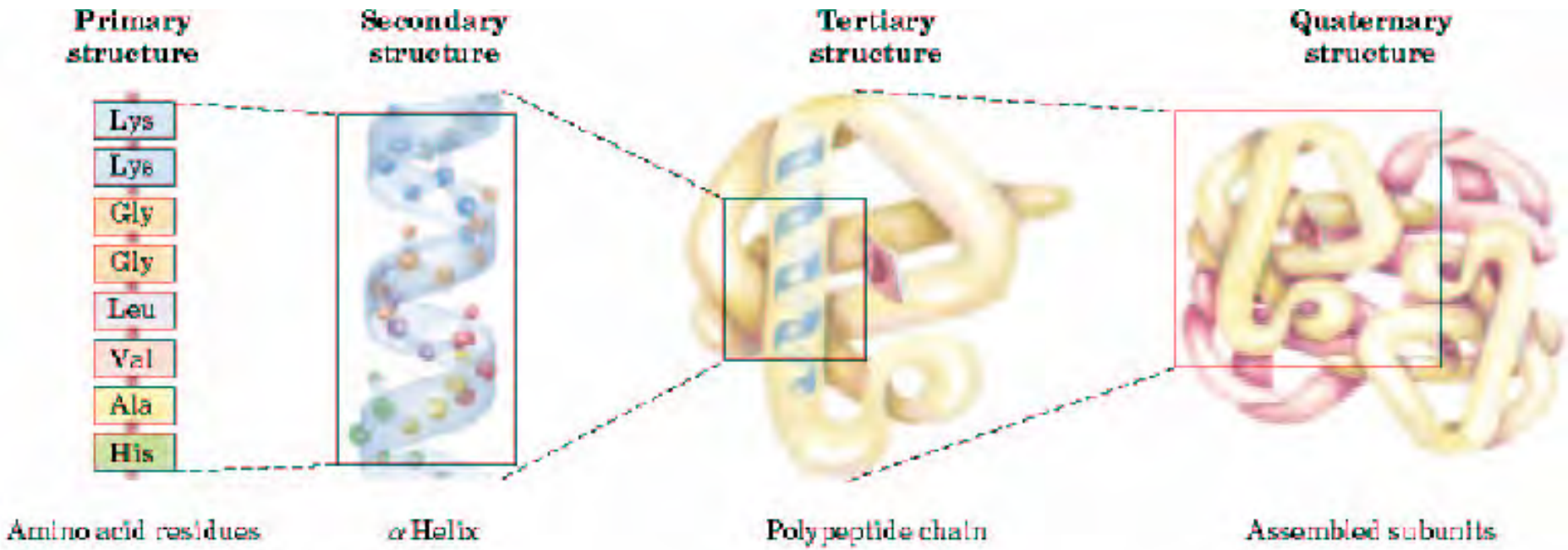
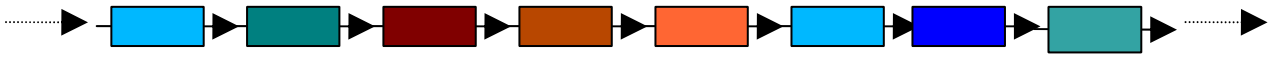
Sekundarne struktura proteina
Fibrilni proteini

Nivoi strukture proteina (strukturna hijerarhija) proteina



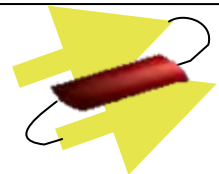
Nivoi strukture proteina

- Primarna struktura



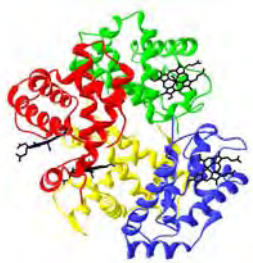
- Sekundarna struktura

- Super-sekundarna struktura



- Tercijarna struktura

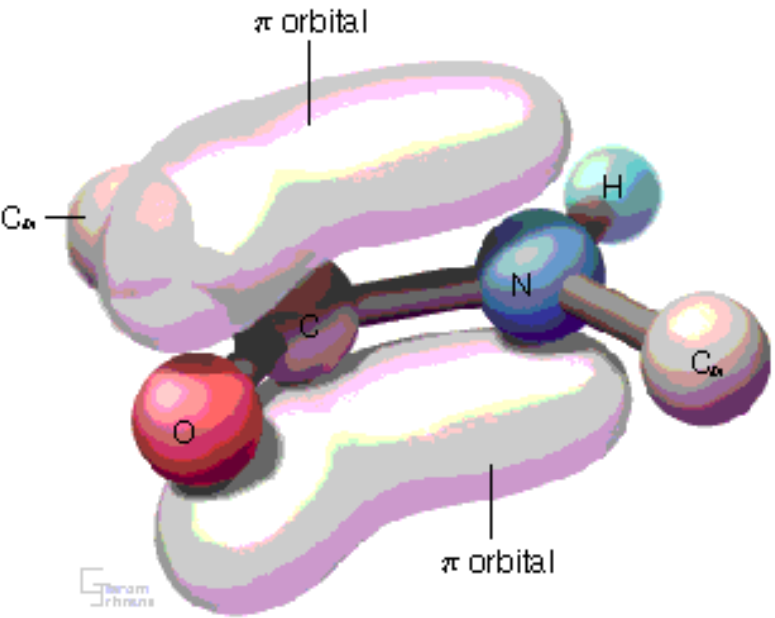
- Kvaternarna struktura



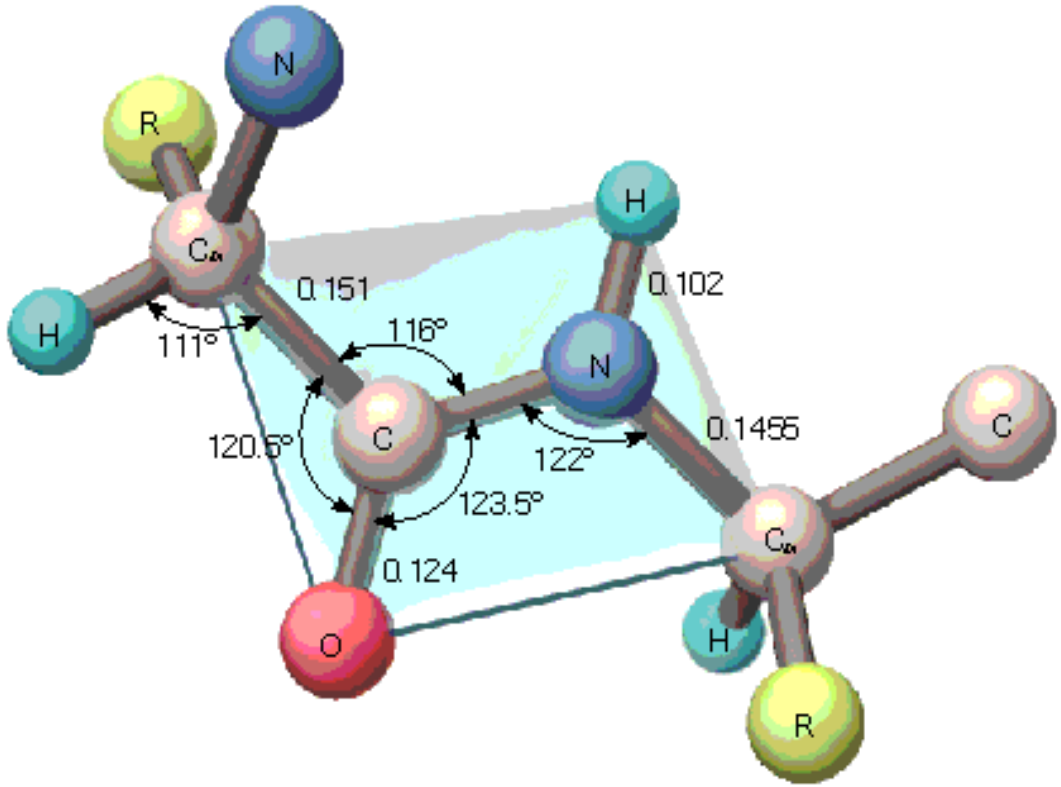
Sadržaj predavanja: Sekundarne strukture

- Šta su sekundarne strukture?
  - Lokalne (uređene) konformacije polipeptidne kičme (bez bočnih ostataka)!
  - α heliks β niz (pločica) β zavijutak
- Zašto se polipeptidni niz uvija u sekundarne strukture?
  - Strukturne osobine peptidne veze
  - Konformaciona analiza peptida
  - Ramachandranov dijagram
  - Stabilizacija sekundarnih struktura

Struktura peptidne veze



(a) Partial double-bond character of peptide bond



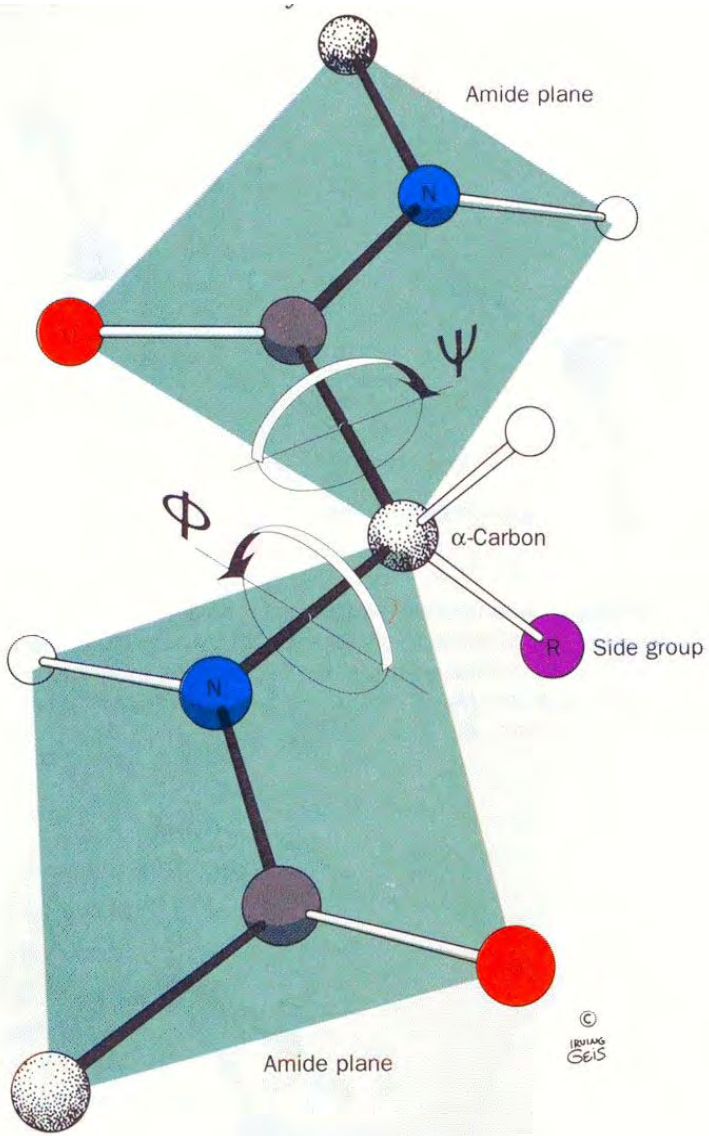
(b) Bond angles and lengths

Prosta C-N veza: 1.49Å

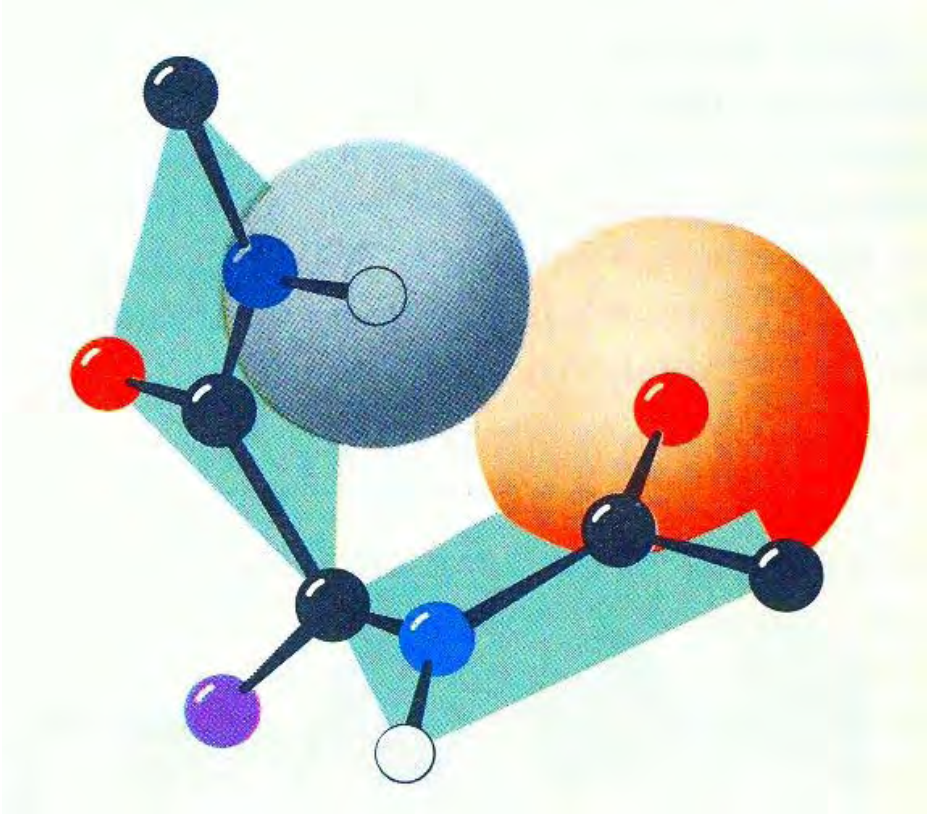
Amidna C-N veza: 1.32 Å (parcijalni dvostruki karakter)

