by an increase in protein content, while the amount of desoxyribonucleic acid remains unchanged.

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THE STRUCTURE OF PROTEINS: TWO HYDROGEN-BONDED HELICAL CONFIGURATIONS OF THE POLYPEPTIDE CHAIN

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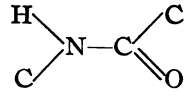
During the past fifteen years we have been attacking the problem of the structure of proteins in several ways. One of these ways is the complete and accurate determination of the crystal structure of amino acids, peptides, and other simple substances related to proteins, in order that information about interatomic distances, bond angles, and other configurational parameters might be obtained that would permit the reliable prediction of reasonable configurations for the polypeptide chain. We have now used this information to construct two reasonable hydrogen-bonded helical configurations for the polypeptide chain; we think that it is likely that these configurations constitute an important part of the structure of both fibrous and globular proteins, as well as of synthetic polypeptides. A letter announcing their discovery was published last year.[1]

The problem that we have set ourselves is that of finding all hydrogen-bonded structures for a single polypeptide chain, in which the residues are

equivalent (except for the differences in the side chain R). An amino acid residue (other than glycine) has no symmetry elements. The general operation of conversion of one residue of a single chain into a second residue equivalent to the first is accordingly a rotation about an axis accompanied by translation along the axis. Hence the only configurations for a chain compatible with our postulate of equivalence of the residues are helical configurations. For rotational angle 180° the helical configurations may degenerate to a simple chain with all of the principal atoms, C, C′ (the carbonyl carbon), N, and O, in the same plane.

We assume that, because of the resonance of the double bond between the carbon-oxygen and carbon-nitrogen positions, the configuration of each residue  is planar. This structural feature has been verified for each of the amides that we have studied. Moreover, the resonance theory is now so well grounded and its experimental substantiation so extensive that there can be no doubt whatever about its application to the amide group. The observed C—N distance, 1.32 Å, corresponds to nearly 50 per cent double-bond character, and we may conclude that rotation by as much as 10° from the planar configuration would result in instability by about 1 kcal. mole^{-1}. The interatomic distances and bond angles within the residue are assumed to have the values shown in figure 1. These values have been formulated[2] by consideration of the experimental values found in the crystal structure studies of DL-alanine,[3] L-threonine,[4] N-acetylglycine[5], and β-glycylglycine[6] that have been made in our Laboratories. It is further assumed that each nitrogen atom forms a hydrogen bond with an oxygen atom of another residue, with the nitrogen-oxygen distance equal to 2.72 Å, and that the vector from the nitrogen atom to the hydrogen-bonded oxygen atom lies not more than 30° from the N—H direction. The energy of an N—H · · · O=C hydrogen bond is of the order

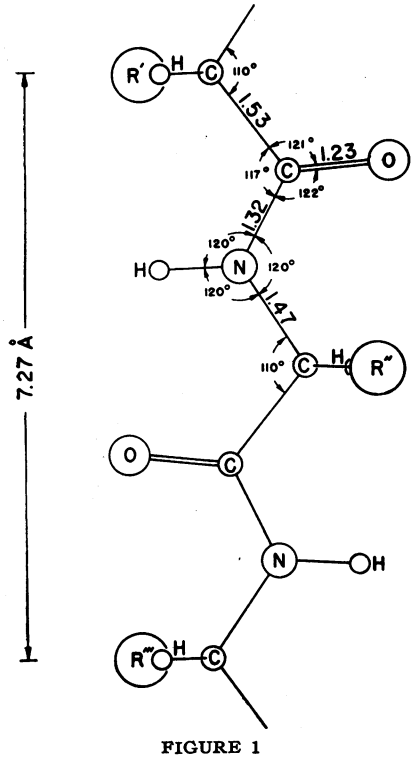


FIGURE 1

Dimensions of the polypeptide chain.

