

units represented by equations (42) geometry of the conductance relations presentation of our numerical results removed in these extreme limits. In that exact solutions of equation of the standard Airy functions and functions and their derivatives, one by the procedure outlined in the that table look up would replace prove cumbersome as a desk calculator of the boundary conditions. It compiled by Smirnov, 1960. In fact that the Russian workers give  $\tau = 0$ , using their notation. This may (28), by reflecting the real axis

in the preparation and processing of and services of the Western Data Production, University of California at Los Angeles the numerical analysis was provided at Riverside as well. This work was

Mathematical Physics (third edition), Special Confluent Hypergeometric Functions, Pergamon Press.

PHYSICAL JOURNAL VOLUME 5 1965

## STEREOCHEMICAL CRITERIA FOR POLYPEPTIDE AND PROTEIN CHAIN CONFORMATIONS

### II. ALLOWED CONFORMATIONS FOR A PAIR OF PEPTIDE UNITS

C. RAMAKRISHNAN and G. N. RAMACHANDRAN

*From the Centre of Advanced Study in Biophysics, University of Madras, Madras, India, and the Biophysics Research Division, University of Michigan, Ann Arbor*

**ABSTRACT** The conformation of a polypeptide or protein chain may be specified by stating the orientations of the two linked peptide residues at each alpha carbon atom in the chain, namely the two dihedral angles  $\phi$ ,  $\phi'$  about the single bonds  $N-\alpha C$  and  $\alpha C-C'$  from a defined standard conformation. By using certain criteria of minimum contact distances between the various atoms, the allowed angles of  $(\phi, \phi')$  have been worked out for three values of the angle  $N-\alpha C-C'$  ( $\tau$ ), namely  $105^\circ$ ,  $110^\circ$ , and  $115^\circ$  for non-glycyl, and  $110^\circ$  and  $115^\circ$  for glycyl residues. The theory is compared with all the available crystallographic data (up to early 1965) on simple (di- and tri-) peptides, cyclic peptides, polypeptide and protein structures, and the observed data fully support the conclusions from theory. The effect of the gamma carbon atom, in its three possible positions, is also discussed, and is found to alter the outer limits of the allowed region of  $(\phi, \phi')$  only slightly. The paper contains exhaustive references to the published data on these structures, using x-ray diffraction.

### INTRODUCTION

The conformation of the backbone of a polypeptide or protein chain can be completely specified by giving the relative orientations of the two linked peptide groups at each  $\alpha$ -carbon atom. When the relative orientations of the peptide group are the same at every  $\alpha$ -carbon atom, then the chain takes up a regular helical folding. In Part I (Ramakrishnan, 1964) methods were described of calculating the parameters of such a helix, mainly the number of residues per turn,  $n$ , and the unit translation of the residue along the helix,  $h$ , from a knowledge of the geometry of the peptide group and the relative orientations of the linked peptide groups. However, not all possible orientations will be stereochemically allowed, because of the short contacts between the atoms of the adjacent residues. A study of this type has been made using certain definite stereochemical criteria and the preliminary results corresponding to the angle  $N-\alpha C-C'$  ( $\tau$ ) =  $100^\circ$  have already been published (Sasisekharan, 1962;

Ramachandran, Ramakrishnan, and Sasisekharan, 1963a and b). This paper describes the fuller details of the results for this value of the angle,  $\tau$ , and also for two other values of  $\tau$ , namely 105 and 115°. In addition, a complete survey of the structures of di- and tripeptides, cyclic peptides, and polypeptides has also been made to check the predicted ranges of allowed conformations. These results are discussed in addition to a study of the conformations which occur in myoglobin.

It may be mentioned that although studies of this type have been reported so far in the literature (Huggins, 1943; Bragg, Kendrew, and Perutz, 1950; Pauling, Corey, and Branson, 1951; Low and Baybutt, 1952; Low and Grenville-Wells 1953; Donohue, 1953; Lindley and Rollett, 1955; Shimanouchi and Mizushima, 1955; Scheraga, 1960), they have not been definitive. Mizushima and Shimanouchi (1961) have taken into account the restrictions or barriers due to the rotation about the two single bonds meeting at the  $\alpha$ -carbon atoms and have preferred nine conformations for the polypeptide chain. More recently, De Santis *et al.* (1965) have considered this problem from potential energy considerations, and Nemethy and Scheraga (1965) have obtained interesting results regarding extended chains and the formation of closed loops containing S-S bridges.

The notation used here for representing the relative orientation of the linked peptide groups is the same as that described in Part I (Ramakrishnan, 1964). The rotations of the two peptide groups are denoted by two dihedral angles ( $\phi$ ,  $\phi'$ ) respectively, these being measured from an initial standard conformation  $\phi = \phi' = 0^\circ$ , in which the planes of the two peptide groups lie in the plane N- $\alpha$ -C' containing the two axes of rotation, and the NH groups of the two residues are pointing towards each other.<sup>1</sup>

#### DETERMINATION OF ALLOWED CONFORMATIONS

In order to determine the allowed conformations, the contact distances between the atoms in the adjacent residues have to be examined using criteria for minimum van der Waals contact distances. This is best done by first working out the positions of

<sup>1</sup> At a recent conference of some of the representative workers in this field held in Bethesda, it was decided to denote the two dihedral angles about the bonds N-C $\alpha$  and C $\alpha$ -C' by  $\phi$  and  $\psi$  respectively, the sense of rotation being the same as that adopted here. The fully extended chain, with N-H and C'=O *trans* with respect to one another, is to be taken as the standard conformation with  $\phi = \psi = 0$ .

It is readily seen that the new  $\phi$  is the same as the old  $\phi$ , but that  $\psi = 180^\circ + \phi'$  (and  $\phi' = 180^\circ + \psi$ ). All the data reported here are thus readily converted into the ( $\phi$ ,  $\psi$ ) coordinates. The diagrams in Figs. 2, 3, and 6 have to be shifted up by 180°, or half the total length, along the vertical direction. In particular, the right- and left-handed alpha helices will have ( $\phi$ ,  $\psi$ ) equal to (133°, 123°) and (227°, 237°). As before, a helix with ( $-\phi$ ,  $-\psi$ ) will be inverse to one with ( $\phi$ ,  $\psi$ ); *i.e.*, it will be of opposite sense, but having the same number of turns per unit.

This paper was finalized well before this meeting, and so the older conventions are adopted here. However, it is proposed to use the new notation in the following papers in this series.

in, 1963a and b). This paper  
value of the angle,  $\tau$ , and also for  
dition, a complete survey of the  
and polypeptides has also been  
conformations. These results are  
ns which occur in myoglobin.

is type have been reported so far  
and Perutz, 1950; Pauling, Corey,  
Low and Grenville-Wells 1953;  
nanouchi and Mizushima, 1955;  
mishima and Shimanouchi (1961)  
ers due to the rotation about the  
nd have preferred nine conforma-  
e Santis *et al.* (1965) have con-  
siderations, and Nemethy and  
ts regarding extended chains and  
ses.

relative orientation of the linked  
art I (Ramakrishnan, 1964). The  
by two dihedral angles ( $\phi$ ,  $\phi'$ )  
standard conformation  $\phi = \phi' =$   
ie in the plane N- $\alpha$ C-C' containing  
two residues are pointing towards

## CONFORMATIONS

the contact distances between the  
ed using criteria for minimum van  
first working out the positions of

workers in this field held in Bethesda,  
t the bonds N-C $\alpha$  and C $\alpha$ -C' by  $\phi$   
s that adopted here. The fully extended  
another, is to be taken as the standard

old  $\phi$ , but that  $\psi = 180^\circ + \phi'$  (and  
adily converted into the ( $\phi$ ,  $\psi$ ) coordi-  
ed up by  $180^\circ$ , or half the total length,  
left-handed alpha helices will have ( $\phi$ ,  
a helix with  $(-\phi, -\psi)$  will be inverse  
out having the same number of turns

i so the older conventions are adopted  
1 the following papers in this series.

the atoms in the two residues for various values of ( $\phi$ ,  $\phi'$ ). Actually, the coordinates of the atoms in the two residues were calculated with respect to a suitably chosen fixed coordinate system, from which the various contact distances were calculated for the various values of ( $\phi$ ,  $\phi'$ ). The following fixed system of coordinates was found to be convenient for this purpose.

The  $\alpha$ -carbon atom C $_2$  at which the two residues [C $_1$ -C $_1'$ O $_1$ -N $_1$ H $_1$ -C $_2$ ] and [C $_2$ -C $_2'$ O $_2$ -N $_2$ H $_2$ -C $_3$ ] are linked together is taken to be the origin of coordinates of a system of axes OXYZ defined as follows. The plane N $_1$ C $_2$ C $_2'$ , which remains unchanged whatever be the rotation of the two groups, is taken as the XY plane with the Z axis upwards. The direction C $_1$ C $_2$ , which lies in the XY plane for  $\phi = 0^\circ$ , is taken as the Y axis. The Z axis is the third perpendicular direction, such that the X, Y, and Z axes form a right-handed system of coordinates. This is shown in Fig. 1.

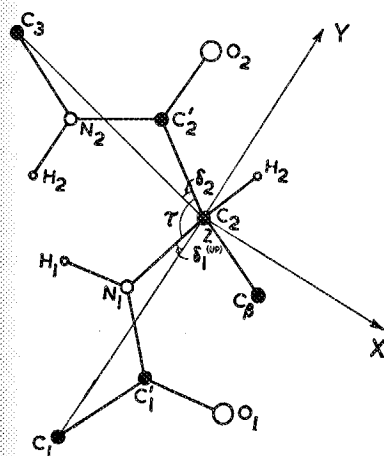


FIGURE 1 The two peptide groups in the initial conformation  $\phi = \phi' = 0^\circ$ . The coordinate axes X, Y, and Z used in the present study are also marked.

Throughout this study, the peptide group has been taken to be planar with NH and CO groups in the *trans* configuration and having the dimensions given by Corey and Pauling (1953).

If  $x, y, z$  and  $x', y', z'$  are the coordinates of an atom before and after rotation, the relations connecting these are given by (Whittaker, 1952)

$$\begin{aligned} x' &= (a^2 + b^2 - c^2 - d^2)x + 2(bc - ad)y + 2(bd + ac)z \\ y' &= 2(bc + ad)x + (a^2 - b^2 + c^2 - d^2)y + 2(cd - ab)z \end{aligned} \quad (1a)$$

$$z' = 2(bd - ac)x + 2(cd + ab)y + (a^2 - b^2 - c^2 + d^2)z$$

where

$$a = \cos(\omega/2), \quad b = L \sin(\omega/2), \quad c = M \sin(\omega/2), \quad d = N \sin(\omega/2) \quad (1b)$$

$\omega$  being the angle of rotation and  $L, M, N$ , the direction cosines of the axis of rotation with respect to the chosen system of coordinates. The sign of  $\omega$  is taken

to be positive, when the rotation is counterclockwise viewing along the axis towards the origin.

The angles of rotation and direction cosines of the axes of rotation corresponding to the two peptide groups about the axes  $N_1-C_2$  and  $C_2-C_2'$  are given in Table I.

The coordinates of the atoms  $C_1$ ,  $C_1'$ ,  $O_1$ , and  $H_1$  were evaluated at intervals of  $10^\circ$  of  $\phi$  and the coordinates of the atoms  $O_2$ ,  $N_2$ ,  $H_2$ , and  $C_2$  were evaluated at intervals of  $10^\circ$  for  $\phi'$ , using the relations (1) for three values of the angle  $\tau$ , namely, 105, 110, and  $115^\circ$ . In fact, all the calculations corresponding to  $\tau = 110$  and  $115^\circ$  were carried out using a desk calculator, while those corresponding to  $\tau = 105^\circ$  were carried out much later using an Elliott-803 electronic computer.

