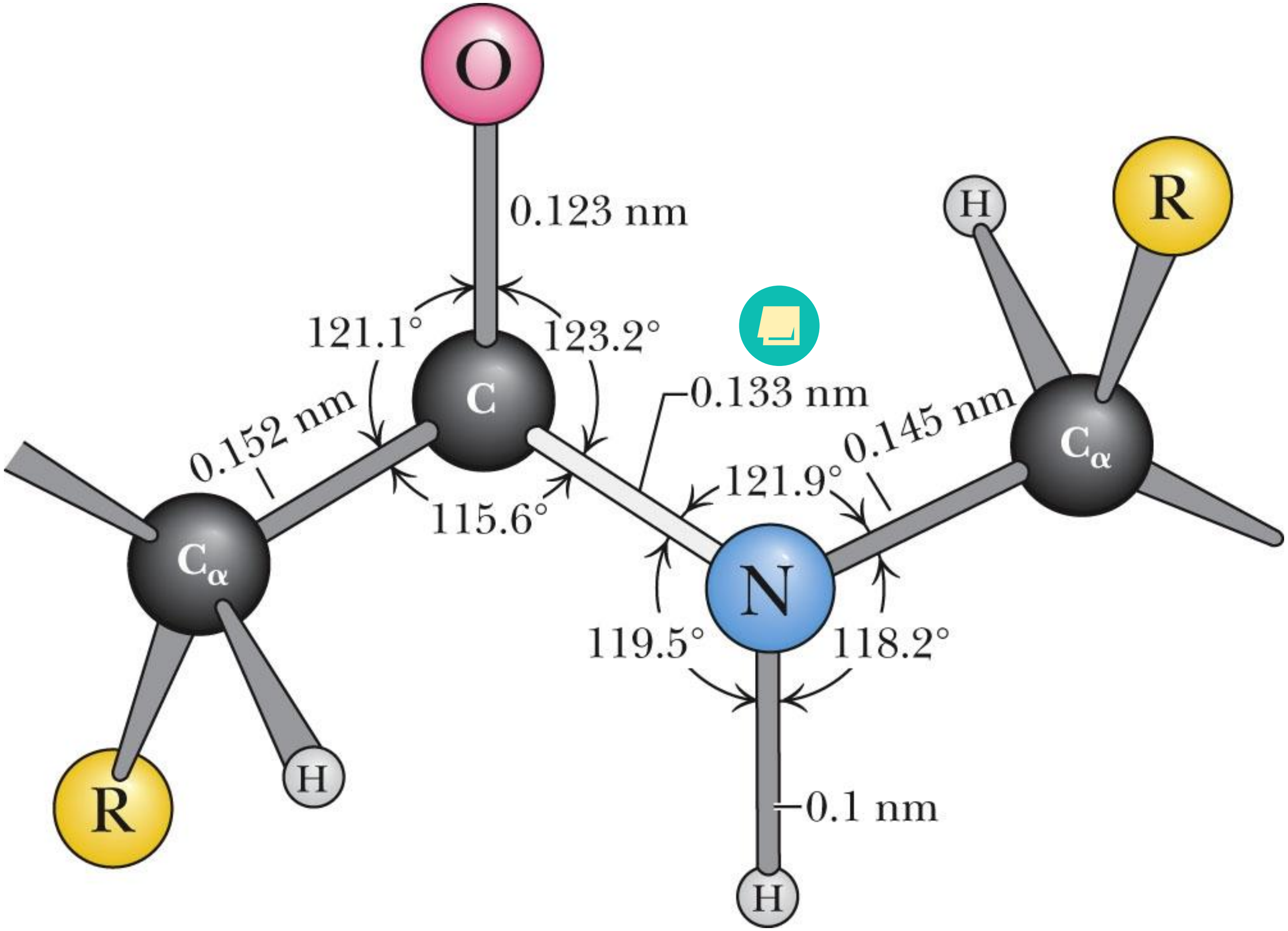
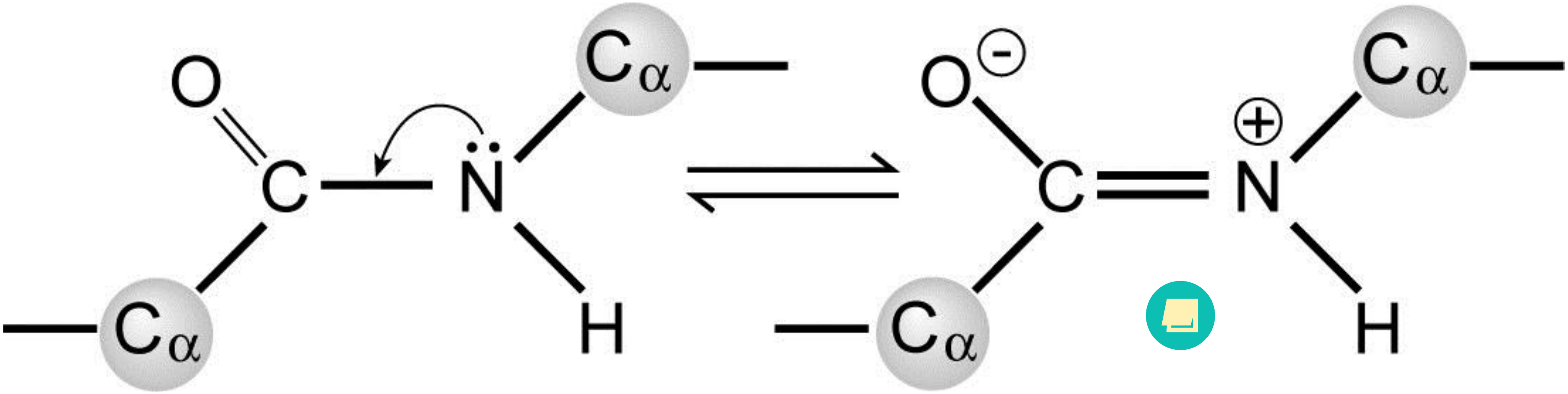
Lecture #4

- Peptide bond
- phi, psi angles
- Ramachandran plot
- Fibrous structural proteins
  - silk
  - keratins
  - collagen

Trans conformation of the peptide (amide) bond



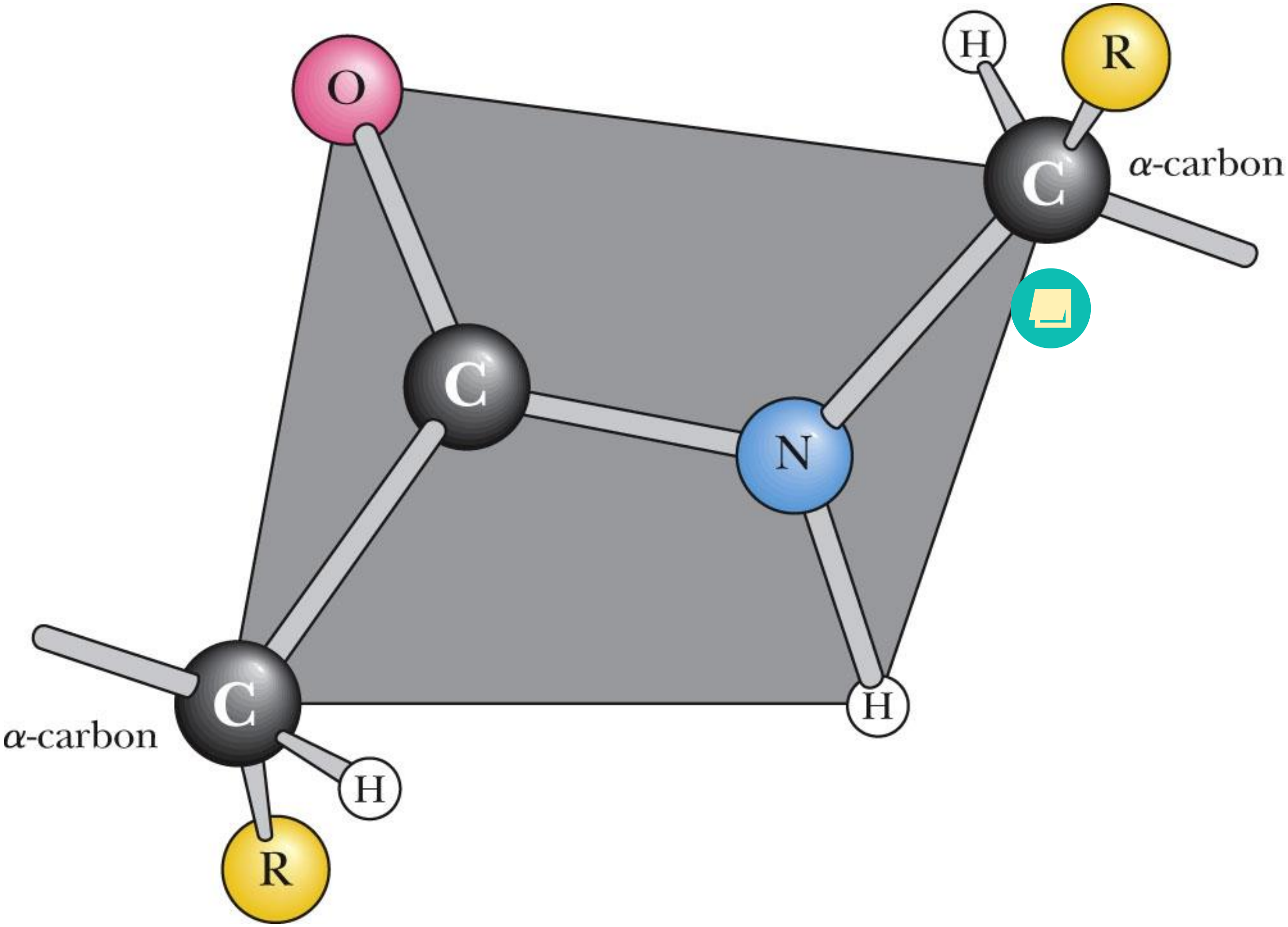
Resonance structures give C-N bond partial double bond character



