SUPRAHELICAL ARRANGEMENTS OF HYDROGEN BONDS IN PEPTIDE HELICES

T. RAMASARMA and M. VIJAYAN
Departments of Biochemistry and Physics, Indian Institute of Science, Bangalore 560–012, India

Received 4 February 1974

The occurrence of helical foldings of polypeptide chain in a variety of structural and functional proteins is well known. Of these, the α-helix (3.6_{13}) is the most stable and is found in several proteins to a varying degree: e.g., α-keratin (100%), paramyosin (100%), serum albumin (46%), aldolase (40%), insulin (20%), cytochrome *c* (10%), α-chymotrypsin (8%). Other helices of the types 3_{10} and π (4.4_{16}) occur to a much smaller extent. Associated with each of these helices there are hydrogen bonds between peptide groups of the main chain which are presently considered to confer additional stability to the helical folding. But a close examination reveals that these intrachain hydrogen bonds themselves form interesting repeating sequences, superimposed on the peptide helix. Each peptide group in the helices can be viewed as being held between two α-carbons and linked to another through a hydrogen bond. This structural feature is common to all the helices and provides continuous helical sequences of alternating peptide groups and hydrogen bonds (· · HN – C – O · · HN – C – O · ·) with the sense of winding opposite to that of the peptide helix. The axis of these helical sequences, however, coincides with that of the peptide helix. This intrinsic structural feature of helical regions in proteins, albeit obvious, has not been recognized and described so far. We propose to refer this as 'Suprahelix' and report in this communication some structural characteristics, including the helical parameters.

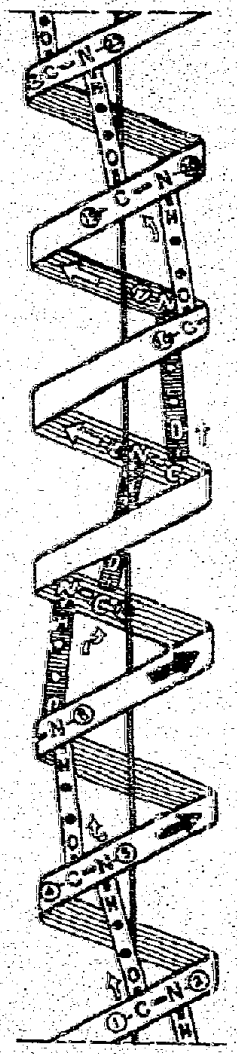

Fig. 1. Schematic diagram showing one of the three suprahelical sequences of hydrogen bonds winding in the opposite sense of α-helix. (N=6, D=4.5 Å, P=27 Å). The number of α-carbons to which N and C of the peptide units are attached are also shown.

α-Helix (3.6_{13})

In the α-helix (3.6 residues per turn, pitch 5.4 Å and repeat distance 27 Å), the carbonyl oxygen atom of the nth peptide unit is hydrogen bonded to the

amino nitrogen atom of the n+3rd peptide unit and the carbonyl oxygen atom of the latter is in turn hydrogen bonded to the amino nitrogen atom of the n+6th peptide unit. Three of these sequences run parallel to one another. One such sequence is shown in fig. 1. This suprahelix advances by a distance of 4.5 Å along the axis and rotates through an angle of 60° per hydrogen bond. Thus the number of hydrogen bonds per turn of the suprahelix is six with a pitch of 27 Å. Viewed along the axis, superposition is obtained with the first and the seventh hydrogen bonds. Hence, the periodic repeat distance and the pitch are the same.

3_{10} Helix

In the 3_{10} arrangement (3 residues per turn, pitch 6 Å and repeat distance 6 Å), the superimposed suprahelix consists of hydrogen bonds connecting the nth and the n+2nd peptide groups, the n+2nd and the n+4th peptide groups, and so on. There are two such suprahelices. In each there are three hydrogen bonds per turn, and the pitch and repeat distance are the same (12 Å).

π-Helix (4.4_{16})

In the π-helix (4.4 residues per turn, pitch 5.06 Å and the repeat distance 25.3 Å), the carbonyl oxygen atom of the nth peptide unit is hydrogen bonded to the amino nitrogen atom of the n+4th peptide group and the n+4th with the n+8th peptide group, and so on. There are four suprahelices associated with the π-helix. Every twelfth hydrogen bond superposes on the first when viewed along the axis. The pitch and repeat distance is 50.6 Å.

The structural parameters are summarized in table 1. One interesting feature is that the pitch and the periodic repeat distance are the same in these suprahelices. The repeat distances of the suprahelices are twice that of the corresponding peptide helices in the 3_{10} and π-helices whereas in the α-helix the two are equal. The pitch of the suprahelices associated with the 3_{10}, α- and π-arrangements are, however, 2X, 5X and 10X that of the corresponding peptide helices, respectively.

It has been suggested that the delocalized π-electron clouds of the peptide units [1] if interconnected through hydrogen bonds could conceivably facilitate mobility of electrons in proteins along molecular networks such as β-structure [2–5]. Electrical conductivity was in fact shown to be greater along than across the layer of hydrogen bonds in single crystals of glycine [2]. A mechanism of enzyme action of α-chymotrypsin was proposed which implicates shift of electrons through a hydrogen bond network

Table 1
Structural parameters of suprahelices

	3_{10} helix	α-helix	π-helix
Number of suprahelices superimposed on peptide helix	2	3	4
Number of hydrogen bonds per turn of the suprahelix (N)	3	6	11
Number of aminoacid residues per turn of suprahelix	6	18	44
Distance along the axis between successive hydrogen bonds (D)	4.0 Å	4.5 Å	4.6 Å
Pitch and the repeat distance of the suprahelix (P)	12.0 Å	27.0 Å	50.6 Å
Radial distance of the midpoint of each hydrogen bond from the axis of the helix (R)	1.3 Å	1.7 Å	2.2 Å
Angle through which suprahelix advances per hydrogen bond	120.0°	60.0°	32.7°

Capital letters of N, D, P and R are used to distinguish from the equivalent parameters of the peptide helix.

connecting Ser 195, His 57 and Asp 102 in the active site [6]. Though the possibility of electron conduction facilitated by hydrogen bonds received the consideration of many workers, experimental or theoretical proof is still awaited. It may be mentioned that, should this prove to be feasible, suprahelices will provide ideal pathways for transporting electrons.

Acknowledgement

It is a pleasure to thank the Director, Dr. S. Dhawan for his encouragement and for bringing together an excellent and inter-disciplinary group of scientists on the campus with whom we had many helpful discussions. We are thankful to Dr. C. Ramakrishnan of the Biophysics Unit for the help in the calculations of the parameters. Support from the Office of Naval Research, U.S.A. (N000 14–71–C–0348) for the project on 'Environmental Stress and Biochemical Adaptation' is acknowledged.

References

[1] Pauling, L., Corey, R. S. and Branson, H. R. (1951) Proc. Natl. Acad. Sci. U.S. 37, 205.
[2] Evans, M. G. and Gergely, J. (1949) Biochim. Biophys. Acta 3, 188.
[3] Szent-Györgyi, A. (1941) Nature 148, 157.
[4] Pullman, A. and Pullman, B. (1962) in: 'Horizons in Biochemistry' (Kasha, M. and Pullman, B., eds.), Academic Press, New York, p. 553.
[5] Eley, D. D. and Leslie, R. S. (1964) in: 'Electronic Aspects of Biochemistry', (Pullman, B., ed.), Academic Press, New York, p. 105.
[6] Blow, D. M., Birktoft, J. J. and Hartley, B. S. (1969) Nature 221, 337.