The next step towards working out the allowed conformations is to choose a set of permitted minimum contact distances between the different types of atoms. Only those conformations ( $\phi$ ,  $\phi'$ ) which do not have any of the contact distances less than these minimum values now become allowed. Two such sets are given in Table II, termed "normally allowed" and "outer limit" contact distances. These are

TABLE I  
ANGLES OF ROTATION AND THE DIRECTION COSINES OF THE  
AXES OF ROTATION USED IN THE RELATIONS (1)

Axis of rotation	Angle of rotation	Direction cosines of the axes of rotation		
		L	M	N
$N_1-C_2$	$\phi$	$-\sin \delta_1$	$-\cos \delta_1$	0
$C_2-C_2'$	$\phi'$	$-\sin \delta_1'$	$\cos \delta_1'$	0

$$\text{where } \delta_1 = C_1\hat{C}_2N_1, \delta_1' = 180^\circ - (\tau + \delta_1) \text{ and } \tau = N_1\hat{C}_2C_2'$$

TABLE II  
MINIMUM CONTACT DISTANCES ASSUMED

Contact	Normally allowed	Outer limit
	<i>A</i>	<i>A</i>
C ... C	3.20	3.00
C' ... C'	2.95	2.90
C ... O	2.80	2.70
C ... N	2.90	2.80
C ... H	2.40	2.20
O ... O	2.70	2.60
O ... N	2.70	2.60
O ... H	2.40	2.20
N ... N	2.70	2.60
N ... H	2.40	2.20
H ... H	2.00	1.90

se viewing along the axis towards

the axes of rotation corresponding and  $C_2-C_2'$  are given in Table I.  $H_1$  were evaluated at intervals of  $[2, H_2, \text{ and } C_3$  were evaluated at three values of the angle  $\tau$ , namely, corresponding to  $\tau = 110$  and  $115^\circ$  those corresponding to  $\tau = 105^\circ$  electronic computer.

ed conformations is to choose a between the different types of atoms. have any of the contact distances owed. Two such sets are given in "limit" contact distances. These are

#### LECTION COSINES OF THE IE RELATIONS (1)

ection cosines of  
axes of rotation

M	N
$-\cos \delta_1$	0
$\cos \delta_1'$	0

$\delta_1$ ) and  $\tau = N_1C_2C_2'$

#### ICES ASSUMED

Outer limit

A

3.00  
2.90  
2.70  
2.80  
2.20  
2.60  
2.60  
2.20  
2.60  
2.20  
1.90

essentially the same as those given by Ramachandran, Ramakrishnan, and Sasisekharan (1963) arrived at from a study of the contact distances observed in structures of various organic compounds. Contact distances in between the two limits have also been observed in actual crystals, but not as frequently as the normally allowed values.

In order that the results can be applied to actual polypeptide and protein structures, the contact distances of the side chain atoms with those of the backbone atoms must also be considered. However, in this study, only the contact distances of the backbone atoms with the  $\beta$ -carbon atom were considered (see Appendix for the effect of  $C_\gamma$ ).

The position of the  $\beta$ -carbon atom was fixed (using a stereographic projection technique) in such a way that the distance  $C_\alpha-C_\beta$  is 1.54 Å and that the angles  $N_1-C_2-C_\beta$  and  $C_2'-C_2-C_\beta$  had tetrahedral values ( $119^\circ 30'$ ). Of the two possible positions of  $C_\beta$ , the one corresponding to the L-type of residues has been used in all these studies and hence the results pertain to L-amino acid residues. However, for D-amino acids, the corresponding allowed conformations will be  $(-\phi, -\phi')$ , where  $(\phi, \phi')$  refers to L-amino acids.

Since the positions of the atoms  $N_1, C_2'$  (which lie on the axis of rotation) and  $C_\beta$  do not change whatever the angle of rotation of the two residues is, only the following contact distances were calculated initially: (a) from  $C_\beta$  and  $C_2'$  to  $C_1, C_1', O_1$  and  $H_1$  for values of  $\phi$  from 0 to  $360^\circ$  at intervals of  $10^\circ$ ; and (b) from  $C_\beta$  and  $N_1$ , to  $O_2, N_2, H_2$ , and  $C_3$  for values of  $\phi'$  for 0 to  $360^\circ$  at intervals of  $10^\circ$ . These calculations were carried out corresponding to all three values of  $\tau$ , namely, 105, 110, and  $115^\circ$ . When the ranges of  $\phi$  and  $\phi'$  allowed by each contact, using the minimum contact distances given in Table III, are combined, the resulting ranges given in the first half (a) of Table III are obtained.

Within the permitted ranges of  $\phi$  and  $\phi'$  given in Table III, the contact distances between the hydrogen atom, H, attached to the  $\alpha$ -carbon atom and the atoms of the backbone were also examined and it was found that for all the three values of  $\tau$ , no further restrictions arise due to these contact distances.

When the remaining contact distances *between* the atoms occurring in the *backbones* of the *two* residues (the positions of which change during the rotations  $\phi$  or  $\phi'$ ) were examined in the permitted range given in Table III, contact distances less than the minimum allowed values were found to occur for some values of  $(\phi, \phi')$  and thus some more conformations became disallowed on account of these short contacts. The resulting diagrams showing the regions of stereochemically allowed conformations are shown in Figs. 2a, b, and c corresponding to the three values of  $\tau$ . In all these figures, the normally allowed regions are shown by continuous lines, while the boundaries of the region allowed by the outer limit values are shown by broken lines.

In order that the results can be applied to the conformations occurring with glycol

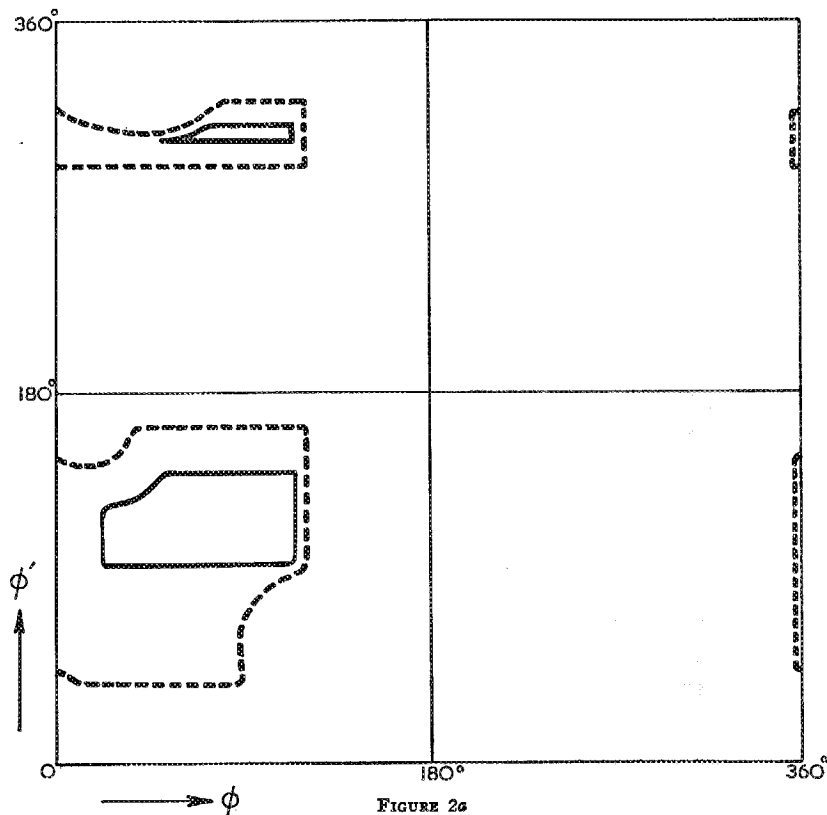


FIGURE 2a

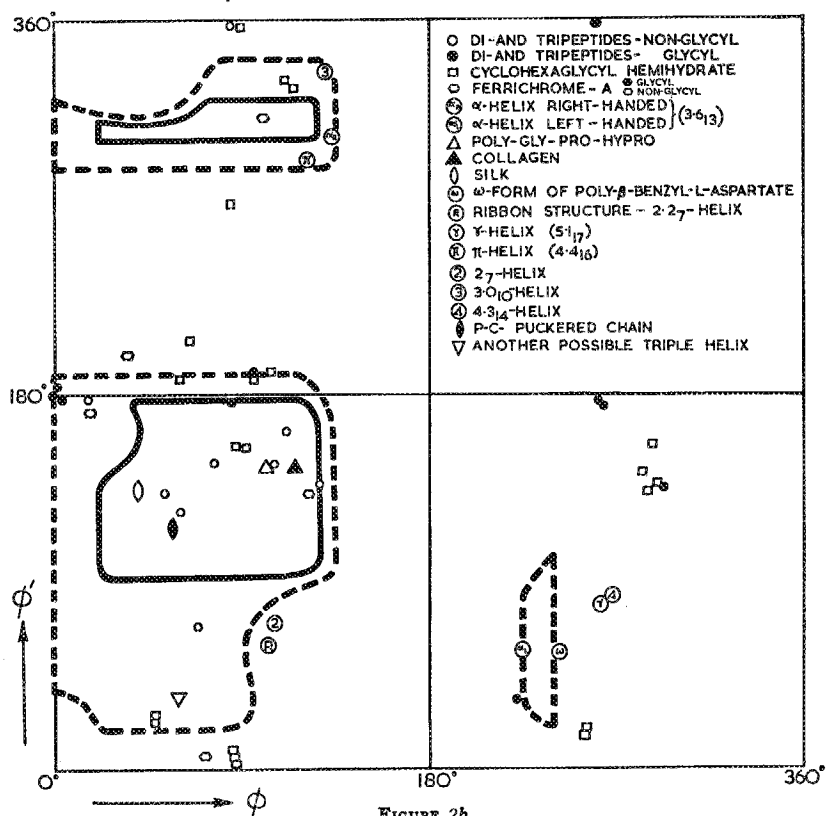


FIGURE 2b

- DI- AND TRIPEPTIDES - NON-GLYCYL
- DI- AND TRIPEPTIDES - GLYCYL
- CYCLOHEXAGLYCYL HEMIHYDRATE
- ◇ FERRICHRROME - A ○ GLYCYL
- FERRICHRROME - A ○ NON-GLYCYL
- ⊙ α-HELIX RIGHT-HANDED
- ⊖ α-HELIX LEFT-HANDED } (3-6)<sub>13</sub>
- ⊙ POLY-GLY-PRO-HYPRO
- △ COLLAGEN
- ◇ SILK
- ⊙ ω-FORM OF POLY-β-BENZYL-L-ASPARTATE
- ⊙ RIBBON STRUCTURE - 2-2<sub>7</sub>-HELIX
- ⊙ γ-HELIX (5<sub>1</sub>1<sub>7</sub>)
- ⊙ π-HELIX (4-4<sub>16</sub>)
- ⊙ 2<sub>7</sub>-HELIX
- ⊙ 3-0<sub>15</sub>-HELIX
- ⊙ 4-3<sub>14</sub>-HELIX
- ⊙ P-C- PUCKERED CHAIN
- ▽ ANOTHER POSSIBLE TRIPLE HELIX

residu  
hydro  
were  
tetra  
It wa  
no sh  
the b  
glycy  
secon  
residu  
3a an  
the no  
It n

RAMAK

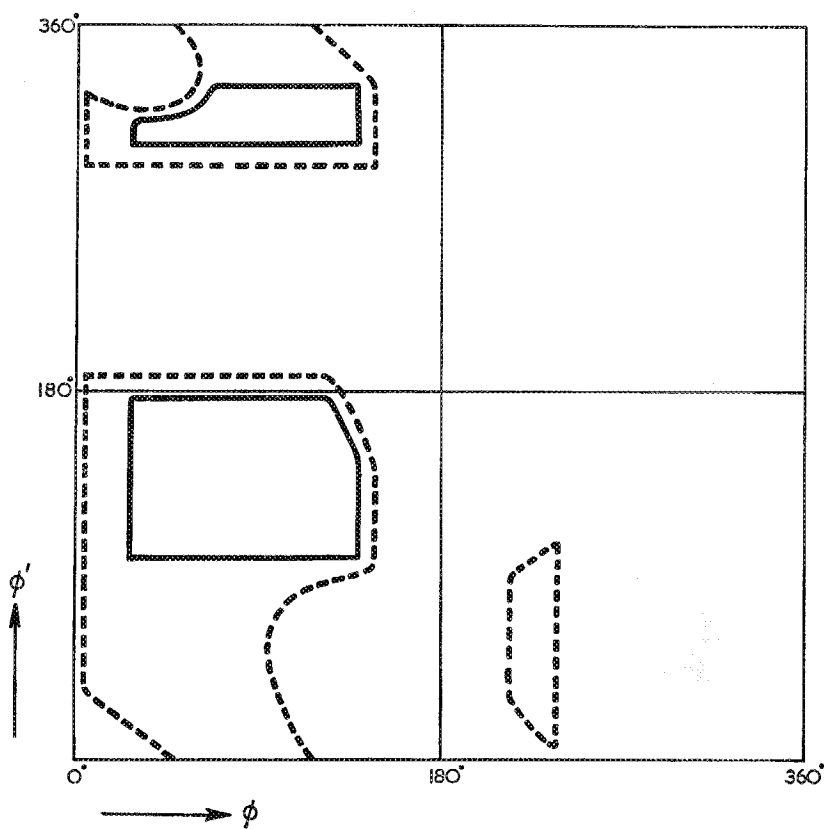
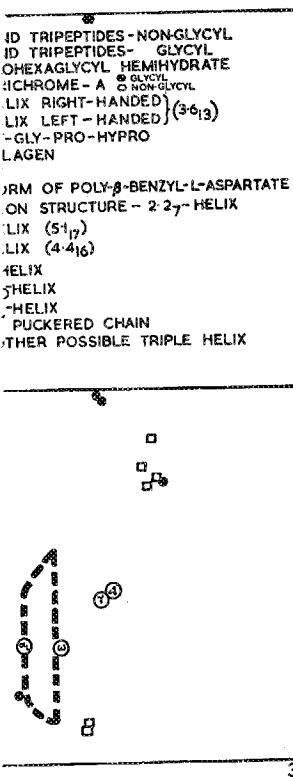
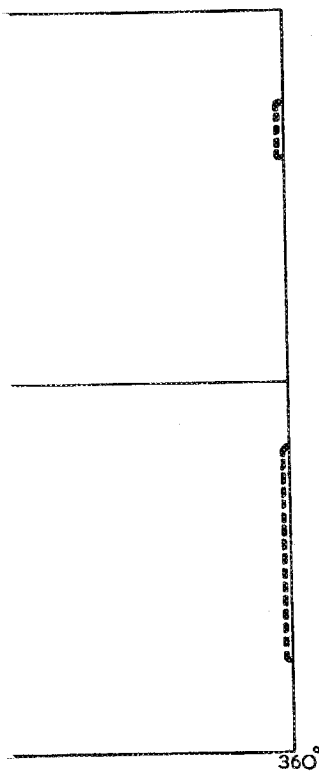