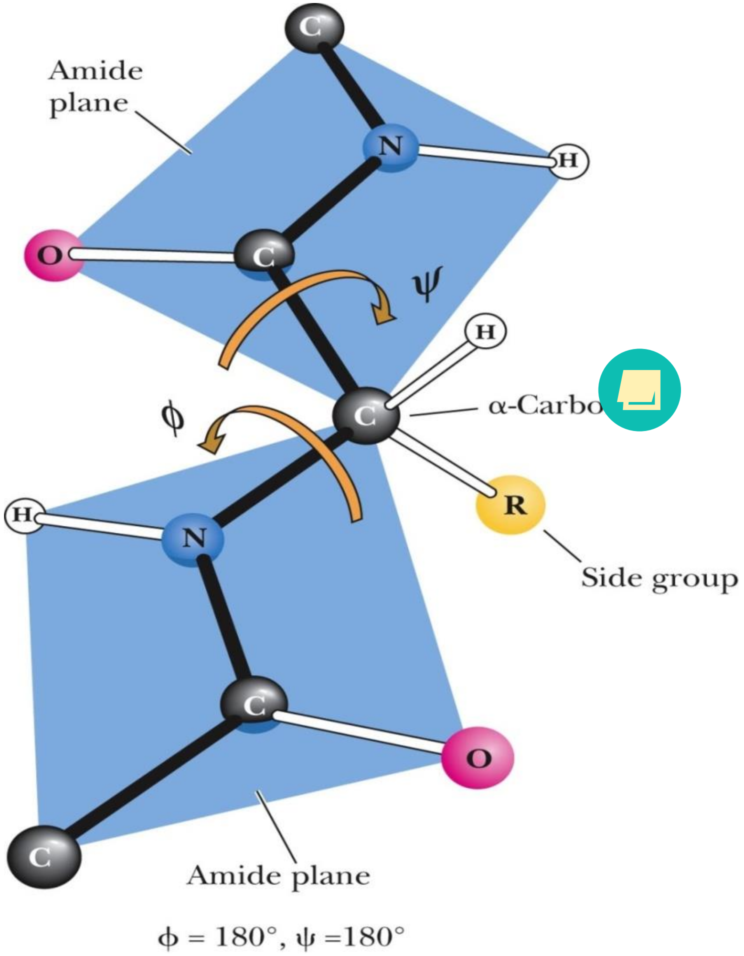
The peptide bond

- The peptide bond is planar and trans between carbonyl O and amide H
- Dihedral angle ω about the peptide C-N bond is fixed at 180°

The peptide bond is planar



The peptide bond planes



Backbone dihedral angles of rotation

- ϕ (phi) is the angle around the N-C_α bond
- ψ (psi) is the angle around the C_α-C=O bond
- ω (omega) is the angle around the C-N (peptide) bond
- χ (chi) angle describes side chain rotation

Protein backbone angles

- The dihedral angle at each backbone bond determines the actual three-dimensional progress of the protein chain.
- Helices and sheets have characteristic backbone angles.

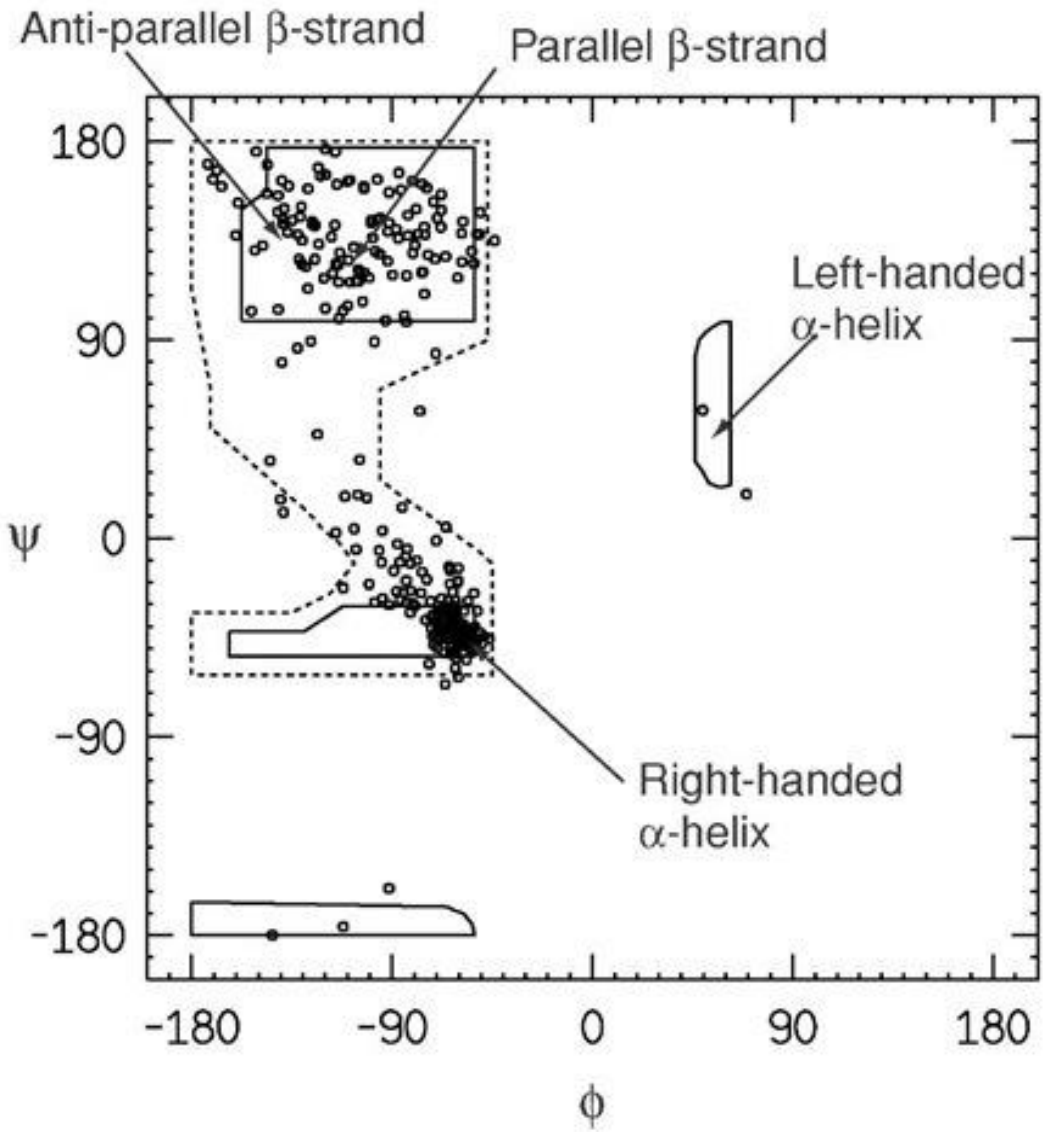
α-helix: (ϕ, ψ)

