94.6 A. These two structures accordingly might well be expected to form a protein such as feather keratin, with a triclinic unit with $a_0 = 9.50$ A, $b_0 = 34.2$ A, $c_0 = 94.6$ A, $\alpha \cong 90°$, $\beta \cong 90°$, $\gamma \cong 90°$.

It seems likely that the pleated sheets are all oriented similarly in the structure—there is no significant indication of a unit with $b_0 = 68$ A, corresponding to two kinds of pleated sheets, with opposite orientations. A pleated sheet is polar: all of the C=O groups point in one direction, and the N—H groups in the opposite direction, and in addition the side chains on one side of the sheet are arranged differently with respect to the residues than are those on the other side of the sheet, so that an isolated sheet would be curved. It is interesting to speculate that this curvature of the pleated sheets may be related to the natural curvature of the feather rachis. An example of a polar sheet in the inorganic field is the kaolin sheet.[6] Curved crystals of the clay minerals have been recently observed with use of the electron microscope, and their curvature has been assumed to result from the polar nature of the kaolin sheets.[7, 8]

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* Contribution No. 1553.

[1] Astbury, W. T., Cold Spring Harbor Symposia on Quantitative Biology, **2**, 15 (1934).

[2] Pauling, L., and Corey, R. B., these PROCEEDINGS, **37**, 251 (1951).

[3] Corey, R. B., and Wyckoff, R. W. G., *J. Biol. Chem.*, **114**, 407 (1936).

[4] Pauling, L., Corey, R. B., and Branson, H. R., these PROCEEDINGS, **37**, 205 (1951); Pauling, L., and Corey, R. B., *Ibid.* **37**, 235 (1951).

[5] Bear, R. S., *J. Am. Chem. Soc.*, **66**, 2043 (1944).

[6] Pauling, L., these PROCEEDINGS, **16**, 123 (1930).

[7] Davis, D. W., Rochow, T. G., Rowe, F. G., Fuller, M. L., Kerr, T. S., and Hamilton, T. K., Electron Micrographs of Reference Clay Minerals, Preliminary Report No. 6 of American Petroleum Institute Project 49 (1950).

[8] Bates, T. F., Hildebrand, S. A., and Swineford, A., Morphology and Structure of Endelite and Halloysite, *American Mineralogist*, **35**, 463 (1950).

THE STRUCTURE OF HAIR, MUSCLE, AND RELATED PROTEINS

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It is thirty years since x-ray photographs were first made of hair, muscle, nerve, and sinew, by Herzog and Jancke.[1] During this period, despite the efforts of many investigators, the photographs have eluded detailed in-

terpretation, and the molecular structures of the proteins have remained undetermined. In the present paper we propose structures for hair, muscle, and related proteins in the extended state (β keratin and β myosin) and the contracted state (α keratin and α myosin), and discuss the extent to which the diffraction data are accounted for by the proposed structures.

The α-Keratin Structure.—It seems not unlikely that the polypeptide chains in unstretched hair, contracted muscle, horn, nail, quill, and other proteins that give the α-keratin x-ray pattern have the 3.7-residue helical configuration[2] (which for convenience we shall call the α helix).