FIGURE 2c

FIGURE 2 The normally allowed (—) and the outer limit (---) regions of ( $\phi$ ,  $\phi'$ ) for (a)  $\tau = 105^\circ$ , (b)  $\tau = 110^\circ$ , (c)  $\tau = 115^\circ$ . The conformations of known simple peptides, polypeptides, and proteins are also marked in Fig. 2b.

residues (*i.e.* where there is no  $\beta$ -carbon atom), the contact distances between the hydrogen atoms attached to the  $\alpha$ -carbon atom and the various backbone atoms were evaluated for  $\tau = 110$  and  $115^\circ$ . The two hydrogen atoms were fixed at tetrahedral directions to  $N_1-C_2$  and  $C_2-C_2'$  and at a distance of 1.0A from  $C_2$ . It was found that both for  $\tau = 110$  and  $115^\circ$ , for all values of  $\phi$  and  $\phi'$ , there were no short contacts between the hydrogen atoms attached to the  $\alpha$ -carbon atom and the backbone atoms. As a result, the permitted ranges of  $\phi$  and  $\phi'$  are larger for glycyll residues than for non-glycyll residues. The permitted ranges are given in the second half (b) of Table III. The regions of allowed conformations for glycyll residues when all the contact distances were taken into account are shown in Figs. 3a and b, where shaded regions are those allowed by only the outer limits, but not the normally allowed contact distances.

It may be mentioned that for glycyll residues the contact distances between any

TABLE III  
 RANGES OF  $\phi$  AND  $\phi'$  ALLOWED BY THE CONTACT DISTANCES BETWEEN  
 THE ATOMS  $N_1, C_2', C_3$  AND THE REMAINING BACKBONE ATOMS IN  
 THE TWO RESIDUES FOR NON-GLYCYL RESIDUES AND BETWEEN  
 THE ATOMS  $N_1, C, H_2'$ , AND THE REMAINING BACKBONE  
 ATOMS FOR GLYCYL RESIDUES

	Normally allowed range		Outer limit range	
	$\phi$	$\phi'$	$\phi$	$\phi'$
(a) Non-glycyl residues				
105°	22 to 115°	95 to 141° and 301 to 309°	0 to 120° and 357 to 360°	38 to 163° and 289 to 322°
110°	22 to 127°	92 to 179° and 300 to 320°	0 to 135° and 225 to 241°	20 to 190° and 289 to 338°
115°	27 to 139°	98 to 177° and 301 to 330°	4 to 147° and 213 to 237°	0 to 188° and 290 to 360°
(b) Glycyl residues				
110°	0 to 127° and 233 to 360°	40 to 320°	0 to 135° and 225 to 360°	22 to 338°
115°	0 to 139° and 221 to 360°	30 to 330°	0 to 147° and 213 to 360°	No restriction

two atoms of the backbone in the adjacent residues for any conformation ( $\phi, \phi'$ ) is the same as for the inverse conformation ( $-\phi, -\phi'$ ) [as can be seen from the relations (1), where, if  $x', y',$  and  $z'$  are the coordinates of a backbone atom for  $\phi$  (or  $\phi'$ ) then the coordinates of the same atom for  $-\phi$  (or  $-\phi'$ ) are  $x', y',$  and  $-z'$ ].

The results shown in Figs. 2 and 3 will be useful in investigating the conformation at an  $\alpha$ -carbon atom when the two dihedral angles  $\phi$  and  $\phi'$  are known. For polypeptide and protein chains, the parameters that are obtainable from x-ray diffraction studies are the number of residues per turn,  $n$ , and the unit translation,  $h$ , (Ramachandran, 1960) along the axis of the helix. Hence, the stereochemically allowed combinations of  $n$  and  $h$  were evaluated using the detailed results of the calculations described in Part I (Ramakrishnan, 1964) and are represented graphically in Figs. 4a, b, and c for the three values of  $\tau$ . In these figures also, the regions of ( $n, h$ ) allowed by the normally allowed contact distances are shown by continuous line boundaries, while those allowed by outer limit values are shown by broken lines. The origins in these figures correspond to  $n = \pm 2$ , and  $h = 0$  A. The positive and



CONTACT DISTANCES BETWEEN  
ADJACENT BACKBONE ATOMS IN  
POLYMER RESIDUES AND BETWEEN  
ADJACENT MAINING BACKBONE  
RESIDUES

Outer limit range	
$\phi$	$\phi'$
0 to 120° and 357 to 360°	38 to 163° and 289 to 322°
0 to 135° and 225 to 241°	20 to 190° and 289 to 338°
4 to 147° and 213 to 237°	0 to 188° and 290 to 360°
0 to 135° and 225 to 360°	22 to 338°
0 to 147° and 213 to 360°	No restriction

...es for any conformation ( $\phi, \phi'$ ) is ...  
'') [as can be seen from the rela-  
inates of a backbone atom for  $\phi$   
or  $-\phi$  (or  $-\phi'$ ) are  $x', y',$  and  $-z'$ ].  
...l in investigating the conformation  
es  $\phi$  and  $\phi'$  are known. For poly-  
are obtainable from x-ray diffrac-  
n,  $n$ , and the unit translation,  $h$ ,  
elix. Hence, the stereochemically  
l using the detailed results of the  
1964) and are represented graphi-  
 $\tau$ . In these figures also, the regions  
distances are shown by continuous  
t values are shown by broken lines.  
2, and  $h = 0$  A. The positive and

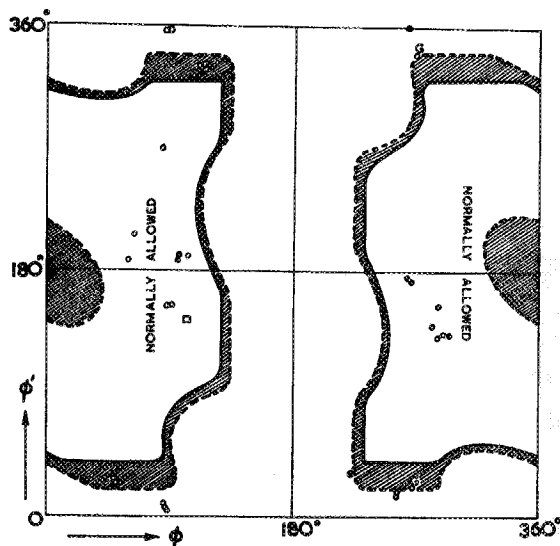


FIGURE 3a

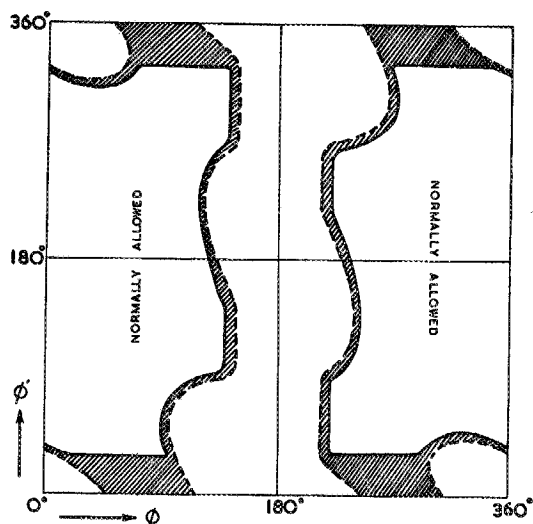


FIGURE 3b

FIGURE 3 Allowed regions of ( $\phi, \phi'$ ) for (a)  $\tau = 110^\circ$ , (b)  $\tau = 115^\circ$ , for glycol residues. The shaded regions represent conformations which are allowed only by the outer limit contact distances. The glycol conformations observed in simple peptides are also marked in Fig. 3a: ● = Di- and Tripeptides; ○ = Cyclic peptides; □ = Polyglycine II.

negative directions of the  $X$  axes correspond respectively to positive and negative values of  $n$ , but  $h$  is always taken to be positive. In other words, plots corresponding to all right-handed helices lie to the right of the  $Y$  axis and similarly points representing all left-handed helices lie to the left of the  $Y$  axis. In Fig. 4*b*, which corresponds to  $\tau = 110^\circ$ , the various observed and postulated polypeptide and protein structures are also plotted.

#### DISCUSSION OF THE RESULTS

From Figs. 2*a*, *b*, and *c*, it can be seen that the general nature of the regions of allowed conformations ( $\phi$ ,  $\phi'$ ) is the same for the three values of  $\tau$ . An interesting feature is that the region around  $(220^\circ, 60^\circ)$ , where the left-handed  $\alpha$ -helix occurs, is not allowed for  $\tau = 105^\circ$ , while it is allowed for  $\tau = 110$  and  $115^\circ$ .

In order to have a quantitative estimate of the results, the area under the allowed regions may be expressed as a percentage of the total area of the plane  $\phi$ - $\phi'$ . These are given in Table IV. There is an appreciable increase in the range of allowed regions with increasing  $\tau$ . Also the allowed region is much larger for glycy residues than when a  $\beta$ -carbon atom is present (about 6 times for normally allowed and 2.5 times for outer limit for  $\tau = 110^\circ$ ). Thus there is more freedom of rotation about the single bonds when the amino acid residue at the  $\alpha$ -carbon atom is glycine than when it contains a  $\beta$ -carbon atom.

Since the  $\alpha$ -carbon atom is not an asymmetric carbon atom in the case of glycine, no D or L isomer is possible. This is reflected clearly in Figs. 3*a* and *b*, which have the symmetry of a center of inversion about  $(180^\circ, 180^\circ)$ .

In order to verify how far the above results from theory agree with observation, the parameters  $\phi$  and  $\phi'$  were evaluated from the available crystal structure data on di- and tripeptides, cyclic peptides, and polypeptides. These were calculated on an IBM 1620 computer. In addition, the two values of  $\phi'$  ( $\phi_1'$  and  $\phi_2'$ ), which alone are relevant in the case of amino acid structures, were also evaluated.

TABLE IV  
AREA OF ALLOWED CONFORMATIONS EXPRESSED AS PERCENTAGE  
OF THE TOTAL AREA OF THE ( $\phi - \phi'$ ) PLANE

$\tau$	Normally allowed	Outer limit
	<i>per cent</i>	<i>per cent</i>
(a) Non-glycyl residues		
$105^\circ$	3.5	12.7
$110^\circ$	7.7	20.3
$115^\circ$	8.8	24.2
(b) Glycyl residues		
$110^\circ$	45.1	57.4
$115^\circ$	56.7	66.8

struct  
N- $\alpha$ C  
L-argi  
acid  
and b  
only r  
are no  
two va  
other  
shown  
given i  
Cor.

ectively to positive and negative  
 other words, plots corresponding  
 axis and similarly points repre-  
 Y axis. In Fig. 4b, which corre-  
 stituted polypeptide and protein

general nature of the regions of  
 three values of  $\tau$ . An interesting  
 re the left-handed  $\alpha$ -helix occurs,  
 $\tau = 110$  and  $115^\circ$ .

esults, the area under the allowed  
 al area of the plane  $\phi-\phi'$ . These  
 ncrease in the range of allowed  
 s much larger for glycyl residues  
 times for normally allowed and  
 ere is more freedom of rotation  
 e at the  $\alpha$ -carbon atom is glycine

arbon atom in the case of glycine,  
 ly in Figs. 3a and b, which have  
 $180^\circ$ .

m theory agree with observation,  
 available crystal structure data on  
 otides. These were calculated on  
 s of  $\phi'$  ( $\phi_1'$  and  $\phi_2'$ ), which alone  
 ere also evaluated.

