

Übersicht zur VL Biophysik

- **Strukturbiologie I**
 - Aufbau von Proteinen
 - Aufbau von Nukleinsäuren
 - Aufbau von Membranen
- **Physikalische Methoden zur Charakterisierung von Biopolymeren**
 - Massenbestimmung
 - Absorption
 - Fluoreszenz
 - Circular dichroismus

Übersicht zur VL Biophysik

- Biothermodynamik
- Intrinsische Kräfte und Energien für die Strukturbildung von Biopolymeren
 - Elektrostatische Wechselwirkungen
 - Hydrophobe Wechselwirkungen
 - Wasserstoffbrücken
 - Van-der-Waals Kräfte
- Wechselwirkungen zwischen Biopolymeren
- Membranen und Transport

Übersicht zur VL Biophysik

- **Strukturbiologie II: Hochauflösende Methoden zur Strukturaufklärung**
 - NMR-Spektroskopie
 - Röntgenkristallographie
 - Kryoelektronenmikroskopie
 - Einzelmolekülspektroskopie

Literatur zur VL Biophysik

- C.R. Cantor, P.R. Schimmel
„Biophysikalische Chemistry“ Vol. 1, 2, 3
W.H. Freeman and Company, 1980
- R. Winter, F. Noll
„Methoden der Biophysikalischen Chemie“
Taschenbuch, Teubner-Verlag, 1998
- R. Cotterill
„Biophysics - An Introduction“
John Wiley, 2003

Literatur zur VL Biophysik

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- W. Hoppe, W. Lohmann, H. Markl, H. Ziegler
„Biophysik“
Springer-Verlag, 1982
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„Molekulare Biophysik“
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Literatur zur VL Biophysik

- H.A. Tritthart
„Medizinische Physik und Biophysik“
Schattauer, 2001

Definition Biophysik

Physik der lebenden Materie

oder

Experimentelle Hilfsmittel zum Studium biologischer Systeme

Entstehung der lebenden Materie

- **Die Proteinwelt**
Urey und Millers (1952-55) -> Entstehung von Aminosäuren in der „Ursuppe“
- **Die RNA-Welt**
RNA-Moleküle sind Informationsspeicher und Biokatalysatoren
- **Die Welt von Prof. Günter Wächtershäuser**
Prog Biophys Mol Biol. (1992), **58**, 85-201; Science 1998, 2000, 2002, 2003

Entstehung der lebenden Materie

- Die Welt von Prof. Günter Wächtershäuser

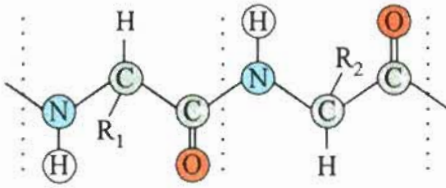
Deduktives Vorgehen:

1. Jede wissenschaftliche Fragestellung beginnt im Kontext existierender Erfahrungen
2. Am Anfang steht eine Theorie oder Hypothese
3. Entwicklung der Theorie: Immer weniger Annahmen um das gleiche Phänomen zu erklären
4. Experimente stützen oder falsifizieren die Theorien

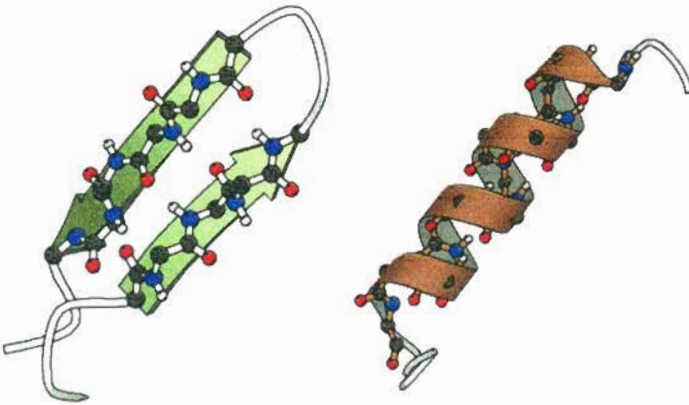
Pyrit-Oberflächen ($\text{Fe}/\text{FeS}/\text{Fe}_2\text{S}_2/\text{Fe}^{2+}$) \rightarrow liefern Energie und Thiosäuren und Thioester mit CO $\rightarrow\rightarrow$ Dipeptide

Protein Architecture

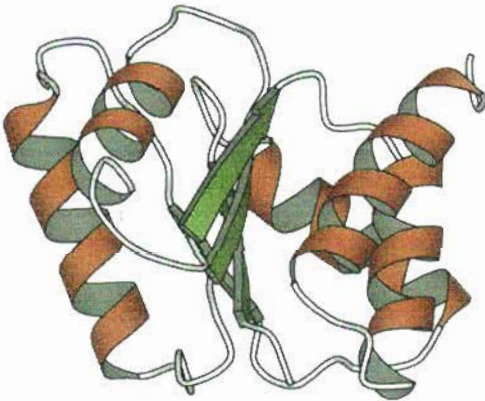
poly- α -amino acid



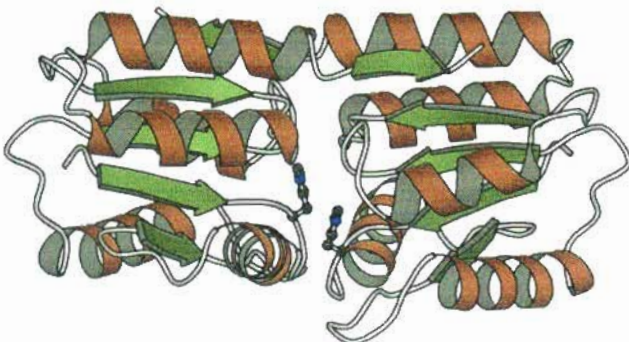
primary structure



secondary structure



tertiary structure



quaternary structure

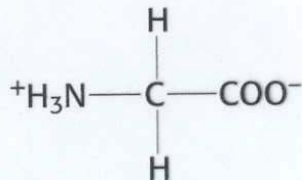
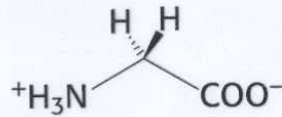
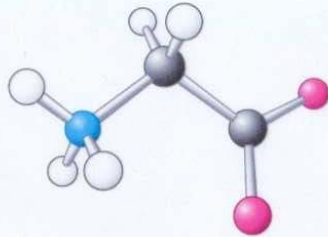
TABLE 1.1