Dvostruka C=N veza: 1.27 Å

Torzioni (rotacioni) uglovi

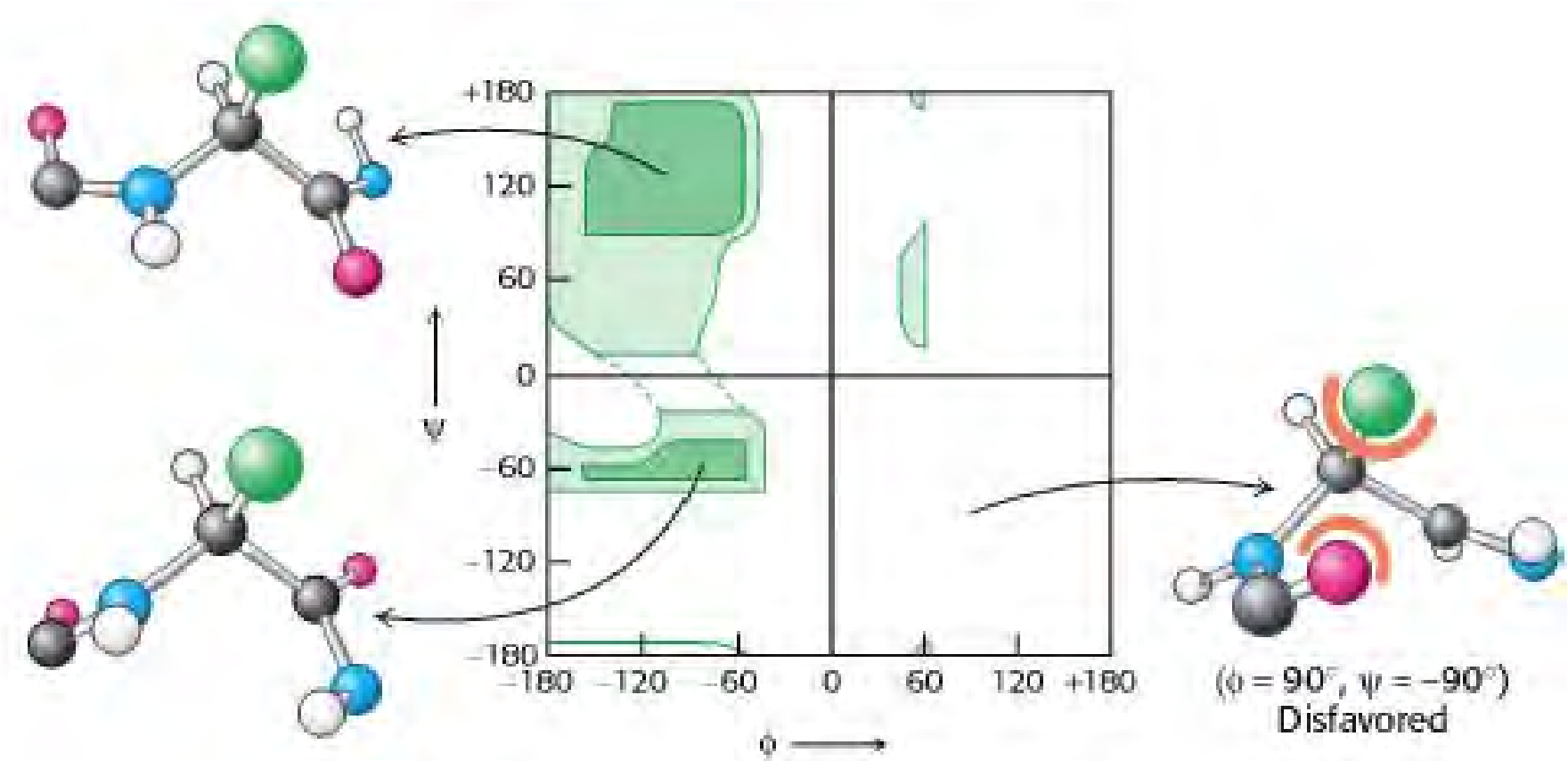


Sterne smetnje

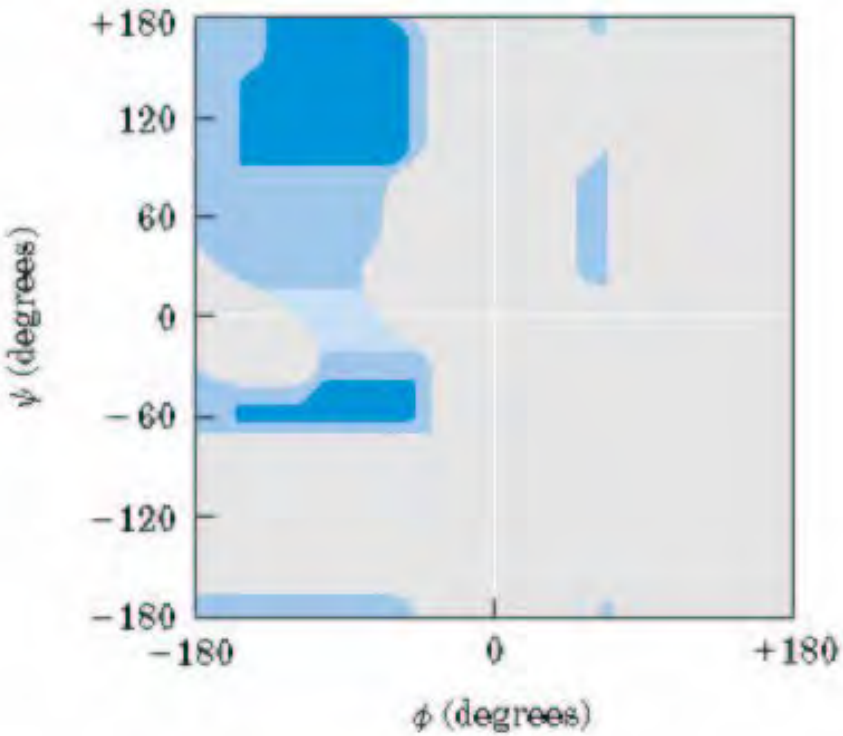


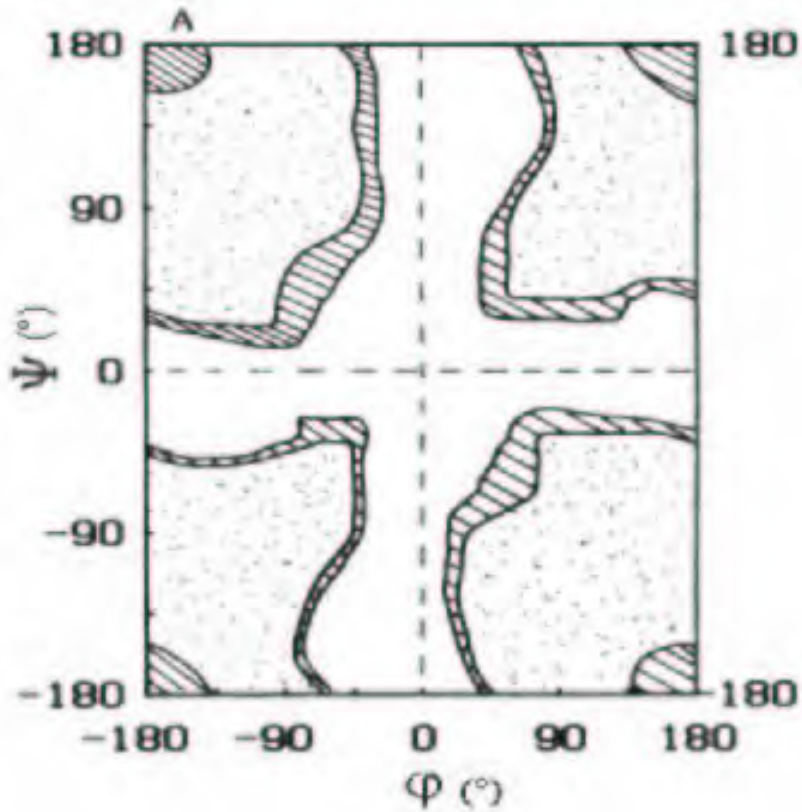
Kriterijum: najmanja (kontaktna) rastojanja među datim atomima nađena u kristalnim strukturama.

Ramachandranov dijagram: ϕ (φ) i ψ uglovi



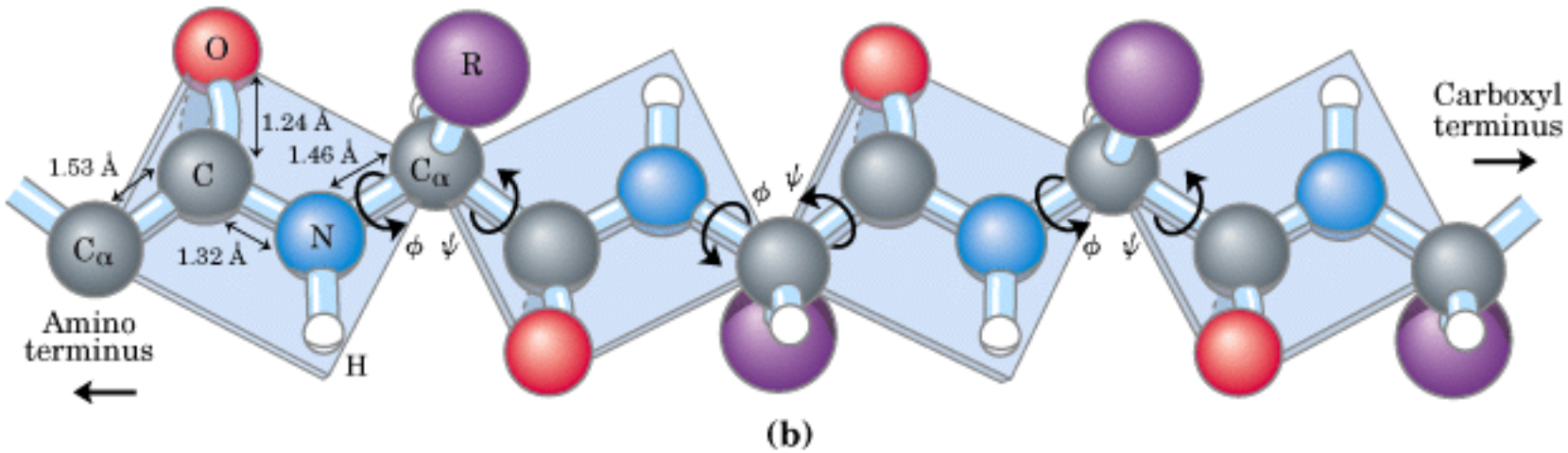
Ramachandranov dijagram za ostatak alanina (levo) i glicina (desno) u peptidu



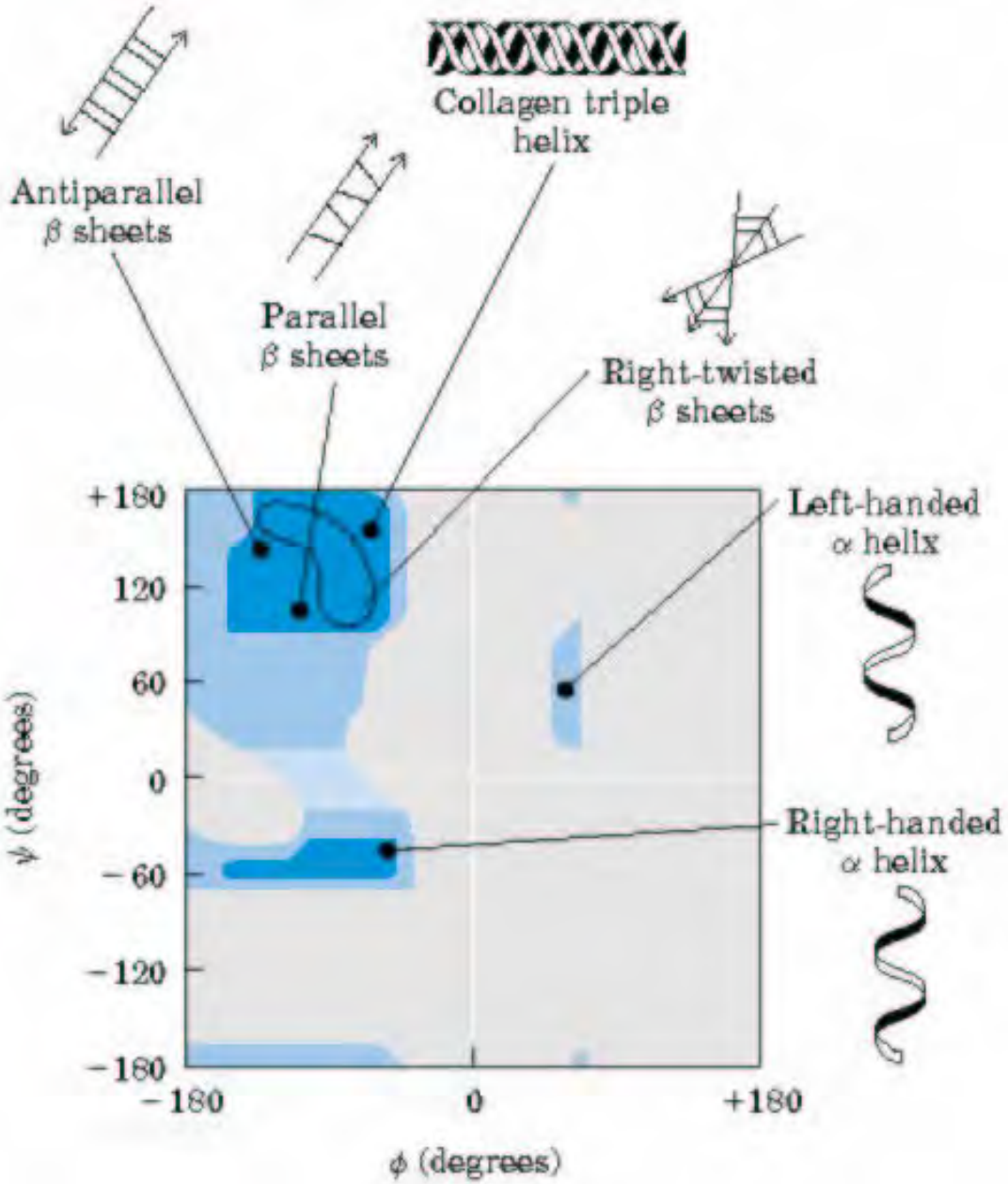


Šta zaključujemo?

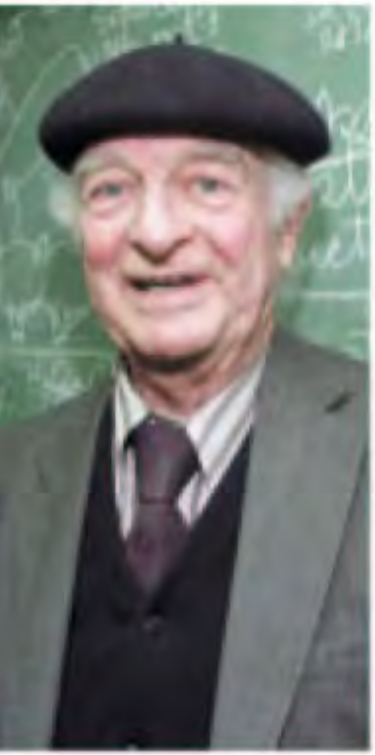
Da li polipeptidni niz može da se uvije u pravilnu ponavljajuću strukturu?



Sekundarne strukture



Linus Pauling i Robert Corey su (1951) predvideli (prvo) α heliks a (potom) i ß niz (pločicu)!



Linus Pauling
1901–1994

Robert Corey
1897–1971

Linus Pauling i Robert Corey su tražili konformacije polipeptidnog niza u kojima su:

-sterne smetnje najmanje.
- vodonično vezivanje između C=O i N-H grupa najveće.

Pomoć:
rendgenska strukturna analiza α-keratina (William Astbury 1930!) koja je ukazivala na α heliks!!!!

Desni α-heliks

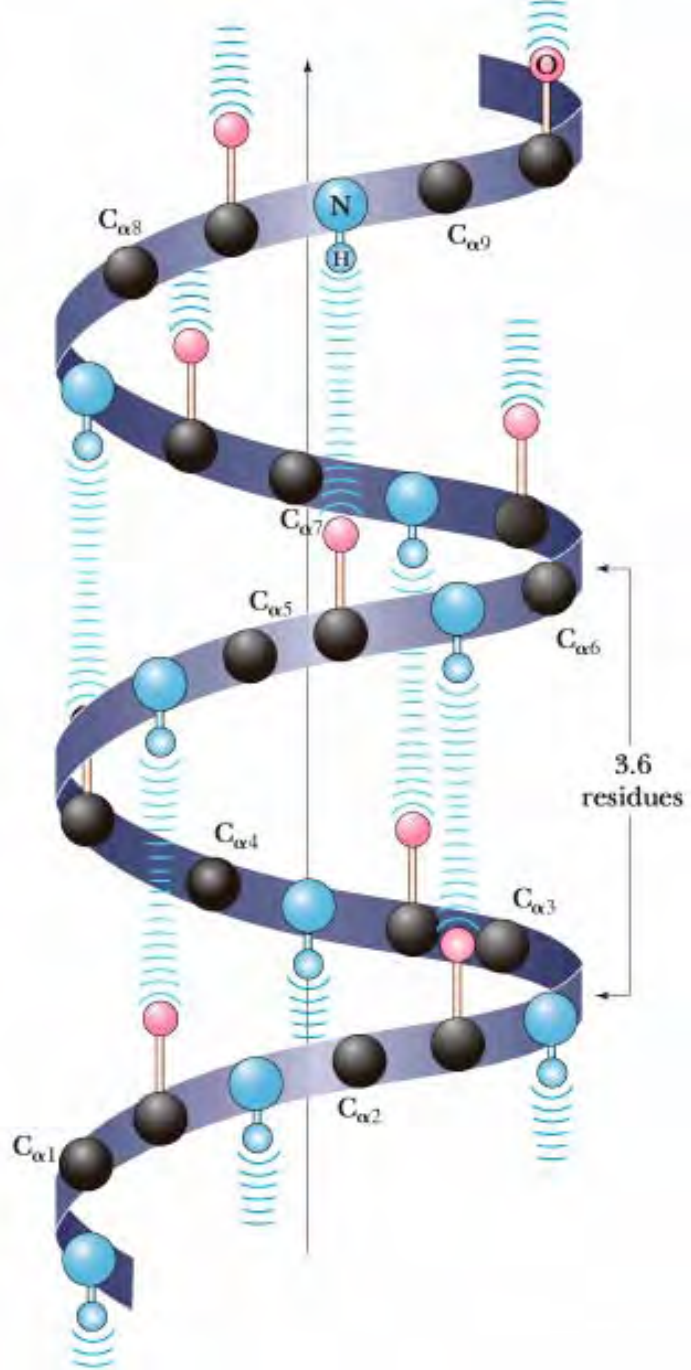
*Peptidne N-H veze ↓

*Peptidne C=O veze ↑

•Vodonična veza između: N-H grupe (ostatka n) i C=O grupe (ostatka n+4).