$= (-\ 60^{o}, -\ 50^{o})$

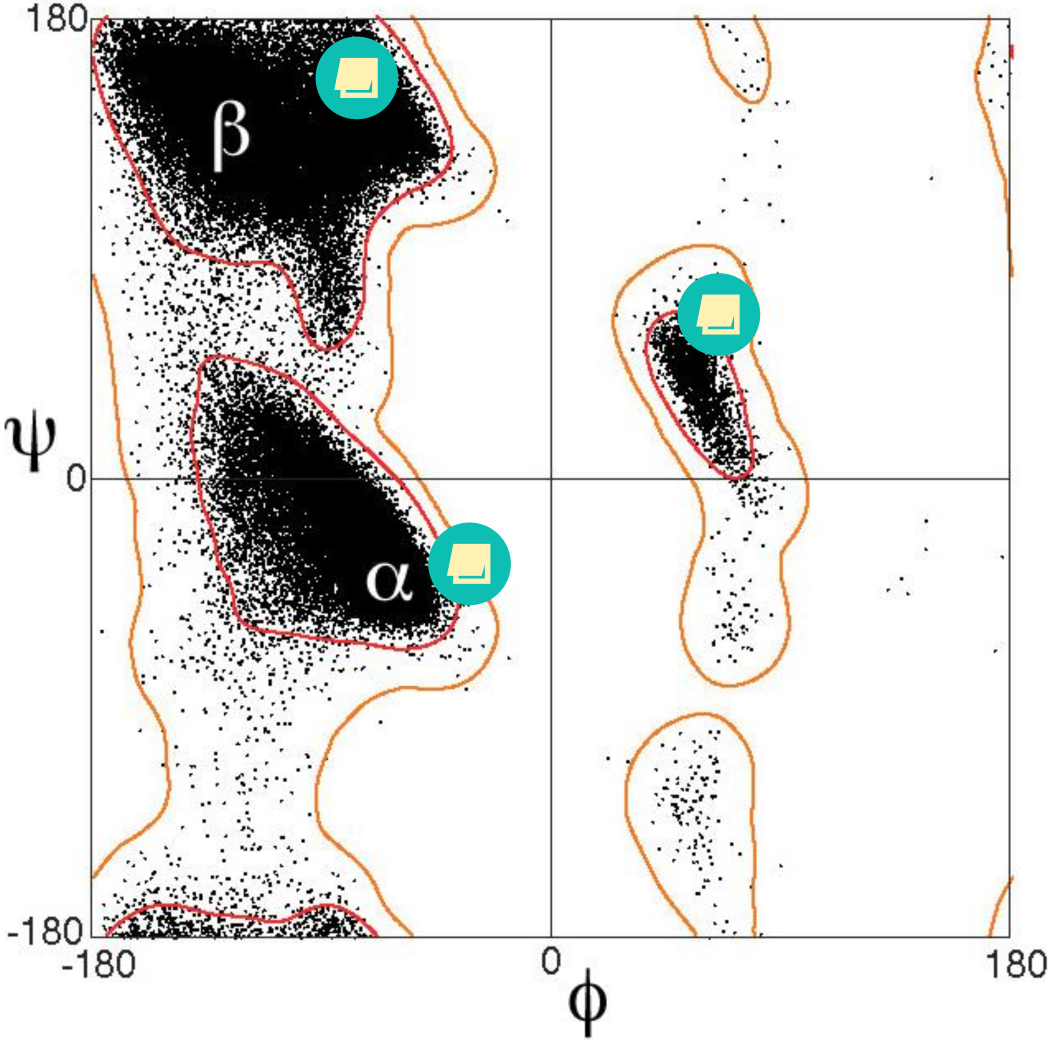
β-sheet: (ϕ, ψ)