Let us consider the structure expected for an aggregate of α helixes. The molecules, with the approximate form of circular cylinders, would be expected to pack in a hexagonal or pseudohexagonal array, as do the synthetic polypeptides poly-γ-methyl-L-glutamate and poly-γ-benzyl-L-glutamate.[3] The average residue weight 120 and approximate density 1.30 g cm^{-3} lead to 11 A as the value of a_0 for the hexagonal unit. The predicted equatorial reflections are $\{10\cdot0\}$ at 9.5 A, $\{11\cdot0\}$ at 5.5 A, $\{20\cdot0\}$ at 4.8 A, $\{21\cdot0\}$ at 3.6 A, $\{30\cdot0\}$ at 3.2 A, etc. The observed pattern of α keratin, as described by Astbury and Street,[4] has a strong equatorial reflection at 27 A, a very strong reflection at about 9.8 A, and a vague region of darkening around 3.5 A. We would attribute the 27-A reflection to a long-range order that can be elucidated only through further study. The 9.8-A reflection is described as covering a range of spacings of about 3 A centered at 9.8 A, which suggests that the packing is only pseudo-hexagonal, and that the hexagonal form $\{10\cdot0\}$ is split into several forms with different spacings. The failure to observe the reflections $\{11\cdot0\}$ and $\{20\cdot0\}$ can be attributed to the smallness of the x-ray form factor for equatorial scattering by the α helix,[5] which has a node at 5 A; indeed, the α-keratin x-ray photographs show a light band which is centered at about 5 A. The form factor then has a maximum at 3.4 A, which corresponds to the vague region of darkening, with center around 3.5 A, reported by Astbury and Street.

The principal meridional feature of the α-keratin x-ray pattern is a strong arc at 5.15 A. This reflection has been accepted as indicating that the c-axis identity distance is 5.15 A or a simple multiple of it, and it has usually been assumed that the c-axis length per residue is either $^1/_3\cdot5\cdot15 = 1.72$ A or $^1/_2\cdot5\cdot15 = 2.58$ A. The 5.15-A arc seems on first consideration to rule out the α helix, for which the c-axis period must be a multiple of the axis distance per turn, which is about 5.6 A. However, it was noted by Bamford, Hanby, and Happey[6] that the "meridional arc" observed on photographs of partially oriented fibers of poly-γ-benzyl-L-glutamate is on other photographs resolved into off-meridional spots in positions corresponding to the value 5.76 A for the c-axis translation. It seems probable that the 5.15-A arc seen on the α-keratin photographs is to be interpreted in a similar way.

A very significant contribution has been made by Herzog and Jancke[7] in 1926 and Lotmar and Picken[8] in 1942. These investigators obtained, by non-reproducible procedures, preparations of rather well crystallized muscle. Herzog and Jancke observed eight forms, and Lotmar and Picken eighteen. Lotmar and Picken's preparation was a piece of posterior-valve-closing muscle (of the mussel *Mytilus edulis*) that had been dried for 48 hours under 10-g tension and then allowed to stand in a can for a year. They indexed their photograph and (also Herzog and Jancke's) with a monoclinic unit with $a_0 = 11.70$ A, $b_0 = 5.65$ A (fiber axis), $c_0 = 9.85$ A, and $\beta = 70.5°$. The fiber-axis translation 5.65 A is in fine accordance with prediction for the 3.7-residue helix.

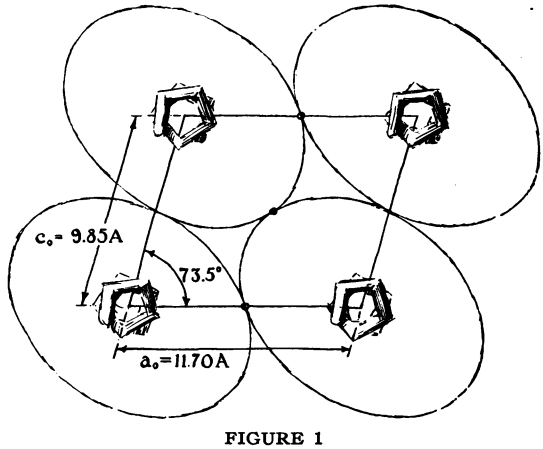

FIGURE 1

Plan of the monoclinic unit proposed for crystalline muscle by Lotmar and Picken, with the 3.7-residue helixes, suggested in the present paper, represented by elliptical cylinders. The dots indicate the positions assumed for side-chain carbon atoms.