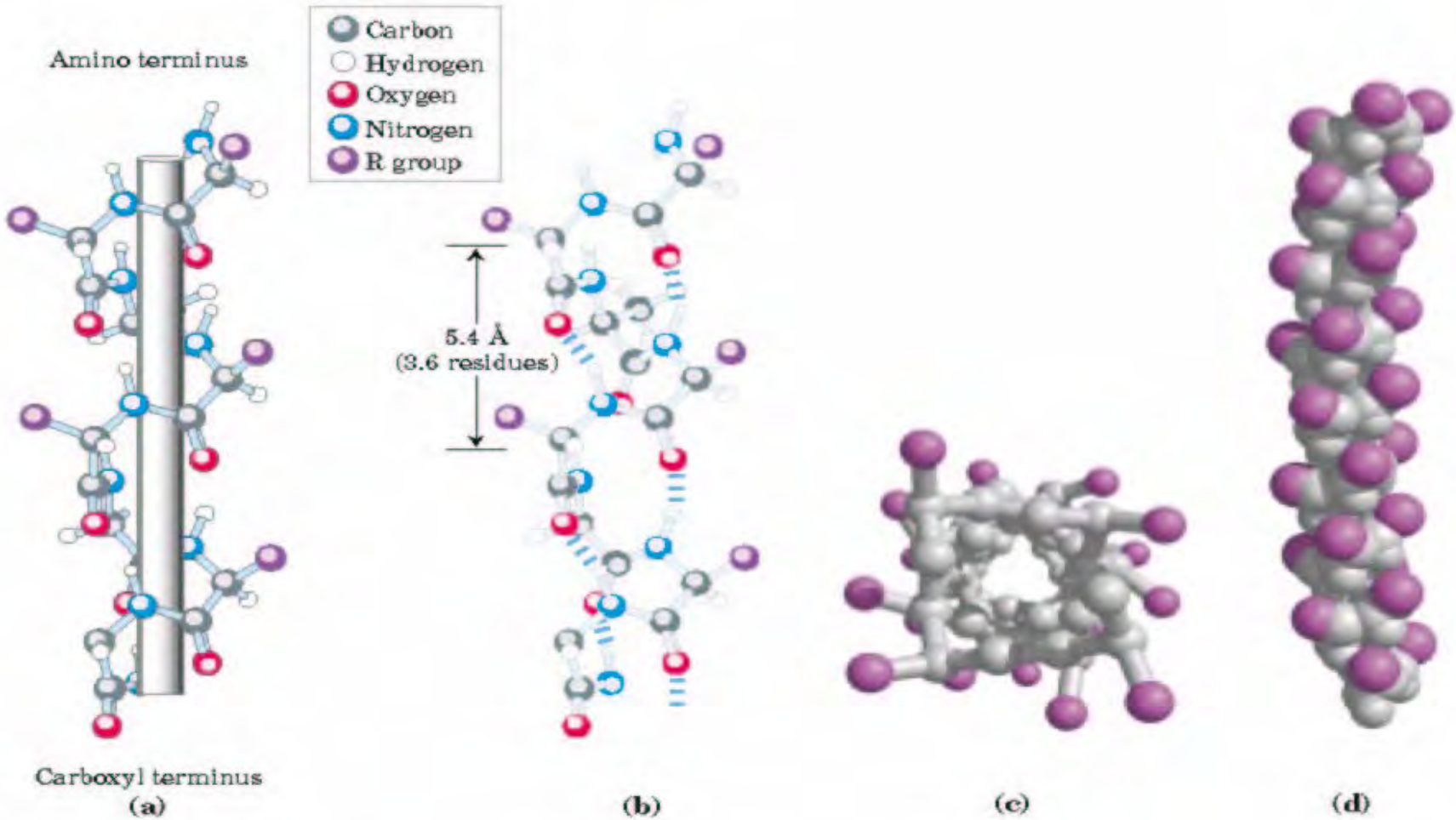
α-heliks ima:

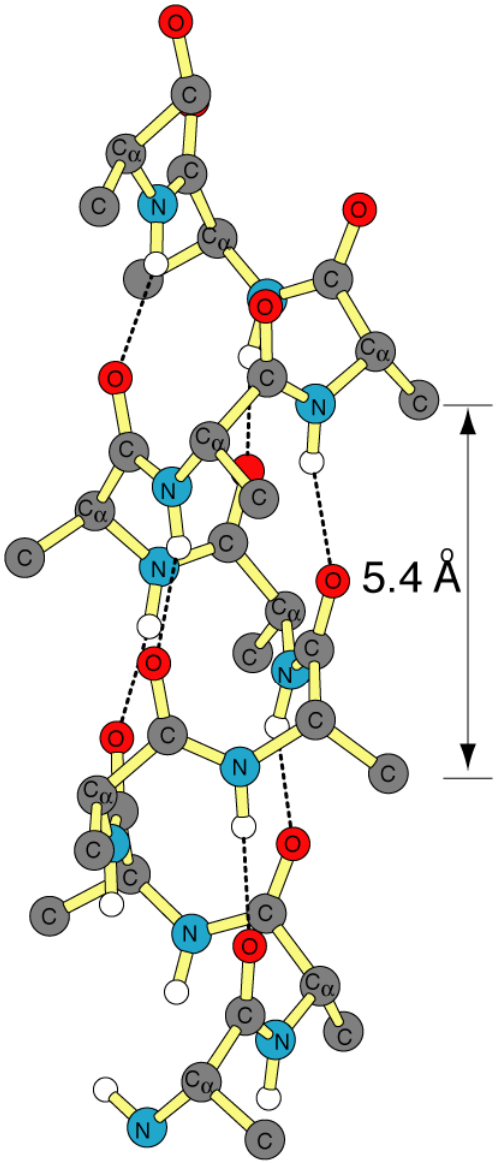
- 3.6 ostatka po zavoju
- rast/ostatak = 1.5 Å
- rast/zavoj = 5.4 Å

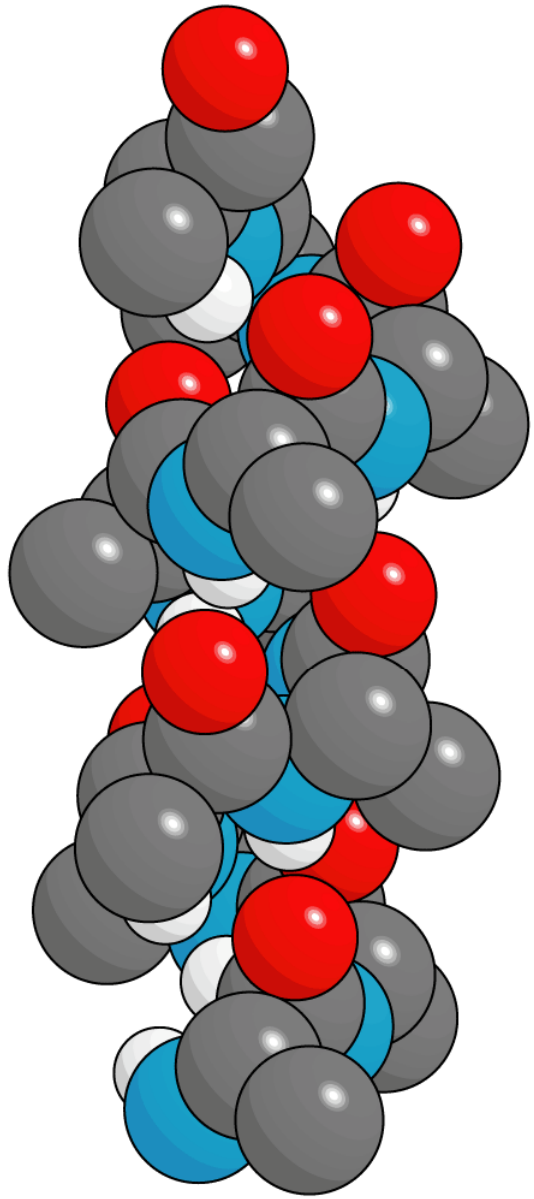


Levi i desni α heliks

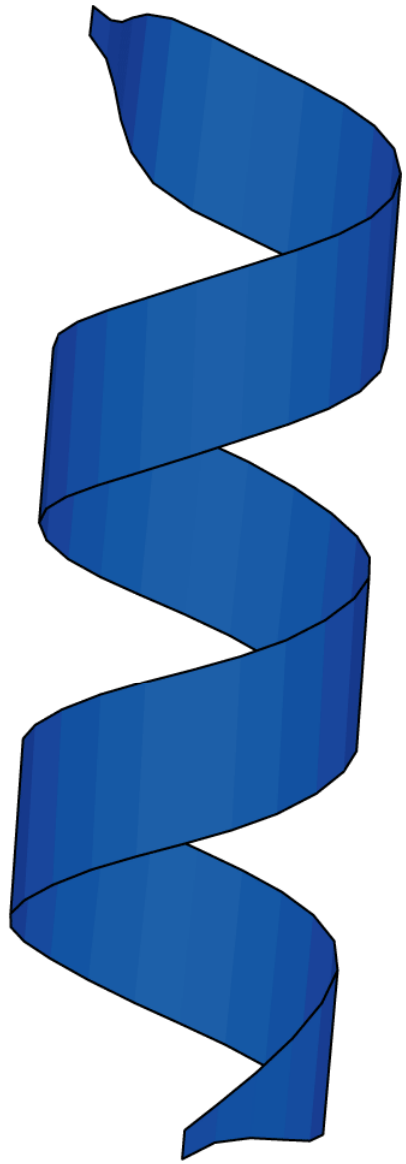
Prikazivanje α heliksa



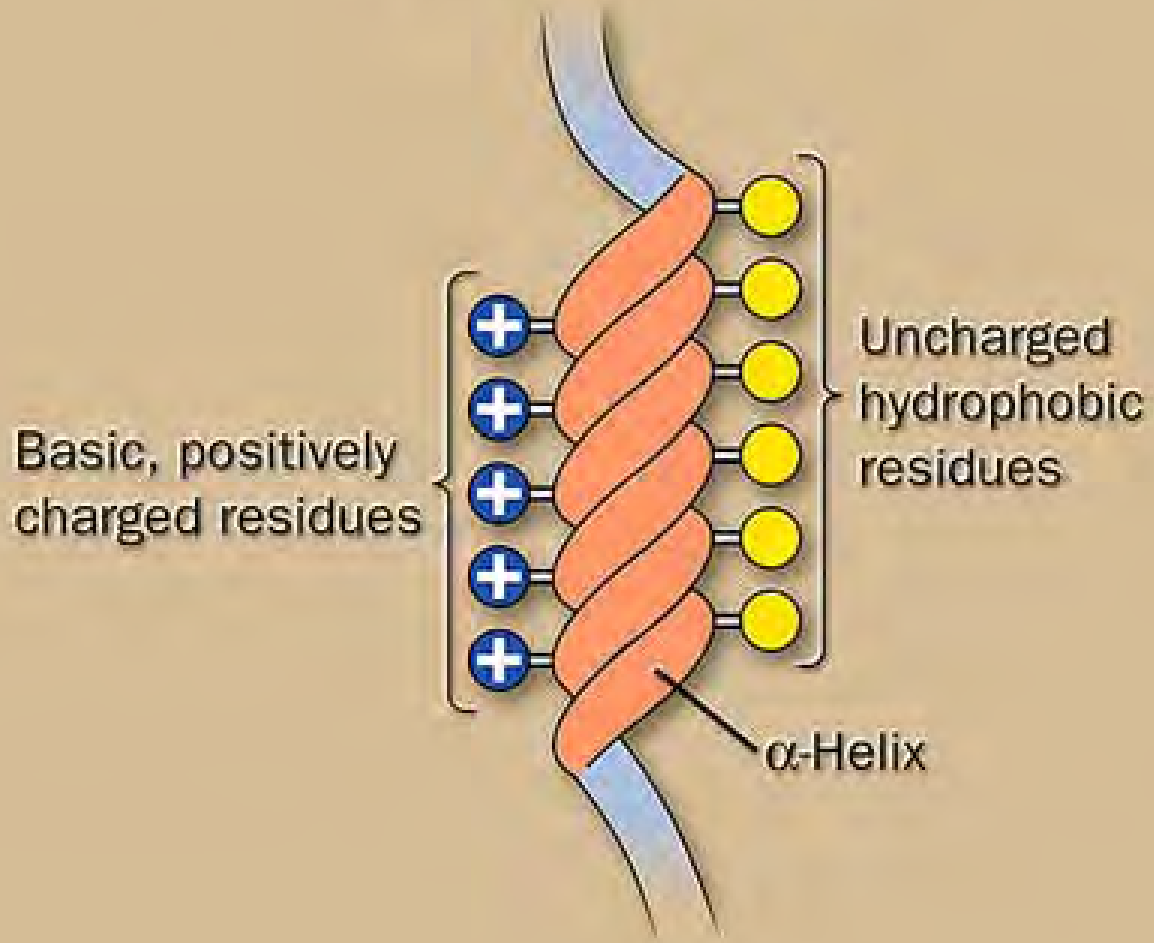




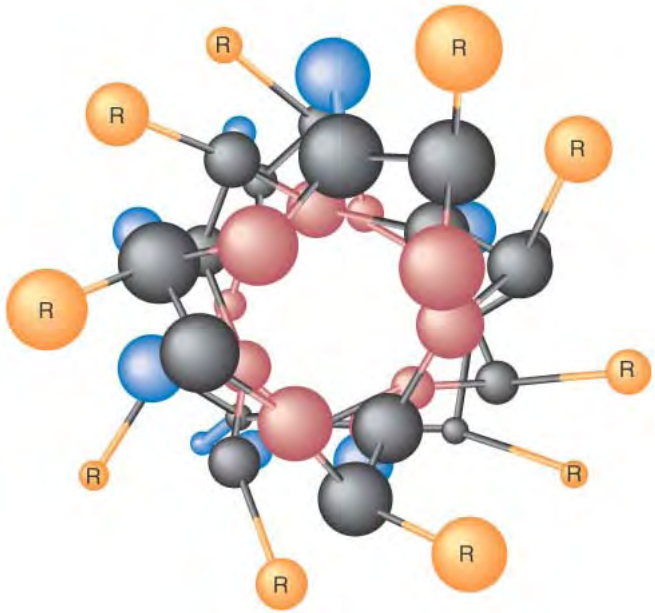
5 Å



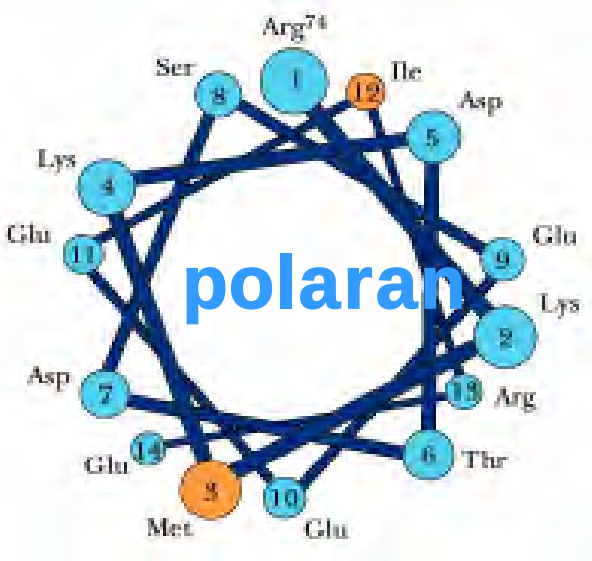
Amphipathic α-Helix



Prikazivanje α-heliksa: Edmundsenov točak

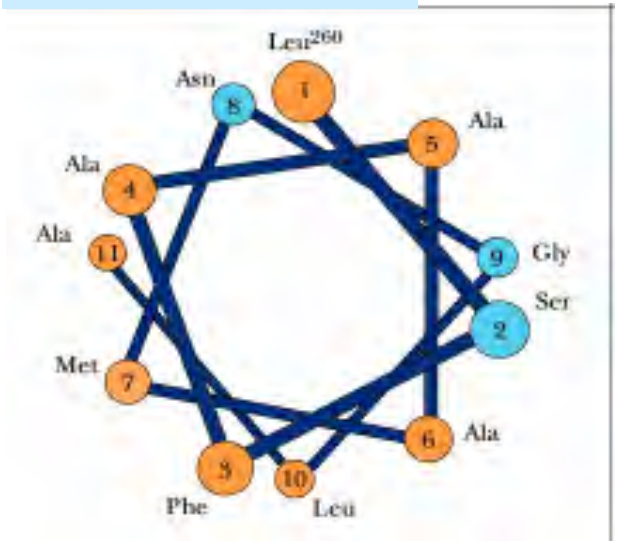


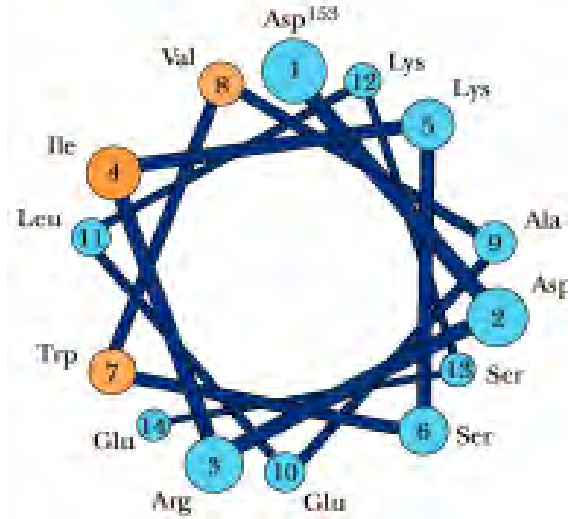
α -heliks može biti:



