Conformational Properties of polypeptide chains

Chapter 5

Proteins

TE Creighton

Conformations

- For small molecules the calssical representations are sufficient.
- Their 3D structure is easy to determine by the bond length and angles.
- Larger polymers such as Proteins can have non interconvertible 3D conformations.
- Different conformations must have the same configuration of atoms.
- Polymers are very flexible and can have a large number of conformations.

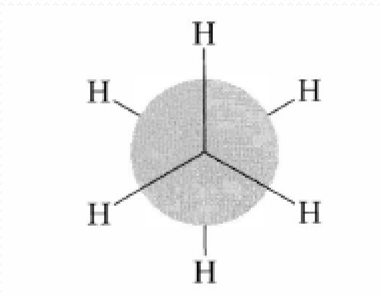
Conformations

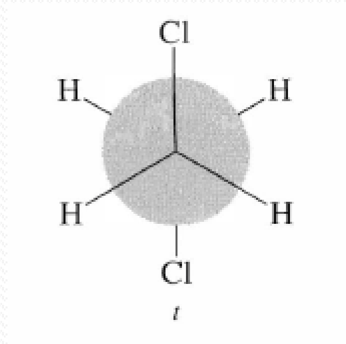
- Proteins:
- Have used this flexibility to adopt a number of fixed conformations.
- Protein structures do have a hierarchy:
- Primary structure- covalent structure of the amino acids.
- Secondary structure- local conformation of the polypeptide backbone.
- Tertiary and quarternary structure- 3D conformation of secondary structures and superstructures.

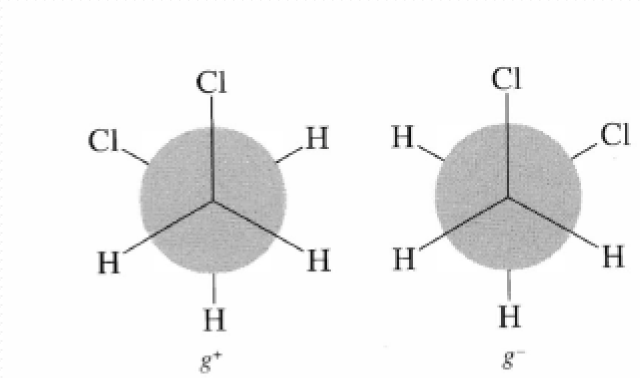
3D Conformations

- How a conformation is defined is not trivial
- Even a small molecule can seem to have an infinite number of conformations.
- Only conformations that have an energetic minimum are considered as stable conformations.
- Representations are shown in Newman projection