$= (-\ 140^{o}, +\ 135^{o})$

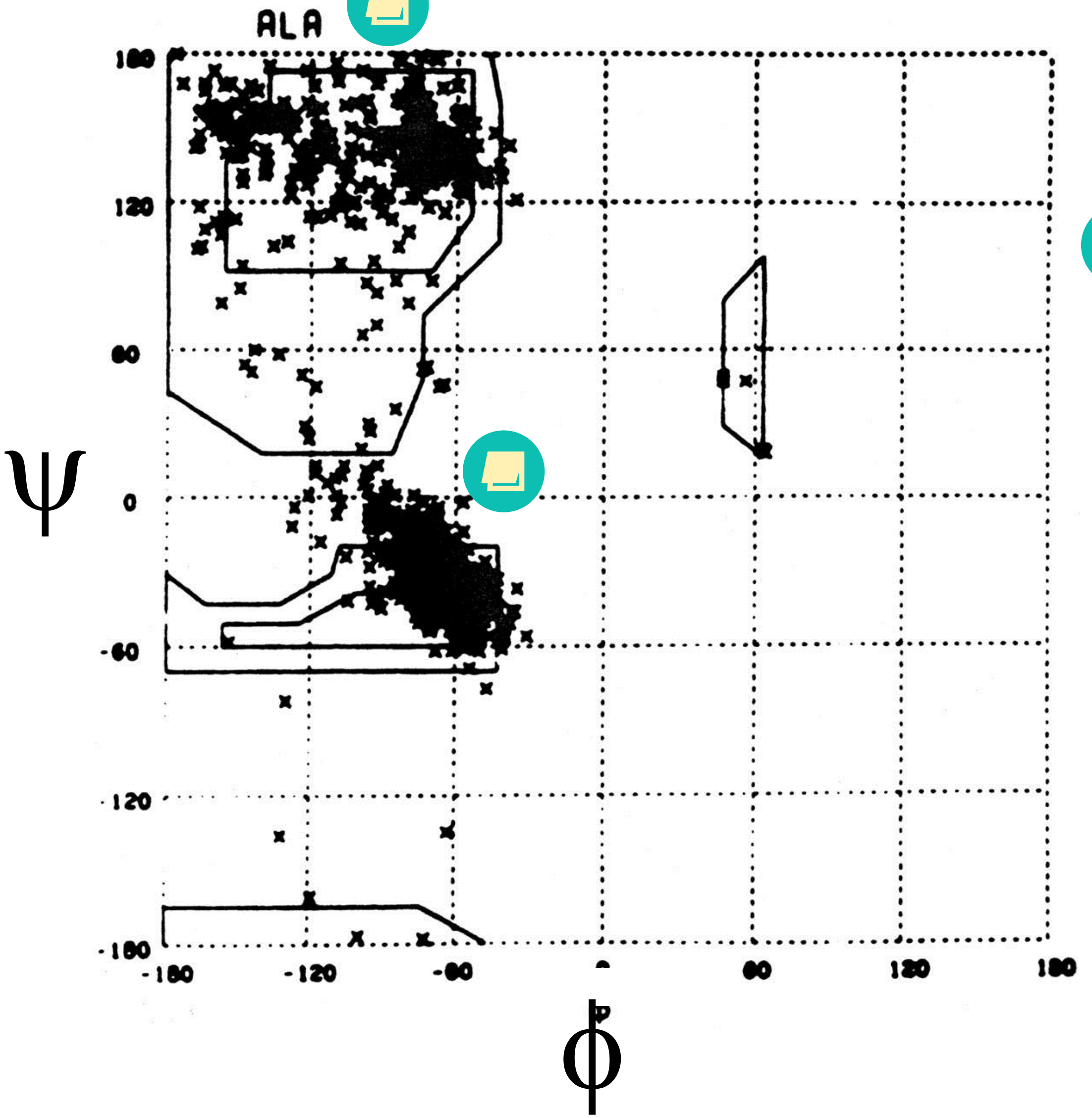
Ramachandran Plot



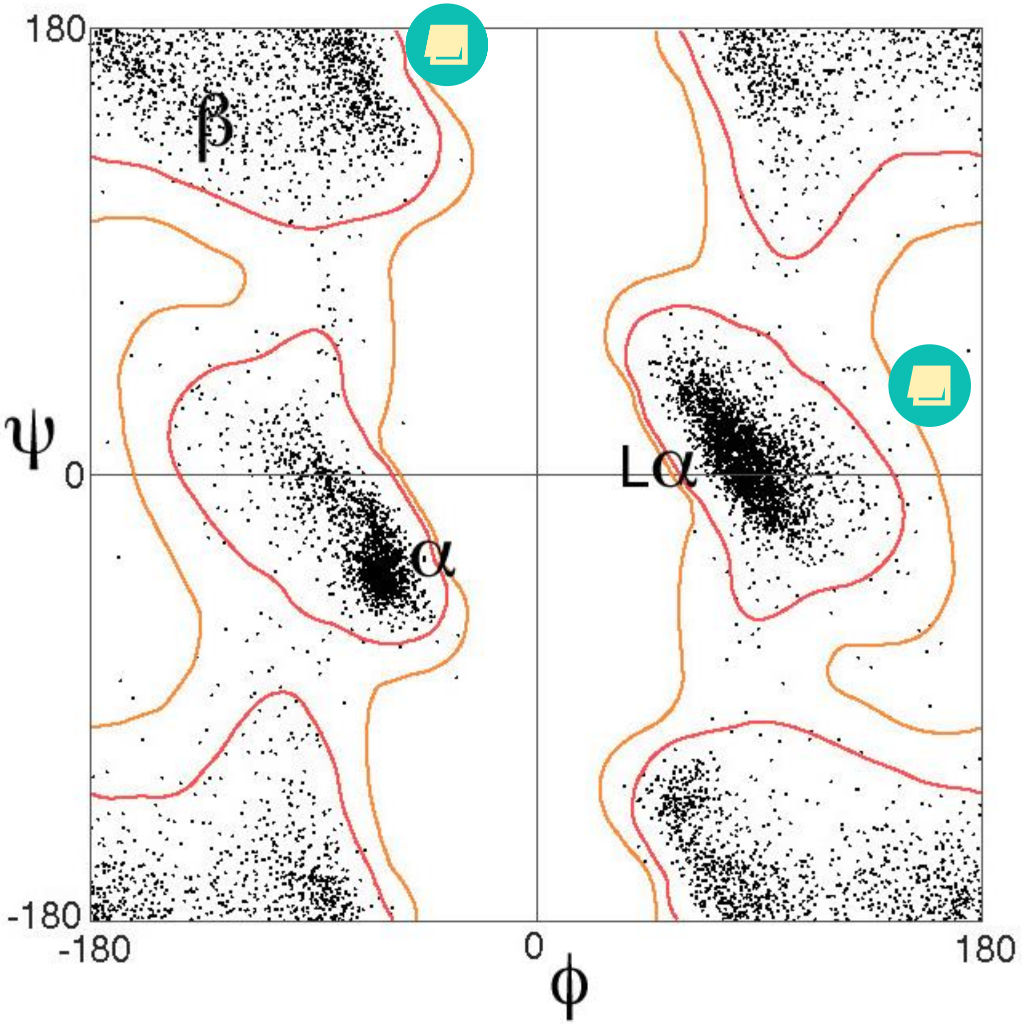
Ramachandran plot of all residues



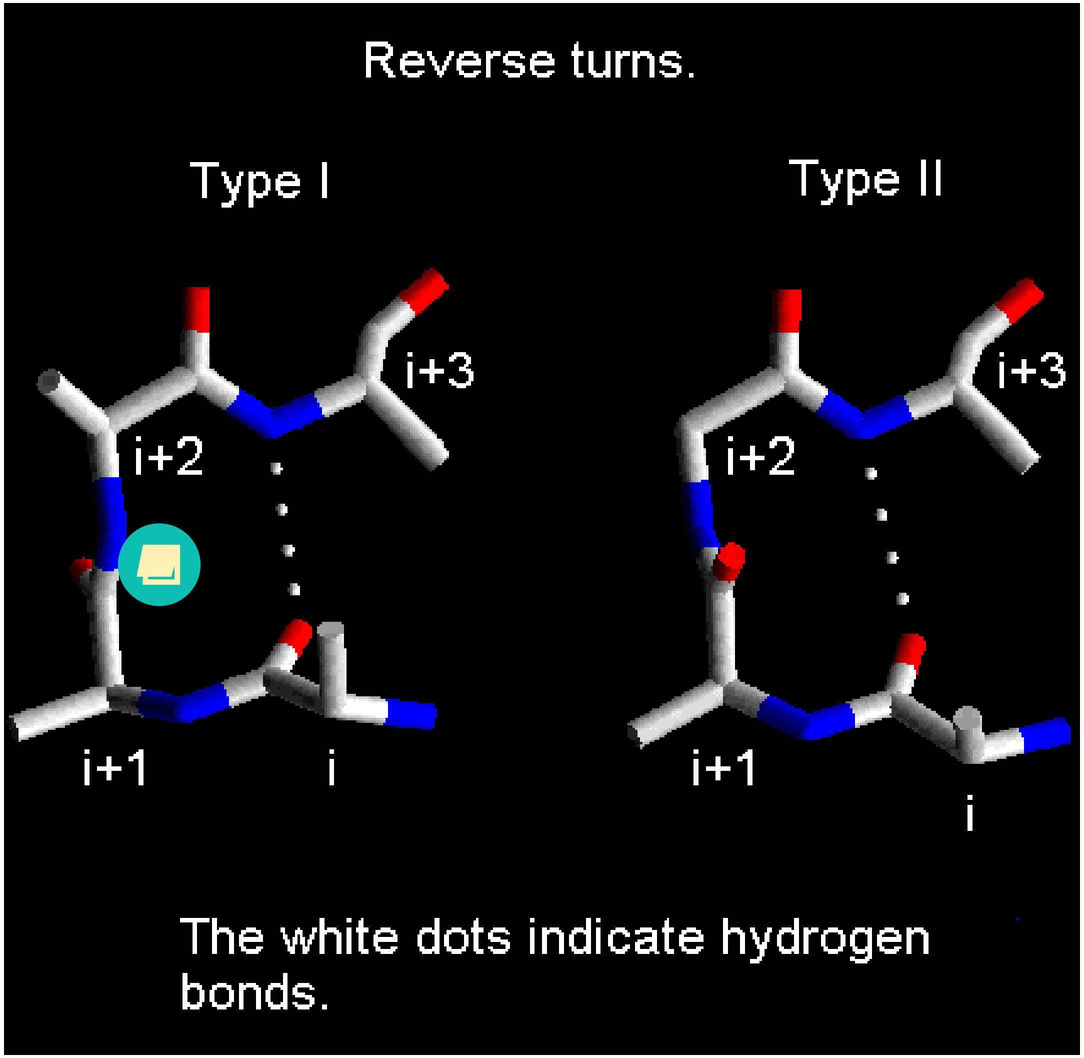
Ramachandran plot of alanine residues in proteins