Lotmar and Picken stated that their excellent photograph presumably shows the x-ray diagram of crystallized myosin, and that there is no sign of the 5.15-A meridional arc. They considered their preparation to represent a new molecular modification of myosin, with two residues per 5.65-A length along the *c*-axis. We think it likely that the process of crystallization has involved only the ordering of the α helixes, as shown in figures 1 and 2, in such a way that the larger side chains are grouped into layers with $x \cong 1/2$, the region near $x = 0$, $z = 1/2$ being free of side chains, thus permitting the helixes to come into close contact at these points.

The occurrence of the 5.15-A arc on the x-ray photographs of poorly ordered aggregates of α-helical molecules can be explained by the consid-

eration illustrated in figure 3. Here a helical curve with pitch 5.65 A is shown on a cylinder with radius 1.81 A, the average radius for the peptide atoms C, N, C′, and O. The angle of inclination of the helix is 26°, and the perpendicular distance between adjacent turns of the curve is 5.65 cos 26° = 5.1 A. We would thus predict strong reenforcement of x-rays scattered by an α molecule in directions about 26° from the fiber axis. (A related pertinent fact is that the maximum for the calculated radial distribution function for the α helix comes at 5.0 A; this function will be reproduced in a later paper.) In the case of a somewhat poorly ordered fibrous aggregate of the molecules or of a crystalline phase with very large unit the intermolecular interference would in general permit strong diffraction maxima with spacing 5.1 A to occur in the near-meridional region, whereas

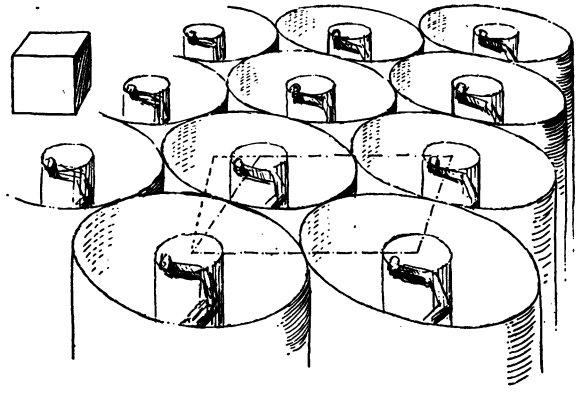

FIGURE 2

Drawing of the proposed structure of α keratin.

for a well-crystallized specimen intermolecular interference could cause these reflections to fail to appear, despite their large molecular form factor.

(Added April 10, 1951: It has been pointed out to us by Professor Verner Schomaker that the foregoing argument is not reliable. He has evaluated the form factor for x-ray scattering by a uniform helix, and has found that the maximum scattering by the helix with the dimensions given above occurs at angles considerably larger than 26° from the meridional direction, and at a Bragg angle corresponding to a spacing of about 4.2 A, rather than 5.1 A. He has further shown that if four main-chain atoms and the β carbon atom are represented by helixes with the correct radii for the 3.7-residue helical structure, and four side-chain atoms are represented by another helix, with the same pitch and with radius 4.0 A, a pronounced maximum is predicted to occur at 26° from the meridional direction and at a Bragg angle corresponding to a spacing of 5.1 A.)

The interplanar distances and estimated intensities of the basal-plane reflections on the x-ray photographs of crystalline muscle reported by Lotmar and Picken and by Herzog and Jancke are given in table 1, together with calculated values of the interplanar distance d, structure factor F, and intensity $I = LPF^2$, with L the Lorentz factor and P the polarization factor. The structure factor is that for the α helix, including a β carbon atom for each residue, evaluated for the case of cylindrical symmetry,[5] plus a side-chain carbon atom per residue at $x = 1/2$, $z = 0$ and another one at $x = 1/2$, $z = 1/2$. If the crystal has monoclinic symmetry, as assumed by Lotmar and Picken, there are 2-fold screw axes passing through these points, and a greater-than-average density of atoms might be expected near these axes; we have accordingly tried to approximate the effect of the side-chain atoms on the structure factor by placing atoms in these positions.