3D Conformations

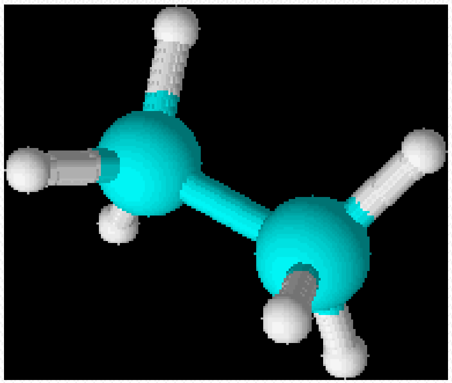


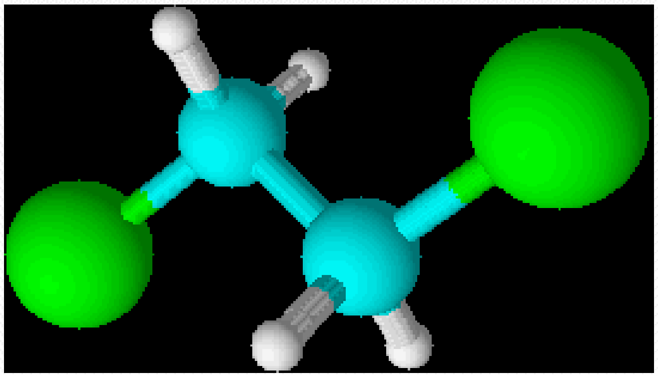




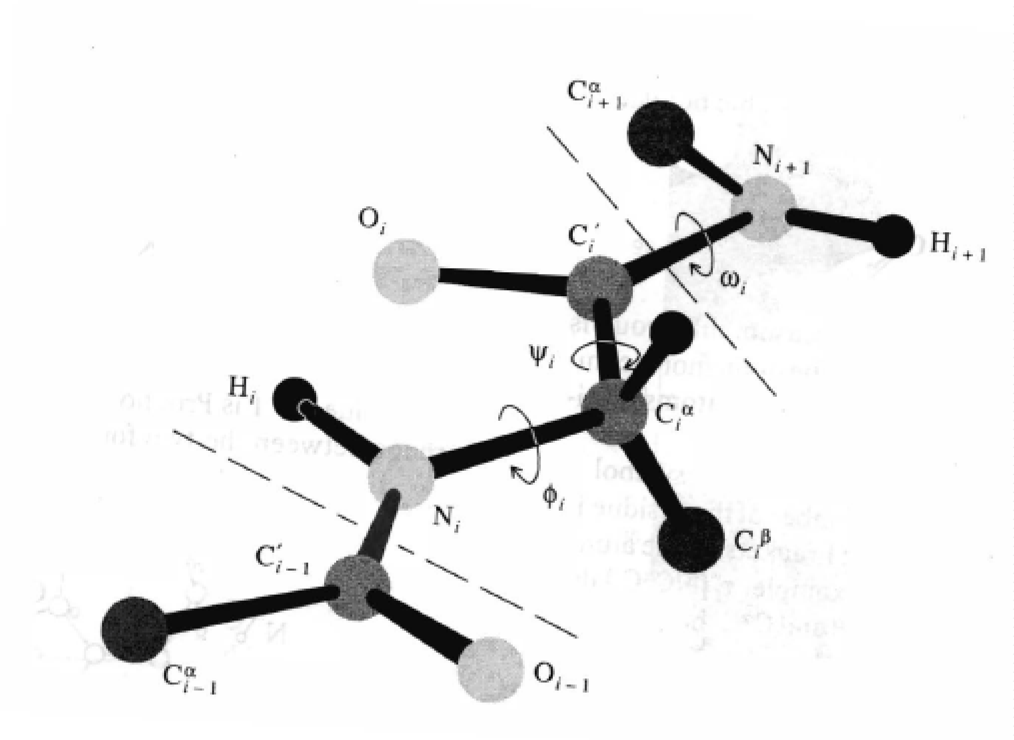
Ethane

1,2 Dichloro etane



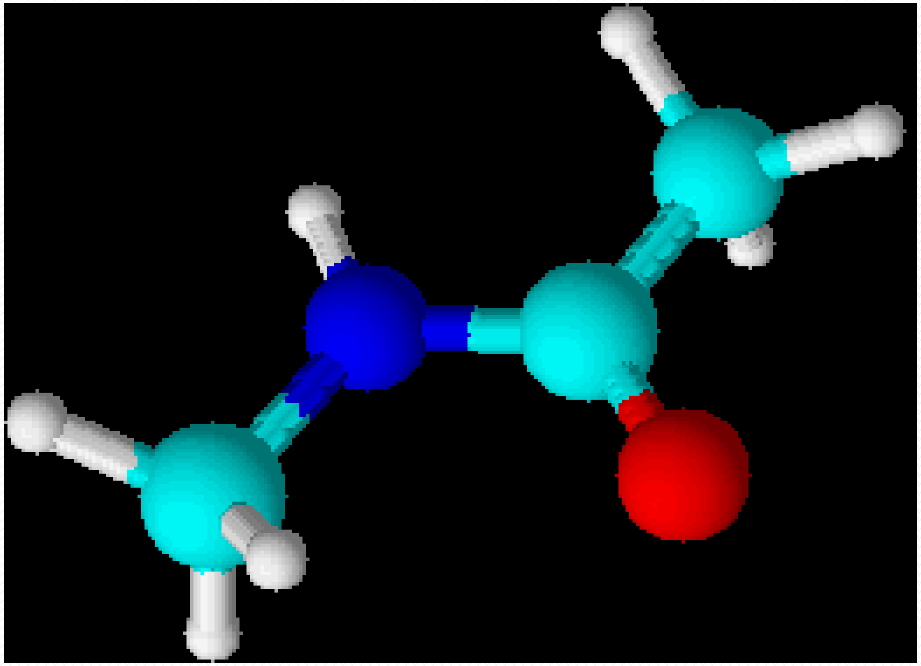


Local restrictions- Ramachandran plot



Local restrictions- Ramachandran plot

- The peptide Bond: Is normally planar



Local restrictions- Ramachandran plot

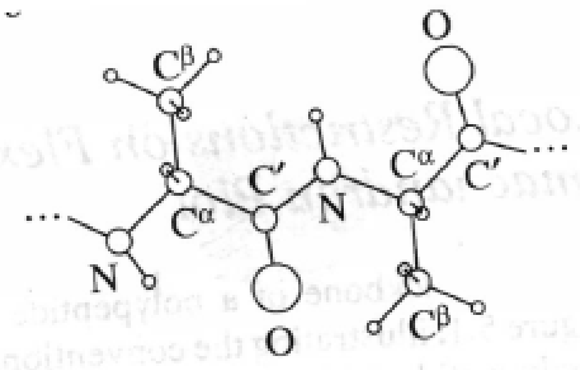
- The angles are callet Tau, describing the angles between $NC^{\alpha}C'$
- Rotations about bonds are described as torsion or dihedral angles
- They are in the range -180 +180 degrees

In trans conformation the angle is 180 deg, in cis conformation the angle is 0 deg.

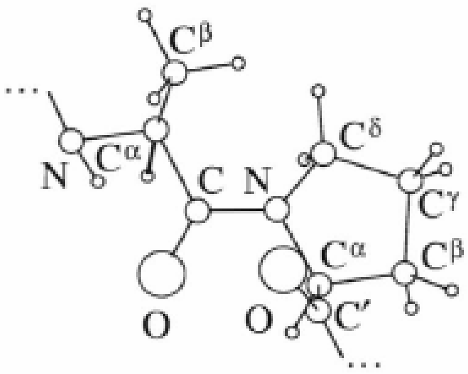
Rotation around this bond: angle + value → rotation clockwise