PRESSED AS PERCENTAGE  
 ( $\phi - \phi'$ ) PLANE

Outer limit
per cent
12.7
20.3
24.2
57.4
66.8

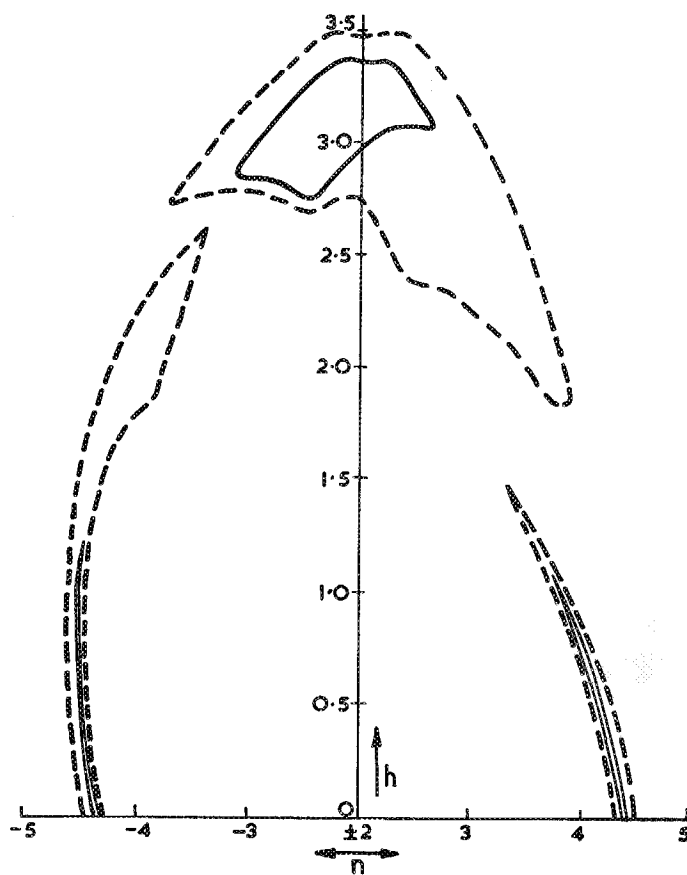


FIGURE 4a

*Amino Acids.* The two values  $\phi_1'$ ,  $\phi_2'$  for the various known crystal structures of amino acids are given in Table V along with the values of the angle N- $\alpha$ C-C' ( $\tau$ ). In general,  $\phi'$  lies between  $\pm 30^\circ$  and  $180^\circ \pm 30^\circ$ , exceptions being L-arginine HCl (Mazumdar, 1964), DL-aspartic acid (Dawson, 1953), L-glutamic acid (Hirokawa, 1955), L-tyrosine HCl and L-tyrosine HBr (Srinivasan, 1959a and b).

*Di- and Tripeptides.* In this case, for the N-terminal residues,  $\phi$  is the only relevant parameter, since the positions of the hydrogen atoms attached to  $N_0$  are not usually available. For the C-terminal residues, there is one value of  $\phi$  and two values of  $\phi'$  corresponding to the two oxygen atoms of the  $C_0^{O-}$  group. For the other residues (middle), there is one value of  $\phi$  and one value of  $\phi'$ . These are shown in Fig. 5, where the  $\alpha$ -carbon atom under consideration is  $C_1$ . The results are given in Table VI along with the value of the angle N- $\alpha$ C-C' ( $\tau$ ).

Considering the N-terminal residues, for which only  $\phi'$  is relevant, the observed

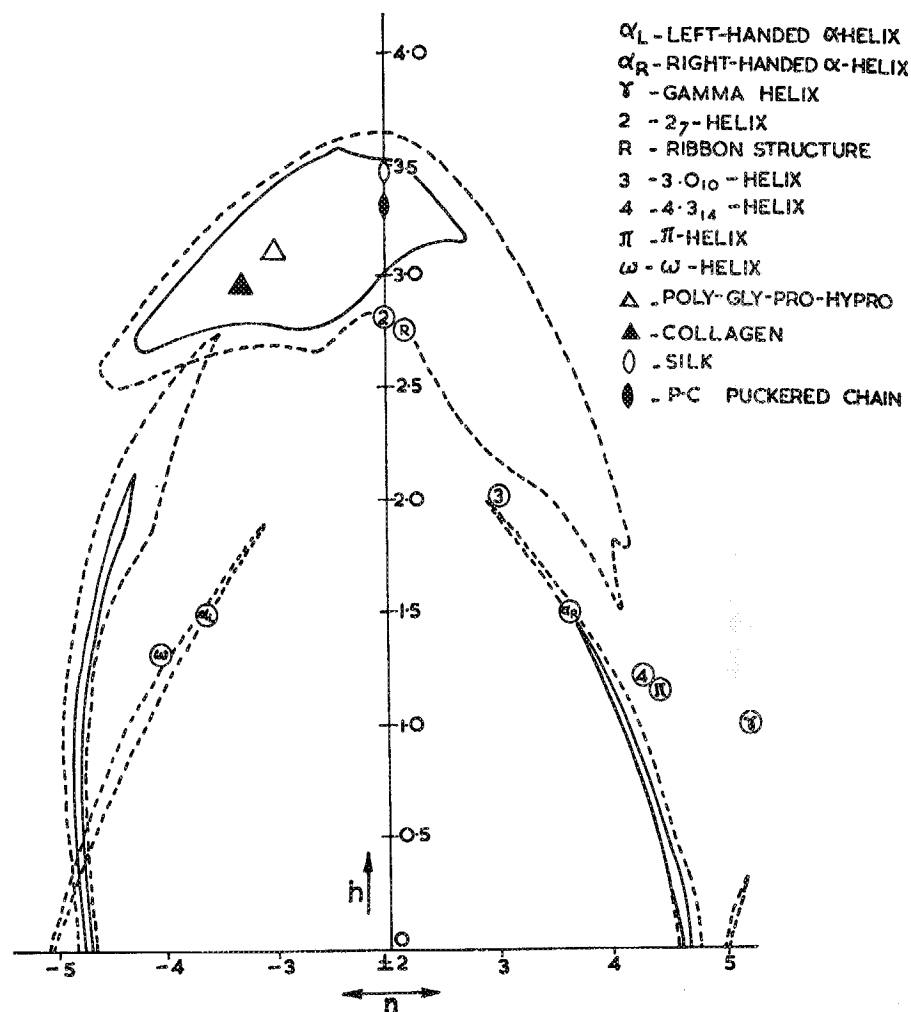


FIGURE 4b

values of  $\phi'$  lie well within the allowed region mentioned in Table III both in the case of glycol and non-glycol residues. In addition,  $\phi'$ , in general, lies between  $180^\circ \pm 30^\circ$  agreeing well with the trend observed in amino acid structures.

In the case of C-terminal and middle residues, the conformations are plotted in Fig. 2b, which also contains the allowed regions of  $(\phi, \phi')$  for  $\tau = 110^\circ$ . For better comparison the conformations at the  $\alpha$ -carbon atoms corresponding to glycol residues are also plotted in Fig. 3a which gives the allowed regions of  $(\phi, \phi')$  for such residues for  $\tau = 110^\circ$ .

Both for glycol and non-glycol residues, almost all the conformations lie within the allowed region. In the case of non-glycol residues it is very interesting to note

- $\alpha_L$  - LEFT-HANDED  $\alpha$ -HELIX
- $\alpha_R$  - RIGHT-HANDED  $\alpha$ -HELIX
- $\gamma$  - GAMMA HELIX
- 2 -  $2_7$ -HELIX
- R - RIBBON STRUCTURE
- 3 -  $3_{10}$ -HELIX
- 4 -  $4_{34}$ -HELIX
- $\pi$  -  $\pi$ -HELIX
- $\omega$  -  $\omega$ -HELIX
- $\Delta$  - POLY-GLY-PRO-HYPRO
- $\blacktriangle$  - COLLAGEN
- $\circ$  - SILK
- $\bullet$  - P-C PUCKERED CHAIN

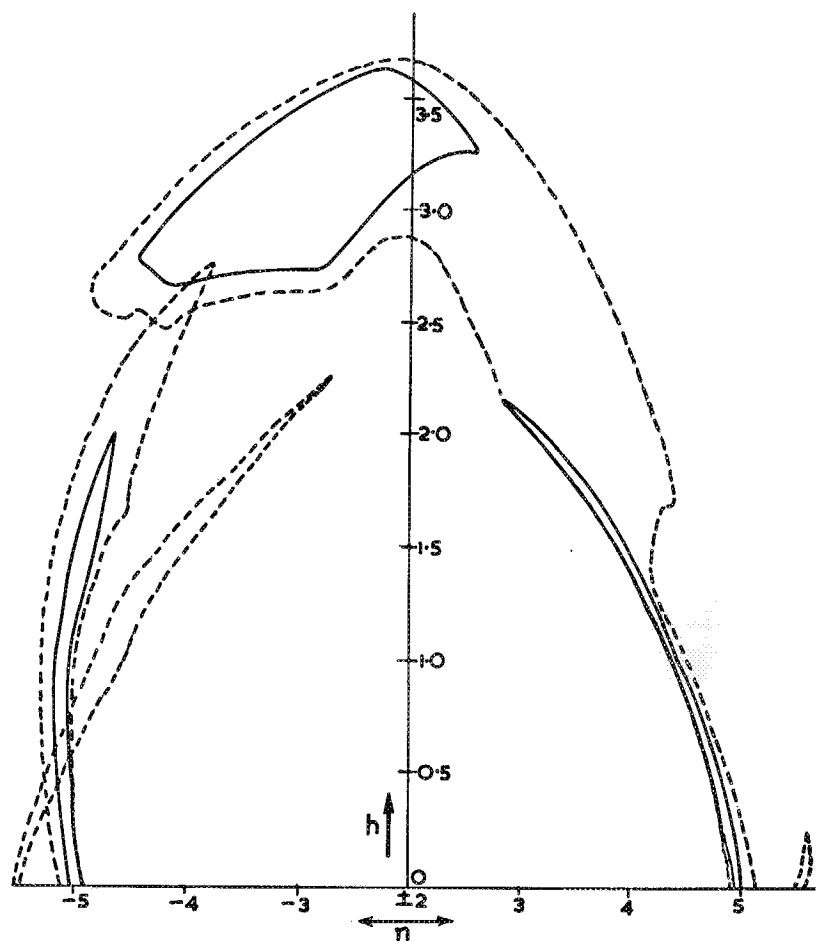
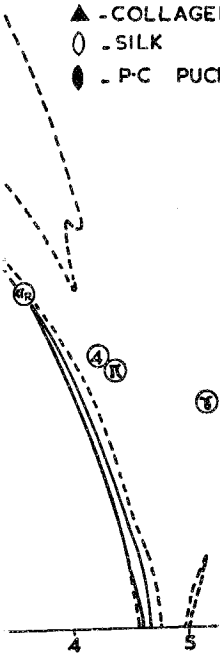


FIGURE 4c

FIGURE 4 The normally allowed (—) and the other limit (---) regions of  $(n, h)$  for (a)  $\tau = 105^\circ$ , (b)  $\tau = 110^\circ$ , (c)  $\tau = 115^\circ$ . The known polypeptide and protein structures are also marked in Fig. 4b— $\alpha_L$  = left-handed  $\alpha$ -helix;  $\alpha_R$  = right-handed  $\alpha$ -helix;  $\gamma$  = gamma helix; 2 =  $2_7$ -helix; R = ribbon structure; 3 =  $3_{10}$ -helix; 4 =  $4_{34}$ -helix;  $\pi$  =  $\pi$ -helix;  $\omega$  =  $\omega$ -helix;  $\Delta$  = poly-gly, -pro, -hypro;  $\blacktriangle$  = collagen;  $\circ$  = silk;  $\bullet$  = P-C puckered chain.

mentioned in Table III both in the definition,  $\phi'$ , in general, lies between  $0^\circ$  and  $180^\circ$  in amino acid structures.

As  $\tau$  increases, the conformations are plotted in the  $(\phi, \phi')$  plane for  $\tau = 110^\circ$ . For better comparison, the conformations corresponding to glycyl residues are also plotted. The allowed regions of  $(\phi, \phi')$  are shown in Fig. 2b.