Chronology of discovery of the chemical composition of proteins

<u>Glycine</u>	Braconnet (1820)
<u>Leucine</u>	Proust (1819), Braconnet (1820)
<u>Tyrosine</u>	von Liebig (1846), Bopp (1849)
Serine	Cramer (1856)
Glutamate	Ritthausen (1866)
Aspartate	Ritthausen (1868)
Phenylalanine	Schulze and Barbieri (1879)
Alanine	Weyl (1888)
Lysine	Drechsel (1889)
<u>Arginine</u>	Hedin (1895)
<u>Histidine</u>	Hedin (1896), Kossel (1896)
<u>Cysteine and the S-S bridge</u>	As cystine: Morner (1899) As cysteine: Mirsky and Anson (1935)
Valine	Fischer (1901)
Proline	Fischer (1901)
Tryptophan	Hopkins and Cole (1901)
Isoleucine	Ehrlich (1903)
Methionine	Mueller (1921)
<u>Asparagine</u>	Vauquetin (1806)
Glutamine	Schulze (1833)
Threonine	Meyer and Rose (1935)
Chromatography	Martin and Synge (1941)
Performic acid treatment of S-S bridges	Toennies and Homiller (1942)
Amino-terminal identification of polypeptide or polypeptide fragments from partial hydrolysis	Sanger (1945)
Separation of S-S bounded insulin chains	Sanger (1949)
Sequence of phenylalanine chain of insulin	Sanger and Tuppy (1951)
Sequence of glycine chain of insulin	Sanger and Thompson (1953)

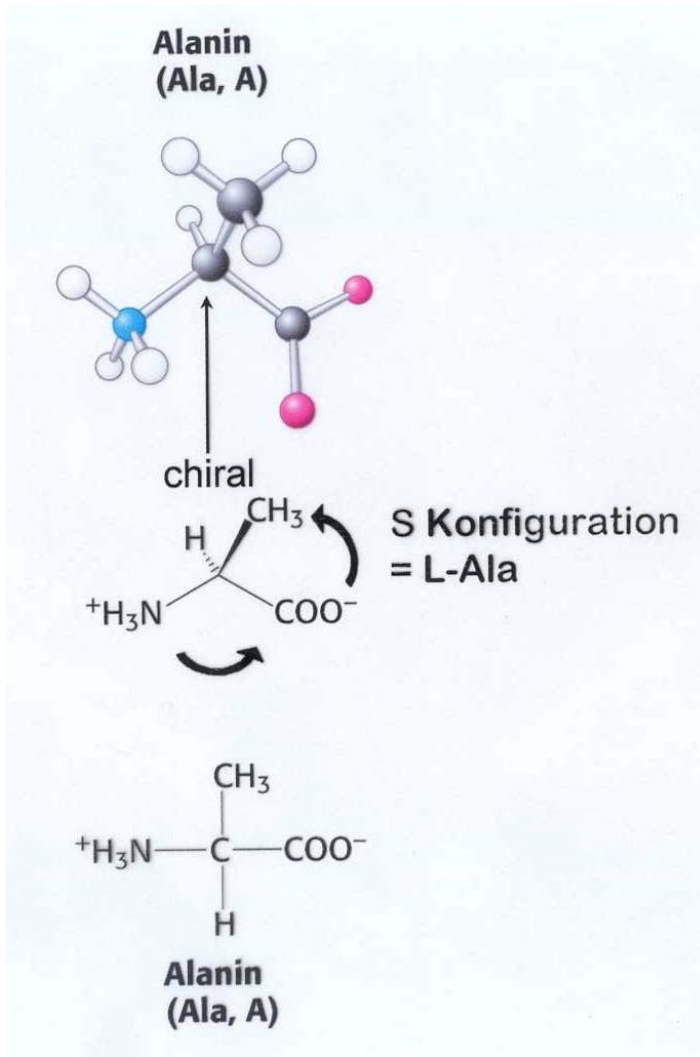
AUS: Robson & Garnier
85WD5050R667

Glycin
(Gly, G)



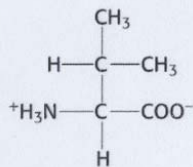
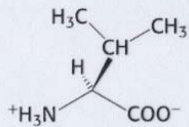
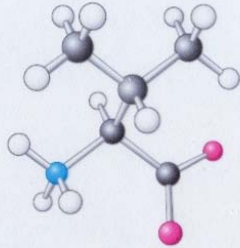
Glycin
(Gly, G)

- keine Seitengruppe
- ungewöhnliche Diederwinkel
- an sterisch engen Stellen
- relativ hoch konserviert, weil andere AS an diesen Stellen nicht passen



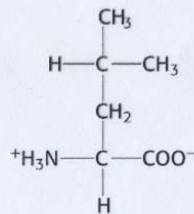
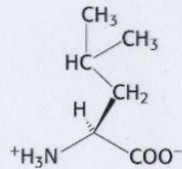
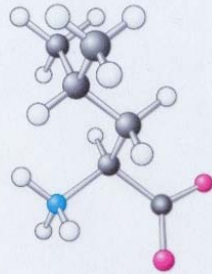
- häufigste Aminosäure
- „billig“ für die Zelle

Valin
(Val, V)



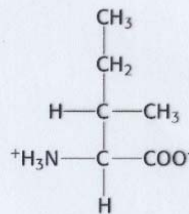
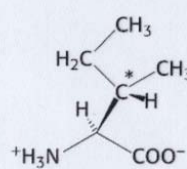
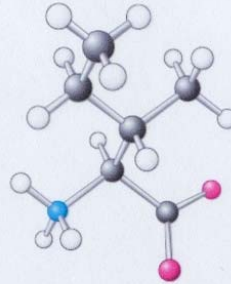
Valine
(Val, V)

Leucin
(Leu, L)



Leucine
(Leu, L)

Isoleucin
(Ile, I)



Isoleucine
(Ile, I)

Hydrophobe Aminosäuren

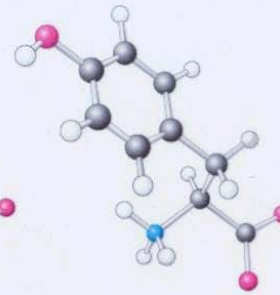
- verzweigte Seitenkette
 - geringe Flexibilität
 - hydrophober Charakter
- > im Proteininneren

Aromatische Aminosäuren

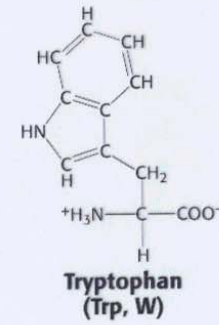
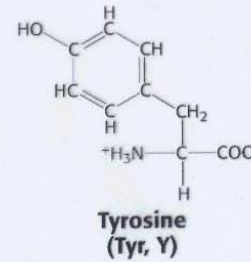
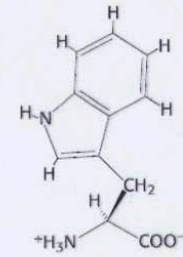
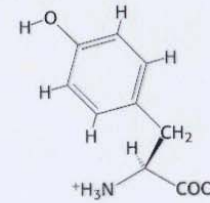
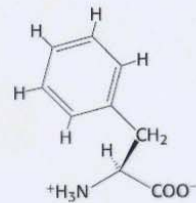
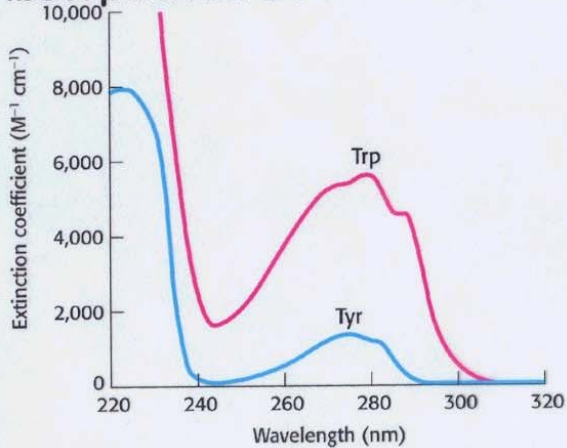
Phenylalanin
(Phe, F)