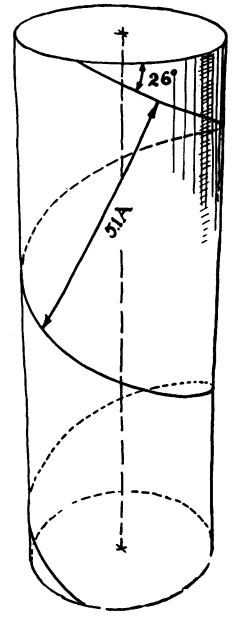

FIGURE 3

Diagrammatic representation of the 3.7-residue helix, indicating the origin of the meridional arc at 5.15 A observed on x-ray photographs.

It is seen that the calculated intensity pattern corresponds surprisingly well with the observed pattern, when it is considered that no variable parameter is involved in the calculation. The only arbitrary decision involved in the calculation is that the side-chain scattering, for about four heavy atoms per residue, can be approximated by placing a carbon atom near each of two 2-fold axes.

The first reflection, A_1, is seen on the reproduction of their photograph in Lotmar and Picken's paper to be very strong—we estimate it to be perhaps ten times as strong as A_2 or A_4. Its breadth is about 3 A, which is enough to include the forms {100}, {001}, and {101}. This spot closely resembles the corresponding spot given by ordinary preparations of α keratin, and described by Astbury and Street as covering a range of about 3 A, centered at 9.8 A. We accordingly think that it is likely that the ordinary preparations of α keratin have in fact a monoclinic structure closely resembling that of crystalline muscle, and only rather slightly disordered. The 27-A reflection seen on photographs of hair and ordinary muscle seems not to be present on Lotmar and Picken's photograph.

The second reflection, A_2, is observed to be strong, and calculated as weak. An additional side-chain carbon atom in phase for this reflection (near the line $x + z = 1$) would bring the value of $I_{calc.}$ to 103. (We have not attempted to find a distribution of side-chain atoms that would give

TABLE 1

COMPARISON OF CALCULATED AND OBSERVED INTENSITIES OF EQUATORIAL REFLECTIONS FOR CRYSTALLINE MUSCLE

TRICLINIC UNIT WITH $a_0 = 11.70$ A, $b_0 = 5.65$ A, $c_0 = 9.85$ A, $\alpha \cong 90°$, $\beta = 73.5°$, $\gamma \cong 90°$

REFLECTION	$h0l$	$d_{calc.}$	$F_{calc.}$	$I_{calc.}$	$I_{obs.LPa}$	$I_{obs.HJa}$	$d_{obs.LPa}$	$d_{obs.HJa}$
A_1	100	11.21 A	10.0	150				
	001	9.44	16.8	353	S(broad)	S(broad)	9.3 A	10.0 A
	101	8.51	14.0	217				
A_2	$10\bar{1}$	6.38	6.1	32	S	M	6.6	6.4
A_3	201	5.56	2.1	3	?[b]	M	6.0	5.8
	200	5.10	9.7	52				
A_4	102	4.87	−9.8	60	S	...	4.78	...
	002	4.72	7.7	35				
	$20\bar{1}$	4.31	−3.1	5				
	202	4.25	5.3	15				
A_5	$10\bar{2}$	3.97	−12.1	73	W	W	3.97	3.94
	301	3.87	−4.3	9				
A_6	300	3.74	−12.7	74	M	...	3.73	...
A_7	302	3.44	−12.4	65	M	...	3.50	...
	103	3.28	−5.0	10				
	$20\bar{2}$	3.19	2.1	2				
	$30\bar{1}$	3.18	−4.9	9				
	003	3.15	−4.9	9				
	203	3.15	−4.9	9				
A_8	401	2.92	−4.4	7	?[b]	...	2.94	
	303	2.84	−4.2	6				
	$10\bar{3}$	2.83	−4.2	6				
	400	2.80	2.9	3				
A_9	402	2.78	2.6	2	W	...	2.75	
	$30\bar{2}$	2.59	−9.6	28				
	$40\bar{1}$	2.50	−3.0	3				
	403	2.47	−2.9	2				
	$20\bar{3}$	2.46	−2.9	2				
A_{10}	104	2.45	−8.8	22	W	...	2.48	
	204	2.44	3.1	3				
	004	2.36	3.2	3				
	501	2.34	−2.4	2				
	304	2.31	−7.8	16				
	502	2.29	−7.7	15	M	...	2.18	
A_{11}	500	2.24	−7.3	13				
	$10\bar{4}$	2.19	−6.9	11				
	$40\bar{2}$	2.16	3.8	5				
	503	2.14	−1.3	0.4				
	$30\bar{3}$	2.13	−1.3	0.4				
	404	2.13	3.9	4				