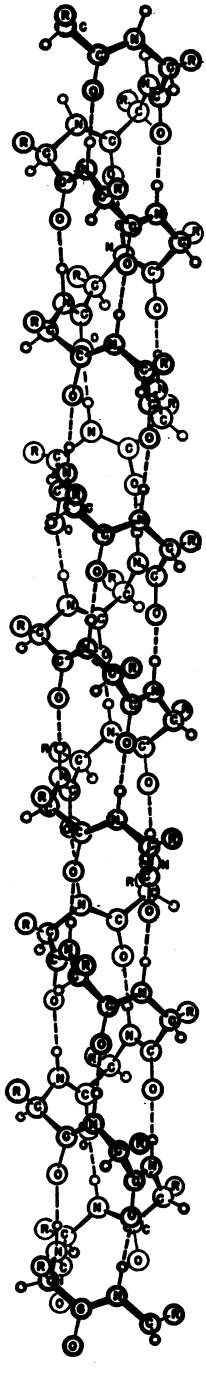


FIGURE 2
The helix with 3.7 residues per turn.

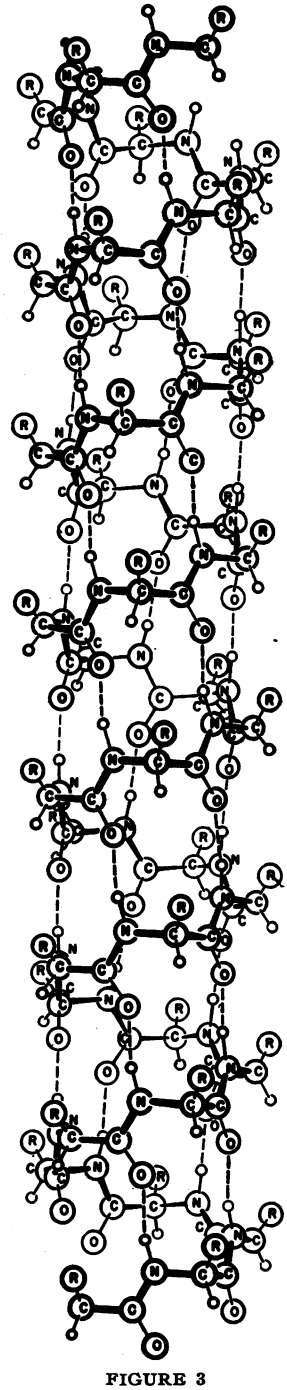


FIGURE 3
The helix with 5.1 residues per turn.

of 8 kcal. mole^{-1}, and such great instability would result from the failure to form these bonds that we may be confident of their presence. The N—H · · · O distance cannot be expected to be exactly 2.72 Å, but might deviate somewhat from this value.

Solution of this problem shows that there are five and only five configurations for the chain that satisfy the conditions other than that of direction of the hydrogen bond relative to the N—H direction. These correspond to the values 165°, 120°, 108°, 97.2° and 70.1° for the rotational angle. In the first, third, and fifth of these structures the >CO group is negatively and the >N—H group positively directed along the helical axis, taken as the direction corresponding to the sequence—CHR—CO—NH—CHR— of atoms in the peptide chain, and in the other two their directions are reversed. The first three of the structures are unsatisfactory, in that the

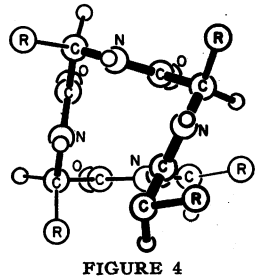


FIGURE 4

Plan of the 3.7-residue helix.

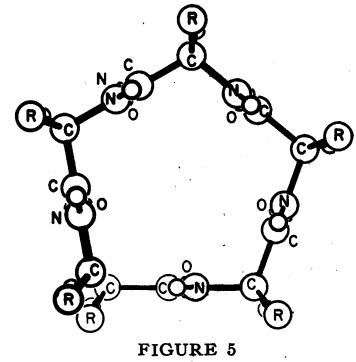


FIGURE 5

Plan of the 5.1-residue helix.