Tyrosin
(Tyr, Y)

Tryptophan
(Trp, W)

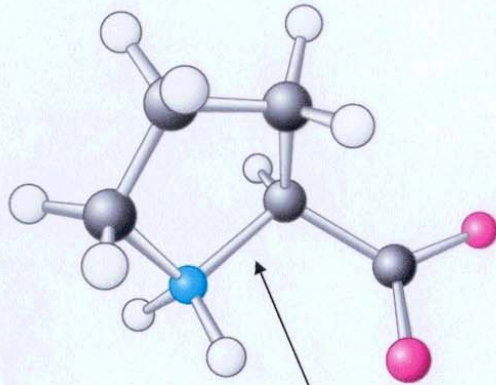


Absorption im UV

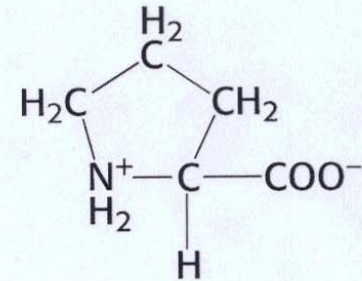
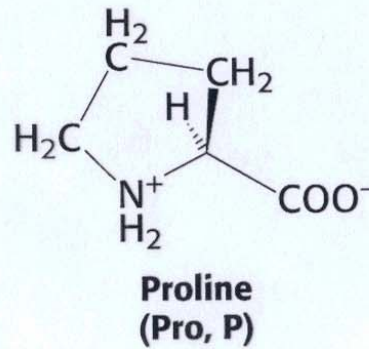


- CH₂-Spacer für die Flexibilität
- hydrophober Charakter
- Tyr: pK_a = 10, H-Brücken

Prolin
(Pro, P)

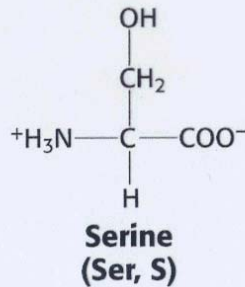
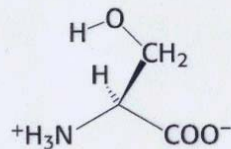
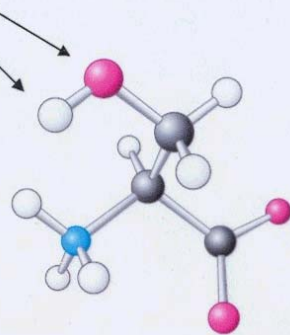


Fünfring fixiert N—C α

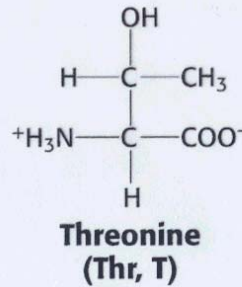
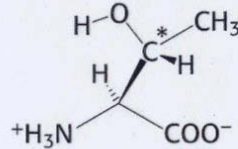
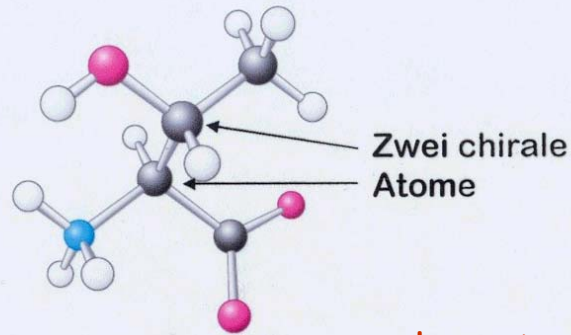


- zyklisches Imin, kein NH Proton, hydrophob
- C γ : „out of plane“
- cis/trans Gleichgewicht

H-Brücken
Serin
(Ser, S)



Threonin
(Thr, T)



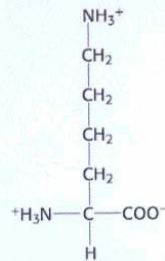
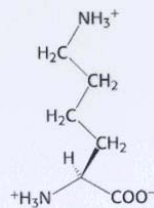
polare Aminosäuren

- Oberfläche
- H-Brückenabsättigung
 -> hydrophob
- Termini von Helices
- an aktiven Zentren

**Basische
Aminosäuren,**

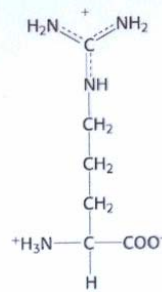
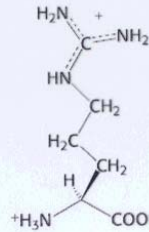
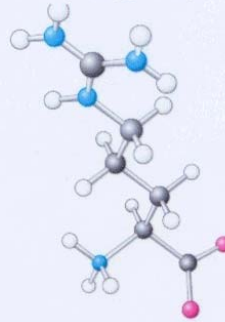
positiv geladen

**Lysin
(Lys, K)**



**Lysine
(Lys, K)**

**Arginin
(Arg, R)**



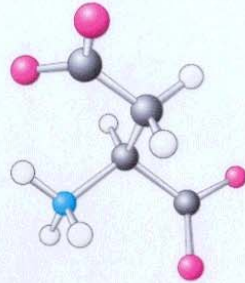
**Arginine
(Arg, R)**

- positiv geladene Oberfläche
- Angriffspunkt für Proteasen (z.B. Trypsin)
- chemisch modifizierbar (z.B. Glutaraldehyd)

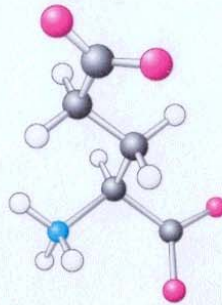
Saure
Aminosäuren
und ihre Amide

- H-Brücken
- Komplexierung von Metallen
- Glycoproteine

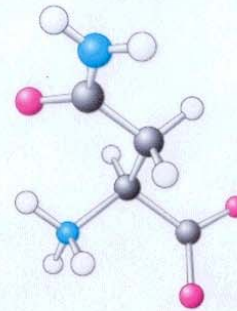
Aspartat
(Asp, D)



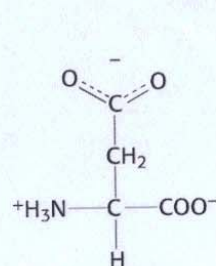
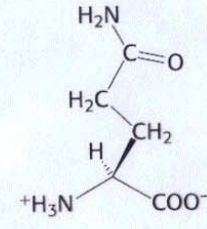
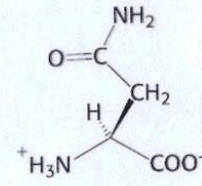
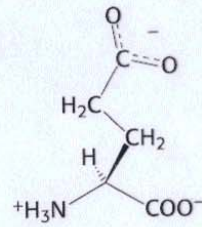
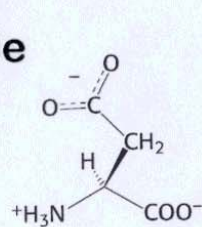
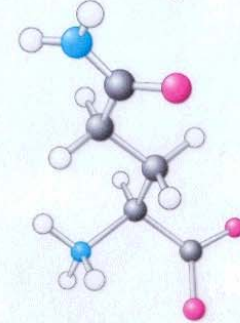
Glutamat
(Glu, E)



