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The Fourier Transform of the Coiled-Coil Model for α-Keratin

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The theory of diffraction by a coiled-coil is applied to α-keratin models and extended to deal with multi-strand ropes of various strand directions. A method of calculating the Fourier transforms of multi-strand ropes is described and important parts of the transforms are given in graphical form.

Introduction

It is now well established that the α-helix described by Pauling, Corey & Branson (1951) occurs in synthetic polypeptides (Elliott & Malcolm, 1959) and in globular proteins (Kendrew, Dickerson, Strandberg, Hart, Davies, Phillips & Shore, 1960). It has also been suggested that α-helices distorted into coiled-coils are the basis of the structure of the *k–m–e–f* group of fibrous proteins (Pauling & Corey, 1953; Crick, 1952, 1953*a*,*b*). A method of calculating the Fourier transform of a coiled-coil has been described by Crick (1953*a*,*b*) and calculations over limited regions have been reported by Lang (1956) and Cohen & Holmes (1963). In the present communication details of the Fourier transforms of various coiled-coil models of α-keratin are given as a first step towards the recognition of such structures from X-ray diffraction patterns.

The coiled-coil model

A continuous coiled-coil may conveniently be described (Crick 1953*a*) by the parametric equations

$$\begin{aligned} x &= r_0 \cos(\omega_0 t+\varphi_0) & x' &= r_1 \cos(w_1 t+\varphi_1) \\ y &= r_0 \sin(\omega_0 t+\varphi_0) & y' &= r_1 \sin(\omega_1 t+\varphi_1) \\ z &= P\omega_0 t/2\pi + z_0 & z' &= 0 \end{aligned} \qquad (1)$$

where x, y, z are the coordinates of the major helix and x', y', z' those of the minor helix. The major helix coordinates refer to a right-handed system of fixed axes and the minor helix coordinates refer to a set of axes which rotate with the major helix as in Crick (1953*a*). The point (x', y', z') traces out the continuous coiled-coil as t is varied and the discontinuous coiled-coil is obtained by supposing a point to occur at $t=t_1$, and further points at fixed intervals of $t=t_0$. The coordinates of the atoms in the seven residues which constitute the asymmetric unit in the α-keratin model were calculated from the expressions given by Crick (1953*a*) and Lang (1956) and the coordinates for an undistorted α-helix listed in Table 1. These coordinates

Table 1. *Coordinates of a residue in an undistorted, right-handed α-helix*

	x_s	y_s	z_s	r_s	φ_s
β-C	3·20	0	0	3·20	0
α-C	2·15	0·75	−0·83	2·28	19·3
N	1·04	1·17	0·03	1·57	48·4
C	−0·11	1·61	−0·44	1·61	93·9
O	−0·39	1·72	−1·64	1·76	102·8
β-C*	−0·56	3·15	1·50	3·20	100·0

are a modified version of those given by Pauling, Corey, Yakel & Marsh (1955). Setting $z_s=\varphi_s=0$ for the β carbon atom as in Table 1 would produce the type of knob-hole packing envisaged by Crick (1953*b*) in his Fig. 6 for poly-L-alanine. The parameters φ_0 and z_0 were taken as zero for convenience and φ_1 calculated from

$$\varphi_1 = \varphi_s + \{(N_1-N_0)/M\}\varphi_M \text{ with } \varphi_M = 2\pi M z_s \cos\alpha/c,$$

where N_0 (=1) is the number of turns of the major helix, N_1 (=36) is the number of turns of the minor helix and M (=126) is the number of residues in the repeat distance c (=186 Å). The coordinates of the thirty-five atoms in the asymmetric unit are given in Table 2 for r_0=5·2 Å. All the formulae used in this account refer to left-handed minor and right-handed major helices so that the coordinates in Table 1 were reflected in the $x0z$ plane for the purposes of calculation and the results again reflected to give the values in Table 2. In addition we have calculated the changes in bond lengths and interbond angles which take place when the α-helix is distorted into a coiled-coil and these are included in Table 2.