N—H group does not extend in the direction of the oxygen atom at 2.72 Å; the fourth and fifth are satisfactory, the angle between the N—H vector and N—O vector being about 10° and 25° for these two structures respectively. The fourth structure has 3.69 amino acid residues per turn in the helix, and the fifth structure has 5.13 residues per turn. In the fourth structure each amide group is hydrogen-bonded to the third amide group beyond it along the helix, and in the fifth structure each is bonded to the fifth amide group beyond it; we shall call these structures either the 3.7-residue structure and the 5.1-residue structure, respectively, or the third-amide hydrogen-bonded structure and the fifth-amide hydrogen-bonded structure.

Drawings of the two structures are shown in figures 2, 3, 4, and 5.

For glycine both the 3.7-residue helix and the 5.1-residue helix could occur with either a positive or a negative rotational translation; that is, as either a positive or a negative helix, relative to the positive direction of the helical axis given by the sequence of atoms in the peptide chain. For other amino acids with the L configuration, however, the positive helix and the negative helix would differ in the position of the side chains, and it might well be expected that in each case one sense of the helix would be more stable than the other. An arbitrary assignment of the R groups has been made in the figures.

The translation along the helical axis in the 3.7-residue helix is 1.47 Å, and that in the 5.1-residue helix is 0.99 Å. The values for one complete turn are 5.44 Å and 5.03 Å, respectively. These values are calculated for the hydrogen-bond distance 2.72 Å; they would have to be increased by a few per cent, in case that a larger hydrogen-bond distance (2.80 Å, say) were present.

The stability of our helical structures in a non-crystalline phase depends solely on interactions between adjacent residues, and does not require that the number of residues per turn be a ratio of small integers. The value 3.69 residues per turn, for the third-amide hydrogen-bonded helix, is most closely approximated by 48 residues in thirteen turns (3.693 residues per turn), and the value 5.13 for the other helix is most closely approximated by 41 residues in eight turns. It is to be expected that the number of residues per turn would be affected somewhat by change in the hydrogen-bond distance, and also that the interaction of helical molecules with neighboring similar molecules in a crystal would cause small torques in the helixes, deforming them slightly into configurations with a rational number of residues per turn. For the third-amide hydrogen-bonded helix the simplest structures of this sort that we would predict are the 11-residue, 3-turn helix (3.67 residues per turn), the 15-residue, 4-turn helix (3.75), and the 18-residue, 5-turn helix (3.60). We have found some evidence indicating that the first and third of these slight variants of this helix exist in crystalline polypeptides.

These helical structures have not previously been described. In addition to the extended polypeptide chain configuration, which for nearly thirty years has been assumed to be present in stretched hair and other proteins with the β-keratin structure, configurations for the polypeptide chain have been proposed by Astbury and Bell,[7] and especially by Huggins[8] and by Bragg, Kendrew, and Perutz.[9] Huggins discussed a number of structures involving intramolecular hydrogen bonds, and Bragg, Kendrew, and Perutz extended the discussion to include additional structures, and investigated the compatibility of the structures with x-ray diffraction data for hemoglobin and myoglobin. None of these authors proposed either our 3.7-residue helix or our 5.1-residue helix. On the other hand, we would

eliminate, by our basic postulates, all of the structures proposed by them. The reason for the difference in results obtained by other investigators and by us through essentially similar arguments is that both Bragg and his collaborators and Huggins discussed in detail only helical structures with an integral number of residues per turn, and moreover assumed only a rough approximation to the requirements about interatomic distances, bond angles, and planarity of the conjugated amide group, as given by our investigations of simpler substances. We contend that these stereochemical features must be very closely retained in stable configurations of polypeptide chains in proteins, and that there is no special stability associated with an integral number of residues per turn in the helical molecule. Bragg, Kendrew, and Perutz have described a structure topologically similar to our 3.7-residue helix as a hydrogen-bonded helix with 4 residues per turn. In their thorough comparison of their models with Patterson projections for hemoglobin and myoglobin they eliminated this structure, and drew the cautious conclusion that the evidence favors the non-helical 3-residue folded α-keratin configuration of Astbury and Bell, in which only one-third of the carbonyl and amino groups are involved in intramolecular hydrogen-bond formation.