Ramachandran plot of glycine residues



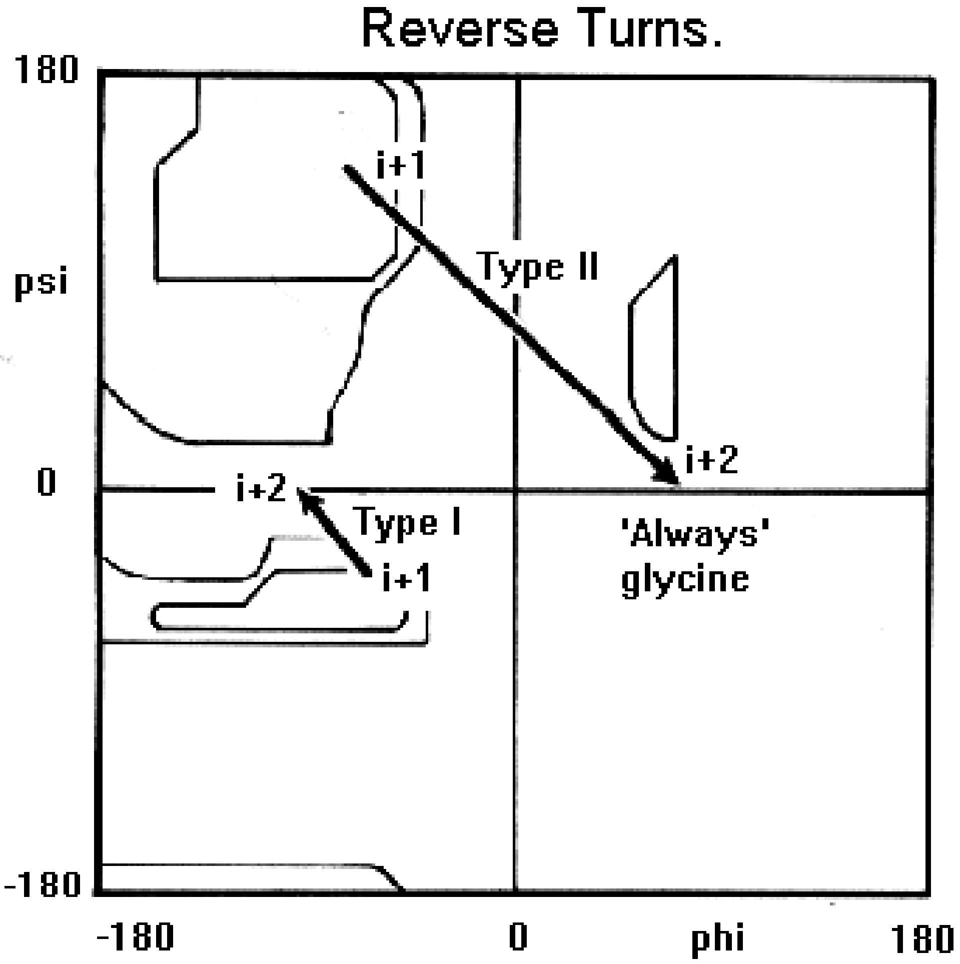
Reverse (β-)turns



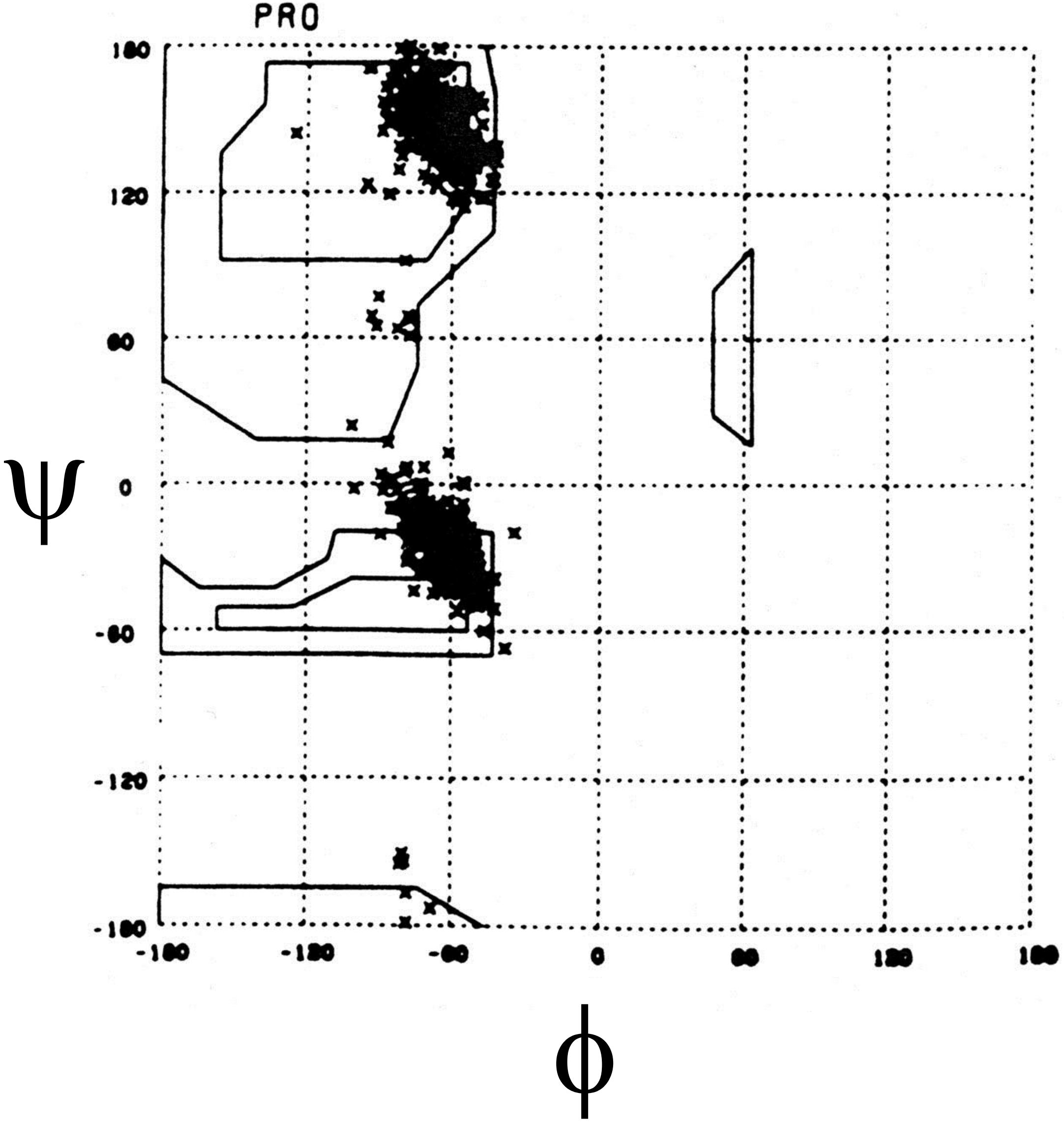
Reverse turns.

The white dots indicate hydrogen bonds.

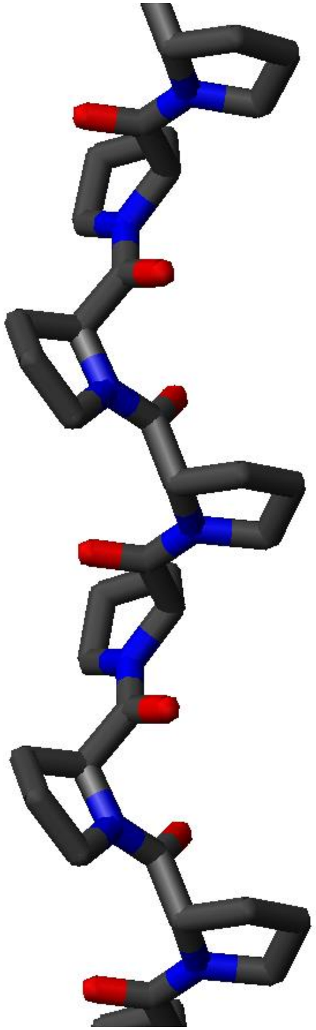
Ramachandran plot of turn residues



Ramachandran plot of proline residues in proteins



Poly-proline helix



Composition to sequence to structure to function

- **Fibrous proteins (silk, wool, collagen)**
- **Structural proteins within cells (cytoskeleton)**
- **Enzymes (globular proteins)**
- **Membrane proteins (transporters, channels, receptors)**

Residue compositions of fibrous proteins

	Gly	Ala	Ser	Glu + Gln	Cys	Pro + Hyp*
Silk	44.6	29.4	12.2	1.0	….	.3
Wool	8.1	5.0	10.2	12.1	11.2	7.5
Collagen	33.0	10.7	4.3	7.1	….	12.2 +9.4*

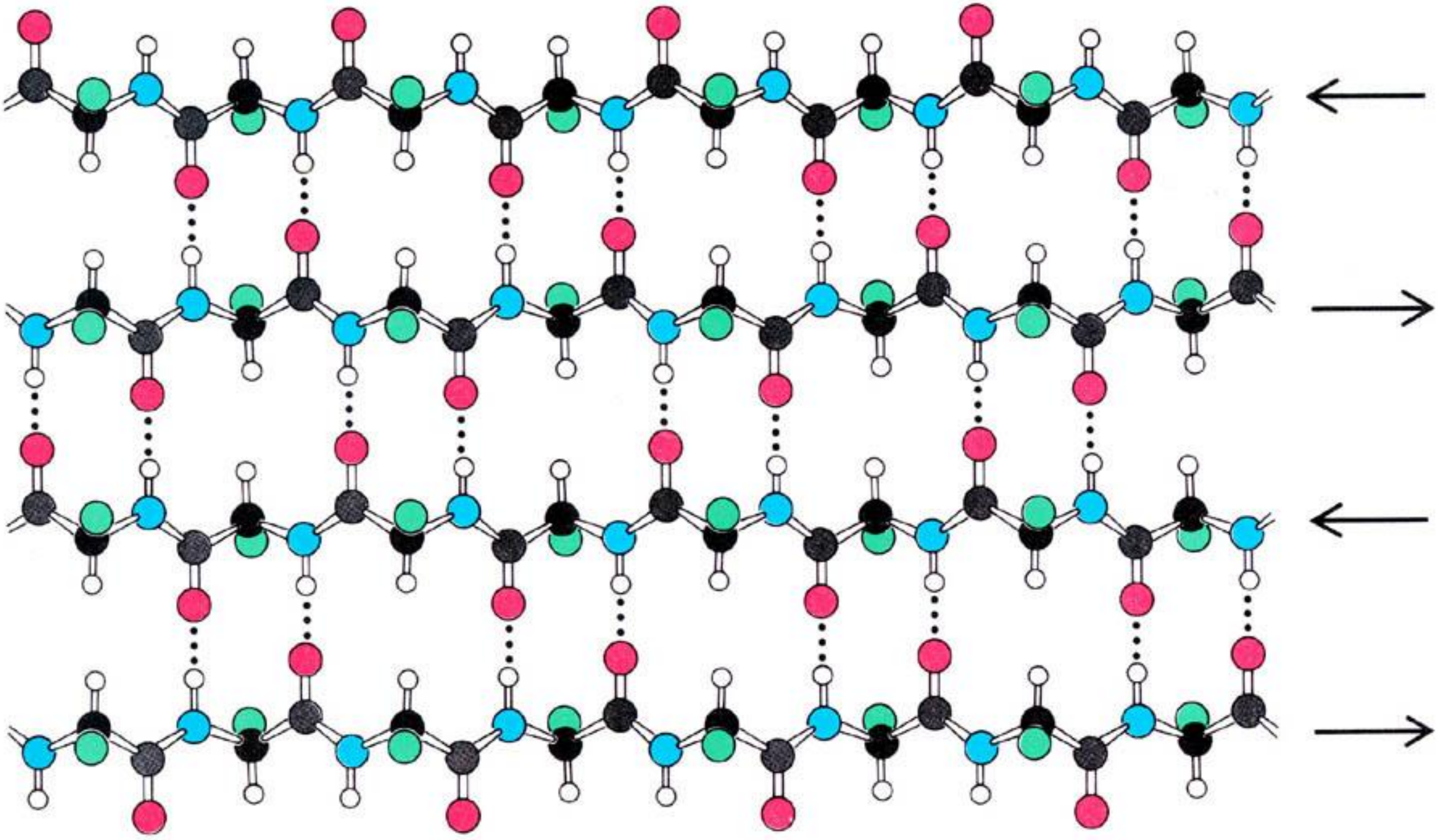
Fibrous proteins: silk

- Silk has repeating unit:

  - Gly-Ser-Gly-Ala-Gly-Ala -

  which is conducive to β-pleated sheets
- Inter-chain H-bonds are formed while side chains are above & below the plane of the sheet