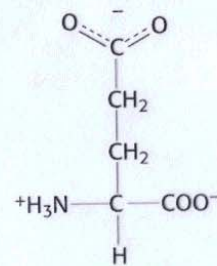
Asparagin
(Asn, N)



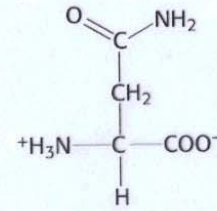
Glutamin
(Gln, Q)



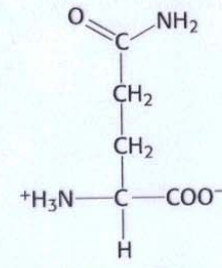
Aspartate
(Asp, D)



Glutamate
(Glu, E)

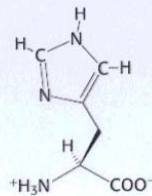
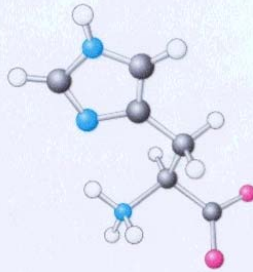


Asparagine
(Asn, N)

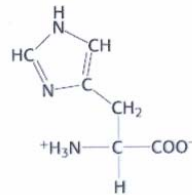


Glutamine
(Gln, Q)

**Histidin
(His, H)**



pK 6-7

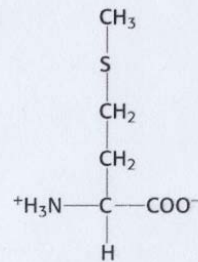
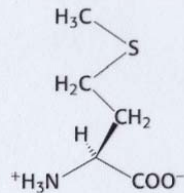
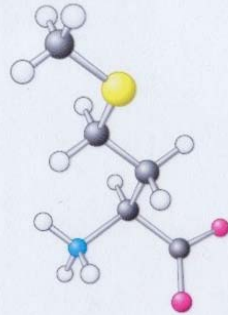


**Histidine
(His, H)**

- sehr oft im aktiven Zentrum
- Amin- >Nukleophil
- Base oder Säure
- Komplexierung von Kationen
- Ni^{2±} Affinitäts chromatographie

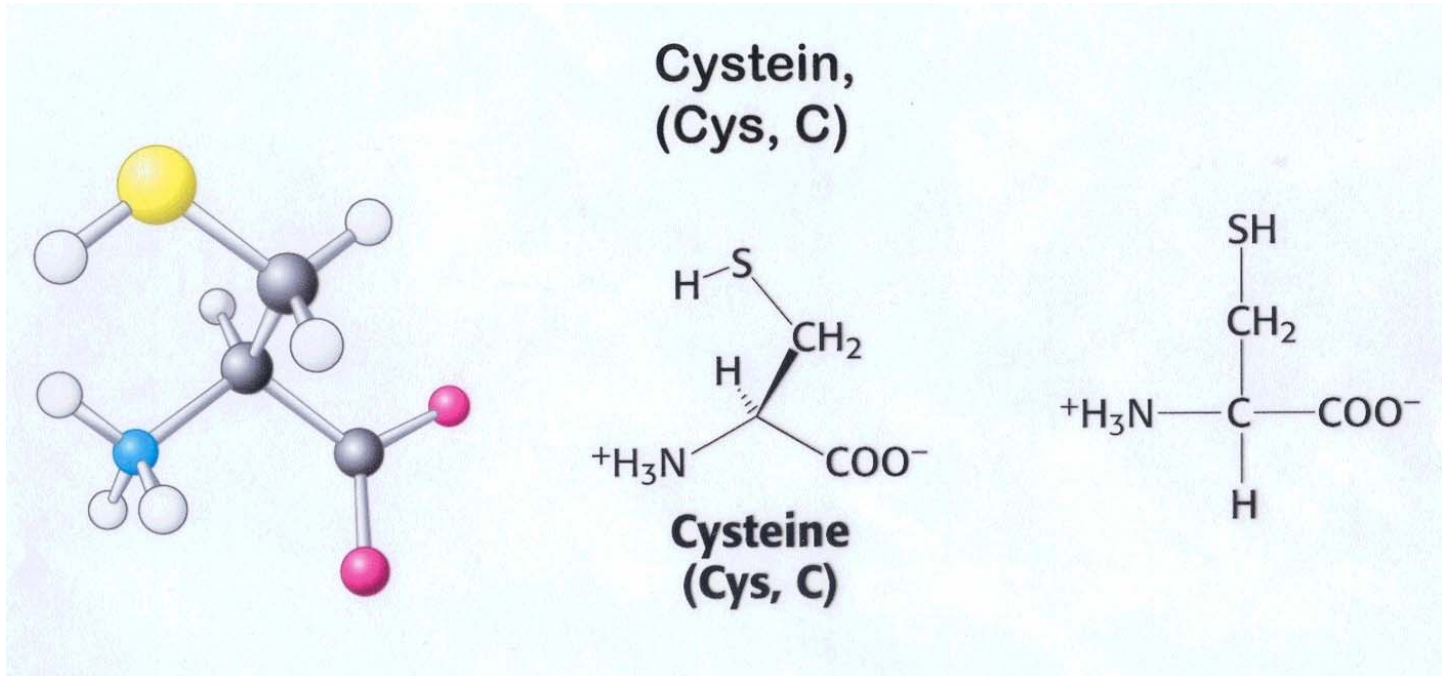
Methionin

(Met, M)



Methionine
(Met, M)

- hydrophob
- S = Nukleophil
- oxidationsanfällig
- spaltbar mit CNBr
(z.B. Fusionsproteine)



- reaktivste Seitengruppe
- $pK_a = 8$
- Thiolatanion: Nukleophiler Angriff
- Anknüpfung von Farbstoffen
- Disulfidbrücken