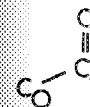
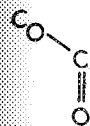
For most all the conformations lie within the allowed region. For cysteine residues it is very interesting to note that six out of nine conformations listed in Table VI lie well within the normally allowed region and two more lie within the outer limit but outside the normally allowed region. The one conformation that lies outside the allowed region is that of the cysteine residue of the compound glutathione. But the value of  $\tau$  in this case is  $115^\circ$  and so the conformation comes into the allowed region corresponding to  $\tau = 115^\circ$  (Fig. 2c). In addition, the value of  $\phi'$  in many cases lies close to  $150^\circ$ , which agrees well with the trend observed in amino acids.

TABLE V  
OBSERVED VALUES OF  $\phi'$  IN AMINO ACIDS. THE VALUE OF THE  
ANGLE N- $\alpha$ C-C' ( $\tau$ ) IS ALSO GIVEN

Amino acid	$\tau$	$\phi_1'$	$\phi_2'$	Reference
	<i>degrees</i>	<i>degrees</i>	<i>degrees</i>	
DL-Alanine	108.4	162.9	-15.3	1
L-Arginine (in L-arginine dihydrate)	110.9	-169.3	12.1	2
*L-Arginine (in L-arginine HBr, H <sub>2</sub> O)	109.5	-173.6	2.8	3
L-Arginine (in L-arginine HBr, H <sub>2</sub> O)	110.2	-151.2	23.9	3
*L-Arginine (in L-arginine HCl, H <sub>2</sub> O)	107.8	-174.2	1.7	3
L-Arginine (in L-arginine HCl, H <sub>2</sub> O)	109.5	-154.3	22.6	3
*L-Arginine (in L-arginine HCl)	109.4	129.2	-45.7	3
L-Arginine (in L-arginine HCl)	108.0	139.6	-41.7	3
Asparagine (in asparagine monohydrate)	110.1	-168.8	6.1	4
DL-Aspartic acid (in DL-aspartic acid HCl)	109.7	-137.8	-42.4	5
L-Cysteine (in L-cysteine HCl)	105.2	169.1	-5.1	6
L-Cysteine (in s-methyl-L-cysteine sulphoxide)	111.1	176.7	-9.8	7
L-Cysteine (in hexagonal L-cysteine)	108.4	-165.8	12.3	8
L-Cystine (in L-cystine dihydrobromide)	108.1	-179.2	0.9	9
L-Glutamic acid	108.3	134.2	-31.9	10
DL-Glutamic acid (in DL-glutamic acid HCl)	110.7	-162.4	18.0	11
L-Glutamine (in glutathione)	110.6	170.5	-12.5	12
L-Glutamine	110.8	160.5	-11.4	13
Glycine (in bis glycino copper monohydrate)	111.3	171.7	-6.1	14
$\alpha$ -Glycine	111.8	-160.9	18.4	15
$\beta$ -Glycine	110.8	-152.7	23.8	16
$\gamma$ -Glycine	110.8	-165.0	11.7	17
Histidine (in dihistidino zinc pentahydrate)	110.8	176.4	-3.9	18
Histidine (in dihistidino zinc dihydrate)	109.0	-168.2	9.1	19
Histidine (in histidine HCl, H <sub>2</sub> O)	109.4	180.0	0.0	20
Hydroxy-L-proline II	110.7	-177.0	2.0	21
D-Isoleucine (in D-isoleucine HBr)	108.5	165.7	-20.6	22
L-Leucine (in L-leucine HBr)	110.1	160.4	-12.3	23
L-Leucine (in L-leucine HCl)	109.7	160.1	-17.2	24
$\alpha$ -Methionine	112.1	146.3	-30.4	25
$\beta$ -Methionine	110.0	150.6	-31.6	25
DL-Norleucine	109.0	144.6	-24.4	26
Proline (in copper proline dihydrate)	109.7	-169.0	11.0	27
DL-Serine	110.1	-176.3	1.2	28
L-Threonine	110.4	153.9	-28.8	29
Tryptophan	111.9	175.8	21.4	30
L-Tyrosine (in L-tyrosine HCl)	110.1	142.1	-25.4	31
L-Tyrosine (in L-tyrosine HBr)	108.4	143.9	-30.4	32
L-Valine (in L-valine HBr)	108.1	168.4	-14.7	33
L-Valine (in L-valine HCl)	105.9	172.2	-8.9	34
L-Valine (in L-valine HCl, H <sub>2</sub> O)	108.2	-173.1	5.3	35

\*In the structures of L-arginine HBr, L-arginine HCl, H<sub>2</sub>O, and L-arginine HCl, there are two molecules per asymmetric unit.

References: (1) Donohue (1951); (2) Karle and Karle (1964); (3) Work done in Madras, Mazumdar (1964); (4) Kartha and De Vries (1961); (5) Dr. B. Dawson, private communication; (6) Work done in



Cons  
Also in  
Gly-Phe  
copper  
for gly

cyclohe.  
Foster,  
four mo  
investiga  
Orn-Orn  
five non

Madras; (  
(1955); (1  
et al. (196  
(19) Krets  
(1952); (22  
(25) Mathi  
et al. (195  
(32) Sriniv  
Madras.

OS. THE VALUE OF THE  
GIVEN

$\phi_1'$	$\phi_2'$	Reference
degrees	degrees	
162.9	-15.3	1
-169.3	12.1	2
-173.6	2.8	3
-151.2	23.9	3
-174.2	1.7	3
-154.3	22.6	3
129.2	-45.7	3
139.6	-41.7	3
-168.8	6.1	4
-137.8	42.4	5
169.1	-5.1	6
176.7	-9.8	7
-165.8	12.3	8
-179.2	0.9	9
134.2	-31.9	10
-162.4	18.0	11
170.5	-12.5	12
160.5	-11.4	13
171.7	-6.1	14
-160.9	18.4	15
-152.7	23.8	16
-165.0	11.7	17
176.4	-3.9	18
-168.2	9.1	19
180.0	0.0	20
-177.0	2.0	21
165.7	-20.6	22
160.4	-12.3	23
160.1	-17.2	24
146.3	-30.4	25
150.6	-31.6	25
144.6	-24.4	26
-169.0	11.0	27
-176.3	1.2	28
153.9	-28.8	29
175.8	21.4	30
142.1	-25.4	31
143.9	-30.4	32
168.4	-14.7	33
172.2	-8.9	34
-173.1	5.3	35

and L-arginine HCl, there are two mole-  
); (3) Work done in Madras, Mazumdar  
private communication; (6) Work done in

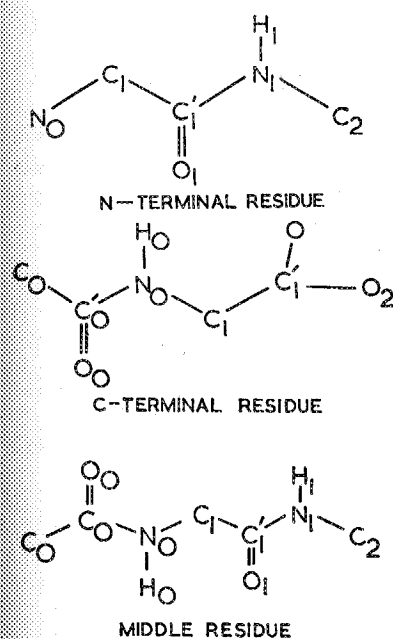


FIGURE 5 The environment around the  $\alpha$ -carbon atom  $C_1$  in the case of N-terminal, C-terminal, and middle residues of peptides.

Considering the glycol residues, almost all of them lie within the allowed region. Also in the case of C-terminal glycol residues of the compounds Cys-Gly NaI and Gly-Phe-Gly and in the case of middle and C-terminal residues in Gly-Gly-Gly copper chloride, the observed conformations are such that they are allowed only for glycol residues.

**Cyclic Peptides.** Recently, the crystal structures of two cyclic hexapeptides, cyclohexaglycol hemihydrate (Karle and Karle, 1963), and Ferrichrome A (Zalkin, Foster, and Templeton, 1964) have been reported. Of these, the former contains four molecules per asymmetric unit and offers twenty four glycol conformations for investigation. The latter hexapeptide (Ferrichrome A) with the sequence Gly-Ser-Ser-Orn-Orn-Orn (Orn standing for ornithine) gives six conformations, one glycol and five non-glycol. The parameters ( $\phi$ ,  $\phi'$ ) for these two hexapeptides are given in

Madras; (7) Hine (1962); (8) Oughton and Harrison (1959); (9) Peterson *et al.* (1960); (10) Hirokawa (1955); (11) Dawson (1953); (12) Wright (1958); (13) Cochran and Penfold (1952); (14) Freeman *et al.* (1964b); (15) Marsh (1958); (16) Itaka (1960); (17) Itaka (1961); (18) Harding and Cole (1963); (19) Kretsinger and Cotton (1963); (20) Donohue and Caron (1964); (21) Donohue and Trueblood (1952); (22) Trommel and Bijvoet (1954); (23) Subramanian (1965); (24) Wright and Marsh (1962); (25) Mathieson (1952); (26) Mathieson (1953); (27) Mathieson and Welsh (1952); (28) Shoemaker *et al.* (1953); (29) Shoemaker *et al.* (1951); (30) Work done in Madras; (31) Srinivasan (1959a); (32) Srinivasan (1959b); (33) Parthasarathy (1962); (34) Work done in Madras; (35) Work done in Madras.

TABLE VI  
THE CONFORMATIONS ( $\phi$ ,  $\phi'$ ) OBSERVED IN DI- AND TRIPEPTIDES.  
THE ANGLE N- $\alpha$ C-C' AT THE CORRESPONDING  $\alpha$ -CARBON  
ATOMS ARE ALSO LISTED

Peptides		$\tau$	$\phi$	$\phi'_1$	$\phi'_2$	Reference*
		degrees	degrees	degrees	degrees	
N-acetyl glycine		110.4	1.5	-176.4	3.3	1
<b>(a) Dipeptides</b>						
$\beta$ -Gly-Gly	N-term-Gly	110.0	—	-155.4	—	2
	C-term-Gly	110.7	-0.8	-180.0	4.7	2
Gly-L-Asp	N-term-Gly	111.2	—	-171.4	—	3
	C-term-Asp	109.5	69.0	-116.7	69.2	3
Gly-L-Tyr	N-term-Gly	112.1	—	173.6	—	4
	C-term-Tyr	111.4	76.6	146.6	-30.9	4
Gly-L-Tyr	N-term-Gly	112.1	—	157.4	—	5
	C-term-Tyr	112.0	106.3	146.7	-23.7	5
N-N' diglycyl cystine	N-term-Gly	109.0	—	-137.1	—	6
	C-term-Cys	109.5	16.5	178.8	-3.7	6
Cys-Gly sodium iodide	N-term-Cys	111.5	—	171.7	—	7
	C-term-Gly	125.7	-136.8	-147.6	33.1	7
Glutathione ( $\gamma$ -Glu-Cys-Gly)	Middle-Cys	115.0	89.3	-2.8	—	8
	C-term-Gly	109.5	95.5	-169.1	10.0	8
<i>p</i> -tosyl-L-Pro-L- hypro	N-term-Pro	106.4	—	163.8	—	9
	C-term-Hypro	117.8	128.5	136.6	-43.6	9
L-Thr-L-Phe	N-term-Thr	106.4	—	140.9	—	10
	C-term-Phe	107.8	61.4	123.5	-67.0	10
L-Leu-Gly	N-term-Leu	109.1	—	-144.0	—	11
	C-term-Gly	112.3	86.4	176.6	2.9	11
<b>(b) Tripeptides</b>						
Gly-Gly-Gly-CuCl <sub>2</sub>	N-term-Gly	107.9	—	169.4	—	12
	Middle-Gly	111.1	-65.6	133.4	—	12
	C-term-Gly	110.7	-94.0	173.3	-4.7	12
Gly-L-Phe-Gly	N-term-Gly	109.9	—	126.8	—	13
	Middle-Phe	107.0	52.9	132.7	—	13
	C-term-Gly	114.7	-96.5	175.4	-0.9	13
L-Leu-L-Pro-Gly	N-term-Leu	107.9	—	152.7	—	14
	Middle-Pro	111.3	112.2	162.5	—	14
	C-term-Gly	114.5	3.7	178.1	0.5	14

\* (1) Donohue and Marsh (1962); (2) Hughes and Moore (1949); (3) Pasternak *et al.* (1954); (4) Smith and Wiebenga (1953); (5) Pasternak (1956); (6) Yakel and Hughes (1954); (7) Dyer (1951); (8) Wright (1958); (9) Fridrichsons and Mathieson (1962); (10) Work done in Madras; (11) Work done in Madras; (12) Freeman *et al.* (1964a); (13) Marsh and Glusker (1961); (14) Leung and Marsh (1958).