Angle – value→ rotation counterclockwise

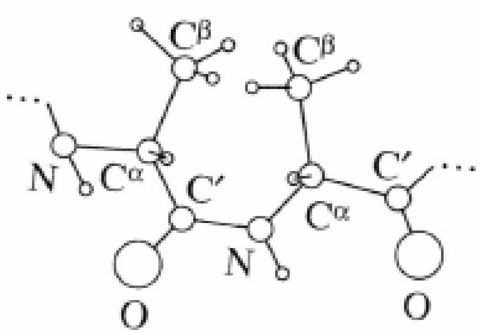
Local restrictions- Ramachandran plot



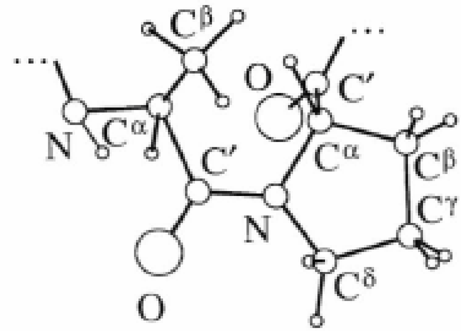
trans



trans

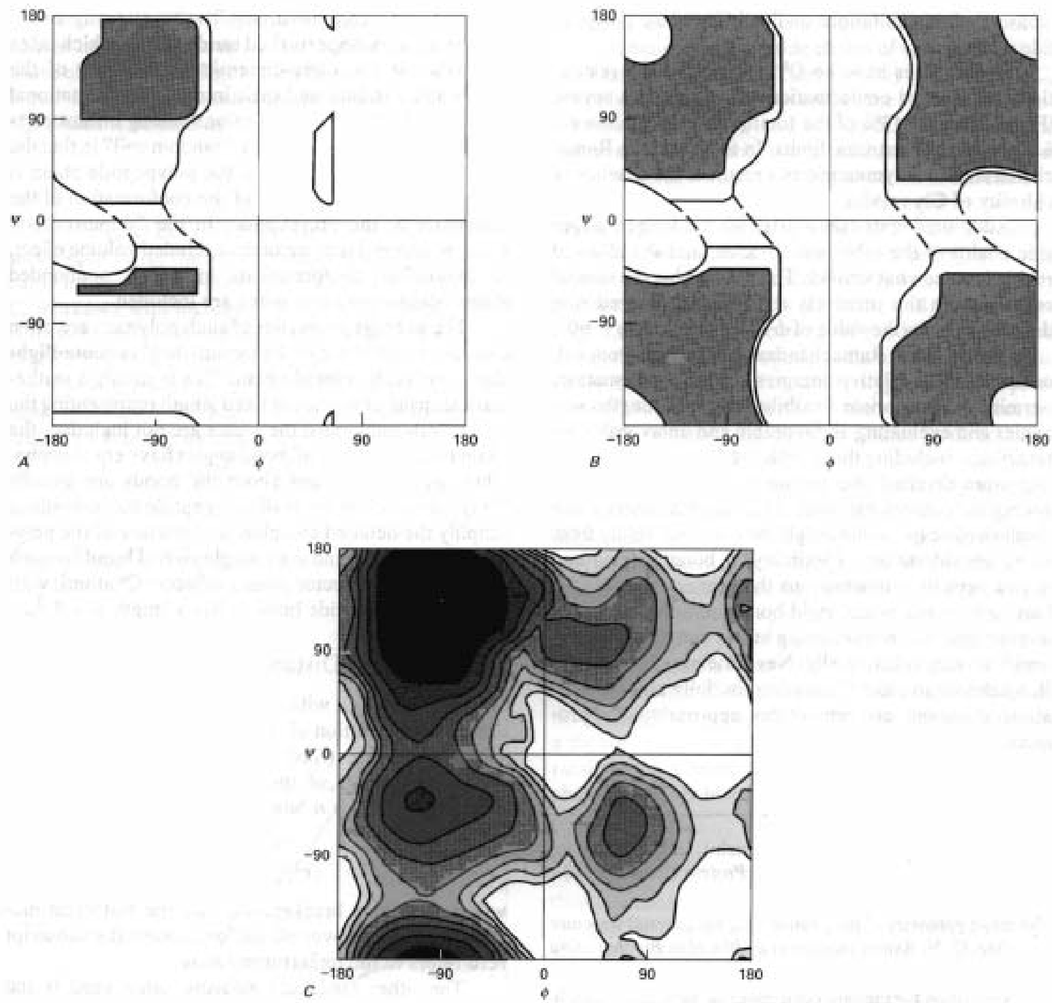


cis



cis

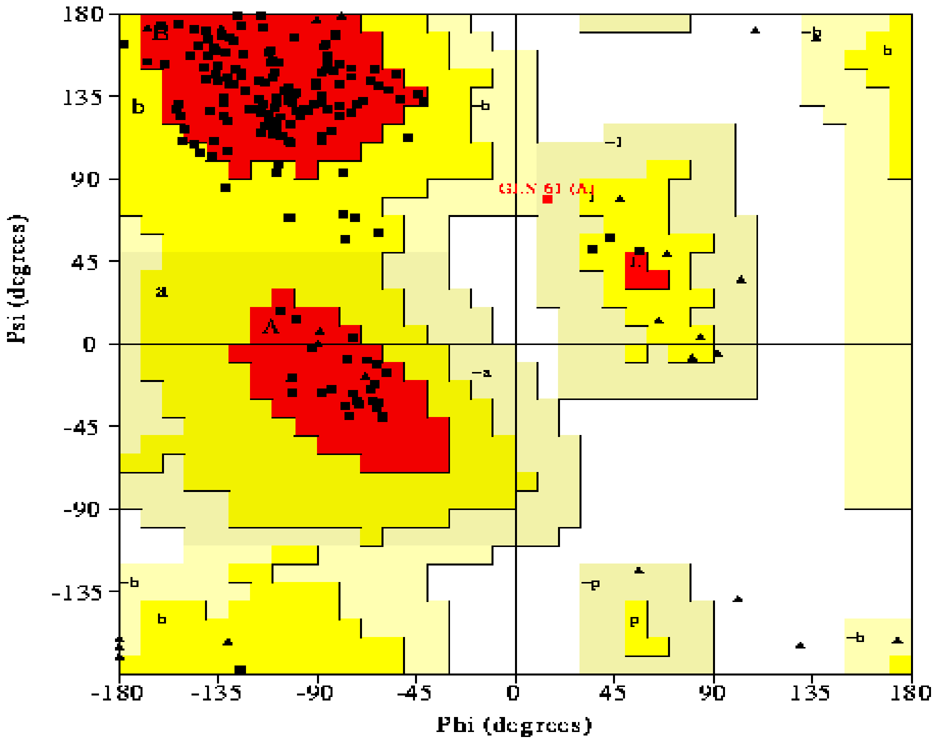
The Ramachandran Plot



PROCHECK

Ramachandran Plot

1abc



Plot statistics

Residues in most favoured regions [A,B,L]	143	69.9%
Residues in additional allowed regions [a,b,l,p]	15	9.4%
Residues in generously allowed regions [~a,~b,~l,~p]	1	0.6%
Residues in disallowed regions	0	0.0%
Number of non-glycine and non-proline residues	159	100.0%
Number of end residues (excl. Gly and Pro)	5	
Number of glycine residues (shown as triangles)	26	
Number of proline residues	15	
Total number of residues	205	

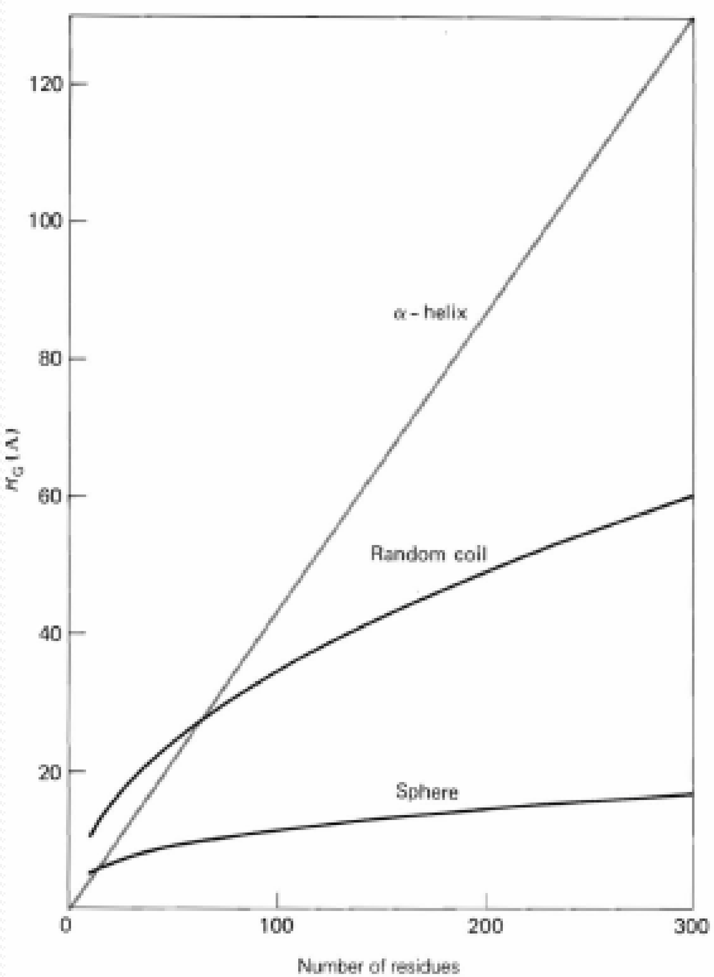
Based on an analysis of 118 structures of resolution of at least 2.0 Angstroms and R-factor no greater than 20%, a good quality model would be expected to have over 90% in the most favoured regions.

1abc_01.ps

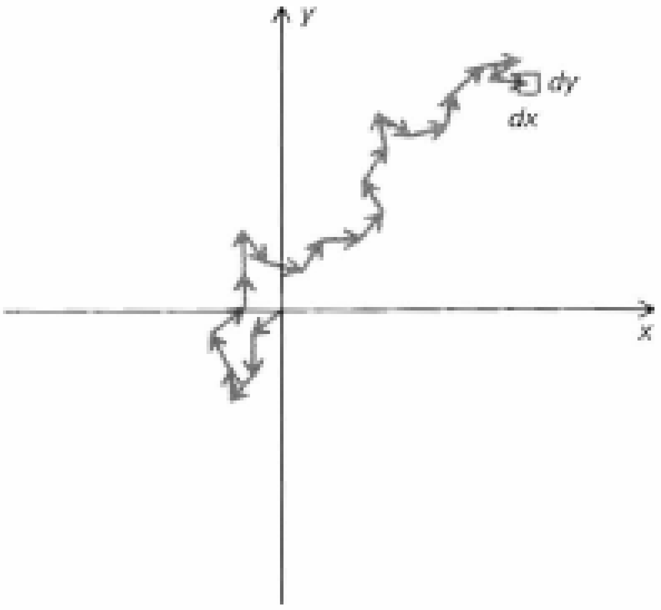
Statistical properties

- The intrinsic conformational property of an individual aa makes it possible to calculate the conformational property of a random polymer chain.
- Statistically averaged over all its many possible conformations
- Therefore the unperturbed random coil is the osrt easy to calculate.