polaran

nepolaran

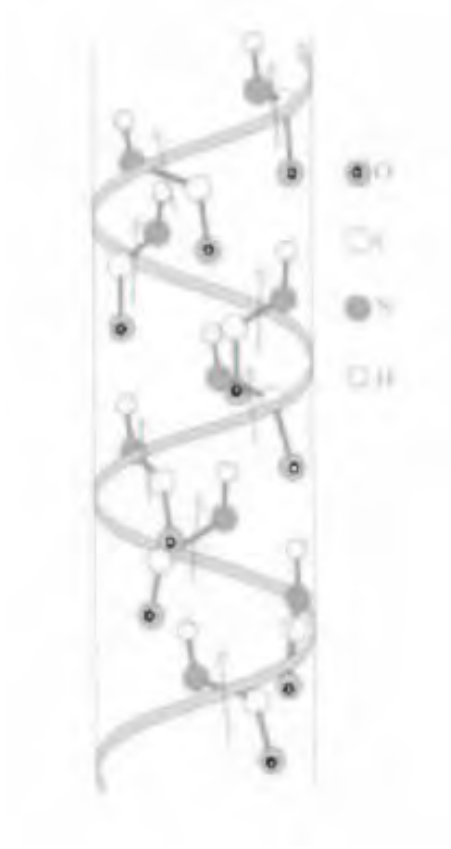




amfipatični

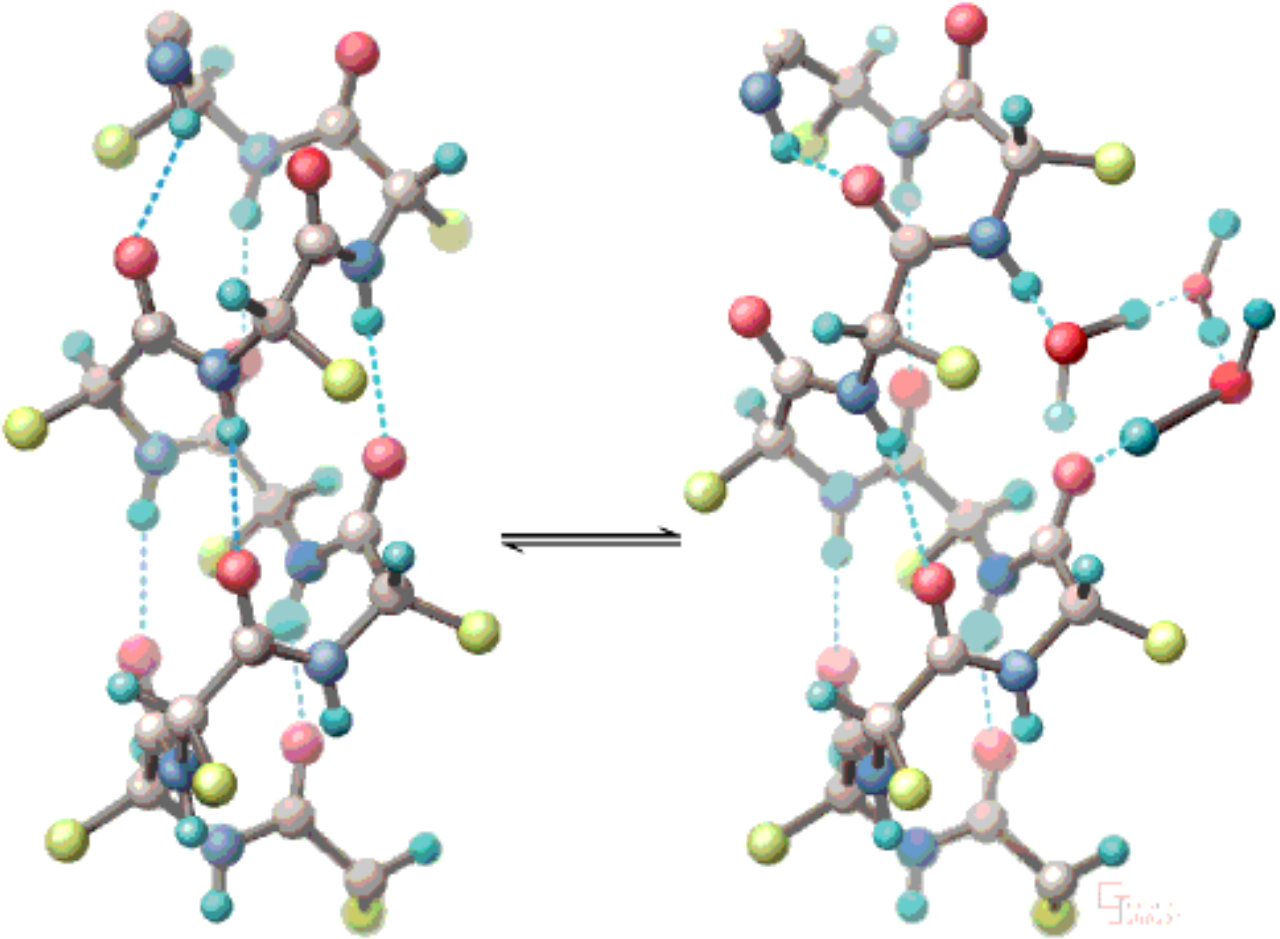
Stabilizacija α heliksa

* vodonično vezivanje između C=O i N-H
* orijentacija amidnih diplola: privlačenje!



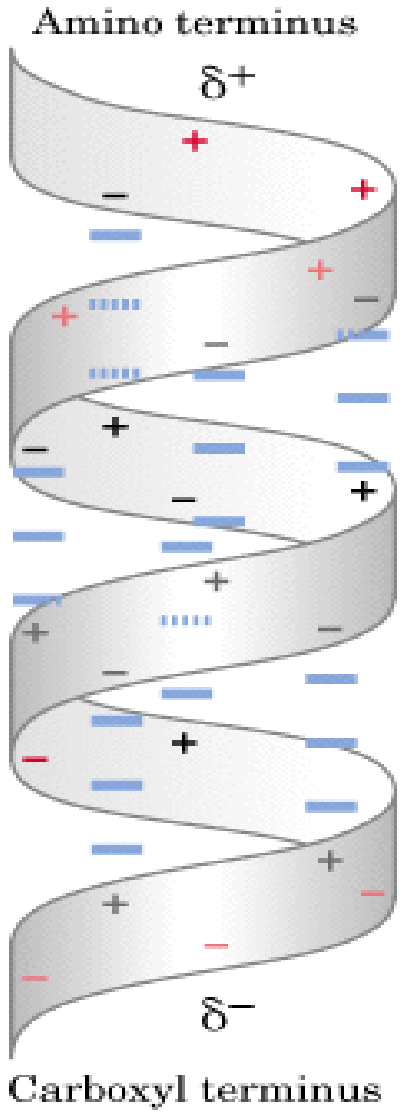
Vodonične veze: kompeticija sa okolnom vodom

Dipoli!!!



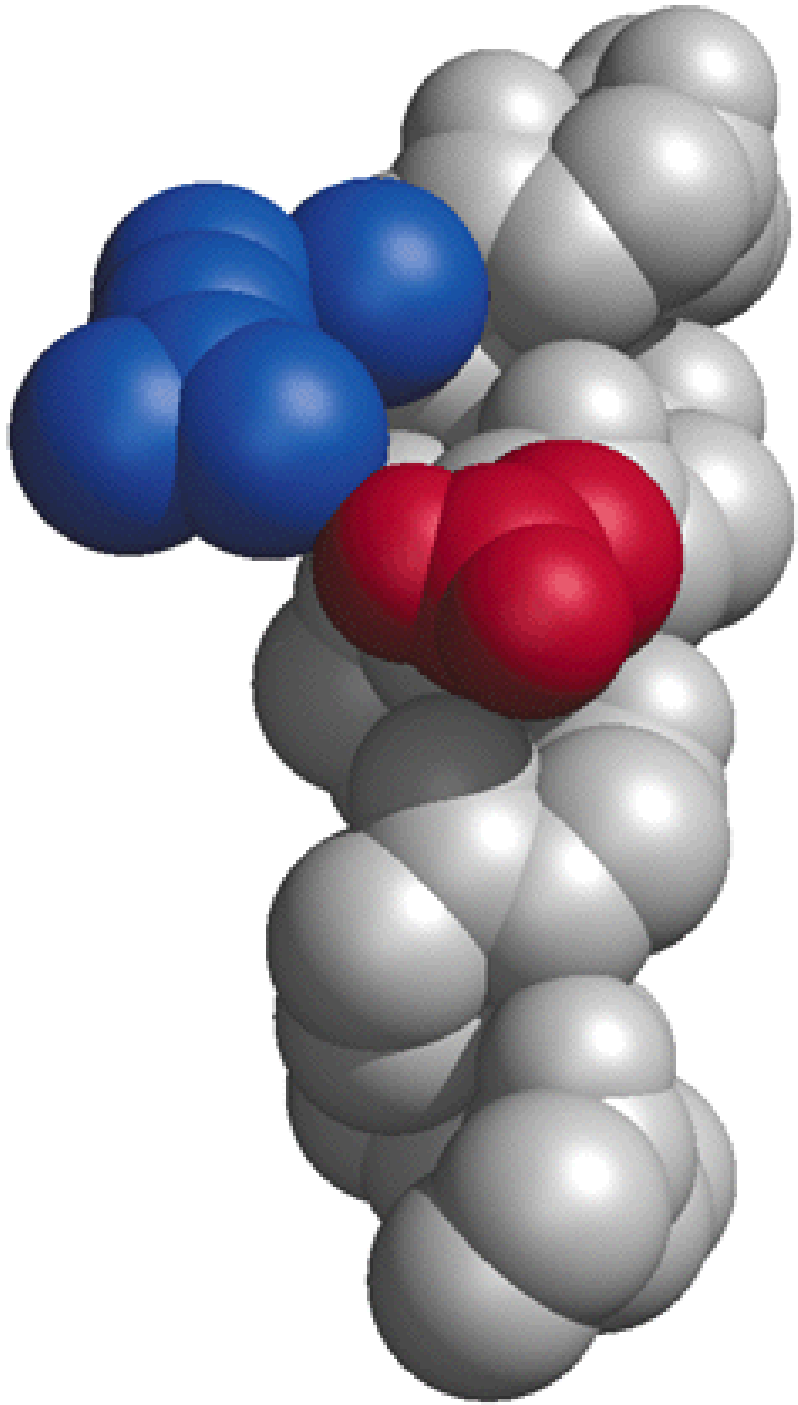
All internal hydrogen bonds; helix intact

Some hydrogen bonds to water; helix broken

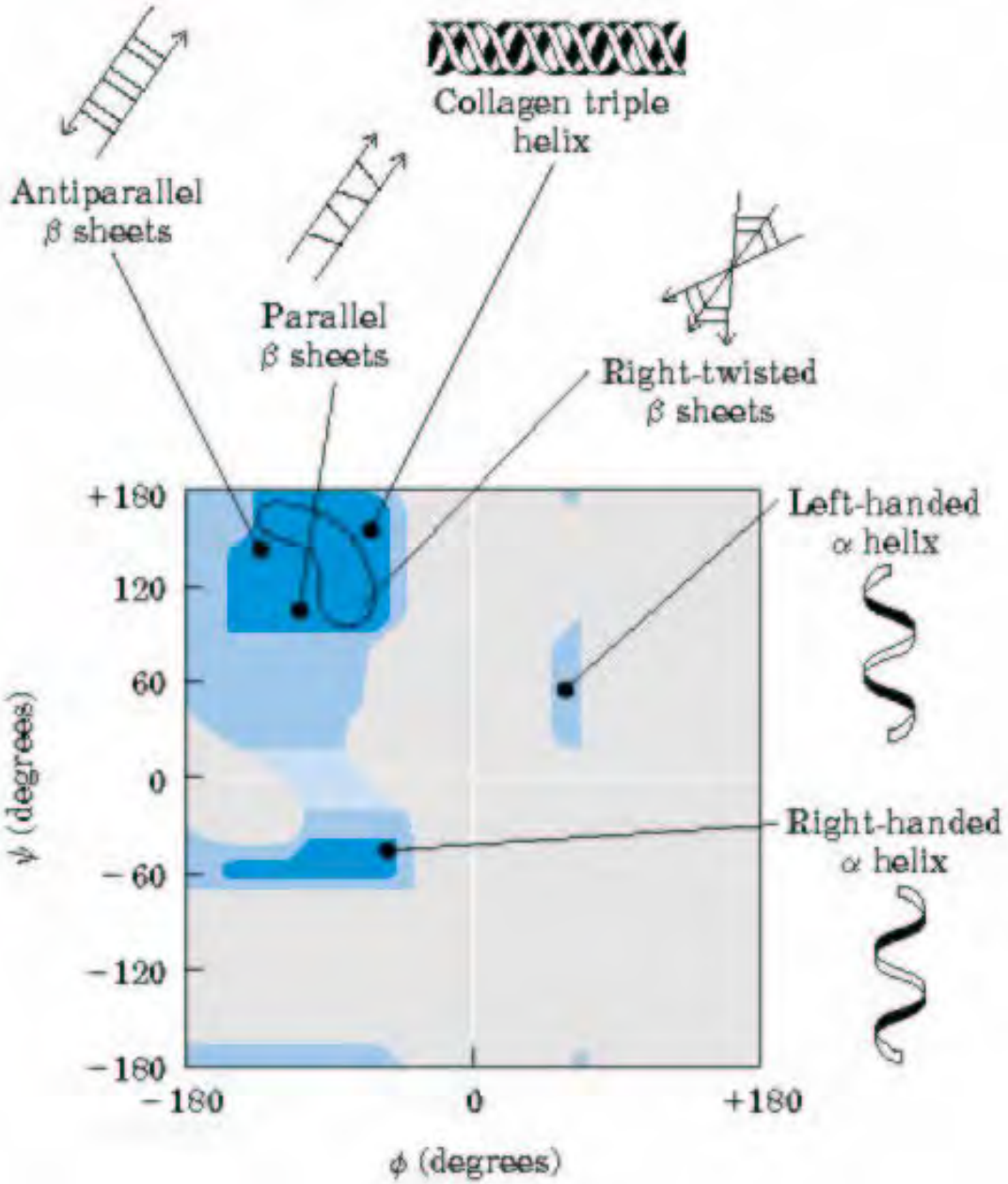


Destabilizacija heliksa!

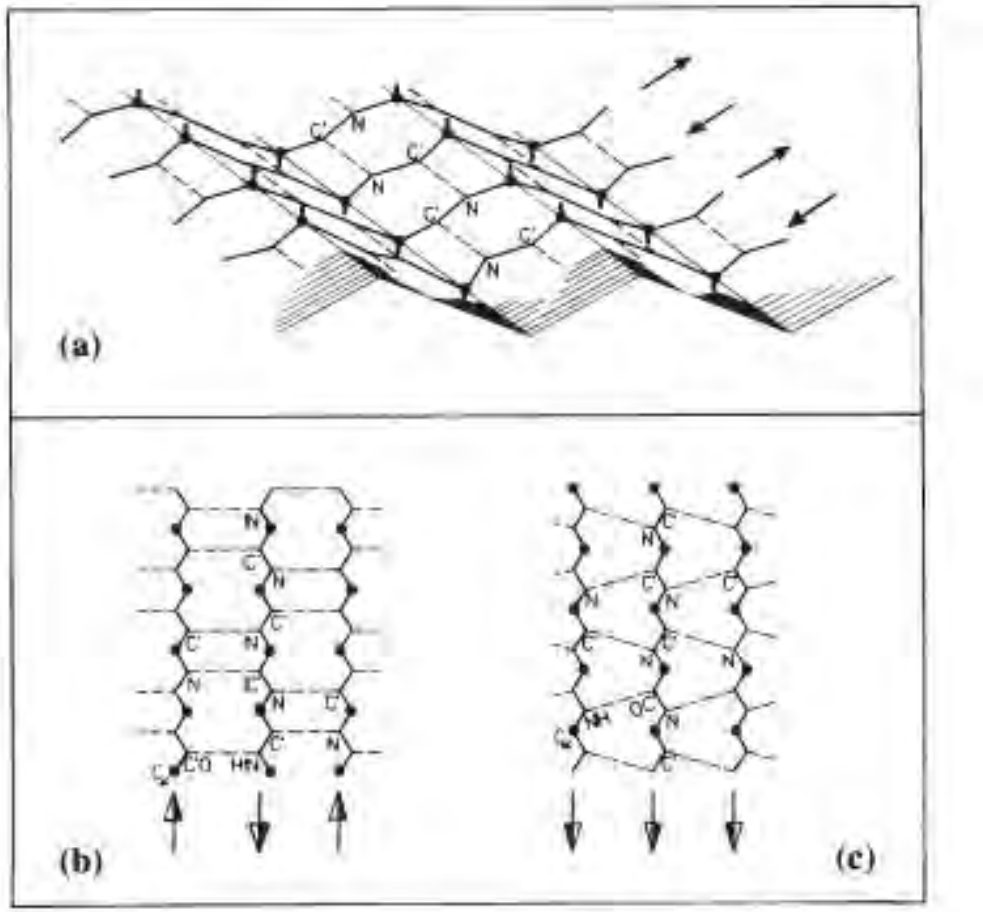
Interakcije između R ostataka u α-heliksu koji su međusobno udaljeni za 3 aminokiselinska ostatka u sekvenci!!!