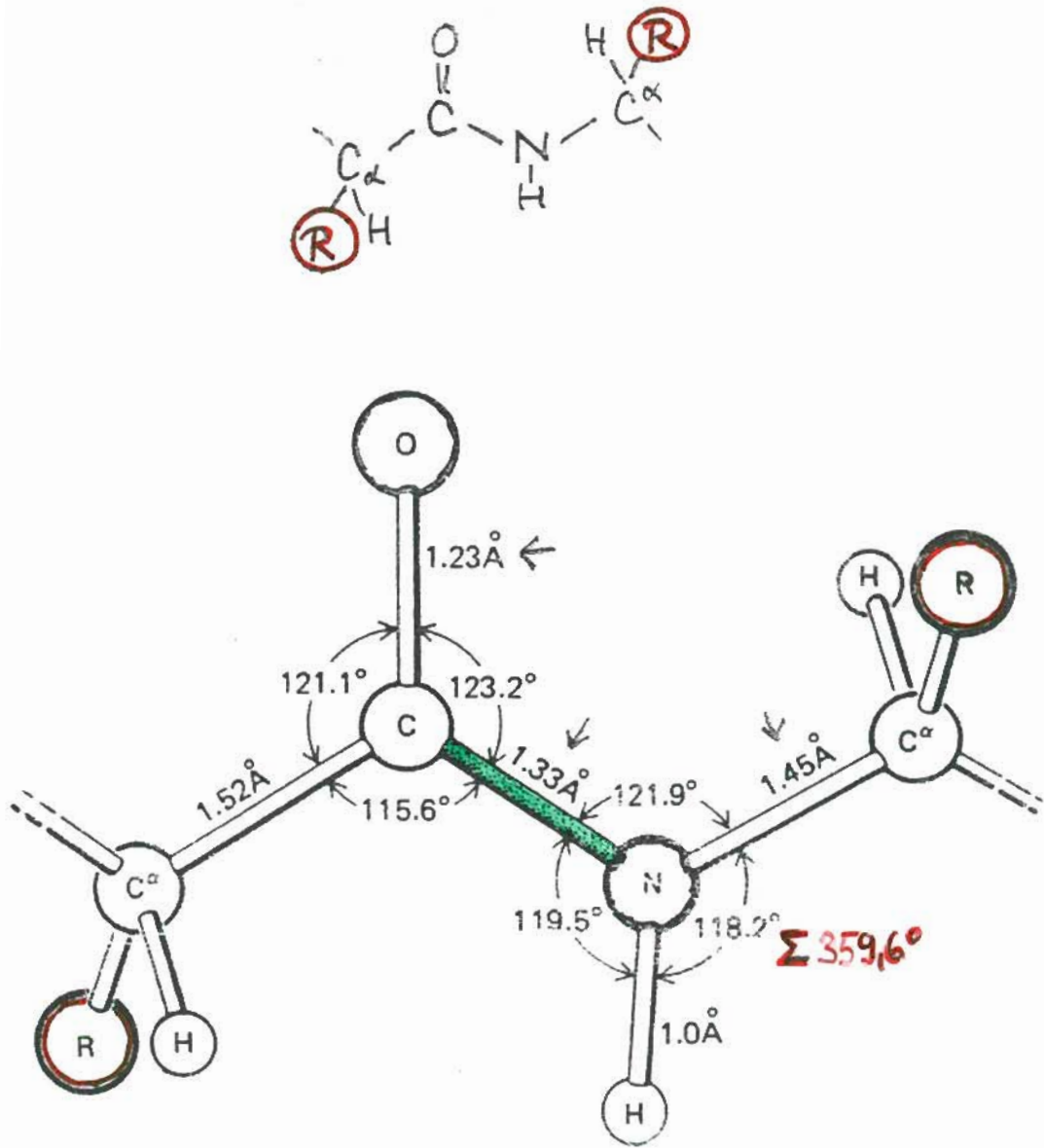


Figure 1-2
 The geometry of the peptide backbone, with a trans peptide bond, showing between two C^α atoms of adjacent residues. The peptide bond is stippled. The values given are the averages observed crystallographically, in amino acids and small peptides from G. N. Ramachandran, et al., *Biochim. Biophys. Acta* 359:298-302, 19

Creighton

- C-N : 1.45 Å
- C=O : 1.25 Å

$\psi = 0^\circ$: N_i & N_{i+1} cis
 $\phi = 0^\circ$: C'_i & C'_{i-1} cis
 $C=O$ $C=O$

Definition
 Dieder \neq

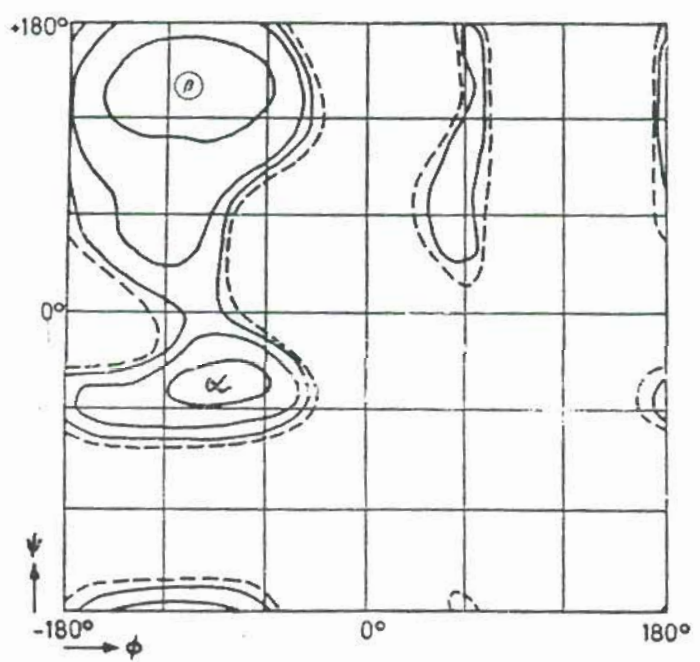
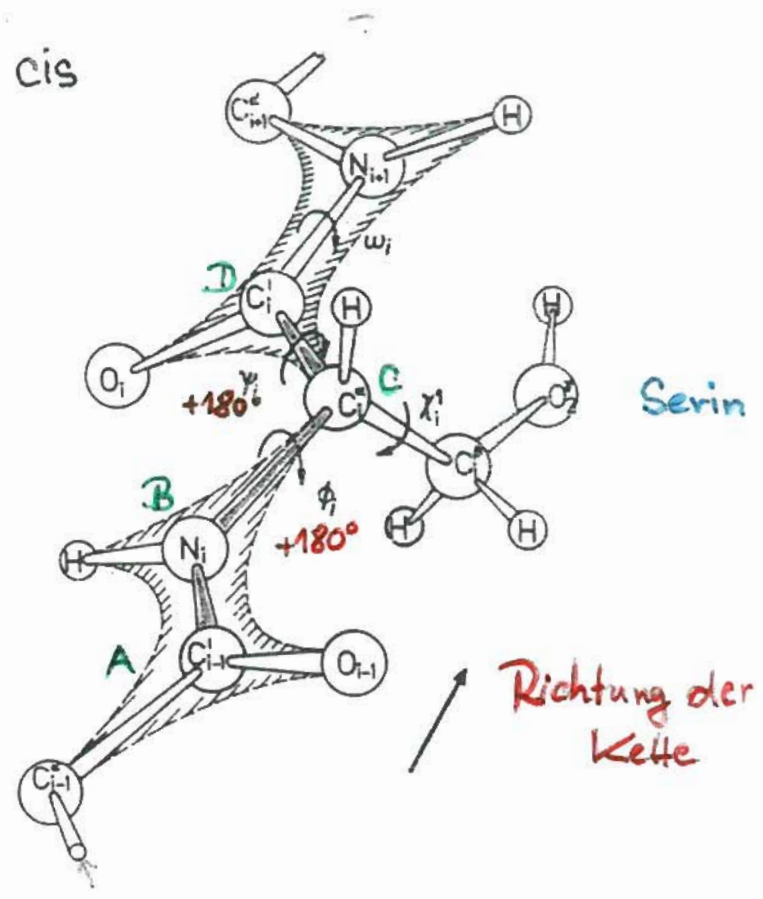
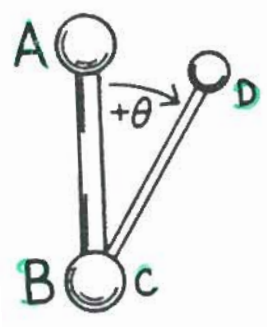
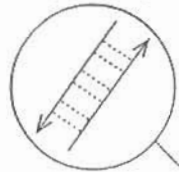