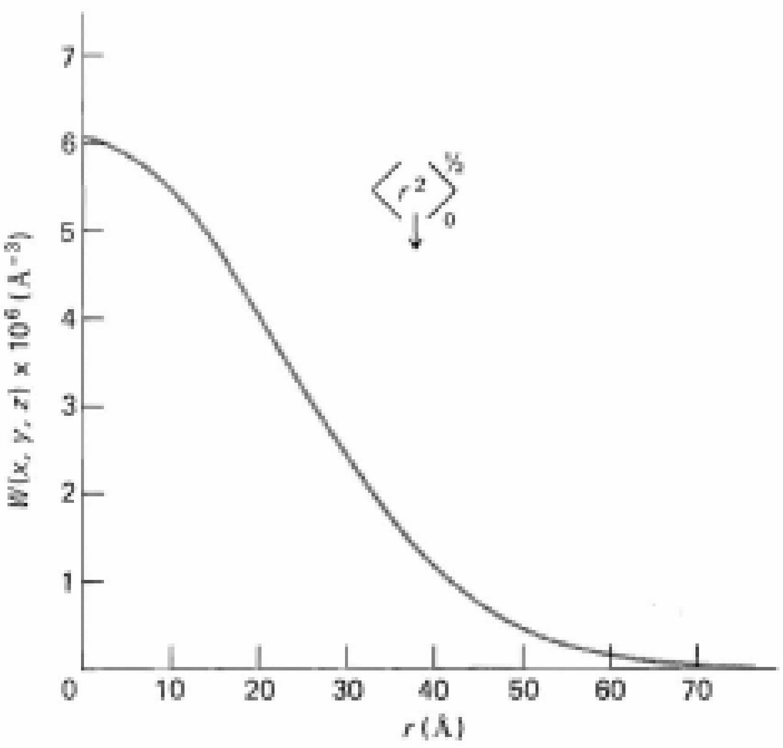
End to End Distances



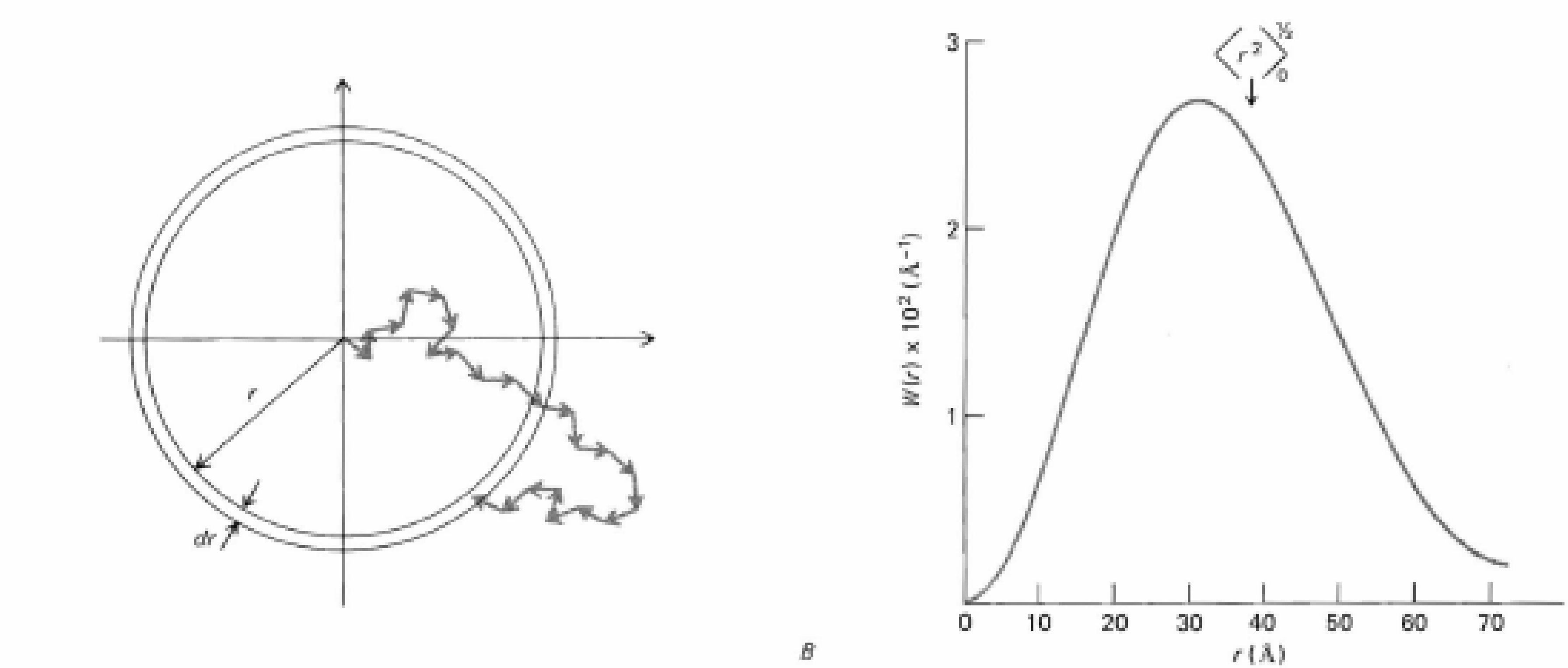
Statistical properties



A



Statistical properties

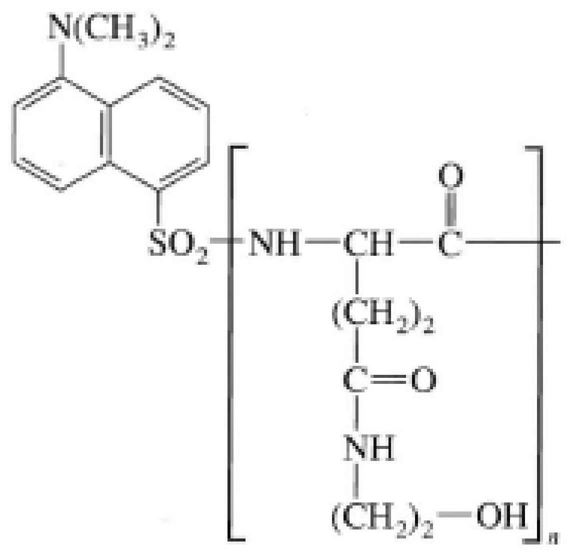


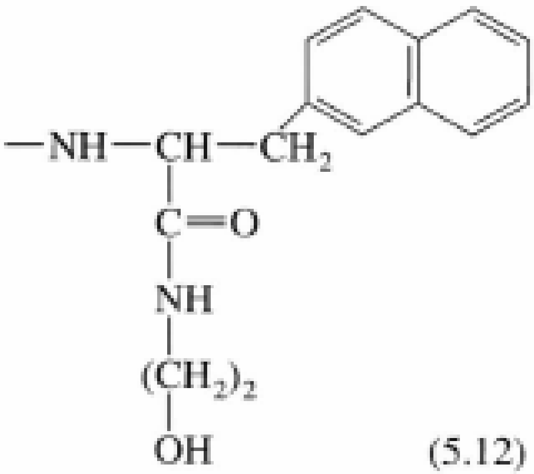
Statistical properties

$$W(x, y, z)\, dx\, dy\, dz = (\beta/\sqrt{\pi})^3\, e^{-\beta^2 r^2}\, dx\, dy\, dz$$

$$W(r)\, dr = (\beta/\sqrt{\pi})^3\, e^{-\beta^2 r^2}\, 4\pi r^2\, dr$$

Statistical Properties





(5.12)

Statistical Properties

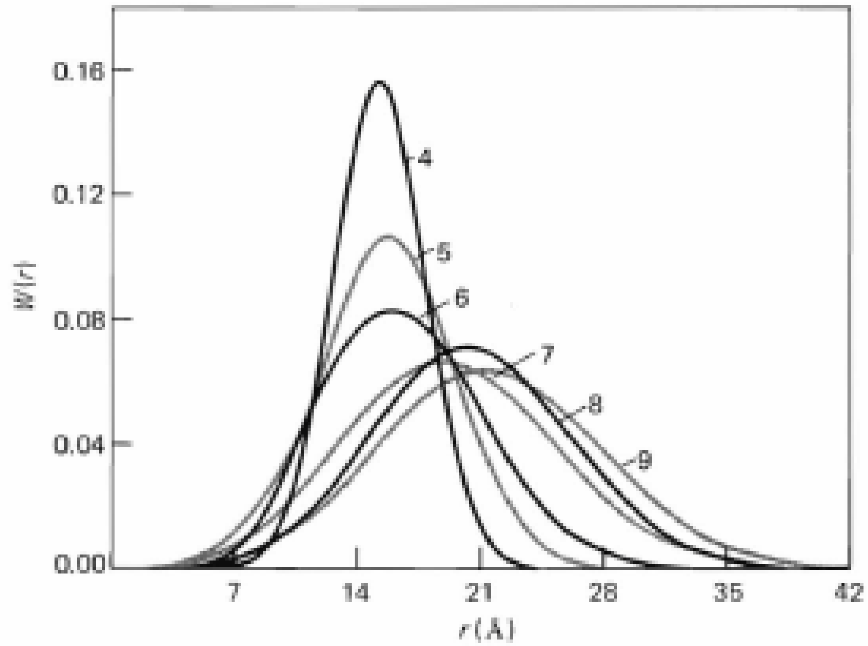


FIGURE 5.5
Radial distribution function of the distances between naphthalene and dansyl groups attached to the ends of peptides of 4–9 residues of *N*-hydroxyethyl-Gln, measured by fluorescence energy transfer. (From E. Haas et al., *Proc. Natl. Acad. Sci. USA* 72:1807–1811, 1975.)