IN DI- AND TRIPEPTIDES.  
SPONDING  $\alpha$ -CARBON  
LISTED

$\tau$	$\phi'_1$	$\phi'_2$	Reference*
rees	degrees	degrees	
1.5	-176.4	3.3	1
—	-155.4	—	2
-0.8	-180.0	4.7	2
—	-171.4	—	3
69.0	-116.7	69.2	3
—	173.6	—	4
76.6	146.6	-30.9	4
—	157.4	—	5
06.3	146.7	-23.7	5
—	-137.1	—	6
16.5	178.8	-3.7	6
—	171.7	—	7
36.8	-147.6	33.1	7
89.3	-2.8	—	8
95.5	-169.1	10.0	8
—	163.8	—	9
28.5	136.6	-43.6	9
—	140.9	—	10
61.4	123.5	-67.0	10
—	-144.0	—	11
86.4	176.6	2.9	11
—	169.4	—	12
65.6	133.4	—	12
94.0	173.3	-4.7	12
—	126.8	—	13
52.9	132.7	—	13
96.5	175.4	-0.9	13
—	152.7	—	14
112.2	162.5	—	14
3.7	178.1	0.5	14

(1) Karle and Karle (1963); (2) Karle and Karle (1963); (3) Pasternak *et al.* (1954); (4) Smith and Hughes (1954); (7) Dyer (1951); (8) Wright and Dyer (1951); (9) Wright and Dyer (1951); (10) Work done in Madras; (11) Work done in Madras; (12) Work done in Madras; (13) Work done in Madras; (14) Leung and Marsh (1958).

Table VII<sup>2</sup> and are plotted in Fig. 2*b*. The glycol conformations are also plotted in Fig. 3*a*.

In the case of cyclohexaglycyl hemihydrate, a majority of the conformations lie within the allowed regions. However, a few of them (1, 5, 7, 10, 12, 13, 15) are clustered around 0° (or 360°) of  $\phi'$ . Although these conformations are not allowed for  $\tau = 110^\circ$ , they do become allowed for higher values of  $\tau$  (see Fig. 3*b*). It can be

TABLE VII  
OBSERVED CONFORMATIONS ( $\phi$ ,  $\phi'$ ) IN CYCLOHEXAGLYCYL  
HEMIHYDRATE AND IN FERRICHRROME A

Residue	$\tau$	$\phi$	$\phi'$
	degrees	degrees	degrees
Cyclohexaglycyl hemihydrate*			
Gly (1)	112.8	85.6	9.9
Gly (2)	111.2	111.6	-29.2
Gly (3)	111.7	85.4	-88.9
Gly (4)	112.6	112.7	-29.3
Gly (5)	110.8	86.6	6.9
Gly (6)	113.0	115.6	-33.0
Gly (7)	112.1	86.8	5.8
Gly (8)	111.5	114.5	-32.6
Gly (9)	110.2	49.4	24.3
Gly (10)	116.2	89.7	-3.8
Gly (11)	110.0	48.2	26.3
Gly (12)	115.4	86.9	-1.6
Gly (13)	114.9	-103.1	16.9
Gly (14)	102.4	87.3	155.1
Gly (15)	113.7	-102.9	18.1
Gly (16)	105.3	-71.8	155.9
Gly (17)	105.3	-71.8	154.9
Gly (18)	109.5	-76.4	141.0
Gly (19)	109.7	-72.3	133.3
Gly (20)	105.3	-68.2	135.3
Gly (21)	110.2	65.0	-153.3
Gly (22)	108.3	60.1	-171.8
Gly (23)	110.0	95.7	-171.1
Gly (24)	109.5	104.1	-169.2
Ferrichrome A†			
Gly	114.7	-98.1	-1.2
Ser 1	114.2	123.7	132.3
Ser 2	104.0	17.3	171.5
Orn 1	113.5	71.6	6.6
Orn 2	113.2	101.4	-47.2
Orn 3	106.1	34.8	-160.7

\*Karle and Karle (1963); marked by the symbol, □, in Fig. 2*b*.

†Zalkin *et al.* (1963); marked by the open hexagon in Fig. 2*b*.

\*The coordinates of the atoms in the cyclic hexapeptide Ferrichrome A has kindly been furnished by Dr. Zalkin to us prior to publication.

seen from Table VII that for all these conformations, the value of  $\tau$  is systematically greater than  $110^\circ$  and thus these conformations also become allowed, under the short contact criteria adopted in this paper.

In the case of the cyclic peptide Ferrichrome A, the conformations corresponding to Ser 1, Ser 2, and Orn 1 lie well within the allowed region. Though the conformation corresponding to Orn 2 apparently lies outside the allowed region, it is allowed on account of the higher value of  $\tau$  ( $114^\circ$ ) at the  $\alpha$ -carbon atom. The corresponding Orn 3 has a short contact  $C_\beta \dots N_2$  according to the present study, but in the actual structure this has a value of 2.96 Å, which is greater than the minimum value given in Table II. Thus this conformation is also allowed. The conformation corresponding to the glycyl residue has a value of  $115^\circ$  for  $\tau$  and hence becomes allowed (Fig. 3*b*). An interesting feature of this conformation is that it is allowed only for a glycyl residue. The value of  $\phi'$  for this conformation lies close to  $360^\circ$  which is also the case with many conformations in the previous cyclic peptide.

*Peptides in the Non-Helical Regions of Myoglobin.* The structure of the crystalline protein myoglobin contains long segments of  $\alpha$ -helices linked by non-helical peptide segments (Kendrew *et al.* 1960, 1961). The conformations at the  $\alpha$ -carbon atoms in these non-helical regions have been plotted by Dr. H. C. Watson of Medical Research Council, Cambridge, England, who has kindly made the plot available to the authors prior to publication. Most of the conformations lie within the allowed regions for  $\tau = 110^\circ$ , with a clustering of conformations around that of the right-handed  $\alpha$ -helix. A few are allowed only for  $\tau > 110^\circ$ . In fact, two conformations lie far outside the allowed limits, namely those of the residues EF3 and HC2. On examination, it is found that the short contact responsible for disallowing those two involve the  $\beta$ -carbon atom, so that they will become allowed if they were glycyl residues. When this fact was communicated to Dr. Watson, it was learned that these were in fact glycyl residues, as expected. The others that lie just outside the allowed regions have  $\phi'$  close to  $0^\circ$  (or  $360^\circ$ ) and hence are likely to have a value of  $\tau$  greater than  $110^\circ$ , in which case they also come within the allowed region.<sup>3</sup>

*Polypeptides and Proteins.* The conformations of the various structures proposed for polypeptides and fibrous proteins have been calculated from the reported coordinates of the atoms and are given in Table VIII along with the data on the number of residues per turn,  $n$ , and the unit translation,  $h$ , along the axis of the axis of the helix. These are plotted in Fig. 2*b* and also in Fig. 4*b*, which gives the allowed combinations of  $(n, h)$  for  $\tau = 110^\circ$ .

All the structures except four ( $\gamma$ -helix, 4.3<sub>14</sub>-helix, 2<sub>7</sub>-helix, and 2.2<sub>7</sub>-helix) lie within the allowed regions, some well within the normally allowed regions and some others only within the outer limit region. These structures are discussed below.

<sup>3</sup> The  $\phi - \phi'$  diagram for myoglobin will be published shortly by Dr. Kendrew and Dr. Watson (private communication).

ons, the value of  $\tau$  is systematically also become allowed, under the

, the conformations corresponding allowed region. Though the con- sies outside the allowed region, it 114°) at the  $\alpha$ -carbon atom. The N<sub>2</sub> according to the present study, 2.96 Å, which is greater than the onformation is also allowed. The e has a value of 115° for  $\tau$  and ig feature of this conformation is ue of  $\phi'$  for this conformation lies onformations in the previous cyclic

*Myoglobin*. The structure of the nents of  $\alpha$ -helices linked by non- (1961). The conformations at the been plotted by Dr. H. C. Watson nd, who has kindly made the plot of the conformations lie within the f conformations around that of the > 110°. In fact, two conformations of the residues EF3 and HC2. On sponsible for disallowing those two come allowed if they were glycy-

r. Watson, it was learned that these ers that lie just outside the allowed ce are likely to have a value of  $\tau$  within the allowed region.<sup>3</sup>

ormations of the various structures have been calculated from the re- Table VIII along with the data on translation,  $h$ , along the axis of the nd also in Fig. 4*b*, which gives the

helix, 2<sub>7</sub>-helix, and 2.2<sub>7</sub>-helix) lie normally allowed regions and some structures are discussed below.

shortly by Dr. Kendrew and Dr. Watson

TABLE VIII

OBSERVED AND POSTULATED CONFORMATIONS ( $\phi$ ,  $\phi'$ ) FOR POLYPEPTIDE AND PROTEIN STRUCTURES. THE PARAMETERS  $n$  AND  $h$  ARE ALSO LISTED

Polypeptide or protein	$\tau$	$\phi$	$\phi'$	$n$	$h$	Reference*
	<i>degrees</i>	<i>degrees</i>	<i>degrees</i>		<i>Å</i>	
$\alpha$ -helix (3.6 <sub>1a</sub> )	109.5	133.0	-57.2	3.615	1.495	1
$\gamma$ -helix (5.1 <sub>17</sub> )	110.1	-96.3	78.0	5.143	0.98	2
2 <sub>7</sub> $\alpha$ -helix	111.3	105.1	69.5	2.000	2.80	1
2.2 <sub>7</sub> -helix (ribbon structure)	111.6	101.9	59.2	2.169	2.75	3
3.0 <sub>10</sub> -helix	111.6	130.7	-25.7	3.000	2.00	3
4.3 <sub>14</sub> -helix	100.5	-91.9	91.7	4.337	1.20	3
$\pi$ -helix (4.4 <sub>10</sub> )	114.9	122.9	-69.7	4.40	1.15	4
Polyglycine II	109.1	102.0	145.8	-3.00	3.10	5
Poly-L-proline II	110.0	102.8	145.9	-3.00	3.12	6
Poly-L-proline II	108.8	103.7	145.1	-3.00	3.12	7
Poly-L-hydroxyproline A	105.5	103.1	147.6	-3.00	3.05	8
$\alpha$ -form of poly- $\beta$ -benzyl-L-aspartate	109.9	-115.6	55.4	-4.00	1.325	9
Collagen type helix	110	116	145	-3.28	2.95	10
Silk	110	40	135	2.00	3.45	11
P-C puckered chain	110	57	118	2.00	3.3	12

\* (1) Bamford *et al.* (1956); (2) Pauling and Corey (1951); (3) Donohue (1953); (4) Low and Grenville-Wells (1953); (5) Crick and Rich (1955); (6) Sasisekharan (1959*a*); (7) Cowan and McGavin (1955); (8) Sasisekharan (1959*b*); (9) Bradbury *et al.* (1962); (10) Ramachandran (1963); (11) Marsh *et al.* (1955); (12) Pauling and Corey (1953).

$\alpha$ -helix. Both the right-handed  $\alpha$ -helix (132°, -57°) and the left-handed  $\alpha$ -helix (-132°, 57°) lie within the outer limit regions only. However, slight perturbations such as changing the value of  $\tau$  would bring the right-handed helix into the normally allowed region but the left-hand  $\alpha$ -helix is always outside the normal limits although it is just allowed by the outer limits. Also the right-handed  $\alpha$ -helix can accommodate L-proline towards an end, since  $\phi' \approx 120^\circ$ , while the left-handed  $\alpha$ -helix cannot. Even in the former case, because the planes of the peptide groups are nearly vertical, short contacts arise between the imino carbon atom, C, and the atoms of the backbone of the residue on top of it, if it is in the middle. It has been found that the two  $\alpha$ -helical portions adjoining the proline ring must be inclined by at least 35° in order that these short contacts may be relieved. Even in this case, there arise two short contacts  $C_2' \dots C_1' = 2.61$  Å and  $C_2' \dots O_1 = 2.45$  Å between atoms in the adjacent residues and these can be relieved only by distorting the planarity of the peptide group.

$\gamma$ -helix. The conformation of the right-handed  $\gamma$ -helix (-96°, 78°) lies well outside the allowed region and hence is not likely to be observed.

*2<sub>7</sub>a-helix*. This type of folding originally proposed by Huggins (1943) and designated as *2<sub>7</sub>*-helix by Bragg *et al.* (1950) has the conformation (105°, 70°) and lies apparently outside the allowed region. But the short contact in this case (as well as in the case of the *2.2<sub>7</sub>*-helix to be discussed next) is O<sub>1</sub>···H<sub>2</sub> (1.93 Å). Since this distance forms part of a possible intrachain hydrogen bond with N<sub>2</sub>···O<sub>1</sub> = 2.72 Å and H<sub>2</sub>N<sub>2</sub>O<sub>1</sub> = 28°30', this is really not a short contact.