[a] LP = Lotmar and Picken, HJ = Herzog and Jancke.

[b] Presumably the symbol means that Lotmar and Picken were doubtful as to the presence of these two spots.

better general agreement with the entire observed pattern, inasmuch as the approximate agreement given by the less arbitrary calculation that we have made seems to us to be more significant.)

The questionable reflections A_3 and A_8 cannot be seen on the reproduced photograph. A_5, which is described by Lotmar and Picken as weak (whereas $I_{calc.}$ is as large for it as for A_6 and A_7, described as strong), lies in a region of general blackening, which may have caused its intensity to be underestimated—it is interesting that Herzog and Jancke report A_5, but not A_6 nor A_7. Whether A_9 can be assigned to the form $\{30\bar{2}\}$ is doubtful; but in any case the appearance of the three reflections A_9, A_{10}, and A_{11} in nearly the calculated positions and with the calculated intensities can hardly be the result of coincidence. The sequence of forms with very small values of $I_{calc.}$ in the regions for which no reflections are reported by Lotmar and Picken and also the rather striking agreement found for the observed reflections strongly favor the conclusion that the assumed structure is not greatly different from the actual structure.

Some evidence for the 3.7-residue helix is provided also by the meridional reflections reported for muscle fibers and porcupine quill by Corey and Wyckoff,[9] MacArthur,[10] and Bear.[11] These reflections correspond to large c-axis identity distances, about 726 A for muscle fiber and 198 A for porcupine quill. The 726-A unit for muscle is shown also in electron micrographs of muscle fibrils treated with osmic acid.[12] We would expect that side chains of different kinds on the α helix would repeat after an integral number of residues, corresponding to an integral multiple of the residue length along the helix axis, about 1.53 A, and that accordingly those orders of basal plane reflection for which the spacing approximated closely to certain multiples of 1.53 A would be enhanced in intensity. It is in fact found that about 80 per cent of the meridional reflections are of this type; for both Venus clam muscle and porcupine quill they are multiples of 1.51 A. The reflections at 1.49 A, 3.05 A, 4.50 A, and 6.19 A for porcupine quill, which represent the first four orders of enhancement, are the strongest features of the wide-angle meridional pattern, except for the 5.2-A arc.

The β-Keratin Structure.—Hair and muscle can be reversibly stretched to about 100 per cent elongation.[13] Some authors have expressed doubt as to whether this elongation is to be attributed to the polypeptide chains, but it seems to us that Astbury's contention that it should be is justified. With a fiber-axis length of 1.53 A per residue for the α helix, an extended chain in the β-keratin structure would be predicted, on this assumption, to have a fiber-axis residue length of about 3.1 A. The principal meridional x-ray reflection of stretched hair, stretched muscle, and other proteins with the β-keratin structure[4] has in fact a spacing reported by Astbury as about 3.32 A, which is presumably the fiber-axis residue length, and would thus correspond to 117 per cent extension of the α helix. That the β-kera-

tin structure involves extended polypeptide chains was first suggested by Brill[14] in 1923, and for the past fifteen years it seems to have been rather generally assumed that the chains are essentially coplanar, and that they alternate in direction in forming hydrogen-bonded non-polar sheets.[15–17, 8] Another hydrogen-bonded layer structure, the pleated sheet, which avoids the difficulty of large steric interference of side-chain groups predicted for the planar sheet, has recently been described.[18] The pleated sheet can easily assume a configuration corresponding to the residue-length 3.32 A, and it seems to us likely that it represents the β-keratin structure.