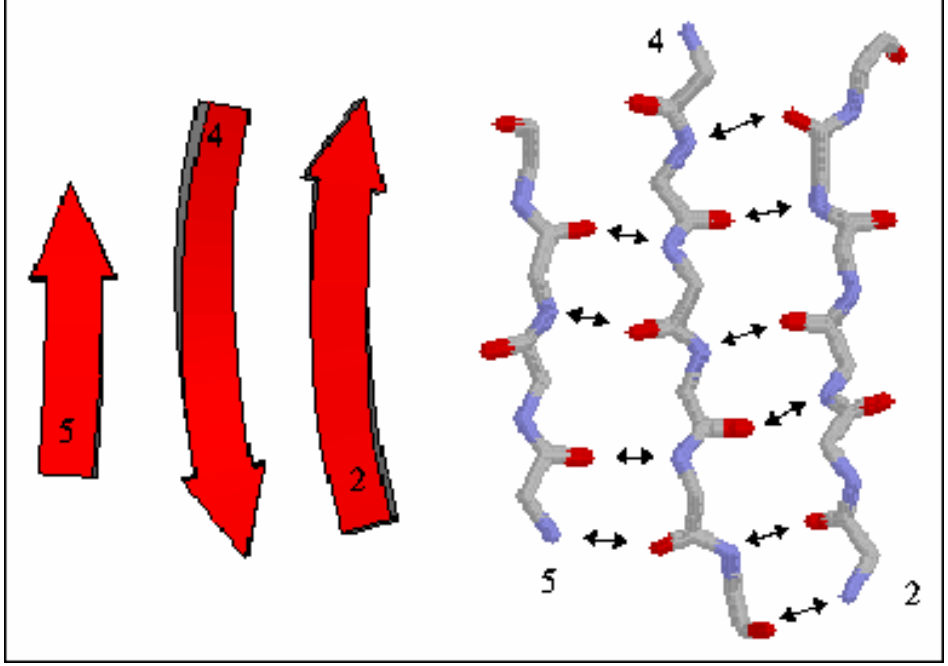


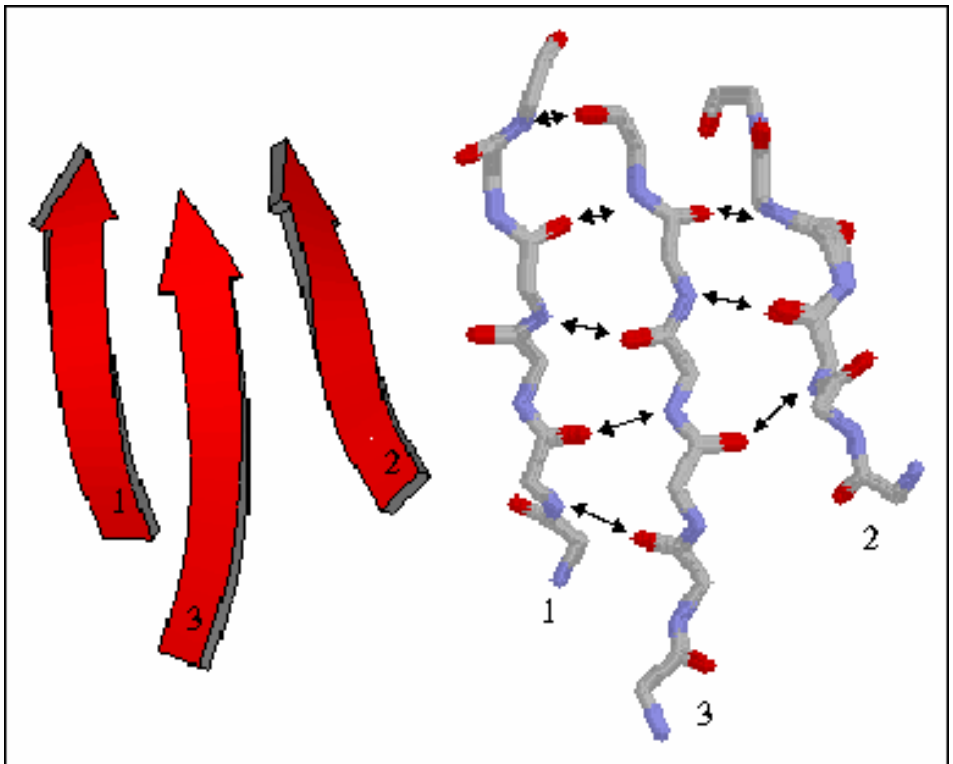
Sekundarne strukture



ß nabrana pločica: paralelna i antiparalelna



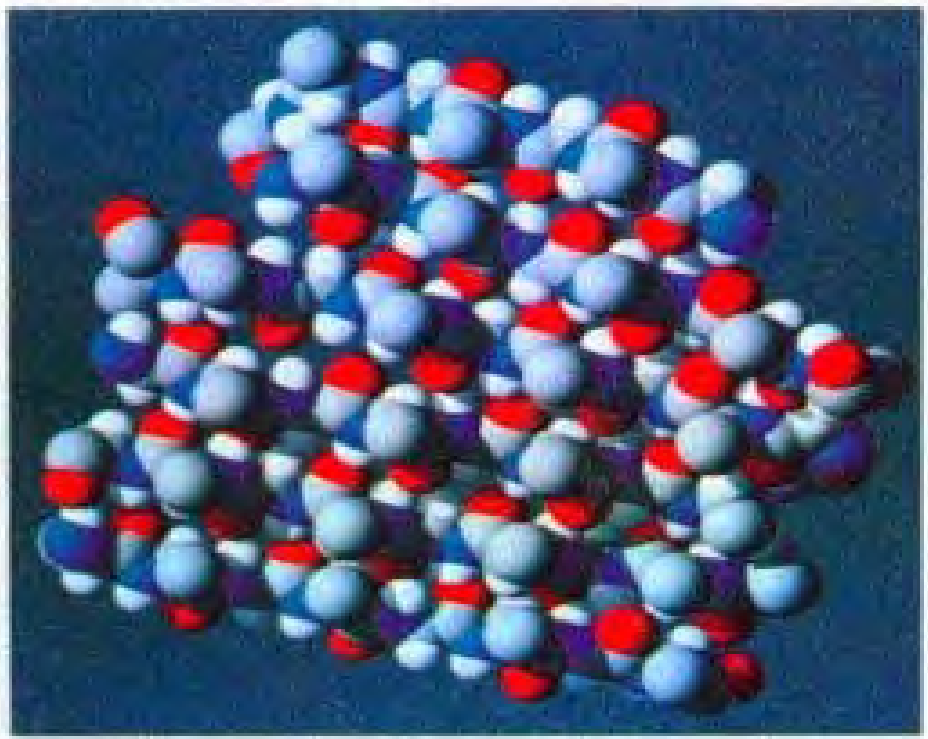

4
5
2
4
5
2

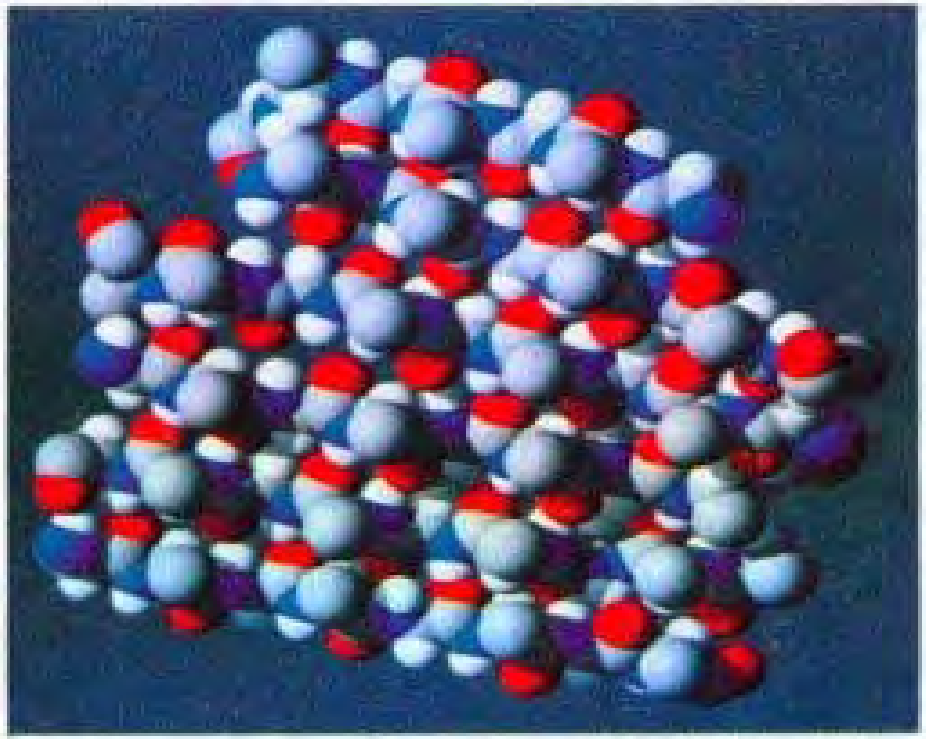

1
3
2
2
1
3

Povezivanje susednih nizova u ß pločici

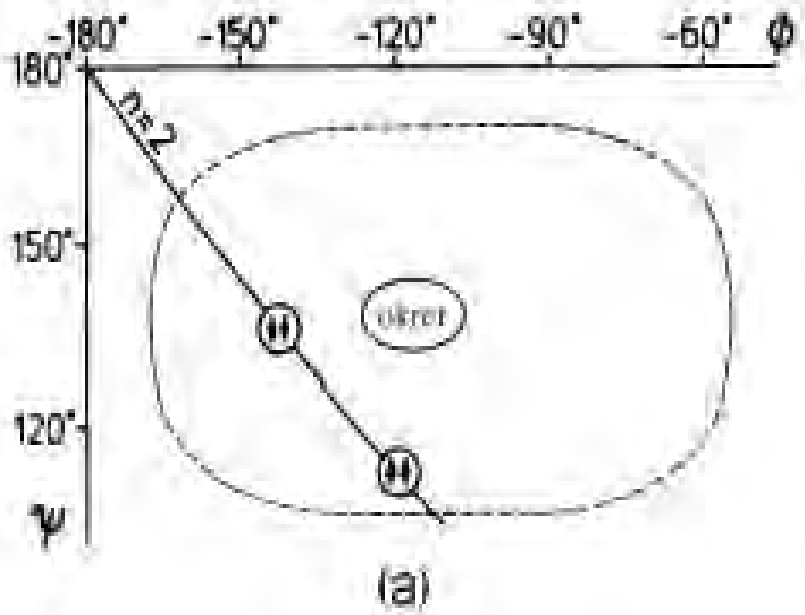
Slika 4.17: Povezivanje susednih nizova u β-pločici: (a) povezivanje susednih antiparalelnih peptidnih nizova vezom tipa ukosnice; (b) desna petlja medju paralelnim nizovima i (c) leva petlja medju paralelnim nizovima. [Na osnovu J.S.Richards, *Adv. Protein. Chem.*, **34**, 290 (1981).]

ß pločica: model ispunjenih sfera





ß pločice nadjene u molekulima proteina se izvijaju udesno

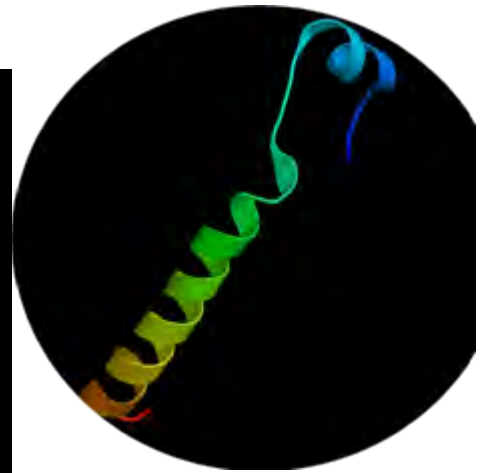


(a)

(b)

Povezivanje sekundarnih struktura: zavoj, zaokret, petlja

ß pločica



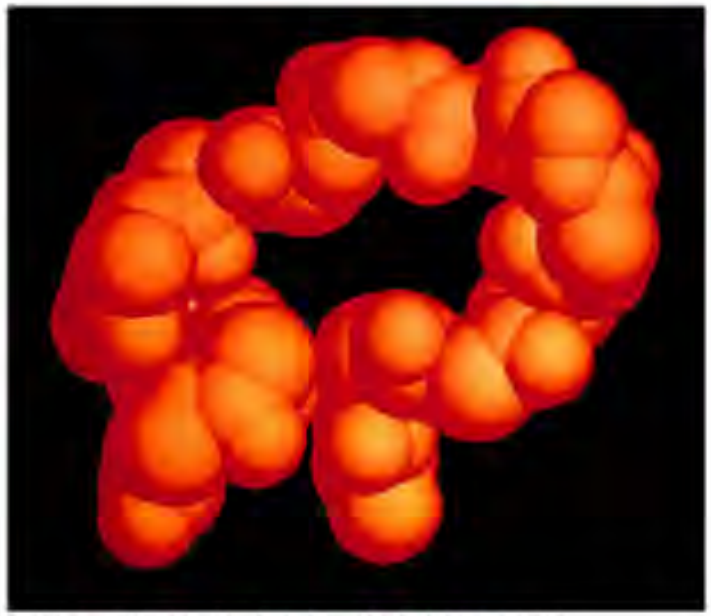
α heliks

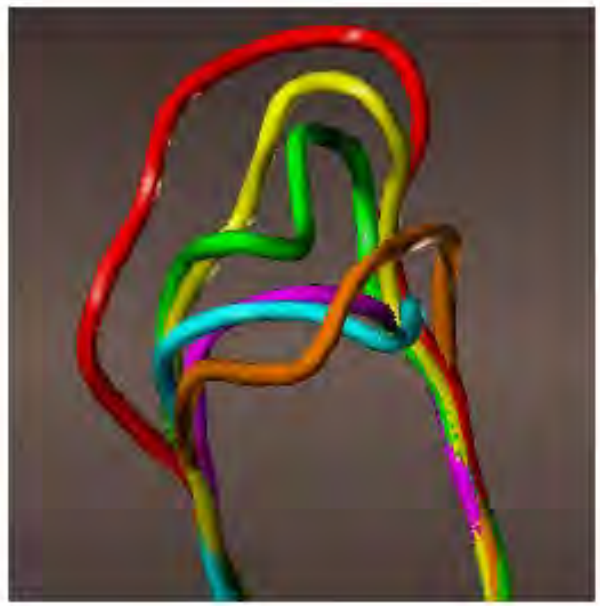
Zavoj

Zaokret

Additional Elements of Structure: Loops

- Irregularly structured elements
- More disordered and flexible than turns
- Connects secondary structure elements
- Variable in length and shape
- Frequently form binding sites and enzyme active sites





The N- and C-terminal arms of proteins are also generally more disordered and irregularly structured.

Verovatnoća nalaženja aminokiselinskih ostataka u sekundarnim strukturama

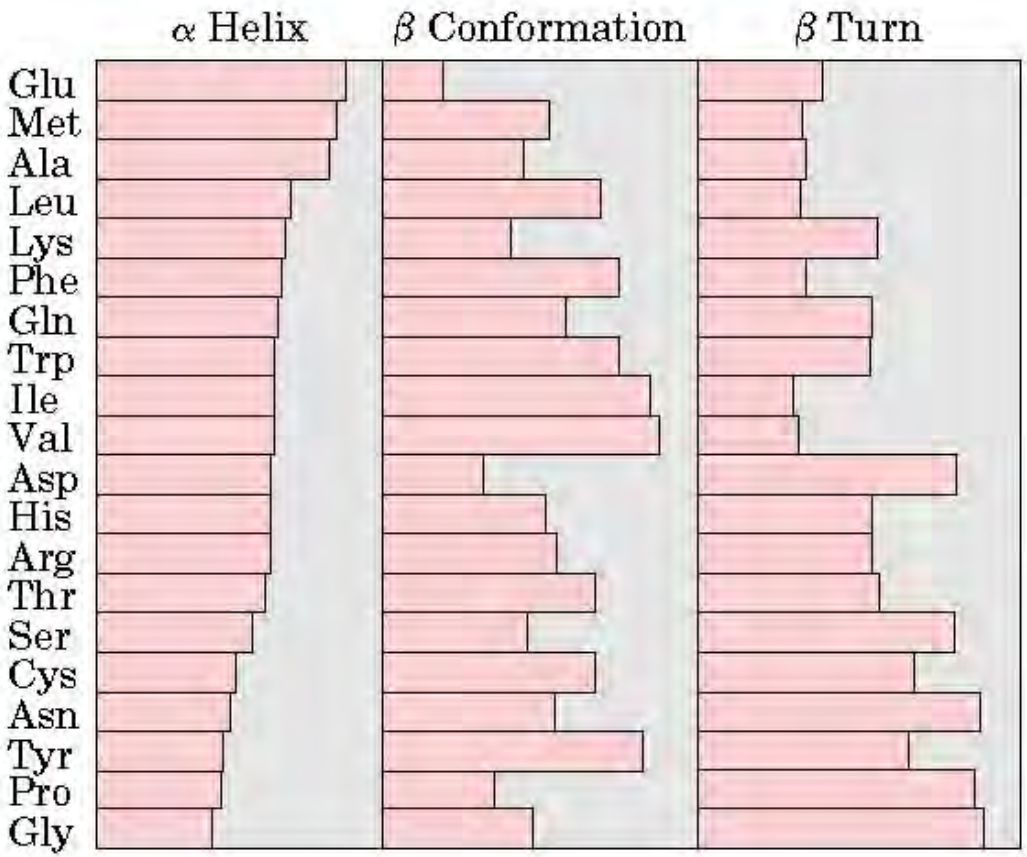
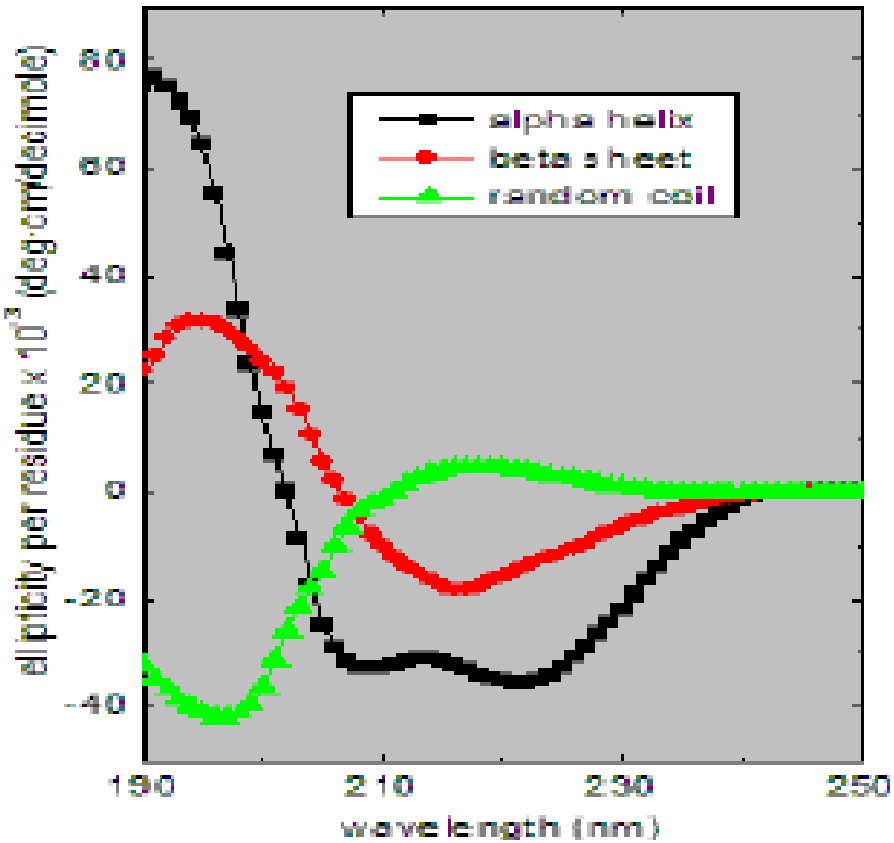


figure 6–10

Relative probabilities that a given amino acid will occur in the three common types of secondary structure.