Transition state theory

$$\Delta S_{conf} = -b - \frac{3}{2} R \ln n$$

$$\nu = \frac{k_B T}{h}$$

$$\ln k_{obs} = \frac{-\Delta H^{\ddagger}}{R}\left(\frac{1}{T}\right) + \frac{\Delta S^{\ddagger}}{R}$$

$$A \underset{}{\overset{K^{\ddagger}}{\rightleftharpoons}} [A^{\ddagger}] \xrightarrow{\nu} P \tag{5.15}$$

$$\Delta G^{\ddagger} = -RT \ln K^{\ddagger} = -RT \ln \frac{[A^{\ddagger}]}{[A]} \tag{5.16}$$

The kinetic equation for the reaction $A \rightarrow P$ is then

$$\frac{-d[A]}{dt} = \frac{d[P]}{dt} = k_{obs}[A] = \frac{k_B T}{h}[A^{\ddagger}] = \frac{k_B T\, K^{\ddagger}}{h}[A]$$

$$= \frac{k_B T}{h}[A] \exp \frac{-\Delta G^{\ddagger}}{RT} \tag{5.17}$$

The observed rate constant k_{obs} is related to the energy of the transition state by

$$k_{obs} = \frac{k_B T}{h} \exp \frac{-\Delta G^{\ddagger}}{RT} \tag{5.18}$$

With the measured value of k_{obs}, the relative free energy of the hypothetical transition state can be calculated:

$$\Delta G^{\ddagger} = RT \ln \frac{k_B T}{k_{obs} h} \tag{5.19}$$

At 25°C with k_{obs} expressed in seconds^{-1}, this equation has the form

$$\Delta G^{\ddagger} = (17.4 - 1.36 \log k_{obs})\ \text{kcal/mol} \tag{5.20}$$

Intrinsic rates of Bond rotation

Table 5.1 *Rotational Relaxation Times in a Random Polypeptide Chain*

Carbon atom		Relaxation time[a] (10^{-9} s)
Ala	C^{β}	0.21
Thr	C^{β}	1.56
	C^{γ}	0.18
Lys	C^{β}	0.81
	C^{γ}	0.54
	C^{δ}	0.60
	C^{ϵ}	0.27
Peptide	C^{α}	1.4 – 2.6

[a] The values were measured at 45°C on performic acid–oxidized ribonuclease A by ^{13}C nuclear magnetic resonance.

From V. Glushko et al., *J. Biol. Chem.* 247:3176–3185 (1972).

Regular conformations

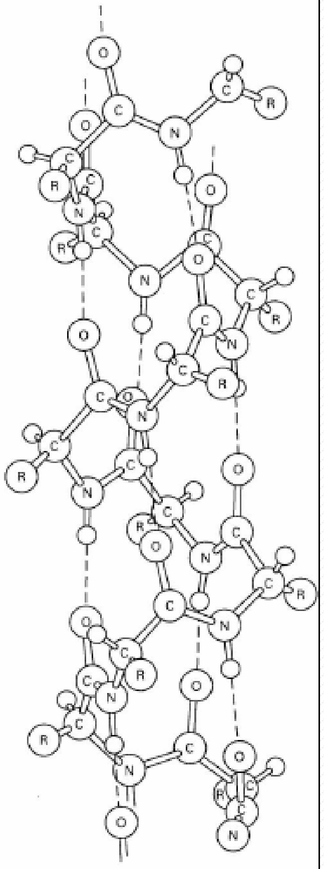


FIGURE 5.6
The classical right-handed α-helix.

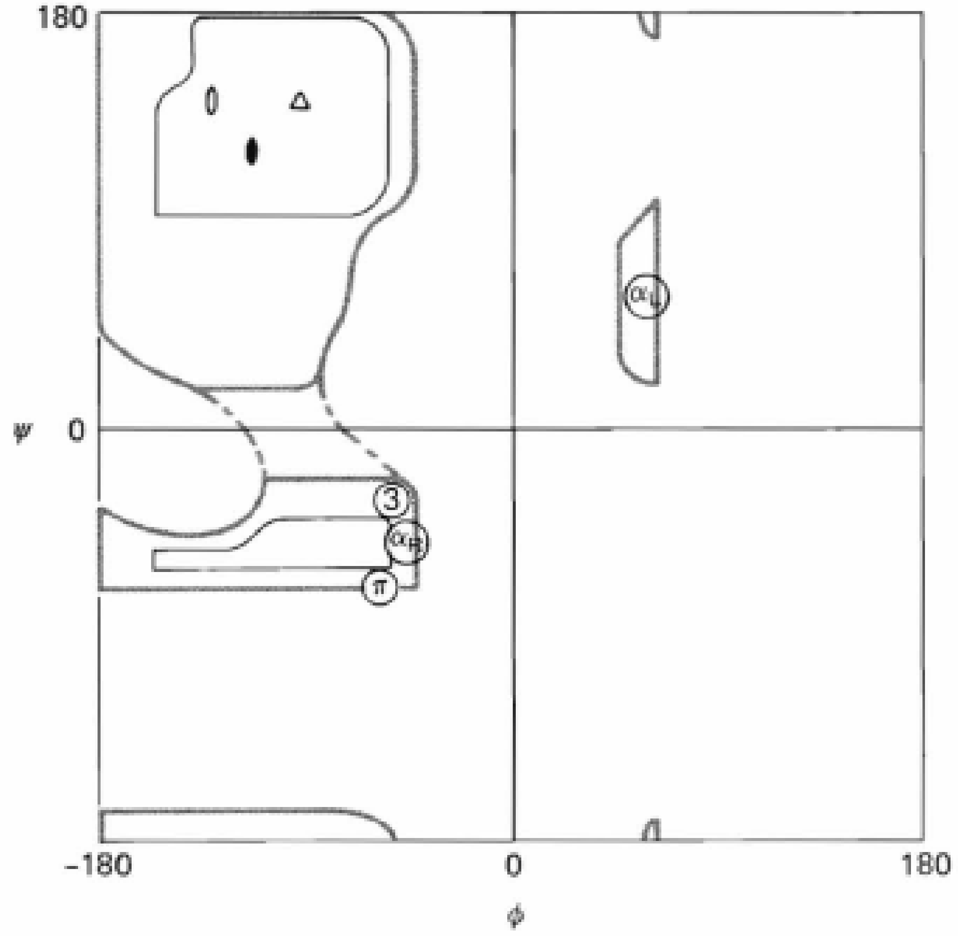
Regular conformations

Table 5.2 *Parameters for Regular Polypeptide Conformations*

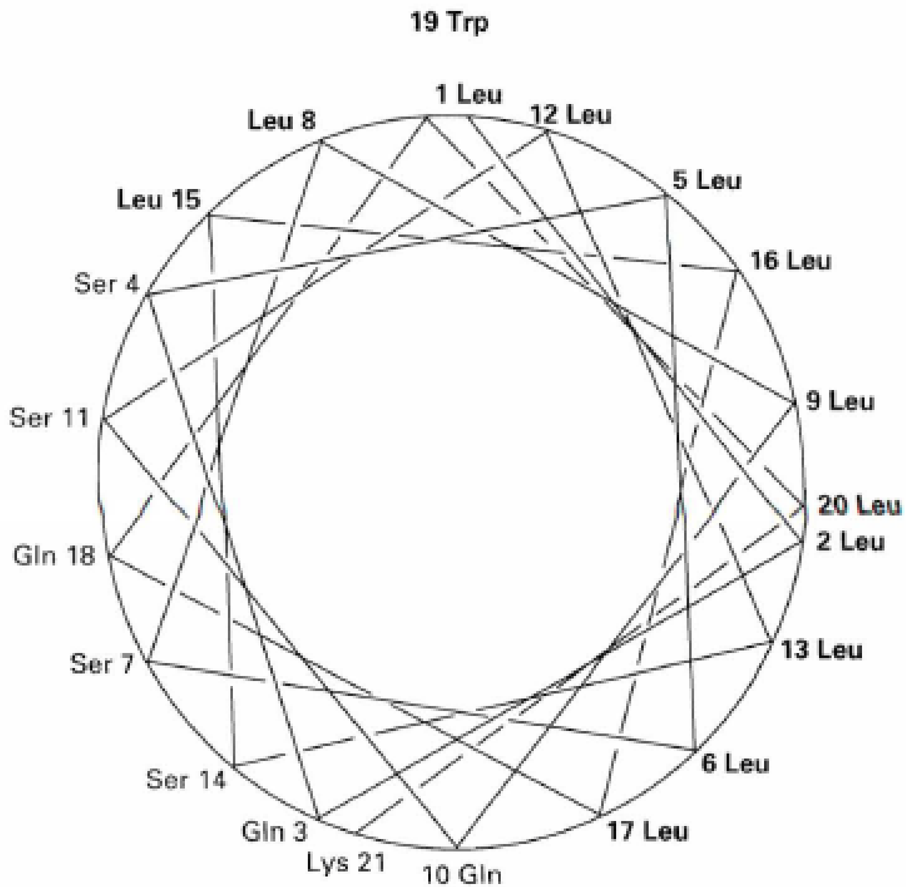
	Bond Angle (deg)			Residues per turn	Translation per residue (Å)
	ϕ	ψ	ω		
Antiparallel β-sheet	−139	+135	−178	2.0	3.4
Parallel β-sheet	−119	+113	180	2.0	3.2
Right-handed α-helix	−57	−47	180	3.6	1.50
3_{10}-helix	−49	−26	180	3.0	2.00
π-helix	−57	−70	180	4.4	1.15
Polyproline I	−83	+158	0	3.33	1.9
Polyproline II	−78	+149	180	3.00	3.12
Polyglycine II	−80	+150	180	3.0	3.1

Adapted from G. N. Ramachandran and V. Sasisekharan, *Adv. Protein Chem.* 23:283–437 (1968); IUPAC–IUB Commission on Biochemical Nomenclature, *Biochemistry* 9:3471–3479 (1970).