At present there is not much direct evidence to support this view. The observed equatorial x-ray reflections[4] at 9.8 A (strong) and 4.65 A (very strong) have been shown by Astbury and Sisson[19] to correspond to the plane of the β-keratin layers and the lateral direction in the layers, respectively. The lack of other equatorial reflections, except one weak reflection at 2.4 A, and lack of knowledge of positions of side-chain atoms make a calculation of intensities of reflection of little value. It may be pointed out, however, that if the one-molecule unit that accounts for the x-ray pattern of crystalline muscle obtained by Lotmar and Picken is correct the α helixes must all be oriented in the same sense, and accordingly this muscle on stretching could be transformed into the pleated sheet, but not into the planar sheet.

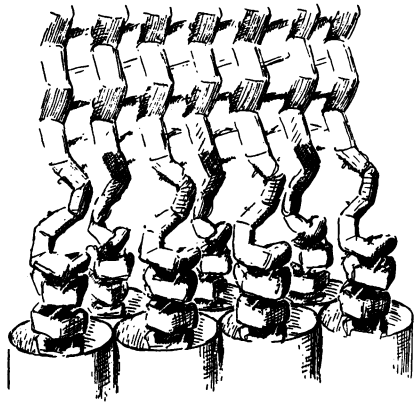

FIGURE 4

Drawing illustrating the proposed mechanism of conversion of a pleated sheet into a double row of 3.7-residue helixes; this is proposed as the process involved in the contraction of muscle.

When hair or muscle is treated with hot water or steam it shortens in the direction of the fiber axis, and swells laterally. The resultant material is called supercontracted keratin. The contraction from the α state is about 30 per cent for both hair[20] and myosin.[21] It is possible that supercontracted keratin has the configuration of the 5.1-residue helix,[2, 5] but there is very little evidence to support this suggestion. The fiber-axis residue length for this helix is about 0.99 A, which corresponds to 35 per cent contraction from the α helix, with residue length 1.53 A. The agreement of this value with the experimental value for the amount of supercontraction provides some support for the suggestion that the γ helix is present in supercontracted keratin. A careful study of the x-ray diagram should permit a decision on this point to be made.

The Mechanism of Contraction of Muscle.—The assignment of the pleated-sheet configuration to extended muscle and of the α-helical configuration to contracted muscle suggests that a discussion be made of the mechanism of contraction of muscle.

We have noticed that in order for a pleated sheet to be converted into a double layer of α helixes it is not necessary that all of the hydrogen bonds in the pleated sheet be initially broken. Instead, it is necessary to break only enough hydrogen bonds, four or five, to liberate four or five residues in each polypeptide chain, these being at about the same horizontal level in the pleated sheet. The liberated chains can then coil into the α-helical configuration, to produce the double layer of packed cylindrical α helixes, as shown in figure 4.