The Fourier transform of the model

We have calculated part of the Fourier transform of the model by means of the theory for simple helices given by Cochran, Crick & Vand (1952) and the coordinates given in Table 2. This provided a useful check on later calculations but is a cumbersome

Table 2.

(*a*) Atomic coordinates of asymmetric unit in a coiled-coil with $r_0 = 5{\cdot}2$ Å (Oz = major helix axis)

	x	y	z		x	y	z
β–C(1)	8·400	0·000	0·000	C(4)	6·488	−0·182	4·182
α–C(1)	7·350	−0·886	−0·696	O(4)	6·466	−0·682	3·043
N(1)	6·243	−1·151	0·235	β–C(5)	7·545	−0·989	6·342
C(1)	5·097	−1·658	−0·152	α–C(5)	6·288	−1·039	5·460
O(1)	4·813	−1·973	−1·312	N(5)	5·147	−0·511	6·205
β–C(2)	4·656	−2·844	2·021	C(5)	4·015	−0·190	5·635
α–C(2)	4·103	−1·842	1·002	O(5)	3·767	−0·300	4·439
N(2)	3·877	−0·547	1·637	β–C(6)	2·631	−0·753	7·624
C(2)	3·658	0·563	0·966	α–C(6)	2·974	0·342	6·619
O(2)	3·603	0·547	−0·256	N(6)	3·507	1·508	7·304
β–C(2)	2·212	1·591	2·710	C(6)	4·123	2·488	6·688
α–C(3)	3·449	1·795	1·861	O(6)	4·311	2·546	5·471
N(3)	4·607	1·960	2·718	β–C(7)	3·395	4·258	8·312
C(3)	5·837	1·892	2·273	α–C(7)	4·600	3·602	7·643
O(3)	6·150	1·692	1·087	N(7)	5·469	3·009	8·664
β–C(4)	6·749	3·508	3·997	C(7)	6·438	2·164	8·376
α–C(4)	6·892	2·100	3·390	O(7)	6·727	1·779	7·225
N(4)	6·679	1·095	4·444				

(*b*) Bond lengths and angles in a coiled-coil compared with values in an undistorted α-helix

Bond	Maximum	Undistorted	Minimum	Angle	Maximum	Undistorted	Minimum
βC–αC	1·540	1·535	1·514	βC–αC–N	110·35	112·46	109·26
αC–N	1·472	1·465	1·450	αC–N–C	123·53	122·55	122·66
N–C	1·318	1·317	1·307	N–C–O	125·33	122·56	124·69
C–O	1·248	1·237	1·226	O–C–αC*	122·53	121·05	121·29
C–αC*	1·556	1·546	1·528	C–αC*–βC*	110·45	110·86	109·12
N–O†	2·864	2·841	2·813	N–C–αC*	113·70	116·39	112·78
				C–N–O†	116·07	114·12	114·97

* Indicates next residue. † Indicates next-but-one residue.

method and not so illuminating as the use of the expression derived by Crick (1953*a*) and Lang (1956) in which only the undistorted α-helix coordinates for one residue are needed. The expression for a single set of points is:

$$\begin{aligned} C(R,\psi,l/c) = \sum_p\sum_q\sum_s\sum_d & J_p(2\pi R r_0) \\ & \times J_q(2\pi R\bar{r}_1) J_s(2\pi(l/c) r_1 \sin\alpha) \\ & \times J_d(2\pi R \Delta) \exp\{i[p(\psi-\varphi_0+\tfrac{1}{2}\pi) \\ & + q(-\psi+\varphi_0+\varphi_1+\tfrac{1}{2}\pi)+s(\pi+\varphi_1) \\ & + d(\psi+\varphi_1-\varphi_0+\tfrac{1}{2}\pi)-m'\varphi_M+2\pi z_0 l/c]\}, \quad (2) \end{aligned}$$

subject to the restriction,

$$N_0 p+(N_1-N_0)q+N_1 s+(N_1+N_0)d = l+Mm' \quad (3)$$

where p, q, s, d and m' may take any integral value. All the published versions of (2) & (3) contain minor misprints or errors. Lang (1956) corrected Crick's formulae but has a misprint in (3) whilst the formula given by Ramachandran (1960) has an erroneous sign for m' in (3). In these formulae:

R, ψ, $l/c(=Z)$ are cylindrical coordinates in reciprocal space; r_0, φ_0, z_0 are the coordinates of the origin of the rotating frame at $t=0$; r_1 is the radius of the minor helix; $\bar{r}_1 = r_1(1+\cos\alpha)/2$ and $\Delta = r_1\,(1-\cos\alpha)/2$ where $\tan\alpha = 2\pi r_0 N_0/c$.

The nature of the solution is most simply described in terms of parameters m and λ which are related to l by

$$Z = l/c = m/h+\lambda/P. \quad (4)$$

This emphasizes the fact that the coiled-coil can be regarded as a simple helix of pitch P with asymmetric units of seven residues distributed at vertical intervals of h and is a most useful device in the general case when c is very large. It follows from the theory of Cochran, Crick & Vand (1952) that the transform will consist of branches emanating from the origin, and a series of points on the meridian distant m/h from the origin, where $m = \pm 1, \pm 2$, *etc.* The separation between each layer line and the next in a branch will be $1/P$. Thus the 5·15 Å meridional reflection would be described by $m=2$, $\lambda=0$, the 1·5 Å meridional by $m=7$, $\lambda=0$ and the 10 Å equatorial group by $m=0$, $\lambda = 0 \pm 1, \pm 2$ *etc.* Equation (2) may be simplified since $\alpha \sim 10°$ and so Δ is small and d is restricted to zero, also we may for convenience choose $\varphi_0 = z_0 = 0$. Restriction (3) can also be simplied, since $M = 7/2N_1$ and $l = mN_1/2 + \lambda N_0$, to

$$(\lambda+q-p)N_0 = (q+s-\tfrac{1}{2}m-\tfrac{7}{2}m')N_1. \quad (5)$$

As only terms in (2) for which *all* the Bessel function orders are small need be considered and since $N_1 \sim 36N_0$ it follows that both brackets in (5) must be zero. Thus the problem reduces to the calculation, for the λth member of the mth branch, of:

$$C(R, \psi, m, \lambda) = \exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\} \sum_{p,q,s,m'} J_p(2\pi R r_0) J_q(2\pi R \bar{r}_1) \times Js(2\pi Z r_1 \sin\alpha) \exp\{i[(q+s) \times (\varphi_1+\pi) - m'\varphi_M]\}, \quad (6)$$

where the summation is restricted to sets of values of p, q, s and m' which satisfy

$$\lambda = p-q, \quad m = 2(q+s)-7m'. \quad (7)$$

It is noteworthy that the amplitude of C is not a function of ψ.

Method of calculation

Equation (6) gives the transform, C, of a single set of points distributed on a coiled coil; the structure factor is thus

$$F(R, \psi, m, \lambda) = \sum_i f_i C_i \quad (8)$$

where f_i is the scattering factor of the ith atom and the summation was taken over the four main-chain atoms plus the β carbon atom.

The only combinations of p, q, s and m' which are required in the summation in (6) are those for which p, q and s are all small and for $m=0$ a single term with $p=\lambda$, $q=s+m'=0$ is sufficient. Expression (8) may be written in the form

$$F(R, \psi, m, \lambda) = \{A(R, m, \lambda)+iB(R, m, \lambda)\} \times \exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\}, \quad (9)$$

and the values of A and B were evaluated at twenty-one points in the interval $R=0-0{\cdot}2$ Å^{-1} for a wide range of m and λ by means of a Ferranti SIRIUS computer. These values enable the intensity $I(R,m,\lambda)$ for the various rope models to be calculated. The value of r_0 suggested by Crick (1953*b*) for the two-strand rope was 5·2 Å and this was used in calculating A and B. In the case of the three-strand ropes r_0 would be somewhat greater, but since 5·2 Å was an arbitrary choice no useful purpose is served by making special calculations for the three-strand ropes. The effect of increasing r_0 is simply to contract proportionally the transform with respect to R.