Optička aktivnost sekundarnih struktura



CD (cirkularni dihroizam) poli-L-lizina

Sadržaj predavanja: Fibrilni proteini

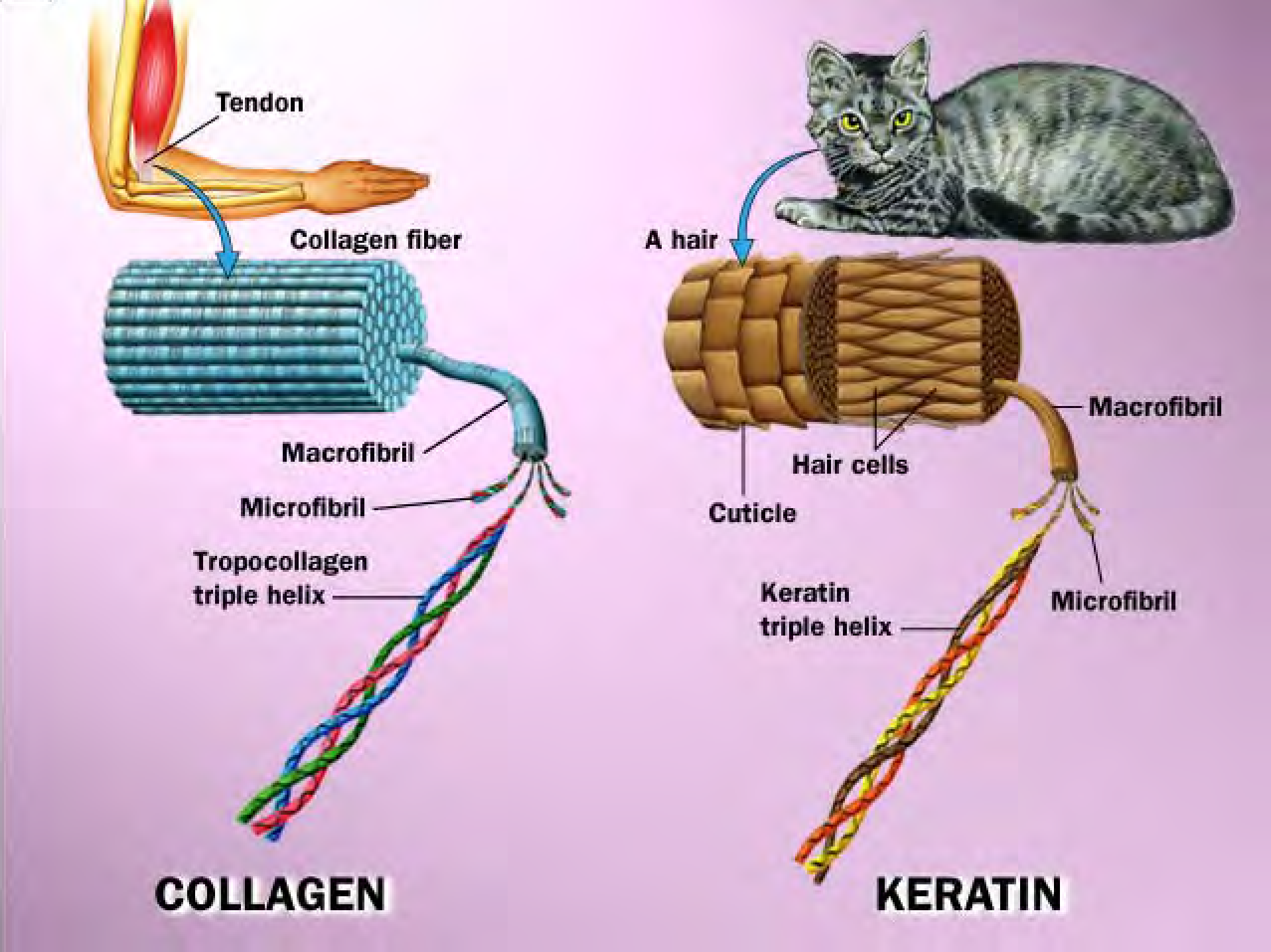
Osnovna struktura, svojstva i funkcija

Primeri:

- α-keratin
- fibroin svile
- kolagen
- elastin

Fibrilni proteini: struktura i funkcija

- Molekuli fibrilnih proteina su izduženi i stvaraju vlakna.
- U molekulu fibrilnih proteina dominiraju sekundarne strukture.
- Imaju strukturnu i zaštitnu ulogu (ekstracelularni matriks, koža, kosa, kosti,...).


Tendon
Collagen fiber
Macrofibril
Microfibril
Tropocollagen
triple helix
COLLAGEN
A hair
Macrofibril
Hair cells
Cuticle
Keratin
triple helix
Microfibril
KERATIN

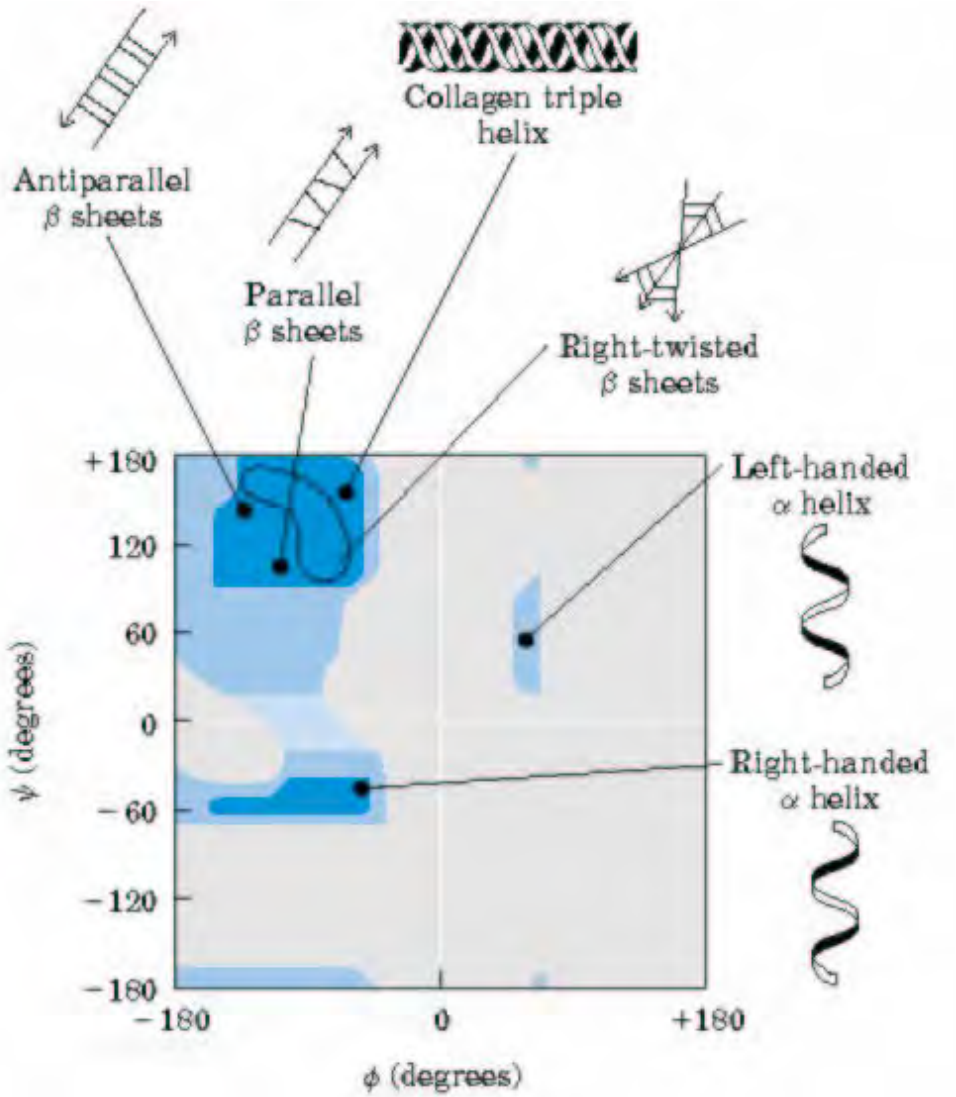
Fibrilni proteini imaju karakterističan aminokiselinski sastav

Tabela 5.2: Poredjenje aminokiselinskog sastava* nekih fibrilnih i globularnih proteina. Istaknute su aminokiseline koje dominiraju u pojedinim fibrilnim proteinima.

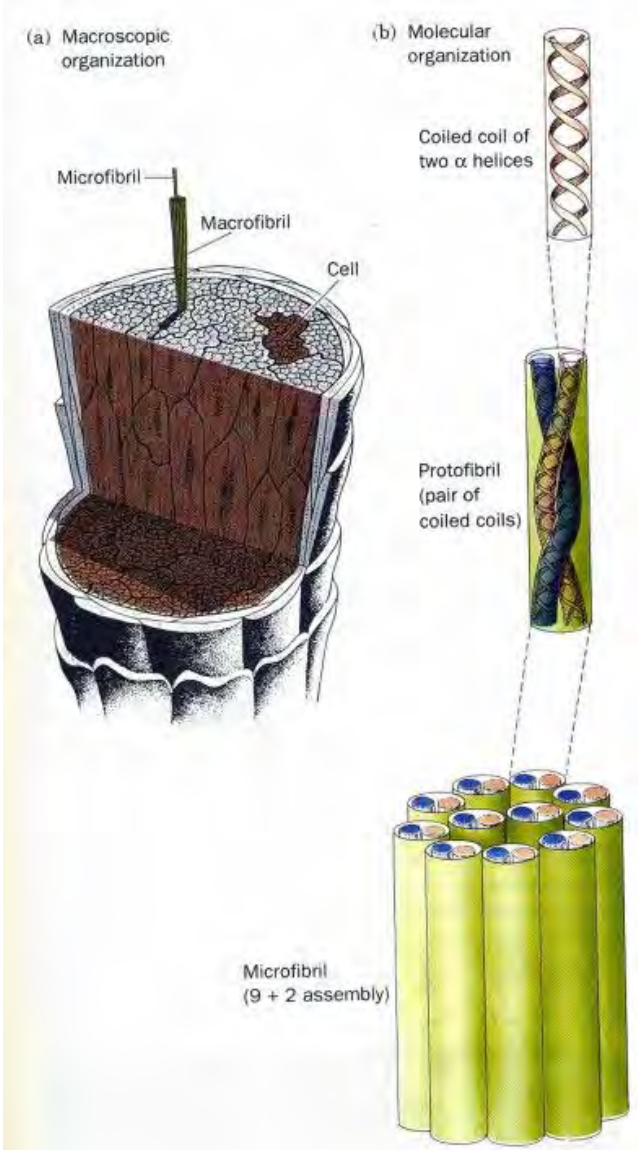
Amino-kiselina	Fibrilni proteini			Globularni proteini	
	Keratin iz vune	Fibroin	Kolagen	Humani hemoglobin	Ribonukleaza govečeta
Ala	5,0	**29,4**	10,7	12,5	9,7
Arg	7,2	0,5	5,0	2,1	3,2
Cys	**11,2**	0,0	0,0	1,1	6,5
Glx	**12,1**	1,0	7,1	5,6	9,7
Gly	8,1	**44,6**	**33,0**	7,0	2,4
His	0,7	0,2	0,4	6,6	3,2
Ile	2,8	0,7	0,9	0,0	2,4
Leu	6,9	0,5	2,4	12,5	1,6
Lys	2,3	0,3	3,4	7,7	8,1
Met	0,5	0,0	0,8	1,1	3,2
Phe	2,5	0,5	1,2	5,2	2,4
Pro	7,5	0,3	**21,6**	4,9	3,2
Ser	**10,2**	**12,2**	4,3	5,6	12,1
Thr	6,5	0,9	2,0	5,6	8,1
Trp	1,2	0,2	0,0	1,1	0,0
Tyr	4,2	5,2	0,4	2,1	4,8
Val	5,1	2,2	2,3	10,8	7,3

*Sadržaj aminokiselina dat je kao molski %

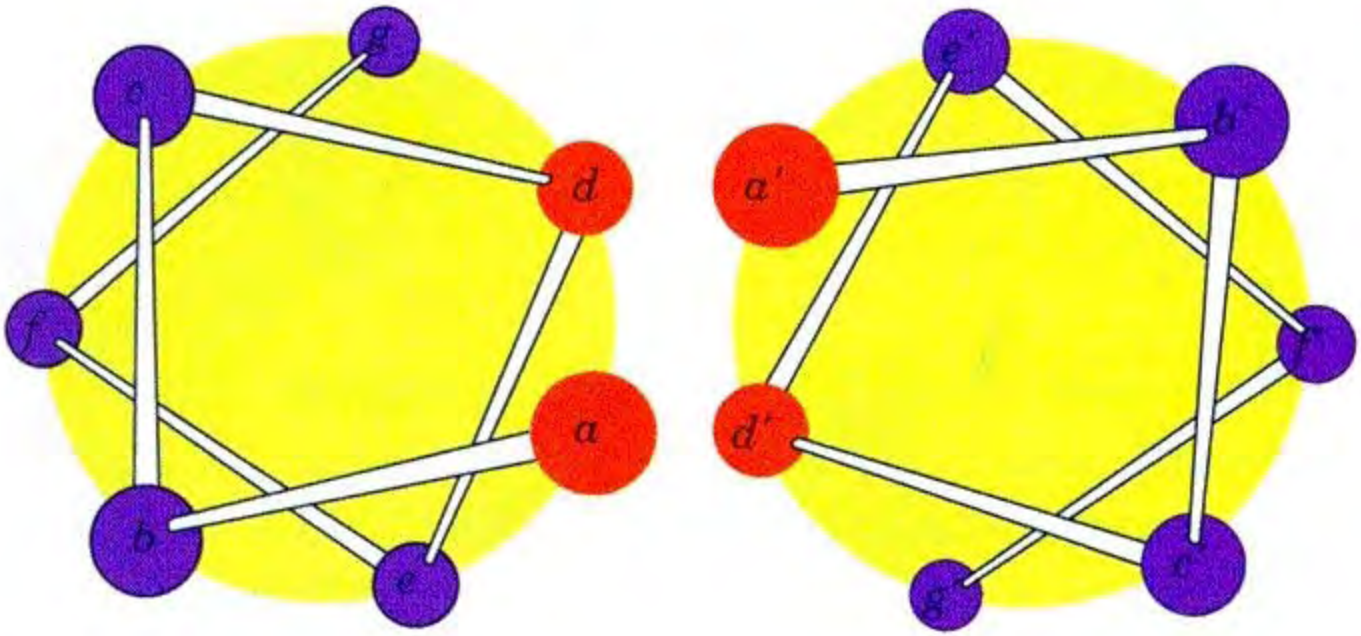
U fibrilnim proteinima dominiraju sekundarne strukture



α keratin: heliks od α heliksa

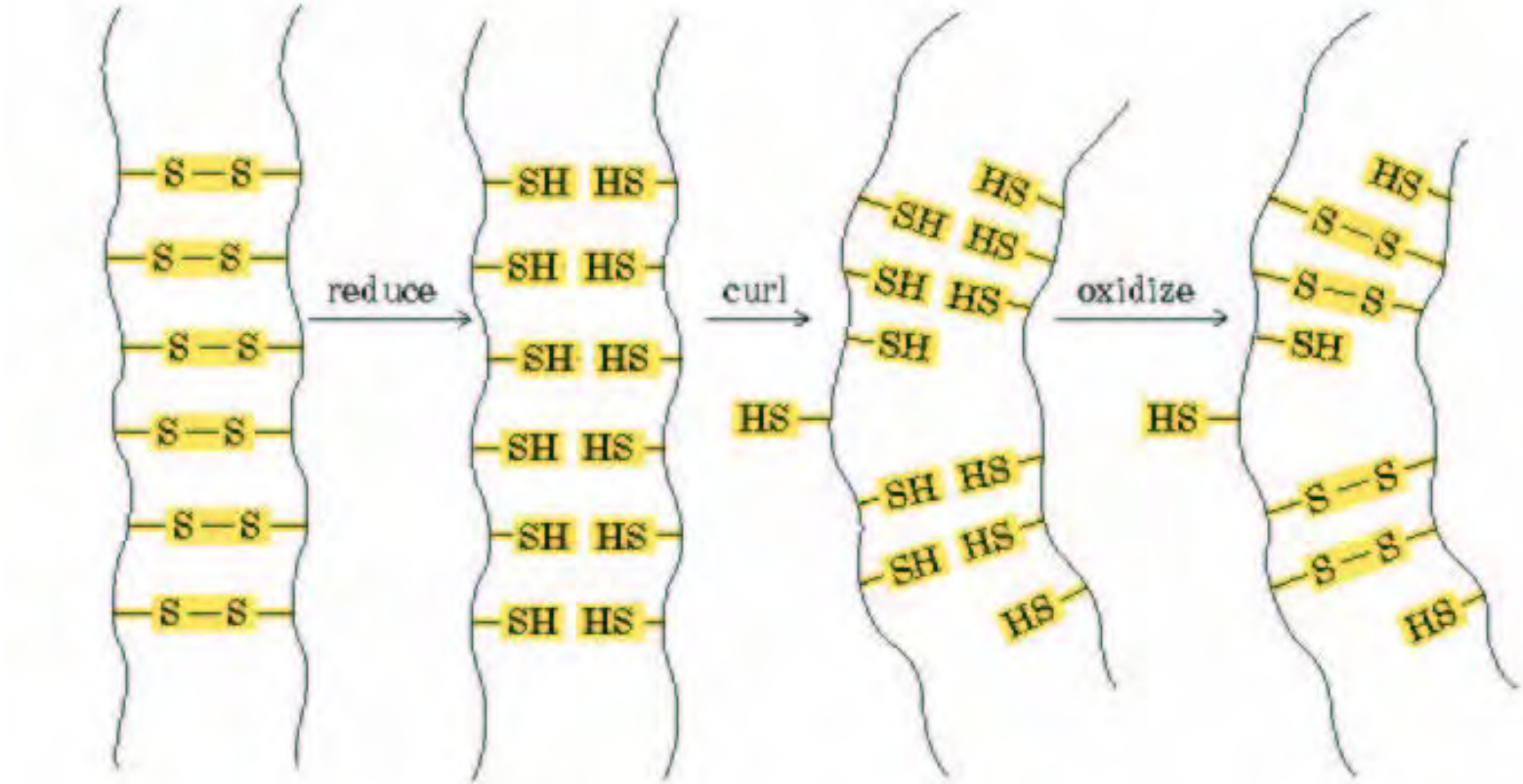


Dodirne površine među α heliksima u keratinu su nepolarne!