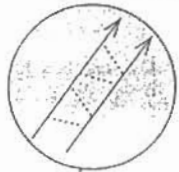
Figure 2-5. Potential energy distribution in the (ϕ, ψ) -plane for a pair of peptide units with an **Ala** residue in between, taken from Ref. (34). The map is calculated on the basis of the Pauling-Corey dimensions of a peptide bond (Figure 2-1a). Contours are drawn at intervals of 1 kcal/mol going negative from zero. The zero contour is dashed. The position of a twisted β -sheet is indicated. Note that this distribution is modified if hydrogen bonds to peptide units farther along the chain (for example in an α -helix) are taken into account.

Ramachandran-Auftragung

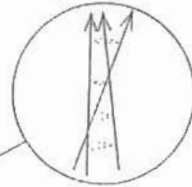
Flat antiparallel β sheet



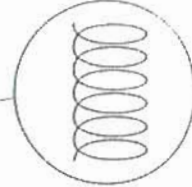
Flat parallel β sheet



Collagen triple helix



Left-handed α helix



α carbon

Amide plane

ψ 180°

α carbon

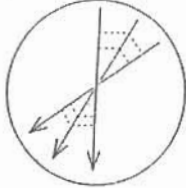
Side group

180°

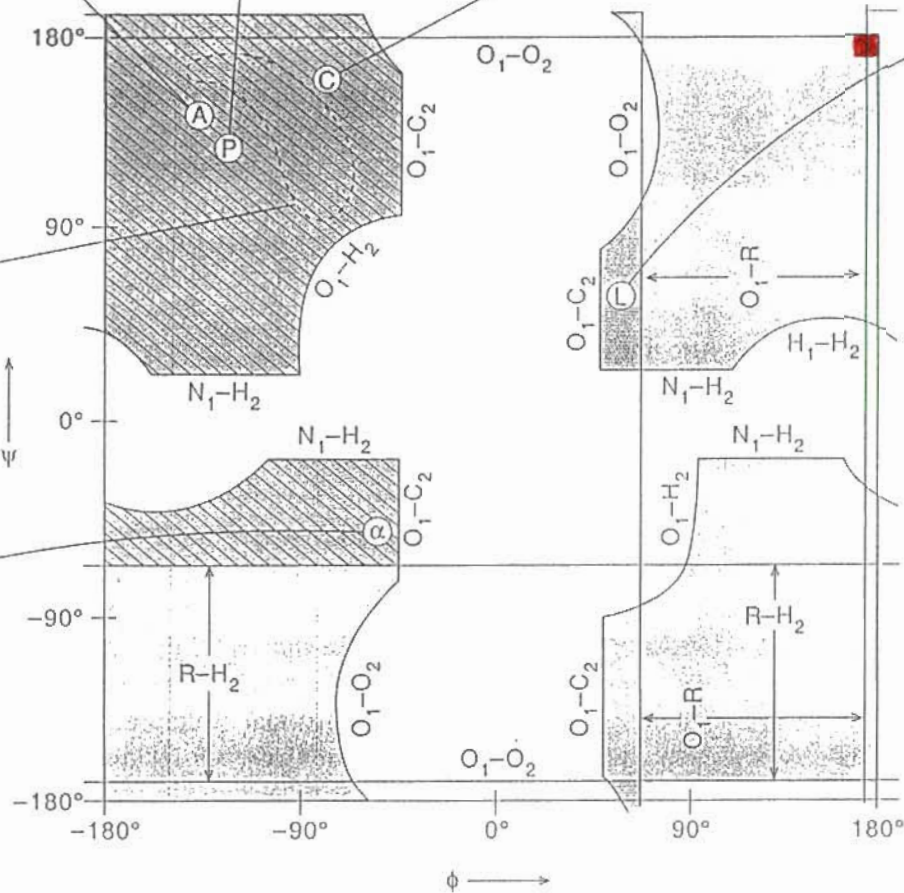
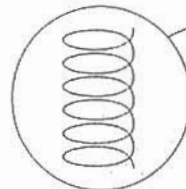
Amide plane