*2.2<sub>7</sub>-helix (ribbon structure)*. This structure proposed by Donohue (1953) has the conformation (102°, 59°) and this also apparently lies outside the allowed region. As in the previous case, the short contact O<sub>1</sub>···H<sub>2</sub> (1.88 Å) forms part of a possible intrachain hydrogen bond and so this conformation becomes allowed. In fact a similar type of folding has been observed by Kakudo *et al.* (1963) in a tetrapeptide.

*3.0<sub>10</sub>-helix*. This structure proposed by Bragg *et al.* (1950) and Donohue (1953) has the conformation (131°, -26°) for the right-handed helix and lies close to the  $\alpha$ -helix conformation, within the outer limit region. This structure is also quite likely to occur.

*4.3<sub>14</sub>-helix*. This structure, also proposed by Donohue (1953), has the conformation (-92°, 92°) for the right-handed helix and lies close to the  $\gamma$ -helix, outside the allowed regions and hence is not likely to occur.

*4.4<sub>16</sub>-helix ( $\pi$ )*. The two slightly different forms of  $\pi$ -helices proposed by Low and Grenville-Wells (1953), one with  $n = 4.3$  and  $h = 1.14$  Å and the other with  $n = 4.4$  and  $h = 1.15$  Å, have the conformations (124°, -69°) and (123°, -70°) lying close to the conformation of  $\alpha$ -helix and are quite likely to occur.

*Poly-Gly, -Pro, -Hypro*. The conformations of these helices (left-handed) lie close to (100°, 150°) well within the normally allowed region. In the case of poly-L-proline and poly-L-hydroxyproline, the value of  $\phi$  is necessarily close to 120° for the imino residues to be accommodated. Also, the right-handed counterparts of these cannot accommodate imino acid residues, since the value of  $\phi$  is close to -120° in these cases.

*$\omega$ -Form of Poly- $\beta$ -Benzyl-L-Aspartate*. The structure of the  $\omega$ -form of poly- $\beta$ -benzyl-L-aspartate has been determined by Bradbury *et al.* (1962) to be a left-handed helix with a fourfold screw axis and with a folding similar to the *4<sub>13</sub>*-helix proposed by Bragg *et al.* (1950). The conformation of this helix is (-116°, 55°) and this lies just outside the allowed region. However, by making the peptide groups non-planar, the short contact that disallows this conformation, namely C<sub>8</sub>···C<sub>1</sub>', can be made to have a value of 3.13 Å, which is allowed by the outer limit. Thus this structure, in the form proposed, also becomes allowed.

*Silk*. Silk has the conformation close to (40°, 135°) which lies well within the allowed region. The structure is slightly buckled with  $h = 3.45$  Å, smaller than that of a fully extended chain ( $h = 3.63$  Å). This is due to the presence of side chains like alanine, etc. In fact, the conformations of other  $\beta$ -forms of polypeptides

proposed by Huggins (1943) has the conformation ( $105^\circ, 70^\circ$ ) and the short contact in this case (as next) is  $O_1 \cdots H_2$  (1.93A). Since hydrogen bond with  $N_2 \cdots O_1 =$  short contact.

proposed by Donohue (1953) apparently lies outside the allowed region.  $O_1 \cdots H_2$  (1.88 A) forms part of this conformation becomes allowed, as proposed by Kakudo *et al.* (1963) in a

proposed by Bragg *et al.* (1950) and Donohue for the right-handed helix and lies in the limit region. This structure is

proposed by Donohue (1953), has the conformation close to the  $\gamma$ -helix, and to occur.

forms of  $\pi$ -helices proposed by Bragg *et al.* (1950) and Donohue (1953) with  $t = 4.3$  and  $h = 1.14$  A and the other conformations ( $124^\circ, -69^\circ$ ) and ( $123^\circ, 69^\circ$ ) and are quite likely to occur.

forms of these helices (left-handed) lie in the allowed region. In the case of the  $\omega$ -form, the value of  $\phi$  is necessarily close to  $180^\circ$ . Also, the right-handed counter-sides, since the value of  $\phi$  is close

The structure of the  $\omega$ -form of the helix proposed by Bradbury *et al.* (1962) to be a  $4_1$ -helix with a folding similar to the  $4_{13}$ -helix. The conformation of this helix is ( $-116^\circ, 135^\circ$ ). However, by making the peptide backbone hydrogen bonds, namely  $N_2 \cdots O_1$ , allows this conformation, namely  $4_1$ -helix, which is allowed by the outer boundary and becomes allowed.

( $40^\circ, 135^\circ$ ) which lies well within the allowed region. With  $h = 3.45$  A, smaller than that of silk. This is due to the presence of side chains of other  $\beta$ -forms of polypeptides

like polyglycine,  $\beta$ -poly-L-alanine,  $\beta$ -poly- $\gamma$ -methyl-L-glutamate have conformations close to silk and are also slightly buckled.

**P-C Puckered Chain.** This chain conformation proposed by Pauling and Corey (1953) for the  $\beta$ -form of proteins has the conformation ( $57^\circ, 118^\circ$ ), close to that of silk. But this is much more buckled and the value of  $h$  in these cases is 3.3 A, less than that for silk (3.45 A). This is fully allowed, but this chain cannot accommodate proline and this has led to the suggestion of an alternative puckered chain (Pauling and Corey, 1953; Ramachandran, 1962; Sasisekharan, 1962).

**Collagen.** The polypeptide chains of the collagen helix ( $n = -3.28$  and  $h = 2.95$  A) has the conformation ( $116^\circ, 145^\circ$ ). Because  $\phi \approx 120^\circ$ , imino acid residues can be readily accommodated. The value of  $\phi'$  close to  $180^\circ$  is also a natural occurrence in the case of amino acids. Consequently, the fact that this conformation provides enough sites for imino acids and that it has a natural value of  $\phi'$  suggest that, even without internal hydrogen bonding, the collagen chain conformation is likely to be quite stable.

The conformation of collagen lies within the normally allowed region. Another interesting feature is that if  $\phi'$  is kept close to  $120^\circ$ , the value of  $h$  does not vary from 2.9 A by more than 5 per cent within the allowed region, thus explaining the relative inextensibility of collagen.

#### CONCLUDING REMARKS

Thus the conformations observed in simple and cyclic peptides are seen to confirm the predictions of the theory, thereby proving the validity of the stereochemical criteria assumed in this study.

Finally, the results obtained in our study agree well with those obtained by others from considerations of potential energy. Thus, Mizushima and Shimanouchi (1961), from a study of the internal rotation of simple molecules have preferred nine orientations. In our notation, these correspond to  $\phi = 0, 120, \text{ and } 240^\circ$ ,  $\phi' = 60, 180, \text{ and } 300^\circ$ . These are given in Table IX, along with the values of the unit twist  $t$  and the unit translation  $h$ . An examination of these in the light of the present study shows that all except  $d, e,$  and  $i$  lie within the allowed region. Even among these conformations,  $i$  becomes allowed because of the formation of a hydrogen bond of the type  $N_2-H_2 \cdots O_1$ , which offsets the short contact, thus leaving the conformation  $d$  and  $e$  alone to be really disallowed.

Recently, De Santis *et al.* (1963) have attempted a study of the stability of helical conformations of linear polypeptide chains from potential energy considerations. Although there is a broad similarity between their potential energy contours and the boundaries of our diagrams, there are some differences, for example a deep potential minimum corresponding to about ( $120^\circ, 300^\circ$ ) and another one at about ( $160^\circ, 60^\circ$ ). Neither of these are particularly populated in Fig. 2b, showing that

TABLE IX  
PREFERRED ORIENTATIONS OF POLYPEPTIDE CHAIN IN OUR  
NOTATION (ACCORDING TO MIZUSHIMA AND SHIMANOUCHI)

Conformation	Twist angles		Unit twist <i>t</i>	No. of residues per turn <i>n</i>	Residue height <i>h</i>
	$\phi$	$\phi'$			
	<i>degrees</i>		<i>degrees</i>		<i>A</i>
a	0	180	180	2.00	3.63
b	0	-60	-96	-3.75	2.45
c	0	60	96	3.75	2.45
d	240	180	84	4.28	2.72
e	240	-60	176	2.05	2.63
f	240	60	-90	-4.00	1.16
g	120	180	-84	-4.28	2.72
h	120	-60	90	4.00	1.16
i	120	60	-176	-2.05	2.63

for a single pair of residues these are not specially favored. The potential energy data that are fed in such studies may have to be further revised.

#### APPENDIX

While evaluating the contact distances for non-glycyl residues, only the  $\beta$ -carbon atom of the side chain was taken into account. It has been possible to extend the study to working out the effect of the  $\gamma$ -carbon atom on the conformation of the two residues. This was made possible since it has been found in Madras, from an analysis of the observed orientation of the side chains in the structures of various amino acids and peptides, that there are three preferred positions for the  $\gamma$ -carbon atom.

The position of  $C_\gamma$  may be represented by a parameter  $\psi$  which measures the rotation of  $C_\gamma$  about the  $C_\alpha-C_\beta$  bond from a standard initial conformation ( $\psi = 0^\circ$ ) in which the atom  $C_\gamma$  lies in the plane  $N-C_\alpha-C_\beta$  and with atoms N and  $C_\gamma$  being in the *cis* configuration with respect to the  $C_\alpha-C_\beta$  bond. Viewing from  $C_\beta$  to  $C_\alpha$ ,  $\psi$  is taken to be positive for an counterclockwise rotation. With this convention, the three positions of  $C_\gamma$  are found to lie close to values of 60, 180, and 300° for  $\psi$ , and these are indicated by indices 1, 2, and 3 respectively.

The contact distances between the  $\gamma$ -carbon atom in these three positions and the backbone atoms were calculated in the range of ( $\phi, \phi'$ ) allowed by the  $\beta$ -carbon atom (given in Table III) for  $\tau = 110^\circ$ . The alterations in the outer limit boundaries thus worked out are shown in Fig. 6, where the shifts in the boundary due to the  $\gamma$ -carbon atom in the three positions are shown by arrows.

In all the three cases, there are some additional restrictions in the allowed ranges of either  $\phi$  or  $\phi'$ , or both, as can be seen from Fig. 6. For the first position of  $C_\gamma$  ( $\psi = 60^\circ$ ), there are restrictions on both  $\phi$  and  $\phi'$ , while for the second position ( $\psi = 180^\circ$ ), the restrictions are on  $\phi'$  only and for the third position ( $\psi = 300^\circ$ ), on  $\phi$  only.

Fig. 6 also contains the conformations of the right-handed and left-handed  $\alpha$ -helices marked in it. It is interesting to note that for the first position  $C_\gamma$  ( $\psi = 60^\circ$ ) the con-

form  
while  
other  
either  
on a  
L-glut  
may  
positi  
explai  
helix

Our th  
the au  
and Th  
author  
Visitin  
very gr

Part I  
Receiv

BAMFO.  
Acad  
BRADBU  
W. E.