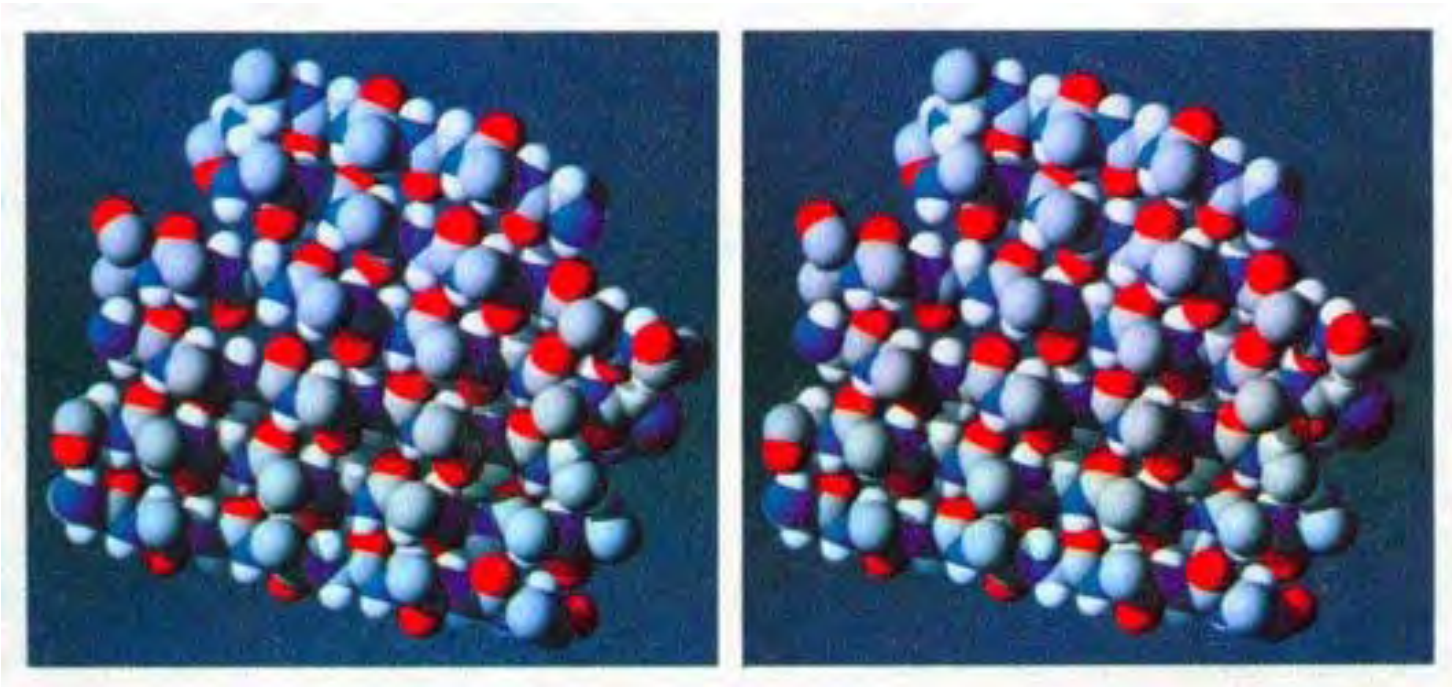


(-A-B-C-D-E-F-G-)n | **NEPOLARNE AK** | **AK GRADITELJI HELIKSA**

“Minival”: permanentno uvijanje kose

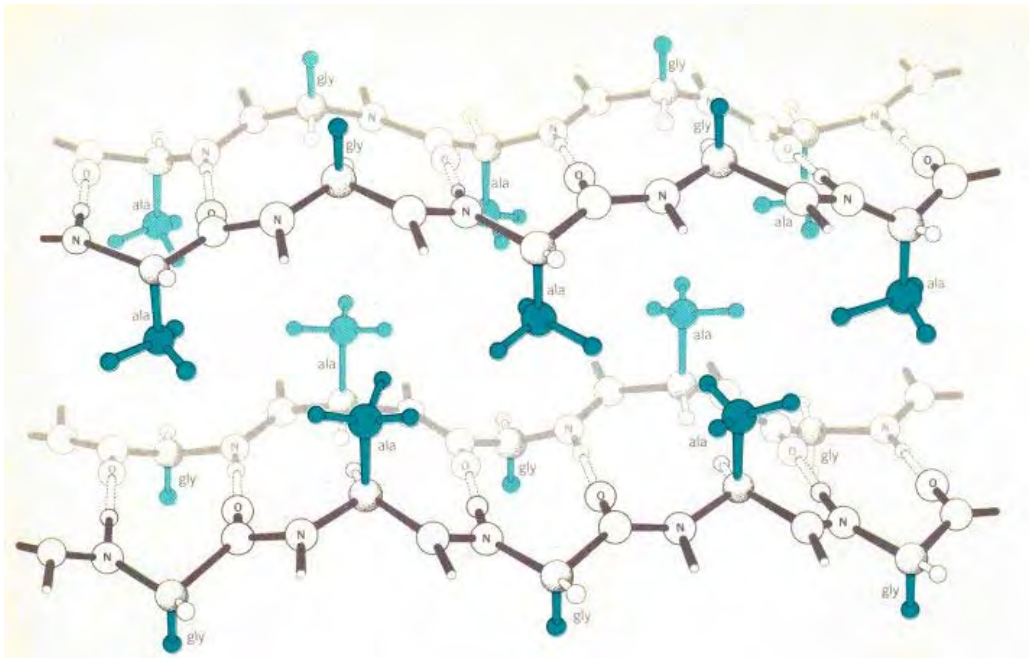


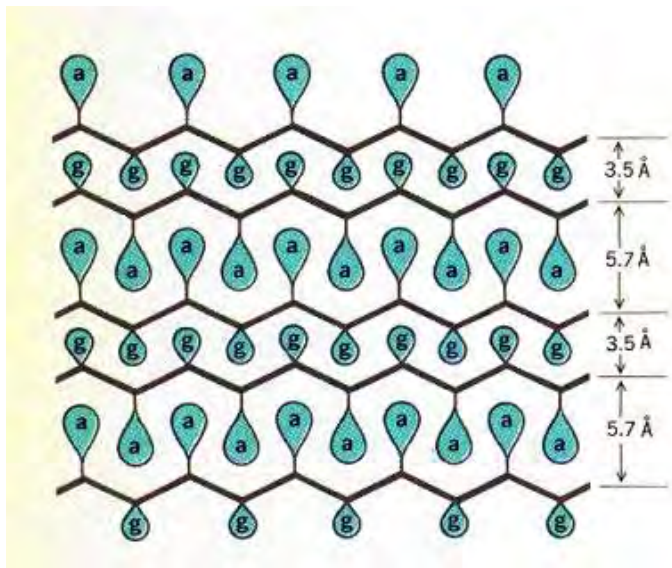
Fibroin svile: ß pločica



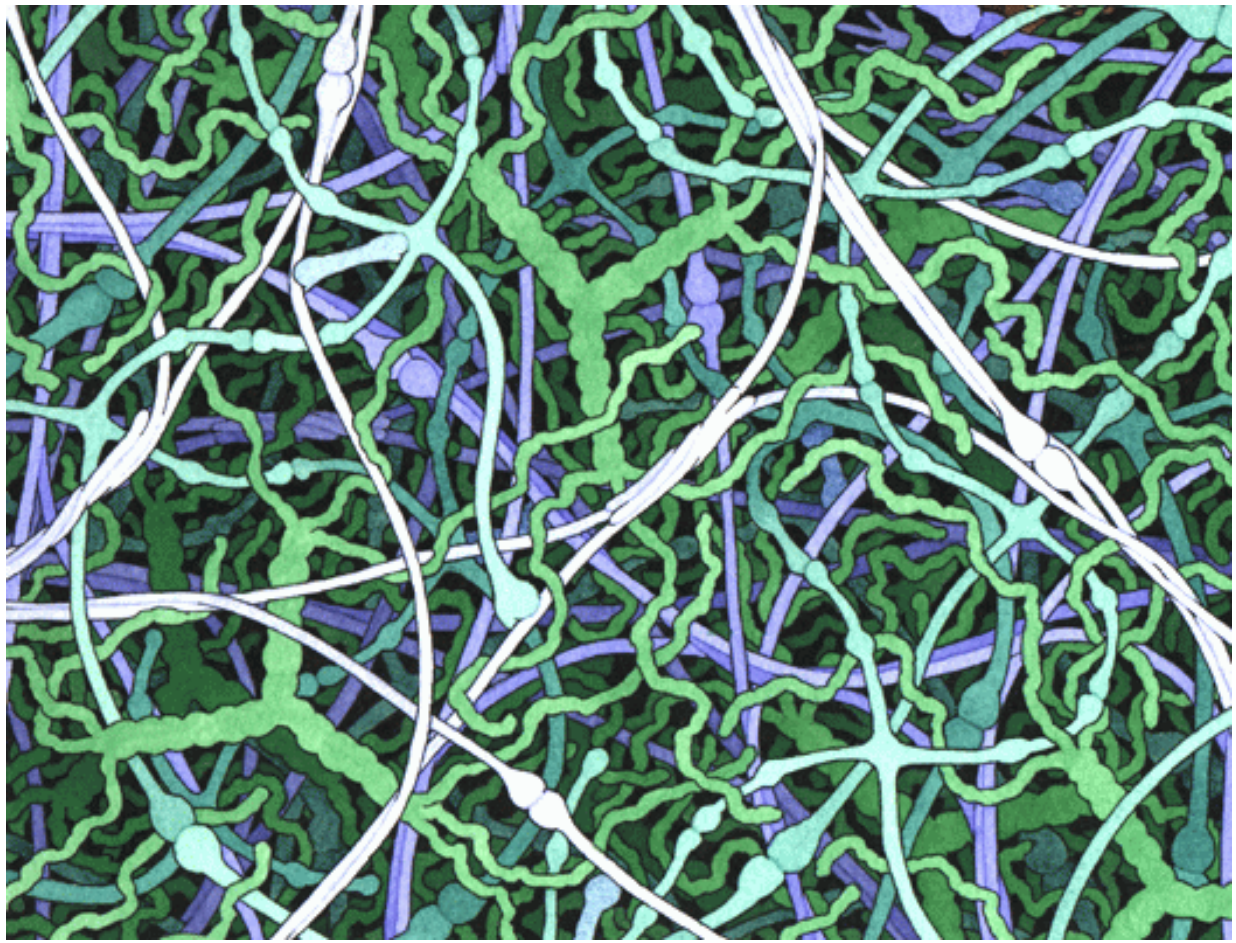
Pakovanje ß pločica u fibrionu svile

(-Gly-Ser-Gly-Ala-Gly-Ala-)n





Kolagen



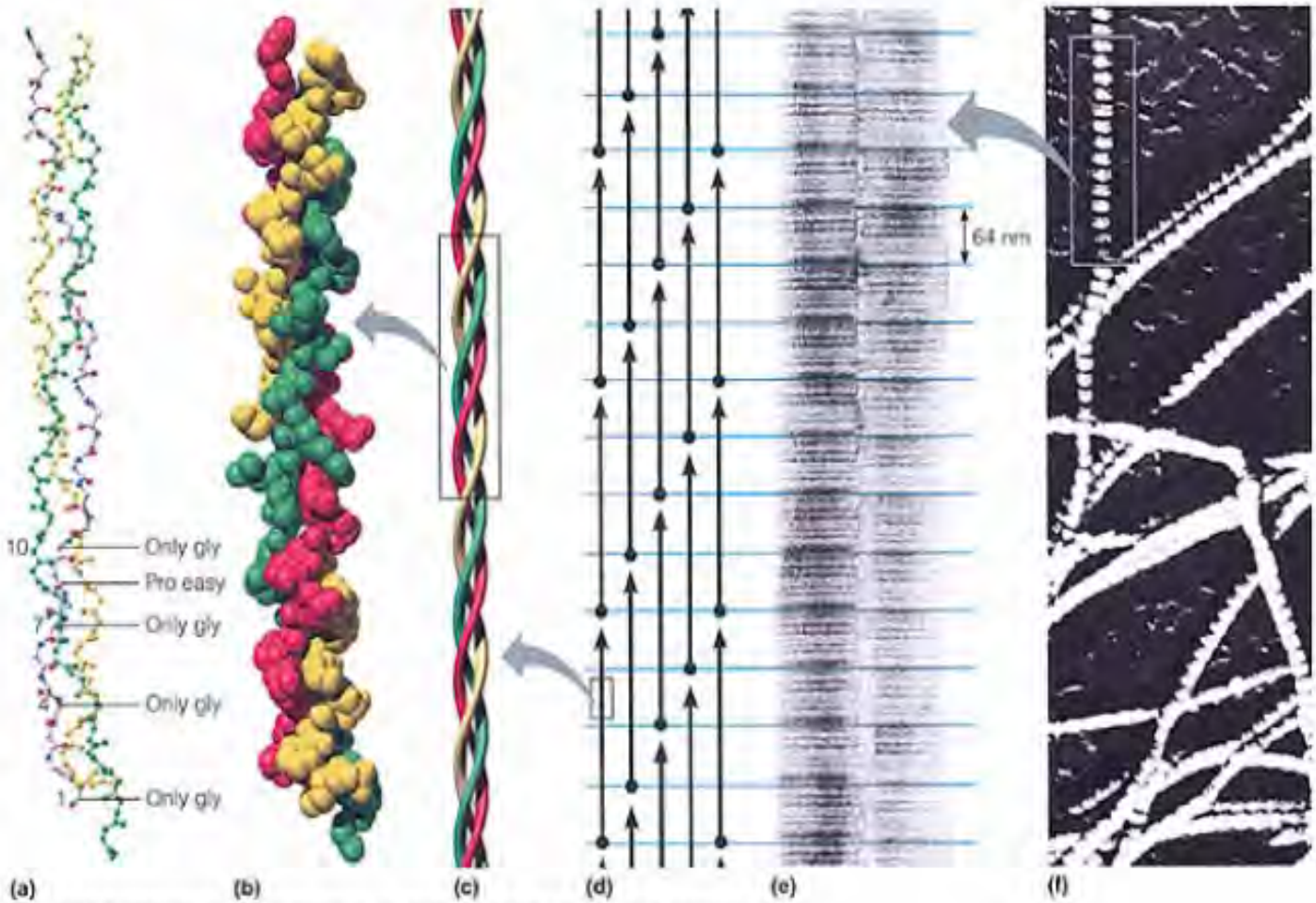
Kolagen u koži

http://www.rcsb.org/pdb/molecules/molecule_list.html

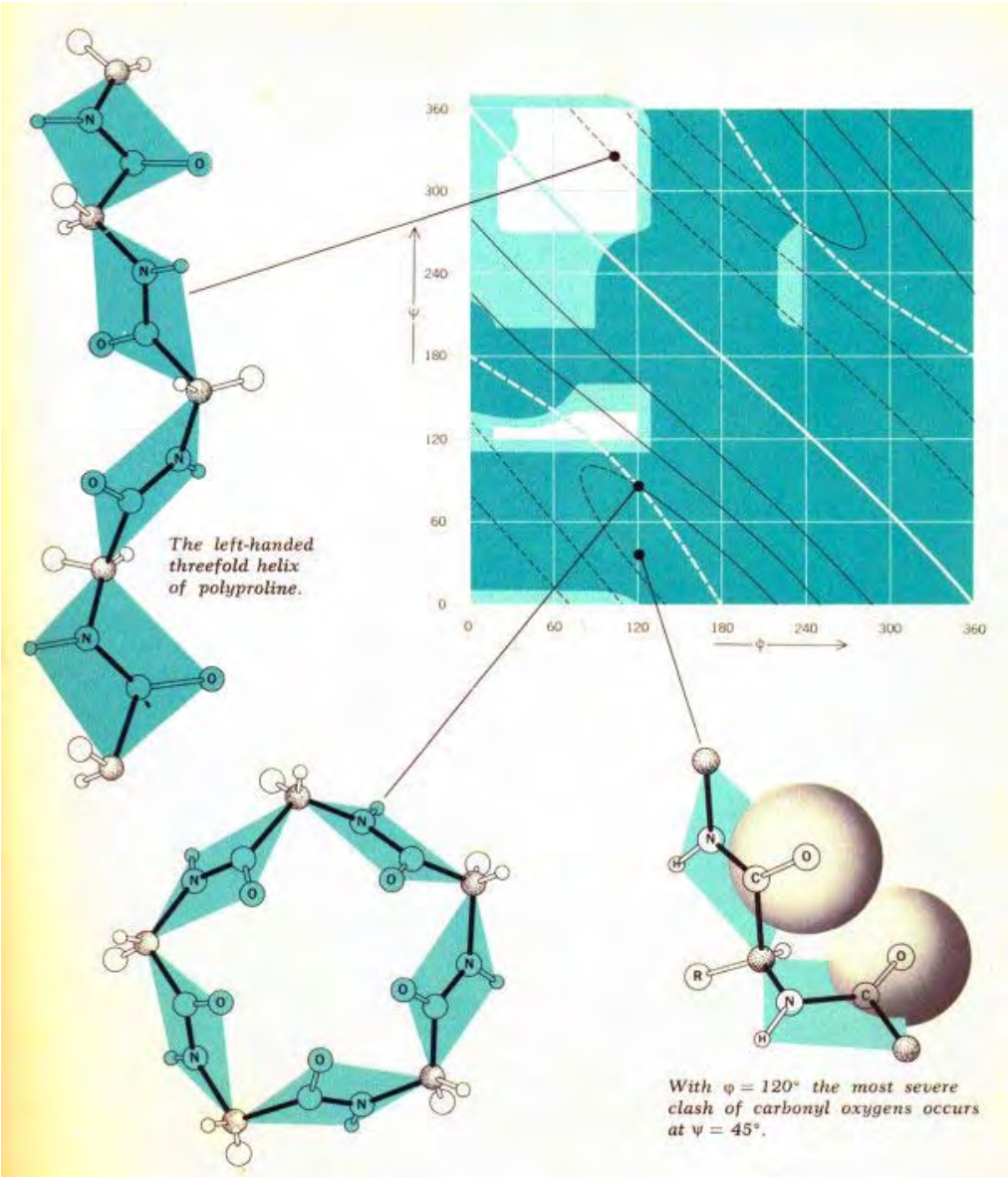
Structure of Collagen Fibers

Collagen is the most abundant vertebrate protein and the major stress-bearing component of connective tissue (bone, teeth, cartilage, tendon) and fibrous matrix of skin and blood vessels.