Coiled-coil ropes

The transforms of the multi-strand rope models described by Crick (1953*b*) can be obtained from that of a single strand by adding together the transforms of the component strands. In the two-strand parallel-chain rope, in which the two strands are related by a rotation axis along Oz, the transform of the second strand is obtained by setting $\psi=\psi-\pi$ in (9), giving for the complete rope, after normalizing,

$$T_{uu}(R,\psi,m,\lambda) = F(R,\psi,m,\lambda)\tfrac{1}{2}\{1+\exp(i\lambda\pi)\}. \quad (10)$$

Thus I_{uu} is zero for odd λ and equal to (A^2+B^2) for even λ. In the two-strand anti-parallel chain rope the second chain is obtained by a rotation of π around Oz followed by a rotation of π around Ox. It is readily shown that the normalized transform for the rope is

$$T_{ud} = A \exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\} \text{ for even } \lambda, \quad (11a)$$

and

$$T_{ud} = iB \exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\} \text{ for odd } \lambda. \quad (11b)$$

Thus $I_{ud}=A^2$ for even λ and B^2 for odd λ. No systematic absences are thus expected for the two-chain anti-parallel rope except near the equator when $q=s=m'=0$ and so $B=O$.

In the three-strand parallel chain rope the three strands are related by a threefold rotation axis along Oz and it follows that

$$T_{uuu} = F.\tfrac{1}{3}\{1+\exp(i\lambda\pi/3)+\exp(i\lambda 2\pi/3)\}. \quad (12)$$

Thus I_{uuu} is zero except when λ is a multiple of 3 and then has the value A^2+B^2. For the 'two up/one down' three-strand rope the transform may be shown to be

$$T_{uud} = (A+\tfrac{1}{3}iB)\exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\}, \quad \lambda = 3n \quad (13a)$$

$$= \tfrac{2}{3}iB\exp\{i\lambda(\psi+\tfrac{1}{2}\pi)\}, \quad \lambda \neq 3n \quad (13b)$$

and thus $I_{uud}=A^2+B^2/9$ for $\lambda=3n$, and $4B^2/9$ for $\lambda \neq 3n$. I_{uud} thus has no systematic absences except for $m=0$.

Discussion

From the sections of the intensity transform shown in Fig. 1 it is clear that if the coiled-coil models are correct it should, in principle, be possible to differentiate between the two- and three-strand ropes and also to determine the combination of chain directions by studying the X-ray diffraction pattern of α-keratin.

An important diagnostic feature of the coiled-coil model is the group of near-equatorial layer lines with $m=0$ and λ small. The separation of these layer lines, δZ, gives a value for the ratio (Number of strands/pitch of major helix). As shown in the analysis this is independent of the combination of chain sense in the rope and has been applied by Cohen & Holmes (1963) to paramyosin in which these layer lines are well resolved and a two-strand rope is indicated. In the case of α-keratin Crick (1953*b*) suggested that the fine structure in the near equatorials reported by MacArthur (1943) indicated a three-strand rope. However recent measurements by the authors put the value of $1/\delta Z$ in the range 70–85 Å which would give $P=210$–255 Å for a three-strand rope or $P=140$–170 Å for a two-strand rope compared with the value 186 Å suggested by Crick. Clearly the question is not yet resolved although the seven-strand cable (Pauling & Corey, 1953) and single-strand coil (Skertchley & Woods, 1960) would seem to be eliminated.