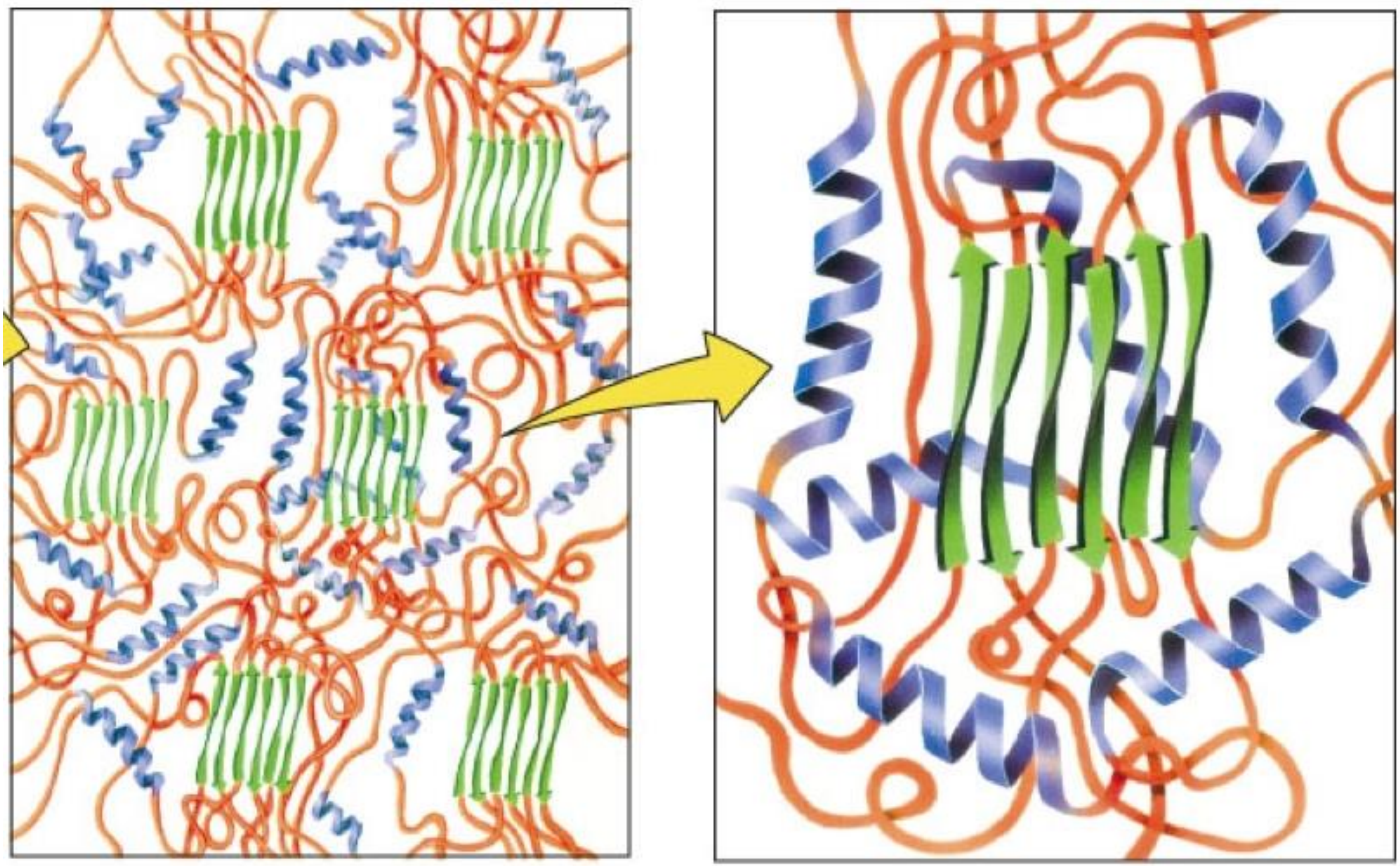
β-pleated sheet



Fibrous proteins: silk

- Small residue Gly allows tight packing
- Hydrogen bond network link β-strands: strong fiber
- Sheets connected by disordered regions: flexible fiber

Structure of silk



Residue compositions of fibrous proteins

	Gly	Ala	Ser	Glu + Gln	Cys	Pro + Hyp*
Silk	44.6	29.4	12.2	1.0	….	.3
Wool	8.1	5.0	10.2	12.1	11.2	7.5
Collagen	33.0	10.7	4.3	7.1	….	12.2 +9.4*

Fibrous proteins: keratins

- Keratins constitute: wool, hair, etc.
- Much lower in Gly (vs. silk), fairly even distribution of helix-forming residues (Ala, Glu)
- 7 amino acid heptad repeat
- Cystine crosslinks

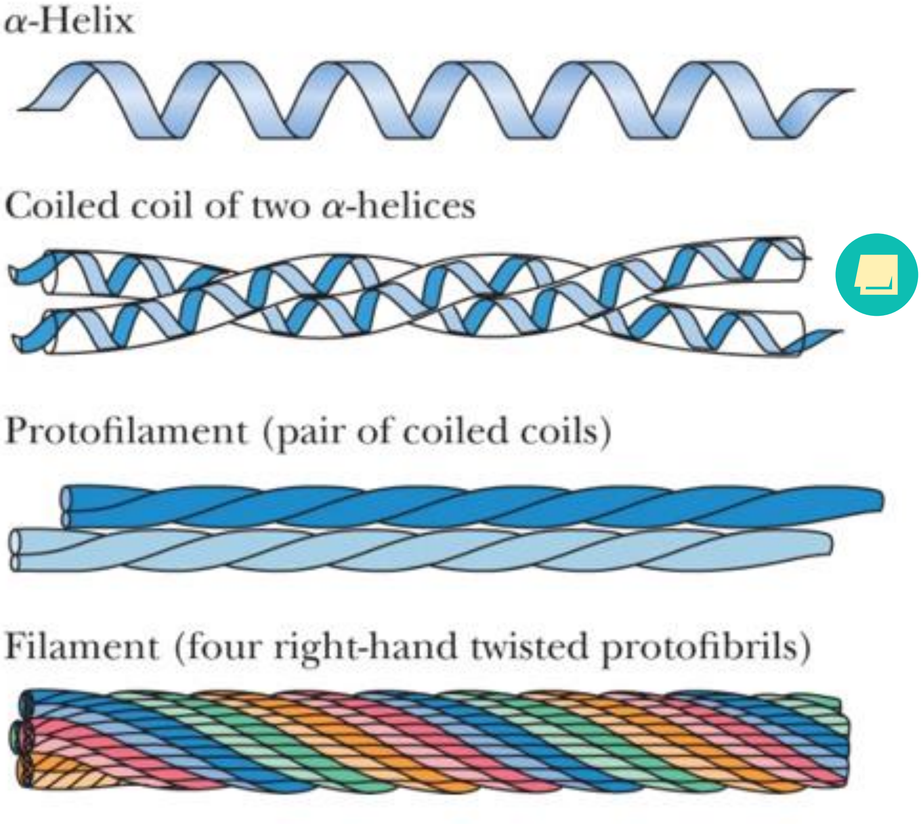
Fibrous proteins: keratins

- **Low-sulfur keratins are ‘soft’: skin, callous**
- **High-sulfur keratins are ‘hard’: horns, claws, hooves**

Fibrous proteins: keratins

- Highly-complex macromolecular structure: each single α-helix is twisted with others into a “protofibril”
- These are packed into a “microfibril” with 9-11 protofibrils, to form a fiber resembling rope

Assembly of keratin filaments



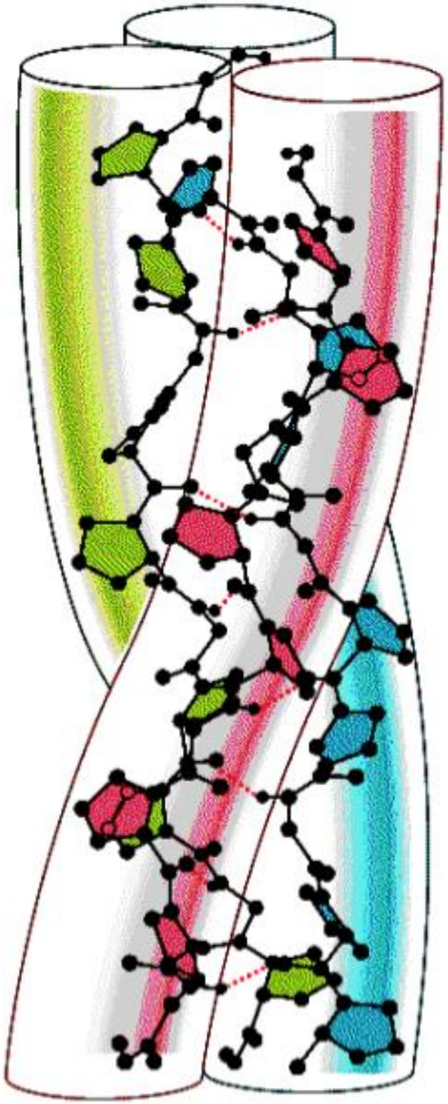
Fibrous proteins: wool

- Wool can be stretched to twice its length
- In the stretched state, intra-helix H-bonds may be broken, and inter-strand H-bonds may form: via an α-helix to β-sheet transition
- Due to sulfur content, disulfide crosslinks constitute the main restoring force