It is our opinion that the structure of α-keratin, α-myosin, and similar fibrous proteins is closely represented by our 3.7-residue helix, and that this helix also constitutes an important structural feature in hemoglobin, myoglobin, and other globular proteins, as well as of synthetic polypeptides. We think that the 5.1-residue helix may be represented in nature by supercontracted keratin and supercontracted myosin. The evidence leading us to these conclusions will be presented in later papers.

Our work has been aided by grants from The Rockefeller Foundation, The National Foundation for Infantile Paralysis, and The U. S. Public Health Service. Many calculations were carried out by Dr. S. Weinbaum.

Summary.—Two hydrogen-bonded helical structures for a polypeptide chain have been found in which the residues are stereochemically equivalent, the interatomic distances and bond angles have values found in amino acids, peptides, and other simple substances related to proteins, and the conjugated amide system is planar. In one structure, with 3.7 residues per turn, each carbonyl and imino group is attached by a hydrogen bond to the complementary group in the third amide group removed from it in the polypeptide chain, and in the other structure, with 5.1 residues per turn, each is bonded to the fifth amide group.

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† Contribution No. 1538.

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CONCERNING NON-CONTINUABLE, TRANSCENDENTALLY TRANSCENDENTAL POWER SERIES

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The main purpose of this note is to show that power series of the kind described in the title can be obtained from a given power series by simply multiplying certain of its coefficients by -1.

Consider the class $\mathfrak{K}$ of power series of the form $\sum_{\nu=0}^{\infty} a_\nu z^\nu$ whose circle of convergence is the unit circle. There are $\mathfrak{c}$ elements in $\mathfrak{K}$ (where $\mathfrak{c}$ denotes the power of the continuum). Let $\mathfrak{C}$ be the class of those series in $\mathfrak{K}$ which can be continued beyond the unit circle, and let $\mathfrak{A}$ be the class of those series in $\mathfrak{K}$ which satisfy an algebraic differential equation. Denote by $\mathfrak{C}'$, $\mathfrak{A}'$, the respective complements of $\mathfrak{C}$, $\mathfrak{A}$, with respect to $\mathfrak{K}$.

There are the following sufficient conditions for a series in $\mathfrak{K}$ to belong to $\mathfrak{C}'$, $\mathfrak{A}'$, respectively:

(*A*)[1] *Let* $\{\lambda_\nu\}$ $(\nu = 1, 2, 3, \ldots)$ *be an increasing sequence of non-negative integers such that* $\lambda_\nu/\nu \to \infty$ *as* $\nu \to \infty$. *If* $\sum_{\nu=1}^{\infty} a_\nu z^{\lambda_\nu}$ *belongs to* $\mathfrak{K}$, *then it also belongs to* $\mathfrak{C}'$.

(*B*)[2] *Let* $\{\lambda_\nu\}$ $(\nu = 1, 2, 3, \ldots)$ *be a sequence of non-negative integers such that* $\lambda_{\nu+1} > \nu\lambda_\nu$ *for every* ν. *If* $\sum_{\nu=1}^{\infty} a_\nu z^{\lambda_\nu}$ *belongs to* $\mathfrak{K}$, *then it also belongs to* $\mathfrak{A}'$.

The series $\sum_{\nu=0}^{\infty} z^\nu$, which represents $(1 - z)^{-1}$ for $|z| < 1$, belongs to $\mathfrak{C}\mathfrak{A}$ (i.e., to both $\mathfrak{C}$ and $\mathfrak{A}$). The series $\sum_{\nu=0}^{\infty} b_\nu z^\nu$, which represents the meromorphic function $\Gamma(z + 1)$ for $|z| < 1$, belongs to $\mathfrak{C}$ and[3] to $\mathfrak{A}'$. According to (*A*), $\sum_{\nu=0}^{\infty} z^{\nu^2}$ belongs to $\mathfrak{C}'$, and it is known[4] that this series belongs to $\mathfrak{A}$. Finally, it follows from (*A*) and (*B*) that $\sum_{\nu=0}^{\infty} z^{\nu!}$ belongs to $\mathfrak{C}'\mathfrak{A}'$. Thus,