It has been pointed out (Fraser & MacRae, 1961) that the spacings of the $m=2$ and $m=7$ meridionals should be in the exact ratio $\frac{7}{2}$ whereas the observed spacings of 5·15 Å and 1·486 Å are not. This discrep-

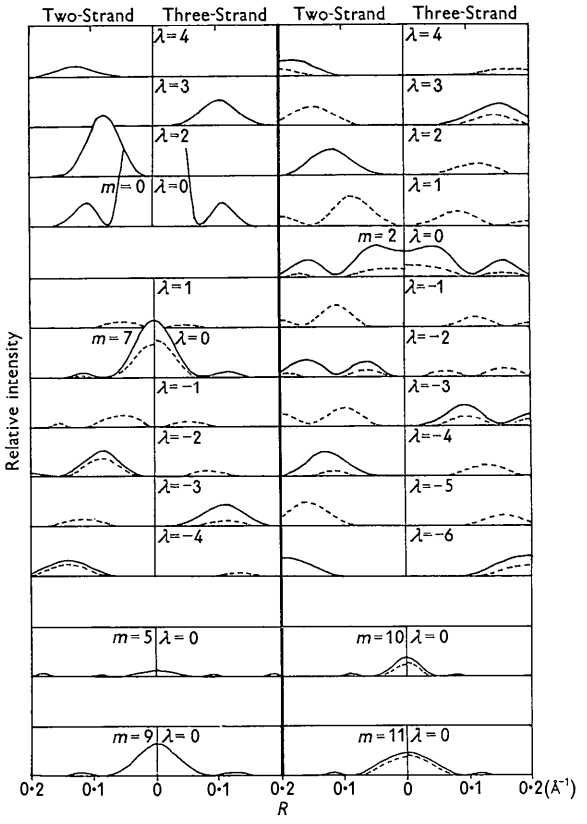

Fig. 1. Sections of the intensity transform of two- and three-strand ropes. The full lines are for parallel strands while the broken lines have one strand running in the opposite direction to the other(s). The scale for $m=0$ has been reduced by a factor of 10.

ancy is readily accounted for in Fig. 1 where it will be seen that for $m=7$ there is considerable intensity on layer lines with $\lambda \leq 0$ and very little for $\lambda > 0$, thus with imperfect resolution the measured spacing of the 'meridional' arc would be greater than the calculated value of 1·476 Å. Detailed discussion of the application of these calculations to α-keratin will be reported elsewhere.

In conclusion, it should be noted that α-helix ropes are likely to be collected into organized fibrils and due allowance must be made for this. The effect will be to superimpose a rapid oscillation on the transform and this effect is clearly apparent on the $m=2, \lambda=0$ layer line of α-keratin. In general the transform of a fibril may be obtained by considering the effect of rotating a rope through an angle φ_0 about Oz, displacing it a distance z parallel to Oz and radially a distance r in a direction making angle φ with Ox. Thus any position and orientation may be achieved, and since the angular dependence of the transform is always of the form $\exp\{i\lambda(\psi+\frac{1}{2}\pi)\}$ the effect of the changed position and orientation may be allowed for by writing

$$T(r, \varphi, z, \varphi_0) = T(0, 0, 0, 0) \times \exp\{i[-\lambda\varphi_0 + 2\pi zZ + 2\pi rR\cos((\psi-\varphi)]\}. \quad (14)$$

The transform for the entire fibril will be obtained by summing a series of such terms, one for each rope in the fibril. It may be shown that in cases where the N ropes are all of the one type the radial average of the normalized intensity transform is given by

$$I = |T|^2/N^2\{N + 2\sum_{j=1}^{N}\sum_{k=j+1}^{N} J_0(2\pi Rr_{jk}) \times \cos(-\lambda\varphi_{0jk} + 2\pi Zz_{jk})\}, \quad (15)$$

which may be compared with the formula given by Oster & Riley (1952) for assemblies of cylinders.

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