α carbon

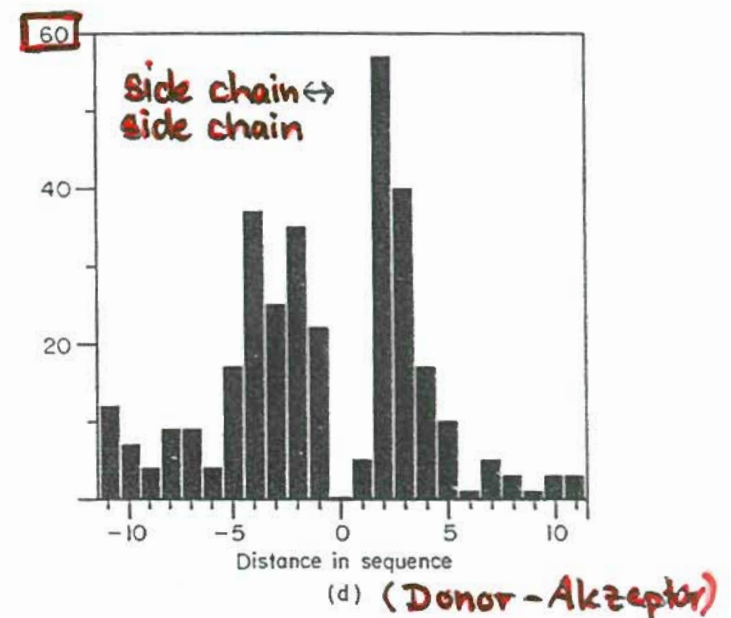
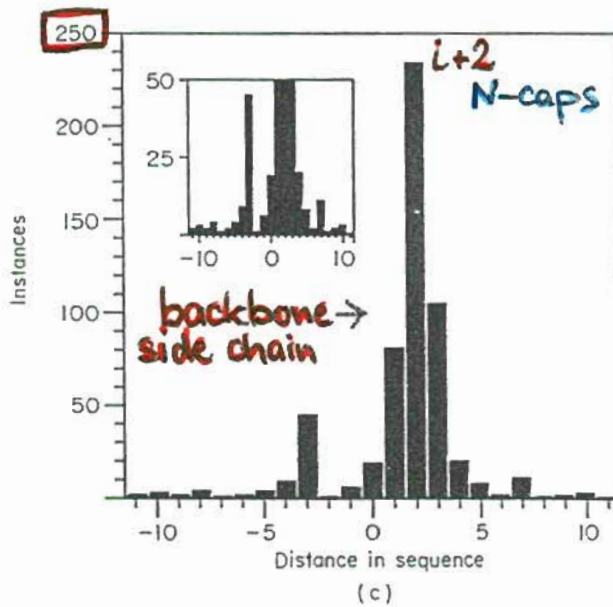
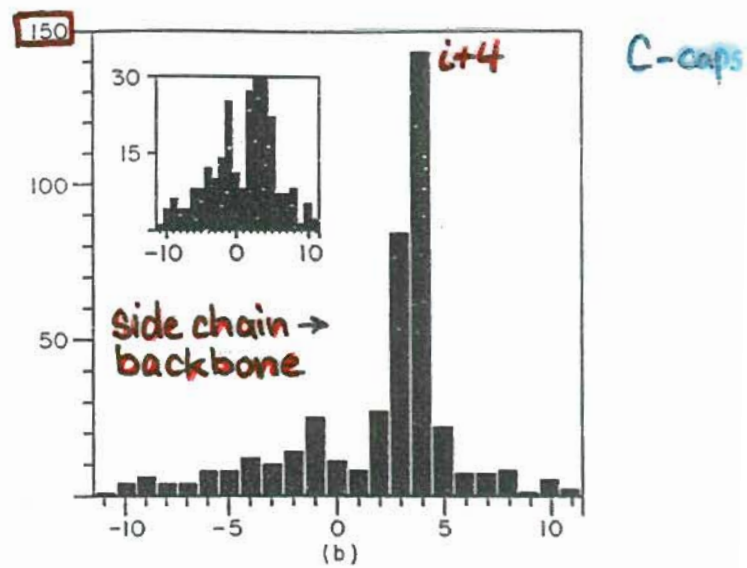
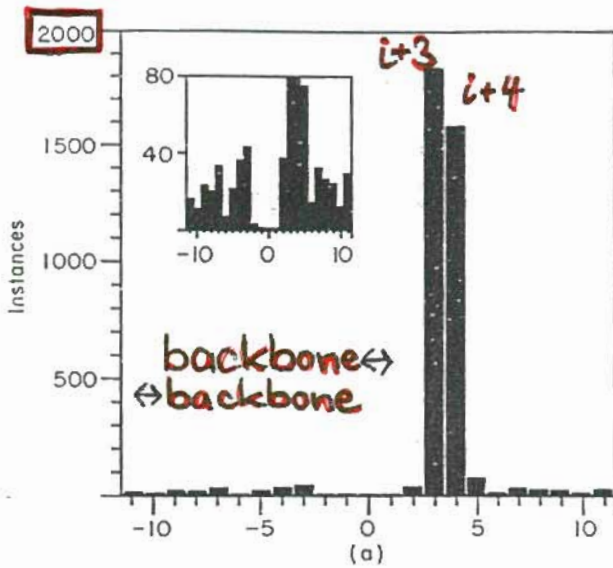
Right-twisted β sheets