RAMAKR

PEPTIDE CHAIN IN OUR  
A AND SHIMANOUCI)

No. of residues per turn $n$	Residue height $h$
	<i>A</i>
2.00	3.63
-3.75	2.45
3.75	2.45
4.28	2.72
2.05	2.63
-4.00	1.16
-4.28	2.72
4.00	1.16
-2.05	2.63

ly favored. The potential energy  
ther revised.

l residues, only the  $\beta$ -carbon atom  
en possible to extend the study to  
conformation of the two residues.  
Madras, from an analysis of the  
ctures of various amino acids and  
ne  $\gamma$ -carbon atom.

eter  $\psi$  which measures the rotation  
l conformation ( $\psi = 0^\circ$ ) in which  
N and  $C_\gamma$  being in the *cis* configura-  
to  $C_\alpha$ ,  $\psi$  is taken to be positive for  
the three positions of  $C_\gamma$  are found  
these are indicated by indices 1, 2,

1 these three positions and the back-  
lowed by the  $\beta$ -carbon atom (given  
outer limit boundaries thus worked  
iary due to the  $\gamma$ -carbon atom in the

restrictions in the allowed ranges of  
or the first position of  $C_\gamma$  ( $\psi = 60^\circ$ ),  
e second position ( $\psi = 180^\circ$ ), the  
( $\psi = 300^\circ$ ), on  $\phi$  only.

nt-handed and left-handed  $\alpha$ -helices  
rst position  $C_\gamma$  ( $\psi = 60^\circ$ ) the con-

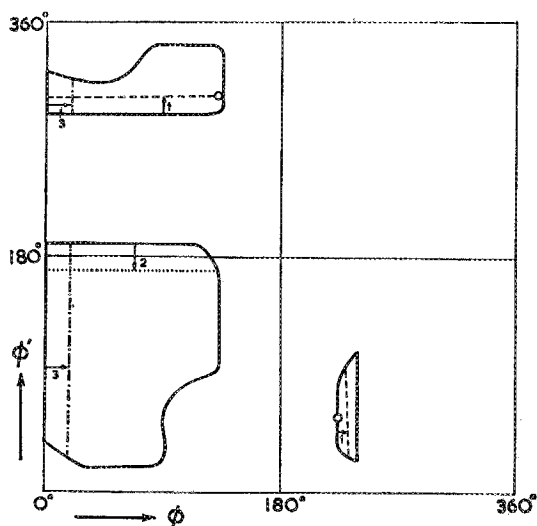


FIGURE 6 The shifts in the boundaries (indicated by  $\rightarrow$ ) of the allowed regions (outer limit) taking into account the restrictions due to  $\gamma$ -carbon atom in the three positions: ———  $C_\gamma$  alone; - - - - with  $C_\gamma$  in position 1; .....  $C_\gamma$  in position 2; - . - . - .  $C_\gamma$  in position 3. The conformations of the right- and left-handed  $\alpha$ -helices are also marked.

formation of the right-handed  $\alpha$ -helix lies just on the boundary of the outer limit region, while the conformation of the left-handed  $\alpha$ -helix goes outside the outer limit. In the other two cases, both are only within the outer limits and there is no obvious case for either the right-handed or the left-handed  $\alpha$ -helix to be more likely. In the analysis made on amino acid side group conformations (Lakshminarayanan, unpublished), both L-glutamic acid and L-glutamic acid HCl have the  $\gamma$ -carbon atom in position 1, which may explain why poly-L-glutamic acid has a right-handed helix. However, the three positions are found to occur fairly distributed in different amino acids, and this explanation will not hold good for the very common occurrence of the right-handed alpha helix in preference to the left-handed one in various polypeptides.

Our thanks are due to Dr. V. Sasisekharan for the discussions which we had with him. One of the authors (C.R.) wishes to thank the Ministry of Scientific Research and Cultural Affairs and The Council of Scientific and Industrial Research, India, for financial support. The other author (G.N.R.) is grateful to the United States National Science Foundation for a Senior Visiting Fellowship, which enabled him to spend a year in the University of Michigan. We are very grateful to Professor J. L. Oncley for his interest in these studies.

Part I of this article appeared in *Proc. Indian Acad. Sc.*, 1964, A59, 327.

Received for publication, July 19, 1965.

#### REFERENCES

- BAMFORD, C. H., ELLIOTT, A., and HANBY, W. E., 1956, *Synthetic Polypeptides*, New York, Academic Press, 260.  
BRADBURY, E. M., BROWN, I., DOWNIE, A. R., ELLIOTT, A., FRASER, R. D. B., and HANBY, W. E., 1962, *J. Mol. Biol.*, 5, 230.

- BRAGG, W. L., KENDREW, J. C., and PERUTZ, M. F., 1950, *Proc. Roy. Soc., London, Series A*, **203**, 321.
- COCHRAN, W., and PENFOLD, B. R., 1952, *Acta Cryst.*, **5**, 644.
- COREY, R. B., and PAULING, L., 1953, *Proc. Roy. Soc., London, Series B*, **141**, 10.
- COWAN, P. M., and MCGAVIN, S., 1955, *Nature*, **176**, 501.
- CRICK, F. H. C., and RICH, A., 1955, *Nature*, **176**, 780.
- DAWSON, B., 1953, *Acta Cryst.*, **6**, 81.
- DE SANTIS, P., GIGLIO, E., LIQUORI, A. M., and RIPAMONTI, A., 1965, *Nature*, **206**, 456.
- DONOHUE, J., 1951, *J. Am. Chem. Soc.*, **72**, 949.
- DONOHUE, J., 1953, *Proc. Nat. Acad. Sc.*, **39**, 205.
- DONOHUE, J., and CARON, A., 1964, *Acta Cryst.*, **17**, 1178.
- DONOHUE, J., and MARSH, R. E., 1962, *Acta Cryst.*, **15**, 941.
- DONOHUE, J., and TRUEBLOOD, K. N., 1952, *Acta Cryst.*, **5**, 419.
- DYER, H. B., 1951, *Acta Cryst.*, **4**, 42.
- FREEMAN, H. C., ROBINSON, G., and SCHOONE, J. C., 1964a, *Acta Cryst.*, **17**, 719.
- FREEMAN, H. C., SNOW, M. R., NITTA, I., and TOMITA, K., 1964b, *Acta Cryst.*, **17**, 1463.
- FRIDRICHSONS, J., and MATHIESON, A. McL., 1962, *Acta Cryst.*, **15**, 569.
- HARDING, M. M., and COLE, S. J., 1963, *Acta Cryst.*, **16**, 643.
- HINE, R., 1962, *Acta Cryst.*, **15**, 635.
- HUKAWA, S., 1955, *Acta Cryst.*, **8**, 637.
- HUGGINS, M. L., 1943, *Chem. Rev.*, **32**, 195.
- HUGHES, E. W., and MOORE, W. J., 1949, *J. Am. Chem. Soc.*, **71**, 2618.
- ITAKA, Y., 1960, *Acta Cryst.*, **13**, 35.
- ITAKA, Y., 1961, *Acta Cryst.*, **14**, 1.
- KAKUDO, M., SASADA, Y., KATSUBE, Y., SAKAKIBARA, S., and AKABORI, S., 1963, in *Aspects of Protein Structure*, (G. N. Ramachandran, editor), London, Academic Press, 69.
- KARLE, I. L., and KARLE, J., 1963, *Acta Cryst.*, **16**, 969.
- KARLE, I. L., and KARLE, J., 1964, *Acta Cryst.*, **17**, 835.
- KARTHA, G., and DE VRIES, A., 1961, *Nature*, **192**, 862.
- KENDREW, J. C., DICKERSON, R. E., STRANDBERG, B. E., HART, R. G., DAVIES, D. R., PHILLIPS, D. C., and SHORE, V. C., 1960, *Nature*, **185**, 422.
- KENDREW, J. C., WATSON, H. C., STRANDBERG, B. E., DICKERSON, R. E., PHILLIPS, D. C., and SHORE, V. C., 1961, *Nature*, **190**, 666.
- KRETSINGER, R. H., and COTTON, F. A., 1963, *Acta Cryst.*, **16**, 651.
- LEUNG, Y. C., and MARSH, R. E., 1958, *Acta Cryst.*, **11**, 17.
- LINDLEY, H., and ROLLETT, J. S., 1955, *Biochim. et Biophysica Acta*, **18**, 183.
- LOW, B. W., and BAYBUTT, R. B., 1952, *J. Am. Chem. Soc.*, **74**, 5806.
- LOW, B. W., and GRENVILLE-WELLS, H. J., 1953, *Proc. Nat. Acad. Sc.*, **39**, 785.
- MARSH, R. E., 1958, *Acta Cryst.*, **11**, 654.
- MARSH, R. E., and GLUSKER, J. P., 1961, *Acta Cryst.*, **14**, 1110.
- MARSH, R. E., COREY, R. B., and PAULING, L., 1955, *Acta Cryst.*, **8**, 710.
- MATHIESON, A. McL., 1952, *Acta Cryst.*, **5**, 332.
- MATHIESON, A. McL., 1953, *Acta Cryst.*, **6**, 399.
- MATHIESON, A. McL., and WELSH, H. K., 1952, *Acta Cryst.*, **5**, 599.
- MAZUMDAR, S. K., 1964, Ph.D. Thesis, Madras University.
- MIZUSHIMA, S., and SHIMANOCHI, T., 1961, *Advanc. Enzymol.*, **23**, 1.
- NÉMETHY, G., and SCHERAGA, H. A., 1965, *Biopolymers*, **3**, 155.
- OUGHTON, B. M., and HARRISON, P. M., 1959, *Acta Cryst.*, **12**, 396.
- PARTHASARATHY, R., 1962, Ph.D. Thesis, Madras University.
- PASTERNAK, R. A., 1956, *Acta Cryst.*, **9**, 341.
- PASTERNAK, R. A., KATZ, L., and COREY, R. B., 1954, *Acta Cryst.*, **7**, 225.
- PAULING, L., and COREY, R. B., 1951, *Proc. Nat. Acad. Sc.*, **37**, 235.
- PAULING, L., and COREY, R. B., 1953, *Proc. Nat. Acad. Sc.*, **39**, 253.



, *Proc. Roy. Soc., London, Series A*,

4.  
*don, Series B*, **141**, 10.

I, A., 1965, *Nature*, **206**, 456.

419.  
*, Acta Cryst.*, **17**, 719.  
*, 1964b, Acta Cryst.*, **17**, 1463.  
*yst.*, **15**, 569.

3.

**71**, 2618.

nd AKABORI, S., 1963, in *Aspects of*  
*on*, Academic Press, 69.

HART, R. G., DAVIES, D. R., PHILLIPS,

KERSON, R. E., PHILLIPS, D. C., and

**16**, 651.

*sica Acta*, **18**, 183.  
**74**, 5806.  
*t. Acad. Sc.*, **39**, 785.

10.  
*Cryst.*, **8**, 710.

**5**, 599.

*mol.*, **23**, 1.  
155.  
**12**, 396.

y.

*Cryst.*, **7**, 225.  
**37**, 235.  
**39**, 253.

PHYSICAL JOURNAL VOLUME 5 1965

PAULING, L., COREY, R. B., and BRANSON, H. R., 1951, *Proc. Nat. Acad. Sc.*, **37**, 205.

PETERSON, J., STEINRAUF, L. K., and JENSON, L. H., 1960, *Acta Cryst.*, **13**, 104.

RAMACHANDRAN, G. N., 1960, *Proc. Indian Acad. Sc.*, **A52**, 240.

RAMACHANDRAN, G. N., 1962, in *Collagen*, (N. Ramanathan, editor), New York, John Wiley & Sons, 1.

RAMACHANDRAN, G. N., 1963, in *Aspects of Protein Structure*, (G. N. Ramachandran, editor), London, Academic Press, 39.

RAMACHANDRAN, G. N., RAMAKRISHNAN, C., and SASISEKHARAN, V., 1963a, in *Aspects of Protein Structure*, (G. N. Ramachandran, editor), London, Academic Press, 121.

RAMACHANDRAN, G. N., RAMAKRISHNAN, C., and SASISEKHARAN, V., 1963b, *J. Mol. Biol.*, **7**, 95.

RAMAKRISHNAN, C., 1964, *Proc. Indian Acad. Sc.*, **A59**, 327.

SASISEKHARAN, V., 1959a, *Acta Cryst.*, **12**, 897.

SASISEKHARAN, V., 1959b, *Acta Cryst.*, **12**, 903.

SASISEKHARAN, V., 1962, in *Collagen*, (N. Ramanathan, editor), New York, John Wiley and Sons, 39.

SCHERAGA, H. A., 1960, *J. Am. Chem. Soc.*, **82**, 3847.

SHIMANOCHI, T., and MIZUSHIMA, S., 1955, *J. Chem. Physics*, **23**, 707.

SHOEMAKER, D. P., DONOHUE, J., SCHOMAKER, V., and COREY, R. B., 1951, *J. Am. Chem. Soc.*, **72**, 2328.

SHOEMAKER, D. P., BARREAU, R. E., and DONOHUE, J., 1953, *Acta Cryst.*, **6**, 241.

SMITH, D. W., and WIEBENGA, E. H., 1953, *Acta Cryst.*, **6**, 531.

SRINIVASAN, R., 1959a, *Proc. Indian Acad. Sc.*, **A49**, 340.

SRINIVASAN, R., 1959b, *Proc. Indian Acad. Sc.*, **A50**, 19.

SUBRAMANIAN, E., 1965, Ph.D. Thesis, Madras University.

TROMMEL, J., and BIJVOET, J. M., 1954, *Acta Cryst.*, **7**, 703.

WHITTAKER, E. T., *A Treatise on Analytical Dynamics of Particles and Rigid Bodies*, Cambridge, Cambridge University Press, 1952, 8.

WRIGHT, D. A., and MARSH, R. E., 1962, *Acta Cryst.*, **15**, 54.

WRIGHT, W. B., 1958, *Acta Cryst.*, **11**, 632.

YAKEL, H. L., and HUGHES, E. W., 1954, *Acta Cryst.*, **7**, 291.

ZALKIN, A., FOSTER, J. D., and TEMPLETON, H., 1964, *Science*, **146**, 261.