Regular conformations



Regular conformations



Regular conformations

Table 5.3 *Relative Helical Tendencies of the Amino Acids Measured in One Peptide*

Amino acid residue	Relative stabilization of α-helical conformation (kcal/mol)
Ala	−0.77
Arg	−0.68
Lys	−0.65
Leu	−0.62
Met	−0.50
Trp	−0.45
Phe	−0.41
Ser	−0.35
Gln	−0.33
Glu	−0.27
Cys	−0.23
Ile	−0.23
Tyr	−0.17
Asp	−0.15
Val	−0.14
Thr	−0.11
Asn	−0.07
His	−0.06
Gly	0
Pro	≈3

Regular conformations

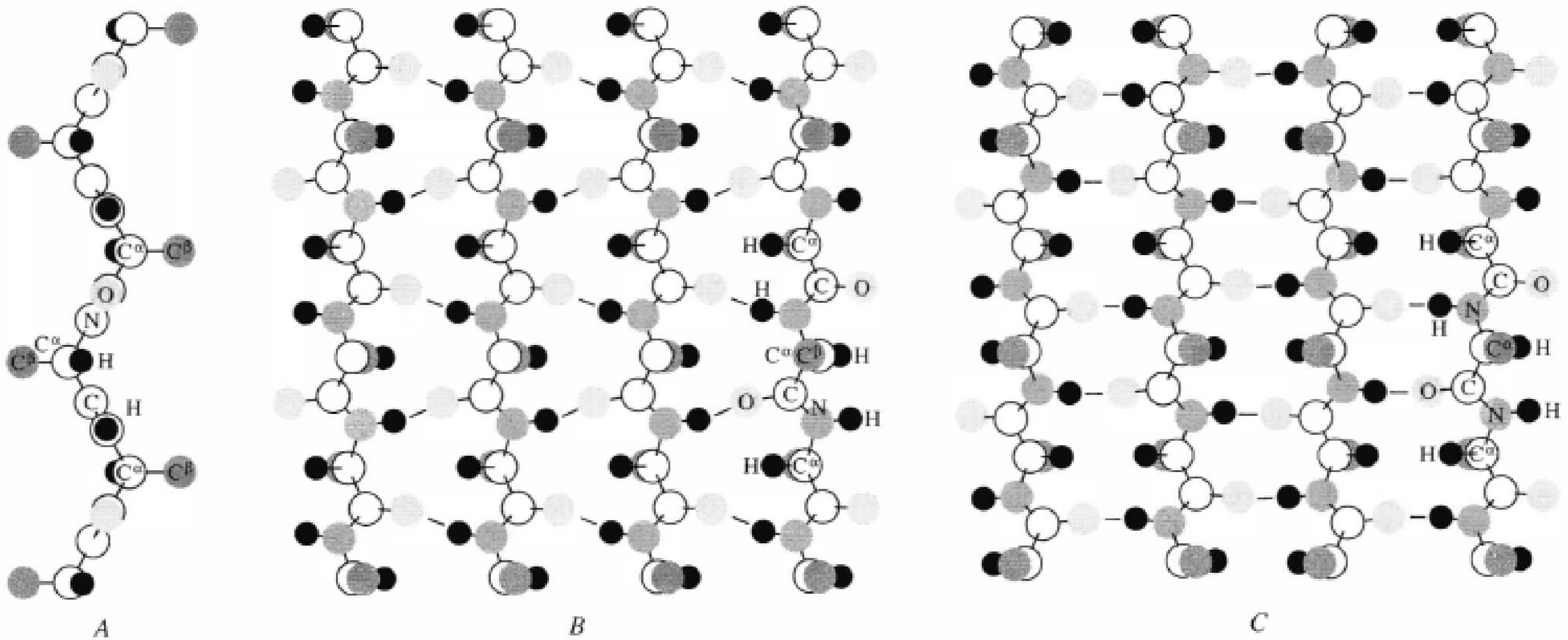


FIGURE 5.9
A single β-strand (*A*) and its incorporation into flat parallel (*B*) and antiparallel (*C*) β-sheets.

Regular conformations

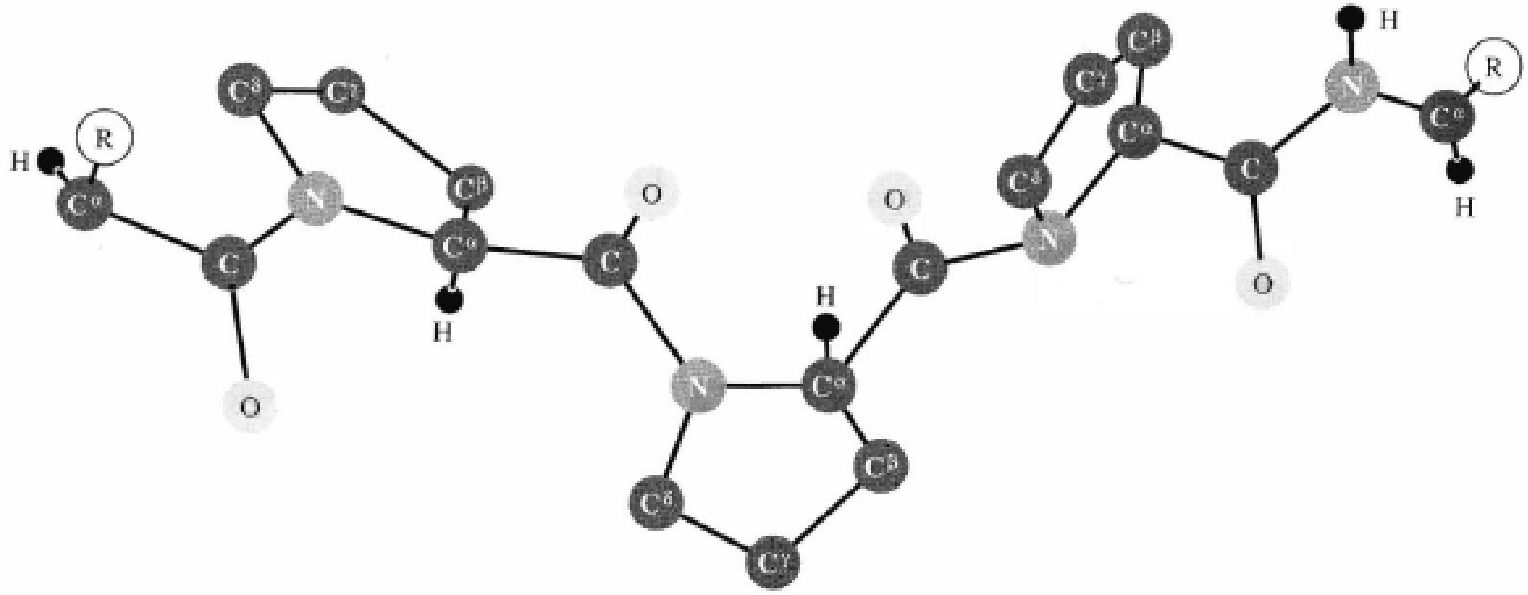
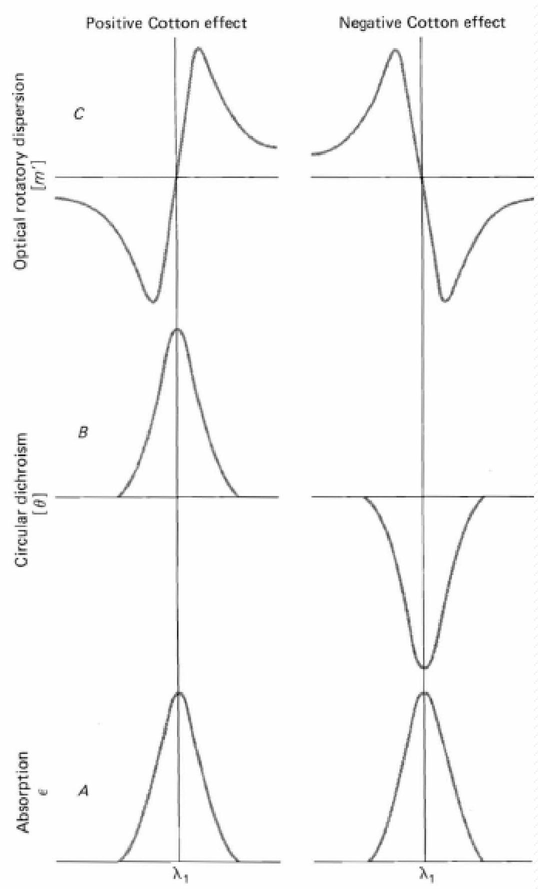