- 3 intertwined left-handed helices
- 3.3 residues/turn
- Repeating Gly-X-Y (X often Pro, Y often Pro or hydroxyPro)

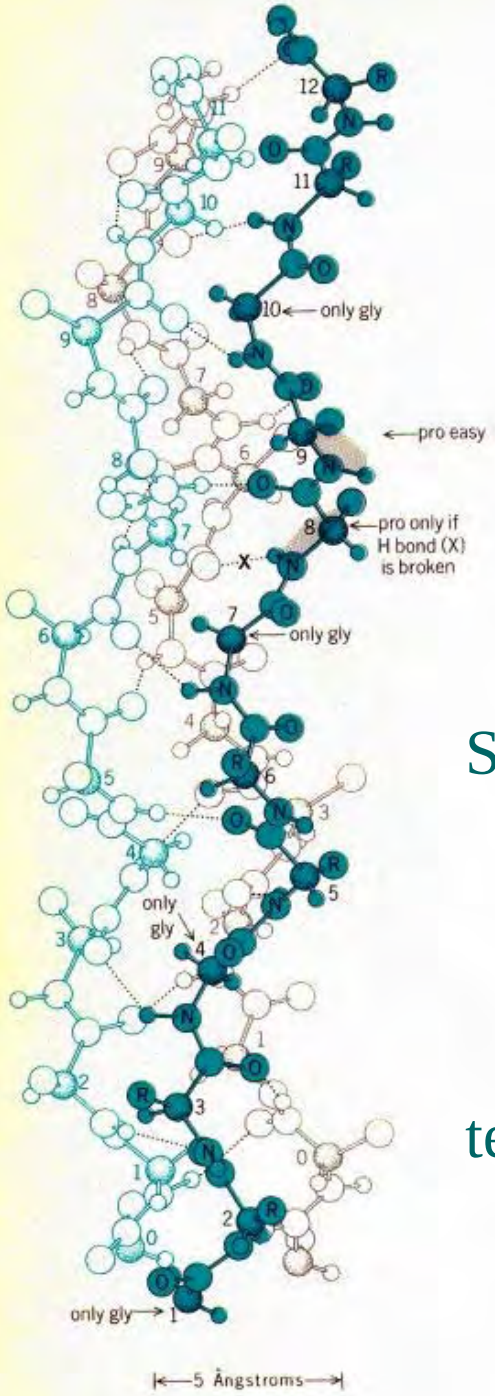


Levi heliks poliprolina (glicina)



Kolagen: trostruki heliks

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



Sekundarna struktura:

- levi heliks
  - 3 ostatka/zavoj
  - 0.9 nm/zavoj
  - nema H-veza unutar lanca

tercijerna/kvaternarna struktura

- 3 niza formiraju desni superheliks

The Collagen Triple Helix (Tropocollagen)

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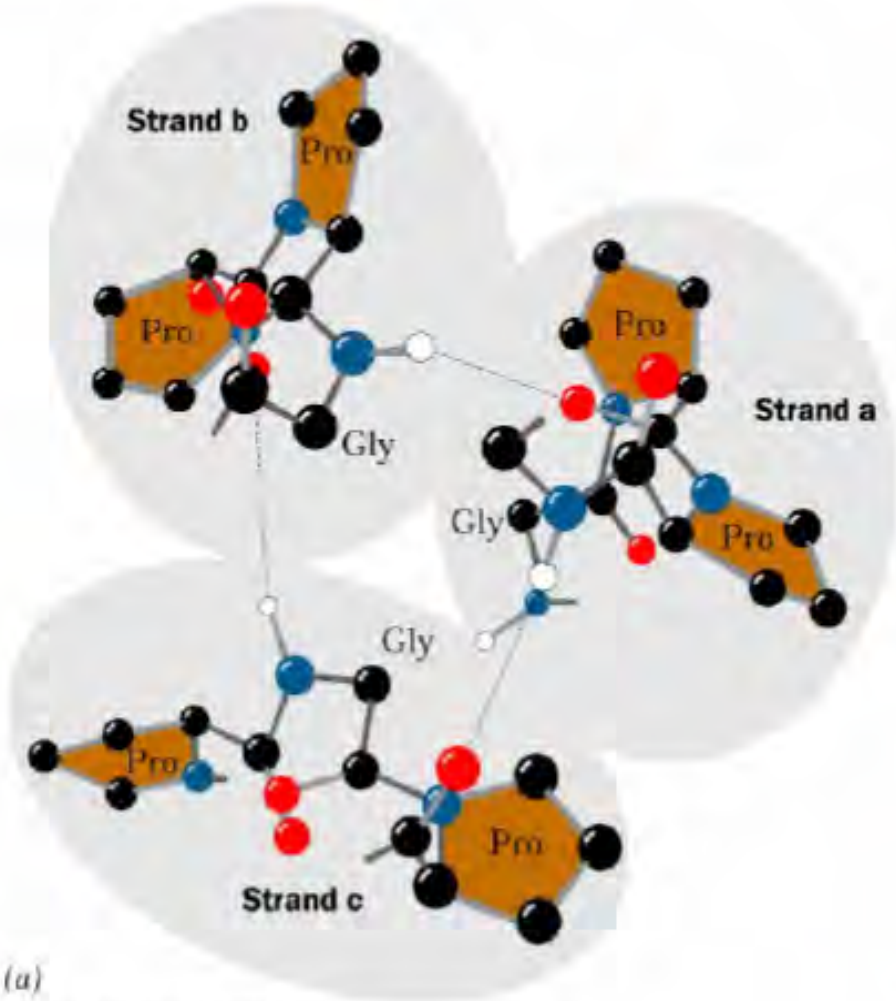


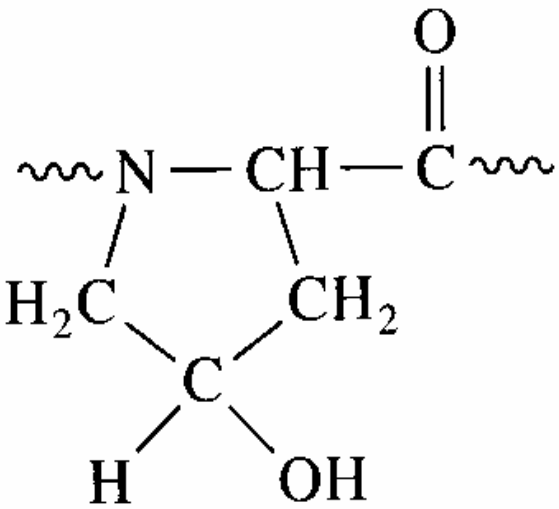
Interactions between strands

G.N. Ramachandran, 1955

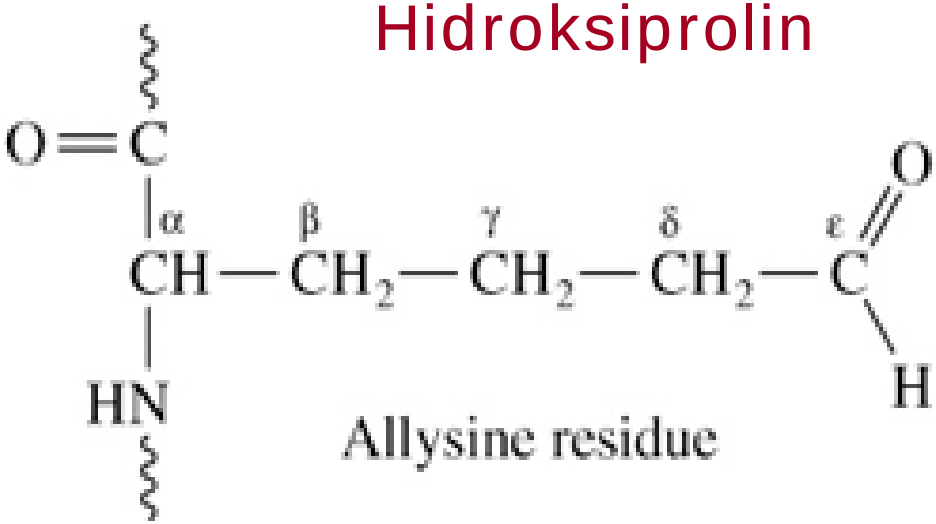
Courtesy of Helen Berman, Rutgers University

Tropocollagen with Gly→Ala substitution (yellow)

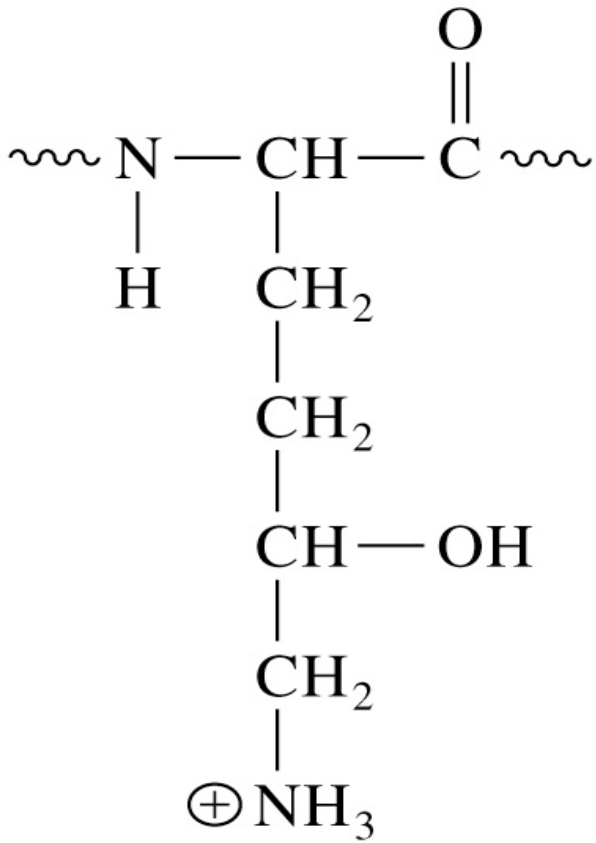
Post-translacione modifikacije u kolagenu



Hidroksiprolin

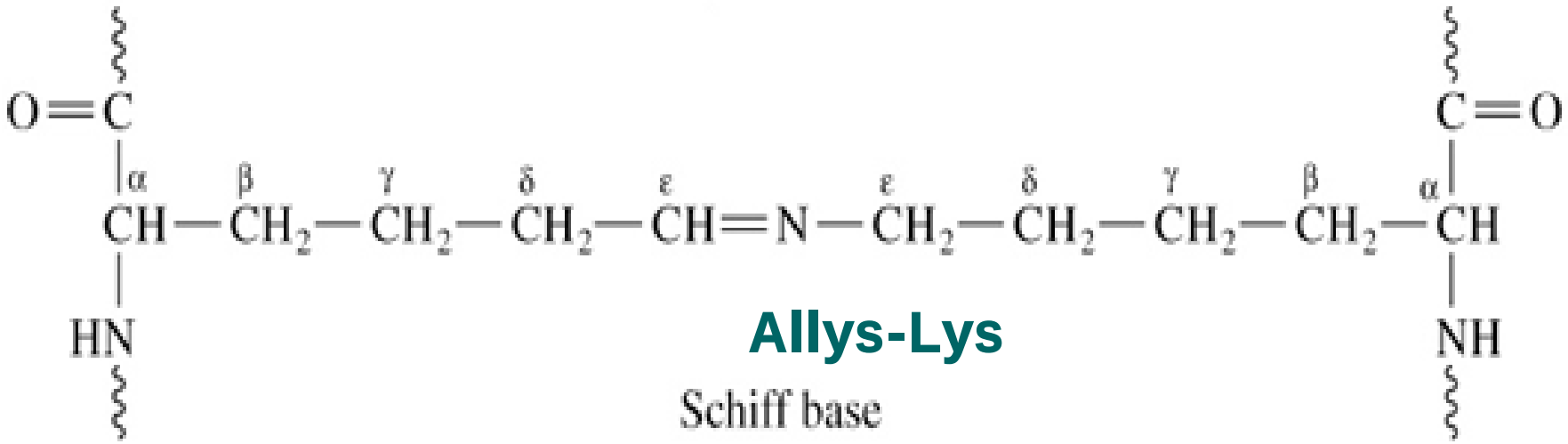


Allysine residue



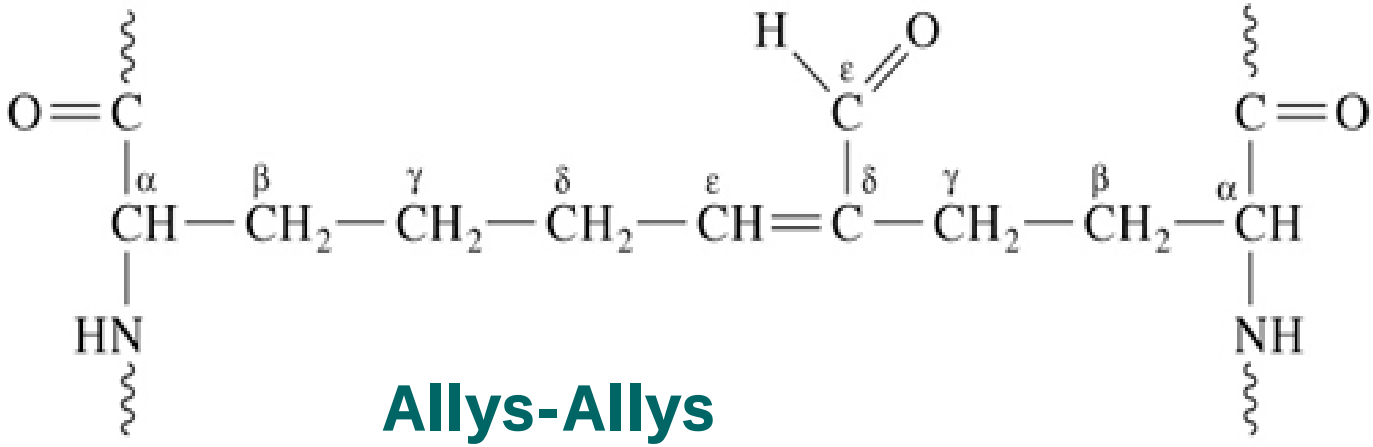
Hidroksilizin

Kovelentno povezivanje nizova u kolagenu



Allys-Lys

Schiff base



Allys-Allys

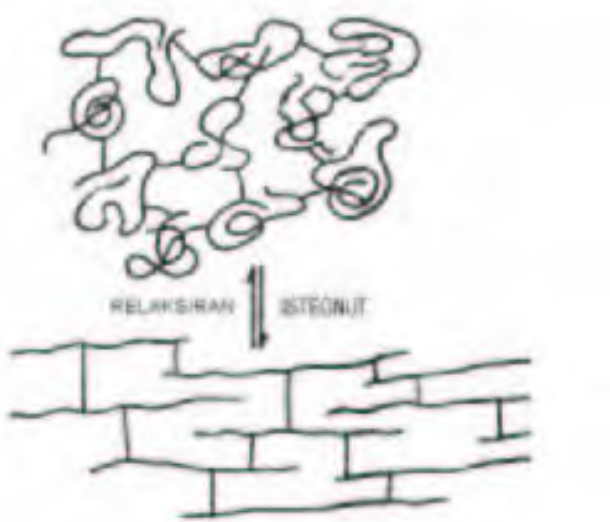
Šta kolagenu daje čvrstinu?

- Vodonično vezivanje medju nizovima pomoću hidroksi-Pro.
- Agregacija trostrukih heliksa daje vlakna.
- Kovalentno povezivanje nizova.

Elastin nema određene sekundarne strukture

Aminokiselinski sastav: najviše Gly, Ala i Val,
malo Pro, hidroksiprolina i hidroksilizina

Gde se nalazi elastin?



Slika 5.9: Povezani neuredjeni monomerni nizovi elastina grade trodimenzionalnu mrežu (matriks) koja može da bude u istegnutom i relaksiranom obliku.