Right-handed α helix

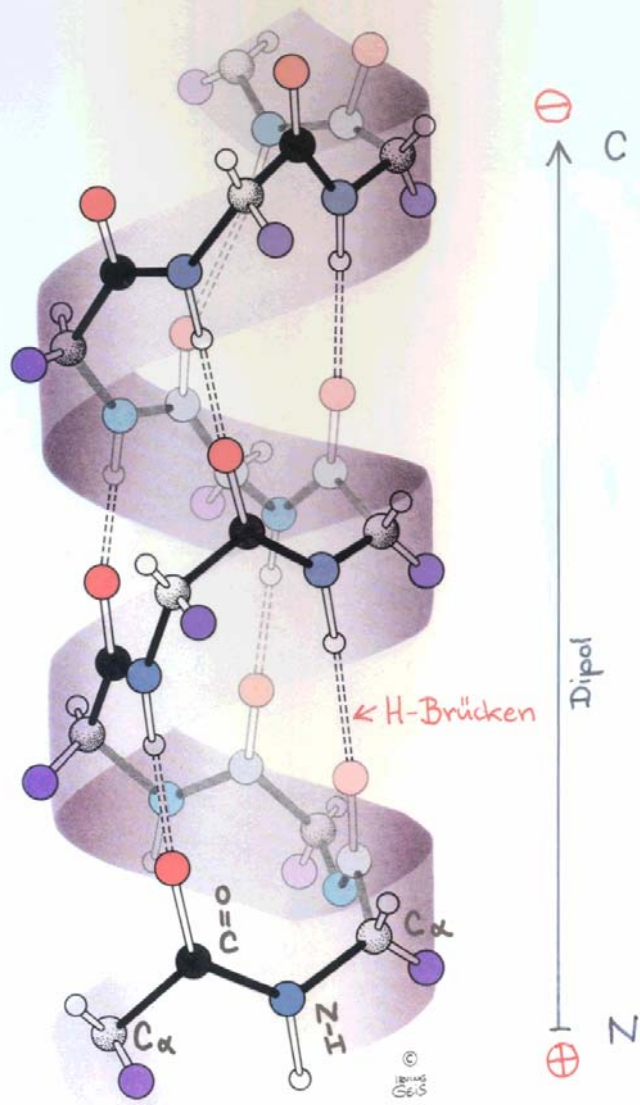


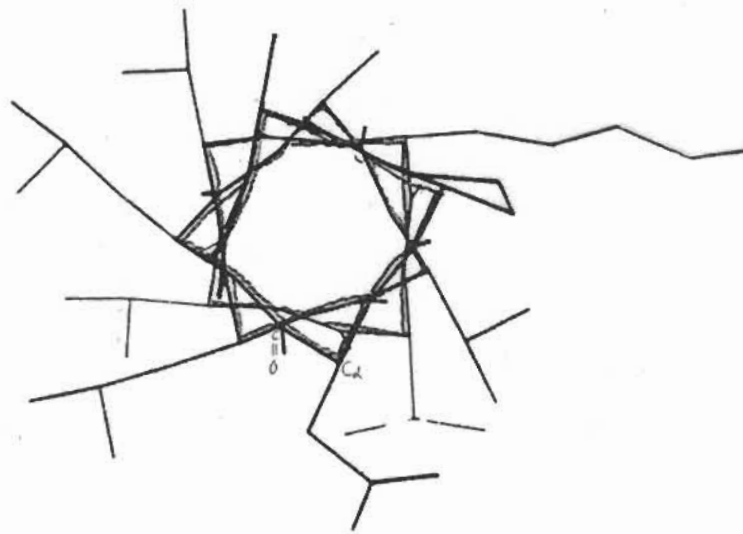
Zusatz: 4. Aufl. S. 84



Verteilung von H-Brücken in Proteinen

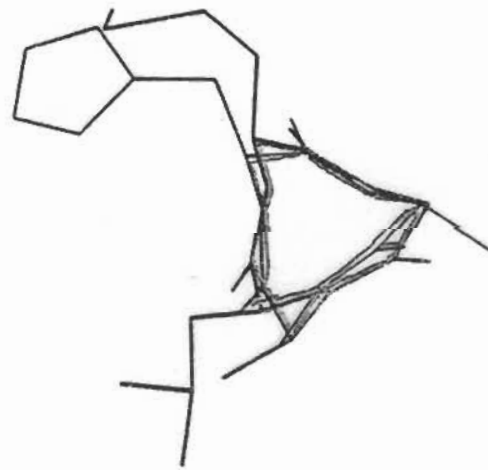
Helix





α -Helix

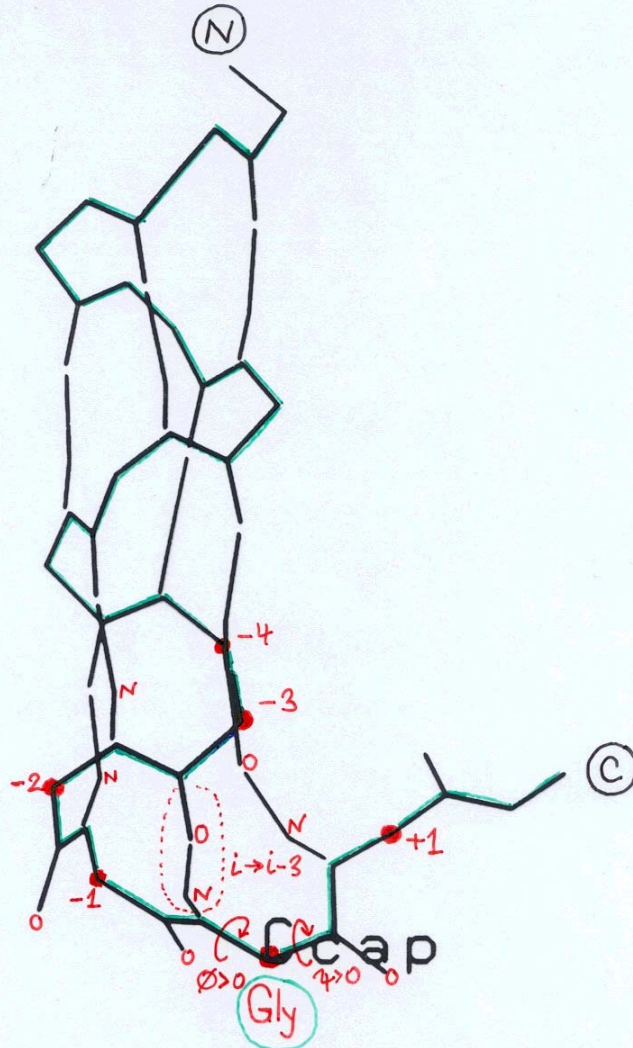
Figure 13. End view of an α helix (2MHR 40-60).



3₁₀-Helix

Figure 16. End view of a 3₁₀ helix (2CYP 171-177), in stereo, showing the distinctively triangular pattern of the backbone.

α -Helix : 3_{10} -C-cap



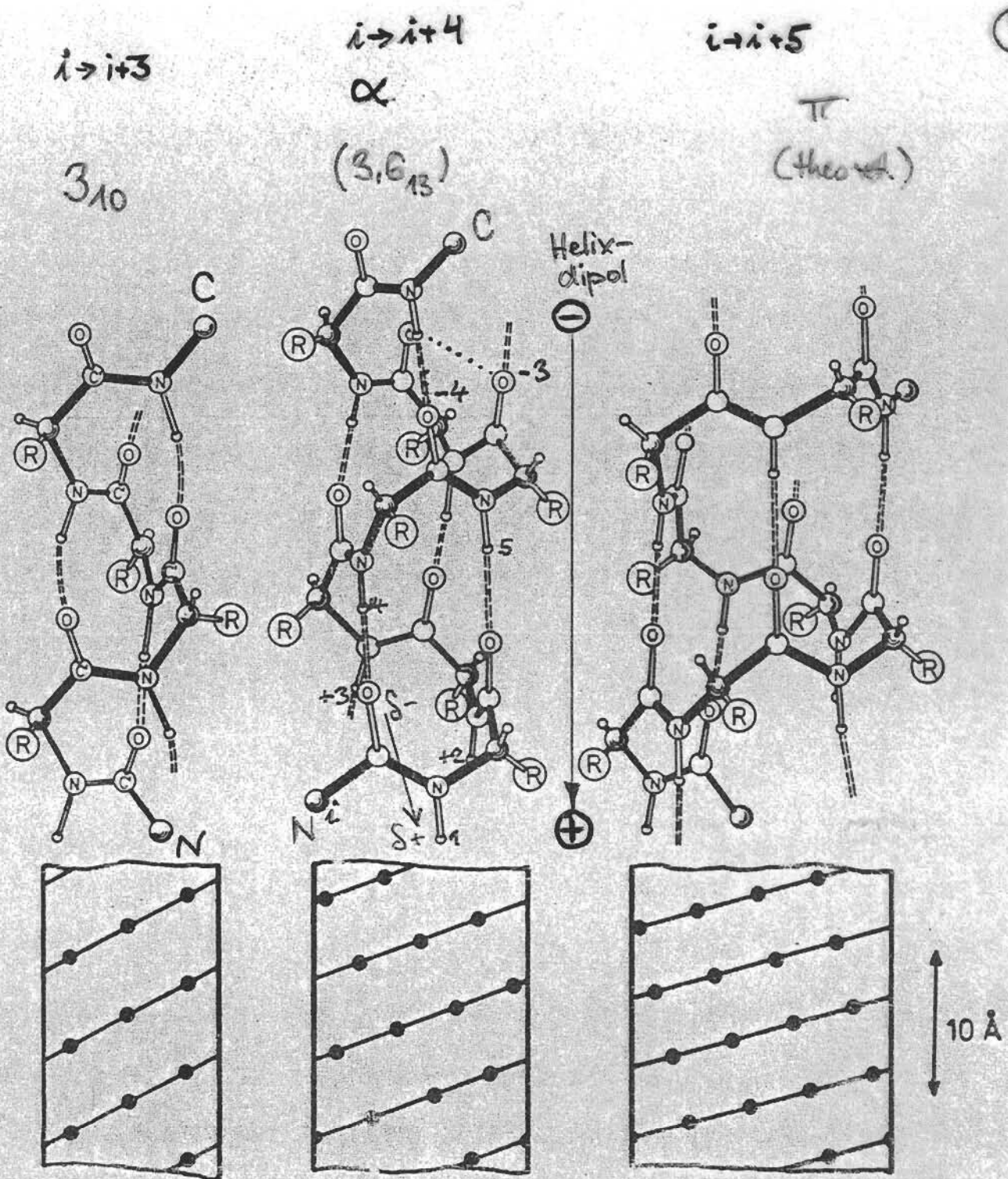


Figure 5-4. Helices of polypeptide chains with internal hydrogen bonds. From left to right: 3_{10} -, α -, and π -helix. Below: cylindrical plots of these helices; the course of the chain and the C_{α} -positions are marked.

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