The sheet configuration is, for a normal protein, somewhat unstable relative to the α helix. This is indicated to be the case for synthetic polypeptides involving residues other than glycine by the fact that these polypeptides have been observed to form crystals of the α type.[6] Indication that the instability of the pleated sheet is due to steric repulsion between side chains is given by the fact that copolymers containing a large fraction of glycine residues assume the β configuration.[6] The steric-hindrance explanation of the instability of the pleated sheet is made reasonable by a consideration of the area available per side chain. In a normal β keratin, with fiber-axis length per residue 3.32 A and side-chain spacing 4.75 A and both sides of the sheet available for side chains, the area per side chain is 31.6 A^2. For the α helix we may take the radius of the side-chain median cylindrical surface to be 4.16 A, which is midway between the centers of the β carbon atoms (radius 3.34 A) and the point of contact with adjacent molecules ($^1/_2c_0$ = 4.98 A); with the fiber-axis residue length 1.53 A, the area per side chain is calculated to be 40.0 A^2, which is 25 per cent larger than for the pleated sheet. Moreover, in the discussion of the pleated sheet we have pointed out that the ideal pleated sheet has fiber-axis length per residue 3.07 A, and that the extension to 3.32 A, as observed in myosin, seems to be associated with a steric interference with the side chains, which causes the residues to rotate out of the position most favorable to hydrogen-bond formation, and thus introduces a strain, essentially of bending, in the hydrogen bonds. The normal hydrogen-bond energy for peptides may be estimated at 7.5 kcal $mole^{-1}$; it is expected to be large, because of the negative charge conferred on the carbonyl oxygen atom and the positive charge conferred on the imino nitrogen atom by the amide resonance. The energy of the strain introduced may be estimated to be of the order of magnitude of about 3 per cent of the hydrogen-bond energy, or 0.22 kcal $mole^{-1}$, which is about 1.8 cal per gram of myosin. Since muscle is about 10 per cent myosin, we estimate (very roughly) the work that could be done by 1 g of muscle to be about 0.18 cal, in a single complete

twitch. Muscle has density 1.06 g cm^{-3}, and 1 g of muscle in the extended state with cross-section 1 cm^2 would be 0.94 cm long. If the entire muscle were to shorten proportionately to the myosin molecules, and these molecules were to shorten from the residue length 3.32 A (for the pleated sheet) to 1.53 A (for the α helix), the contracted length would be 0.43 cm, the contraction being by 54 per cent. The contracting pleated sheet would be predicted to exercise the same force throughout its contraction; for initial cross-section 1 cm^2 (in the extended state) this force is calculated from the assumed strain energy 0.18 cal per g of muscle, assuming it to be free energy, to have the value 1.53 kg.

The foregoing rough calculation agrees well with experiment in some respects. A. V. Hill has reported[22] that the maximum force exerted in a twitch by frog's muscle at 0°C is 1 to 2 kg cm^{-2}, which agrees well with the value 1.5 kg cm^{-2} calculated above. It is interesting also that the observed maximum shortening,[23] by 50 to 60 per cent for toad muscle, is close to the predicted shortening, 54 per cent, for the transition from the pleated sheet to the α helix. The heat liberated by frog's sartorius muscle on tetanic contraction has been measured,[24] and found to be about 400 g cm per cm of shortening and per cm^2 cross-section, or 0.05 cal per g of muscle, assuming complete contraction (by 54 per cent). Somewhat smaller values were found in a later study.[23] These values are considerably smaller than the estimated energy difference of the extended and the contracted forms of the myosin of muscle, as given above (0.18 cal g^{-1}).

In order to account for the observed mechanical properties of hair (great extension under a load of 500 to 2000 kg cm^{-2}, depending on humidity) in the same way, it must be assumed that the strain of the β configuration is very much greater, about 10 cal $mole^{-1}$ per residue. Moreover, the great dependence on humidity shows that side-chain interactions, which are changed by hydration, are involved.

The pleated-sheet configuration of extended muscle is metastable. In order for the polypeptide chains to contract an excitation energy would be needed, the energy of breaking four or five hydrogen bonds, to liberate four or five residues, in each chain. We suggest that the mechanism whereby the reaction of contraction is initiated may involve the production in or transfer to this region of the muscle of a number of hydrogen-bond-forming molecules, which can attack the hydrogen bonds of the pleated sheet, and through the formation of hydrogen bonds with the carbonyl and imino groups of the chains decrease the energy of activation of the sheet-disrupting process. As the α helixes are formed these molecules are liberated, and might continue to attack hydrogen bonds in the pleated sheet. It is, however, not necessary that they do so, in order for the process of formation of α helixes to continue, once that it is started: as the freed residues coil into the α helixes, and form more stable hydrogen bonds within these helixes, they would exercise a mechanical strain, communicated along the

polypeptide chain, on the adjacent residues that are still held by hydrogen bonds in the pleated sheet, and this strain would have the effect of reducing the activation energy for the liberation of further residues. Accordingly once that the reaction were initiated, it would be expected to continue until all of the pleated sheet had been converted into a double row of α helixes.