FIGURE 5.10
The poly(Pro) II helix. (From A. G. Walton, *Polypeptides and Protein Structure*, Elsevier-North Holland, New York, 1981.)

Spectral properties



A typical electronic absorption band (*A*), which can have either a positive or negative Cotton effect. The two types circular dichroism (*B*) and optical rotatory dispersion (*C*) spectra that result are illustrated. (From A. J. Adler et al., *Methods Enzymol.* 27:675–735, 1973.)

Spectral properties

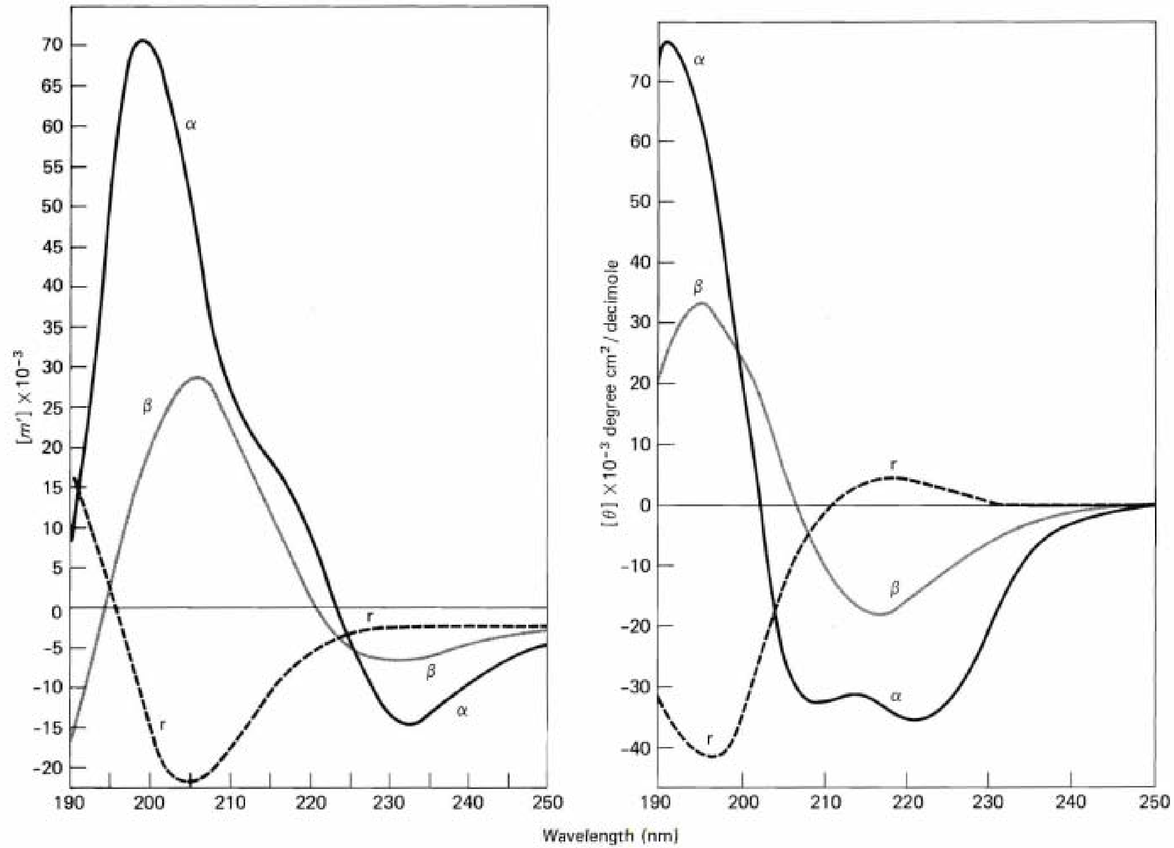


FIGURE 5.12
Optical rotatory dispersion *(left)* and circular dichroism *(right)* spectra of poly(Lys) in the α-helical (α), antiparallel β-sheet (β), and random-coil (r) conformations. (From N. J. Greenfield et al., *Biochemistry* 6:1630–1637, 1967; 8:4108–4116, 1969.)

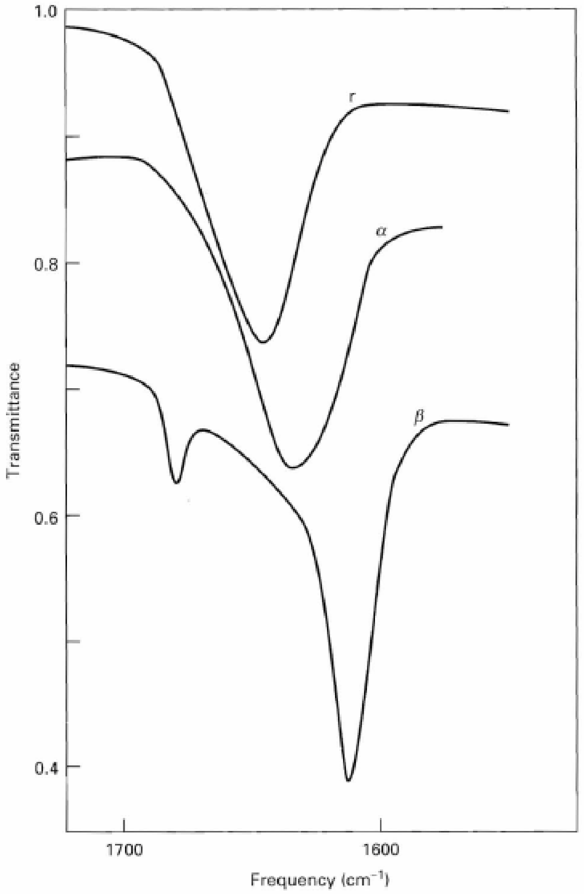
Spectral properties

Table 5.4 Characteristic Infrared Bands of the Peptide Linkage

Designation	Approximate frequency (cm^{-1})	Description
A	~3300	NH stretching in resonance with (2 × amide II) overtone
B	~3100	
I	1600–1690	C═O stretching
II	1480–1575	CN stretching, NH bending
III	1229–1301	CN stretching, NH bending
IV	625–767	OCN bending, mixed with other modes
V	640–800	Out-of-plane NH bending
VI	537–606	Out-of-plane C═O bending
VII	~200	Skeletal torsion