Residue compositions of fibrous proteins

	Gly	Ala	Ser	Glu + Gln	Cys	Pro + Hyp*
Silk	44.6	29.4	12.2	1.0	….	.3
Wool	8.1	5.0	10.2	12.1	11.2	7.5
Collagen	33.0	10.7	4.3	7.1	….	12.2 +9.4*

Collagen triple helix



Each strand is a “polyproline helix” with repeat distance of three residues/turn

Fibrous proteins: collagen

- About 1/3 of our protein is collagen
- Universal occurrence
- Rigid, inert material, resistant to stretching
- Used for connective tissue, skin, tendons

Fibrous proteins: collagen

- Composition: 33% Gly,
  22% (Pro + Hydroxy-Pro)
- Sequence: Gly in every third position
- Fundamental unit: triple helix

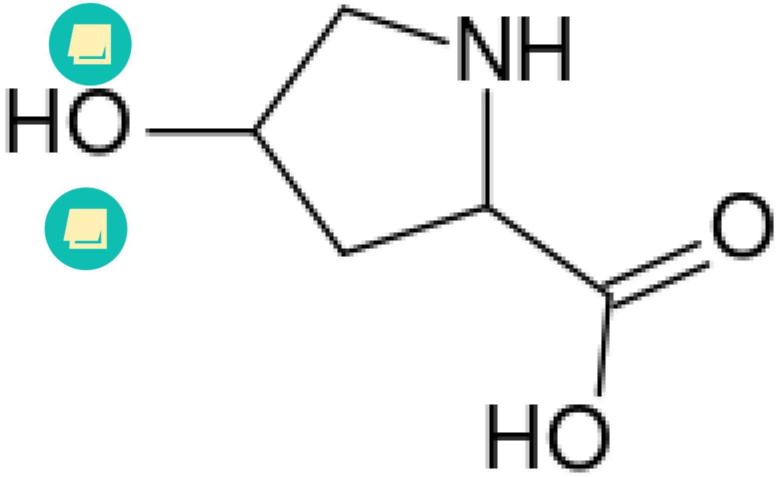
Fibrous proteins: collagen

- Not α-helix, but “polyproline” helix
- Typical amino acid sequence:

- Gly-Pro-X-Gly-X-Pro-

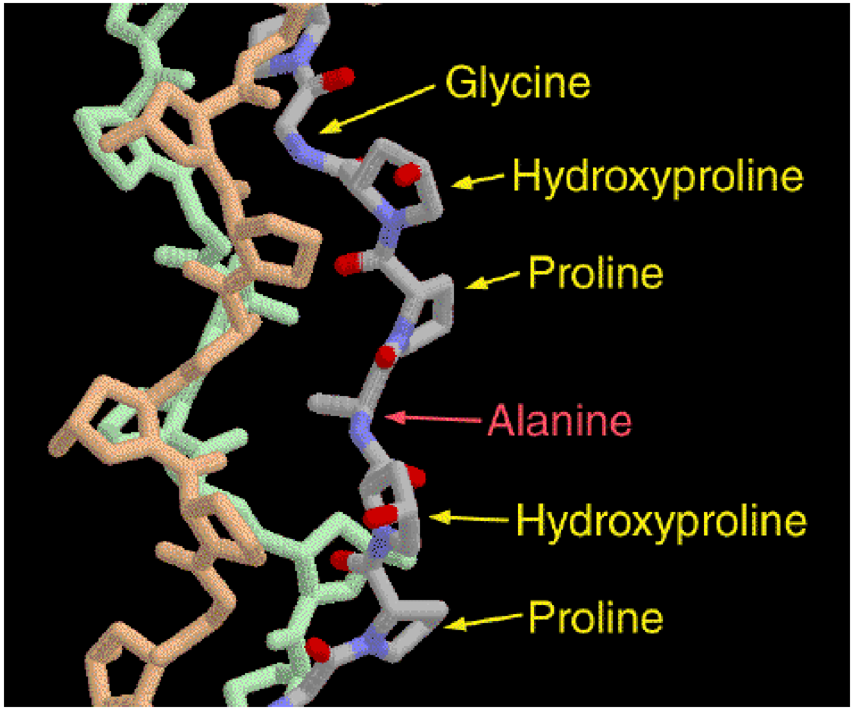
Gly-X-X-Gly-Pro-Hyp -

Hydroxy-proline (Hyp)



- -OH group used to form H-bond cross-links between collagen strands
- -enzyme proline hydroxylase adds –OH group to proline side chain in pro-collagen protein

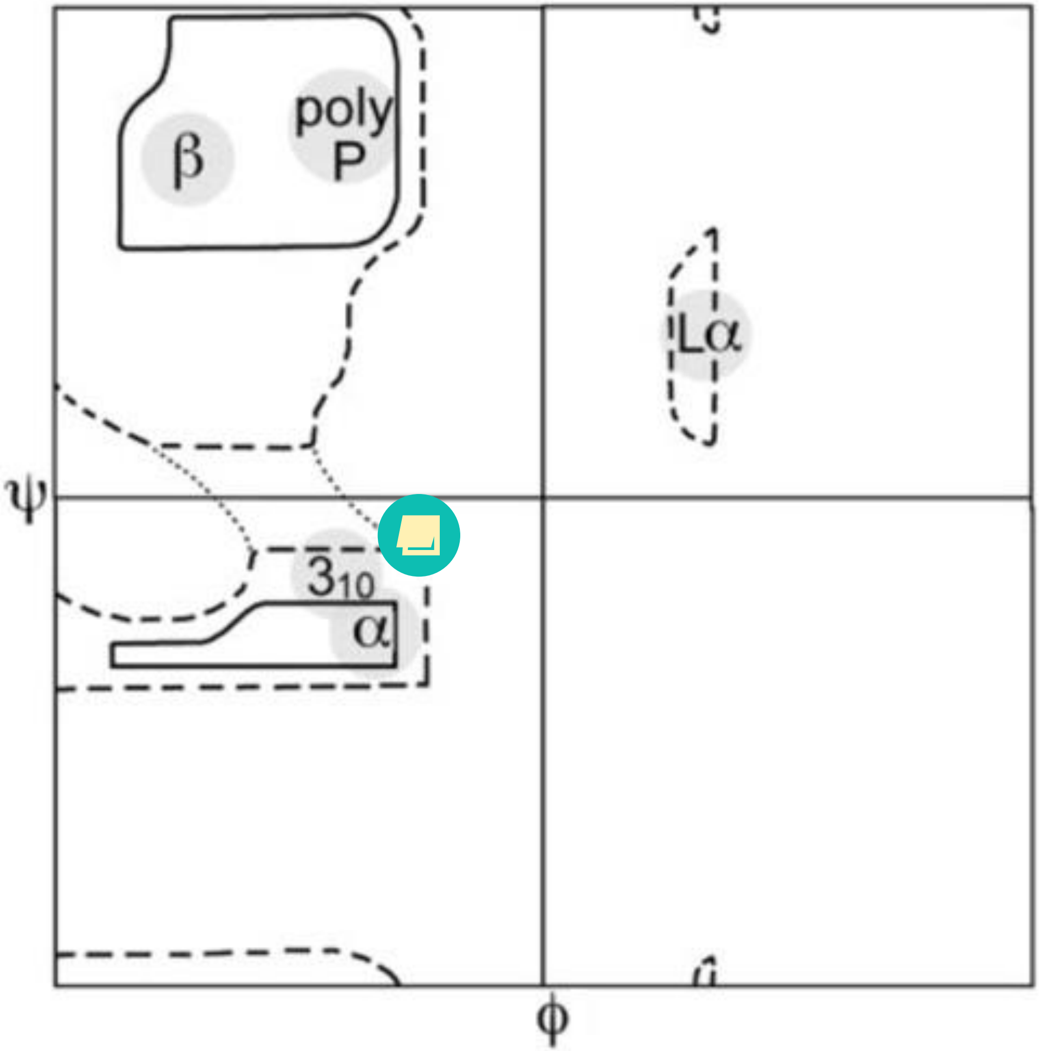
Basic coiled-coil structure of collagen



PDB molecules

Three left-handed single-chain helices wrap around one another with a right-handed twist

Ramachandran plot



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Poly-proline helix

Note **(ϕ, ψ)** comparison:

3.6

α-helix:
(ϕ, ψ) = (- 60^{o}, - 50^{o})

2.0

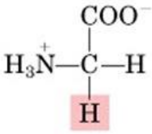
β-sheet:
(ϕ, ψ) = (- 140^{o}, + 135^{o})

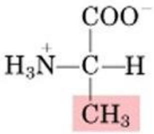
3.0

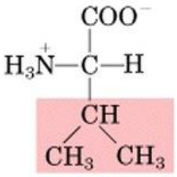
polyproline helix:
(ϕ, ψ) = (- 60^{o}, +135)