It is not so easy to suggest a single reasonable way in which the muscle can be reconverted to the stretched state. There are many conceivable ways in which this could be done, with the use of chemical reactions of various sorts—especially the change in the nature of the environment of the α helixes. One possibility, suggested over twenty years ago by Meyer and Mark,[25] is that through a change in the ionic environment in the muscle the polypeptide chain is provided with a sequence of similarly charged side chains, not paired with neutralizing charges of the opposite sign. The electrostatic repulsion of these side chains would then tend to cause the chains to stretch out into the pleated-sheet configuration. It is of interest that Meyer and Mark illustrated this mechanism with use of a simple helical curve for the molecule of contracted muscle.

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* Contribution No. 1554.

[1] Herzog, R. O., and Jancke, W., "Festschrift der Kaiser Wilhelm Gesellschaft," 1921.

[2] Pauling, L., Corey, R. B., and Branson, H. R., these PROCEEDINGS, **37**, 205 (1951).

[3] Pauling, L., and Corey, R. B., *Ibid.*, **37**, 241 (1951).

[4] Astbury, W. T., and Street, A., *Phil. Trans. Roy. Soc.*, **A230**, 75 (1931).

[5] Pauling, L., and Corey, R. B., these PROCEEDINGS, **37**, 235 (1951).

[6] Bamford, C. H., Hanby, W. E., and Happey, F., *Proc. Roy. Soc.*, **A205**, 30 (1951).

[7] Herzog, R. O., and Jancke, W., *Naturwiss.*, **14**, 1223 (1926).

[8] Lotmar, W., and Picken, L. E. R., *Helv. Chim. Acta*, **25**, 538 (1942).

[9] Corey, R. B., and Wyckoff, R. W. G., *J. Biol. Chem.*, **114**, 407 (1936).

[10] MacArthur, I., *Nature*, **152**, 38 (1943).

[11] Bear, R. S., *J. Am. Chem. Soc.*, **66**, 2043 (1944).

[12] Jakus, M. A., Hall, C. E., and Schmitt, F. O., *Ibid.*, **66**, 313 (1944).

[13] Astbury, W. T., and Woods, H. J., *Nature*, **126**, 913 (1930).

[14] Brill, R., *Ann. d. Chem.*, **434**, 204 (1923).

[15] Astbury, W. T., *Trans. Faraday Soc.*, **29**, 193 (1933).

[16] Huggins, M. L., *J. Org. Chem.*, **1**, 407 (1936).

[17] Pauling, L., *J. Am. Chem. Soc.*, **62**, 2643 (1940).

[18] Pauling, L., and Corey, R. B., these PROCEEDINGS, **37**, 251 (1951).

[19] Astbury, W. T., and Sisson, W. A., *Proc. Roy. Soc.*, **A150**, 533 (1935).

[20] Astbury, W. T., and Woods, H. J., *Phil. Trans. Roy. Soc.*, **A232**, 333 (1933).

[21] Astbury, W. T., and Dickinson, S., *Proc. Roy. Soc.*, **B129**, 307 (1940).

[22] Hill, A. V., *Proc. Roy. Soc.*, **B136**, 243 (1949).

[23] Hill, A. V., *Ibid.*, **B136**, 195 (1949).

[24] Hill, A. V., *Ibid.*, **B126**, 136 (1938).

[25] Meyer, K. H., and Mark, H., "Der Aufbau der hochpolymeren organischen Naturstoffe," Akademische Verlagsgesellschaft M.B.H., Leipzig, 1930.