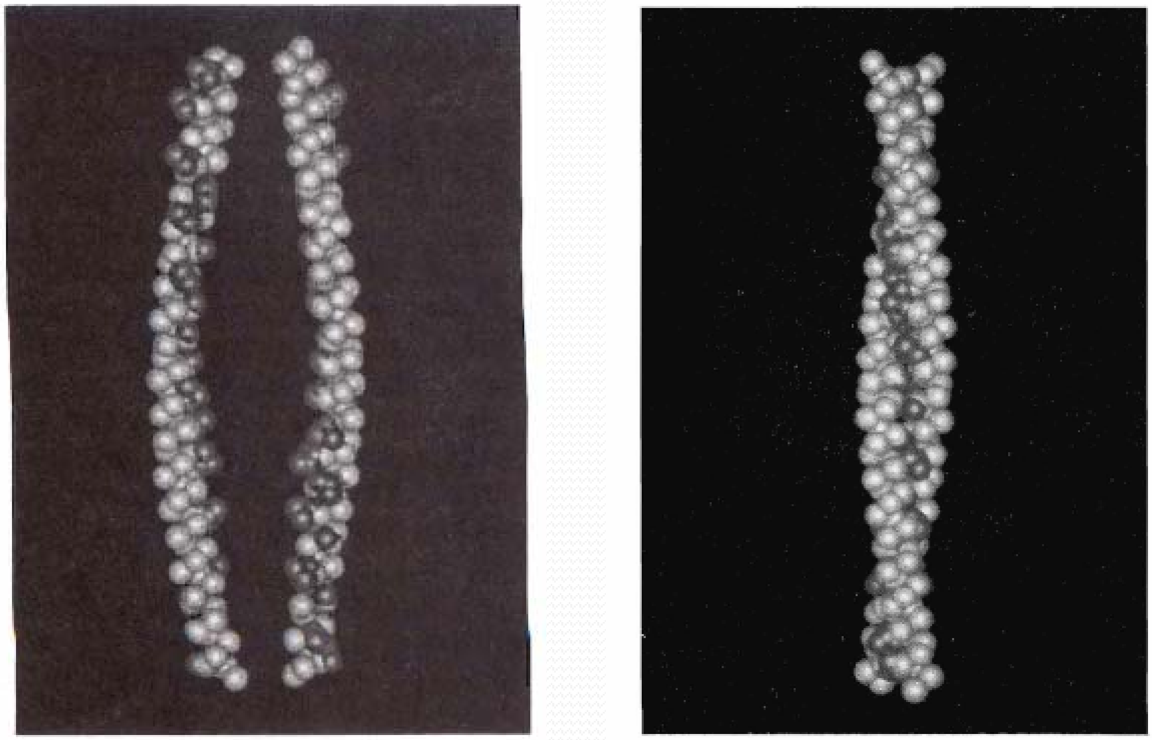
From H. Susi, *Methods Enzymol.* 26:455–472 (1972).

Spectral properties



The amide I band of poly(Lys) in the random coil (r), α-helix (α), and antiparallel β-sheet (β) conformations, as measured by infrared spectroscopy in ^2H_2O. The characteristic frequencies for this synthetic polyamino acid are somewhat different from those found in other polypeptides and proteins. (From H. Susi, *Methods Enzymol.* 26:455–472, 1972.)

Fibrous Proteins

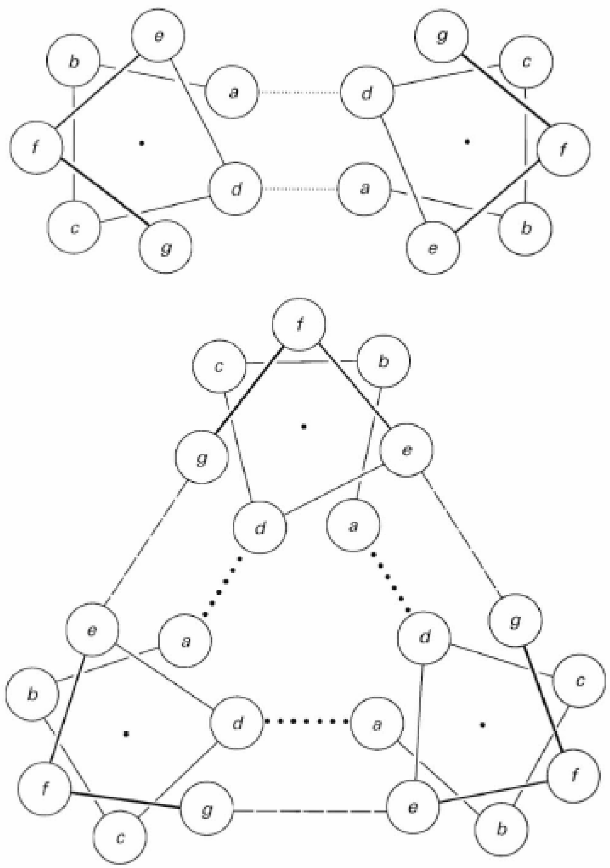


A

B

The structure of α-helical coiled coils. *A* shows two parallel α-helices twisted slightly as they are when interacting. The shaded atoms make up the apolar stripe of residues *a* and *d* of the heptad repeat that pack together in the parallel dimer (*B*). (From C. Cohen and D. A. D. Parry, *Proteins: Struct. Funct. Genet.* 7:1–15, 1990.)

Fibrous Proteins



Helical wheel representations of one heptad repeat of the individual α-helices, illustrating how the side chains of residues *a* and *d* pack together in the two- or three-stranded coiled coils. (From A. C. Steven et al., *J. Mol. Biol.* 200:351–365, 1988.)

Fibrous Proteins

Table 5.5 *Frequency of Occurrence of Amino Acids in the Heptad Repeats of Coiled-Coil Proteins*

Amino acid	Average Occurrence at Different Positions (%)						
	a	*b*	*c*	*d*	*e*	*f*	*g*
Ala	10.2	12.3	8.1	22.2	4.4	11.1	9.3
Cys	0.9	0.0	0.4	0.3	0.2	0.5	0.1
Asp	0.1	13.4	13.0	1.0	4.0	9.8	8.0
Glu	0.8	21.2	19.3	5.5	31.5	14.7	20.1
Phe	2.0	0.4	1.4	2.1	0.4	0.4	0.0
Gly	0.6	1.7	3.5	1.0	1.3	4.2	1.2
His	1.2	2.7	1.6	1.1	0.8	2.6	0.7
Ile	13.2	0.9	2.2	6.3	2.4	2.2	2.2
Lys	7.7	15.3	11.5	0.6	9.0	10.5	14.9
Leu	32.2	1.6	3.9	34.7	6.4	3.9	5.6
Met	4.9	0.9	0.9	2.3	0.9	1.0	0.4
Asn	3.6	4.3	4.6	1.1	5.7	4.8	2.7
Pro	0.0	0.2	0.1	0.0	0.0	0.0	0.0
Gln	0.8	8.7	7.5	4.1	14.0	6.1	13.2
Arg	5.5	6.2	8.2	0.9	6.6	13.2	10.7
Ser	2.1	3.6	8.1	2.2	5.2	8.1	4.5
Thr	1.2	3.8	3.7	2.2	5.1	3.6	3.5
Val	8.9	1.9	1.9	6.0	1.9	3.1	2.7
Trp	0.1	0.0	0.0	0.7	0.0	0.1	0.0
Tyr	4.1	0.9	0.3	5.7	0.3	0.2	0.2

The average occurrences of the various amino acid residues at positions *a-b-c-d-e-f-g* were tabulated from the heptad repeats of tropomyosin, myosin, paramyosin, and intermediate filament proteins.

From C. Cohen and D. A. D. Parry, *Proteins: Struct. Funct. Genet.* 7:1–15 (1990).

Model for the three-stranded collagen structure, represented as the repeating sequence -Gly-Pro-γOH Pro-. The three-stranded structure is on the *left*, a single strand on the *right*. (From R. D. B. Fraser et al., *J. Mol. Biol.* 129:463–481, 1979.)