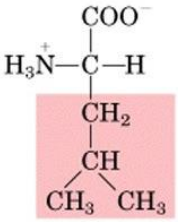
Residues/ turn

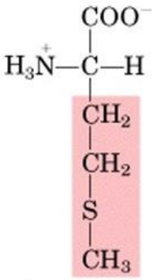
Nonpolar, aliphatic R groups

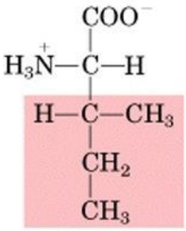

Glycine


Alanine

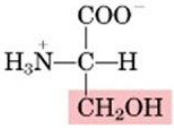

Valine

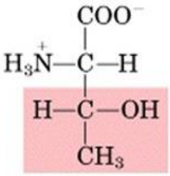

Leucine

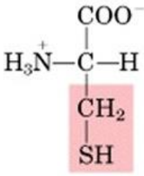

Methionine

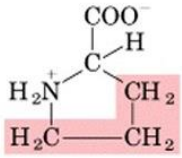

Isoleucine

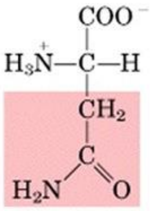
Polar, uncharged R groups

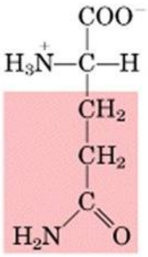

Serine


Threonine

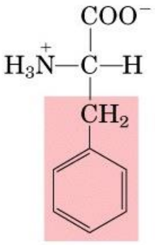

Cysteine

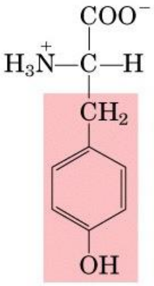

Proline

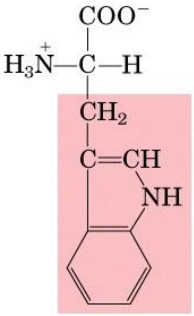

Asparagine


Glutamine

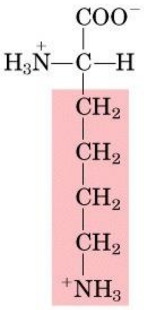
Aromatic R groups

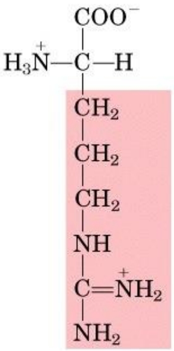

Phenylalanine

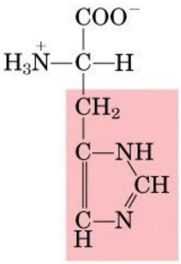

Tyrosine


Tryptophan

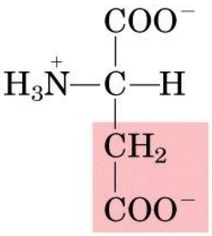
Positively charged R groups

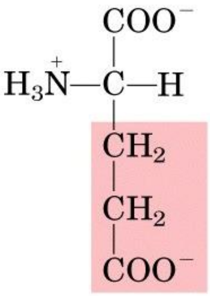

Lysine


Arginine

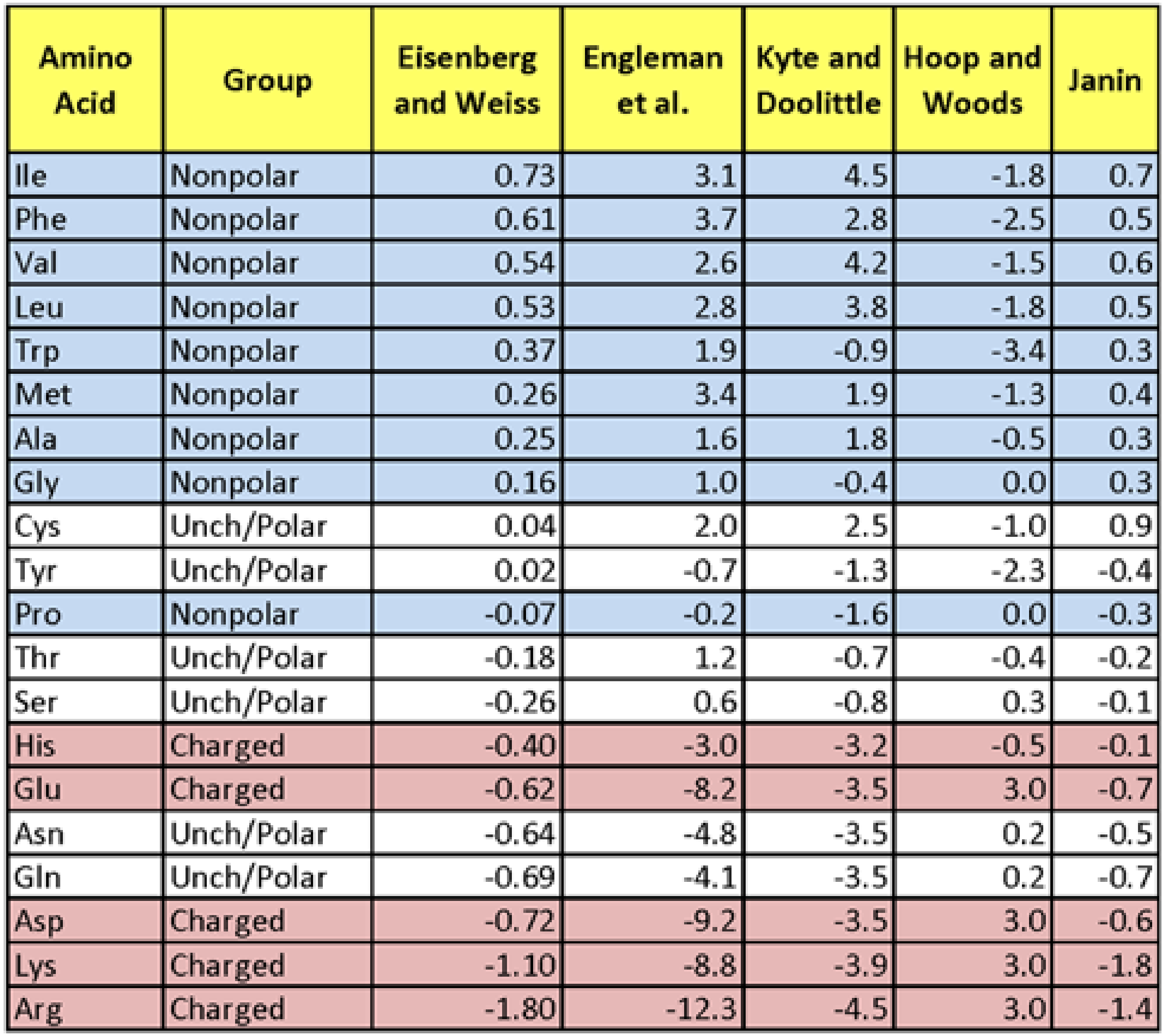

Histidine

Negatively charged R groups


Aspartate


Glutamate

Hydrophobicity scales



Amino Acid	Group	Eisenberg and Weiss	Engleman et al.	Kyte and Doolittle	Hoop and Woods	Janin
Ile	Nonpolar	0.73	3.1	4.5	-1.8	0.7
Phe	Nonpolar	0.61	3.7	2.8	-2.5	0.5
Val	Nonpolar	0.54	2.6	4.2	-1.5	0.6
Leu	Nonpolar	0.53	2.8	3.8	-1.8	0.5
Trp	Nonpolar	0.37	1.9	-0.9	-3.4	0.3
Met	Nonpolar	0.26	3.4	1.9	-1.3	0.4
Ala	Nonpolar	0.25	1.6	1.8	-0.5	0.3
Gly	Nonpolar	0.16	1.0	-0.4	0.0	0.3
Cys	Unch/Polar	0.04	2.0	2.5	-1.0	0.9
Tyr	Unch/Polar	0.02	-0.7	-1.3	-2.3	-0.4
Pro	Nonpolar	-0.07	-0.2	-1.6	0.0	-0.3
Thr	Unch/Polar	-0.18	1.2	-0.7	-0.4	-0.2
Ser	Unch/Polar	-0.26	0.6	-0.8	0.3	-0.1
His	Charged	-0.40	-3.0	-3.2	-0.5	-0.1
Glu	Charged	-0.62	-8.2	-3.5	3.0	-0.7
Asn	Unch/Polar	-0.64	-4.8	-3.5	0.2	-0.5
Gln	Unch/Polar	-0.69	-4.1	-3.5	0.2	-0.7
Asp	Charged	-0.72	-9.2	-3.5	3.0	-0.6
Lys	Charged	-1.10	-8.8	-3.9	3.0	-1.8
Arg	Charged	-1.80	-12.3	-4.5	3.0	-1.4