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Acta Cryst. (1956). **9**, 436

An X-ray Study of α-Keratin. I. A General Diffraction Theory for Convoluted Chain Structures and an Approximate Theory for Coiled-Coils

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(*Received* 10 *June* 1955)

A fibre structure is examined consisting of a periodic distribution of electron density along an infinite line which is folded or coiled in space in a pattern arbitrarily complex but repeating regularly along the fibre axis. The electron-density distribution on the spiral is expressed as a Fourier series, periodic in the distance measured along the line, and the same holds for each of the cartesian coordinates of a point of the spiral. The expression for the structure amplitude on any layer can be written as a product of Fourier coefficients of these four series. The approximate theory for the coiled coil regards the compound helix as a minor helix deformed with the periodicity of the major helix, the scattering contribution of each turn of the minor helix being thereby modulated in phase and amplitude. The diffraction pattern of a three-strand cable composed of α_1 helices has been calculated in the region of meridional spacing 6·1–4·7 Å and shows qualitative agreement with the observed porcupine-quill pattern.

Introduction

Pauling & Corey (1951*a*) proposed a structure for α-keratin consisting of α-helices packed together in alignment with the fibre axis, and Perutz (1951) pointed out that the observation of a relatively strong meridional 1·5 Å reflection in materials such as horse hair and porcupine quill gave strong support to this idea. On the other hand, the projection on the fibre axis of the electron density of the α-helix shows no periodicity corresponding to the helix repeat distance, and so the strong meridional arc at 5·18 Å, characteristic of the α-keratin pattern, cannot be explained by the simple model of α-helices in parallel array. The way out of this difficulty was shown in principle by Crick (1952) and Pauling & Corey (1953), who suggested that the α-helix axis was inclined to the fibre axis and itself followed a larger helix. It is easily seen that the projection on to the fibre axis of such a coiled-coil structure possesses a periodicity corresponding roughly to the α-helix repeat, and hence will give some approach to the observed meridional diffraction pattern. The apparently complex calculation of the diffraction pattern of a structure containing coiled-coils can be much simplified by regarding the structure as a grating composed of a repetition of single turns of the minor helix (i.e. the α-helix) with a superimposed modulation in scattering amplitude and phase, the modulation wavelength being the major helix axial-repeat distance. On this basis the writer has derived a simple approximate theory for the rapid calculation of the meridional and near-meridional diffraction pattern of coiled-coils assembled in multi-strand cables. An exact theory for the calculation of the whole diffraction pattern of coiled coils has been developed independently by Crick (1953*a*).

The present paper describes a general diffraction theory applicable to fibres consisting of atomic chains folded in arbitrarily complex fashion. This reduces to Crick's formula as a special case. An account is then given of the approximate theory. It is compared with the exact theory, and applied to calculate the diffrac-

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tion pattern given by a three-strand cable of α-helices in the region of the 5·18 Å meridional arc.

General diffraction theory for convoluted chains

In this discussion a chain structure will be defined as a periodic distribution of electron density along an infinite line. Thus, if a parameter t is taken as proportional to the distance along the line, the variation of scattering power along the line, measured in appropriate units, may be represented by the Fourier series

$$A_0 = \sum_{p=-\infty}^{\infty} \varrho_p \exp(-2\pi i p t/t_m),$$

where t_m is the value of t after which the distribution repeats. In the convoluted chain structure the infinite line is subjected to a three-dimensional coiling and folding of any complexity provided that after t increases by a finite amount t_0 the configuration repeats. Take any point on one such convoluted line as origin, and let the direction joining this point with another on the line differing from it by t_0 in t value define the z axis of a rectangular coordinate system. Usually the direction of the z axis so chosen will be coincident with the fibre axis. In the possible case of a fibre composed of a web of several differently convoluted chains, the structure may be reduced to one form of chain by combining segments of chains of different forms so that the whole configuration is made to repeat in the direction of the fibre axis.

For the line passing through the origin let t have there the value $t = 0$, and let $z = z_c$ at $t = t_0$. Then the constant $\varepsilon \equiv z_c/t_0$ measures the average rate of progression of z with t. The periodic variation of the x, y and z coordinates due to the convolutions can always be represented by Fourier series, most conveniently in the form of sine and cosine series. Thus,

$$\left.\begin{aligned} x &= \sum_{u=0}^{\infty} (a_u \cos 2\pi u t/t_0 + b_u \sin 2\pi u t/t_0), \\ y &= \sum_{u=0}^{\infty} (c_u \cos 2\pi u t/t_0 + d_u \sin 2\pi u t/t_0), \\ z &= \varepsilon t + \sum_{u=0}^{\infty} (e_u \cos 2\pi u t/t_0 + f_u \sin 2\pi u t/t_0). \end{aligned}\right\} \quad (1)$$

It should be remembered that these series are not independent, since at every point on the line we have $\lambda dt^2 = dx^2+dy^2+dz^2$, λ being a constant.

The transform of the convoluted chain at the point (ξ, η, ζ) in reciprocal space is

$$T(\xi, \eta, \zeta) = \int_{-\infty}^{\infty} A_0 \exp 2\pi i[x\xi + y\eta + z\zeta]\, dt.$$

Putting $\xi^2+\eta^2 = R^2$, $\tan\psi = \eta/\xi$, $\omega = 2\pi u t/t_0$, and substituting for x, y and z from equations (1), this becomes

$$\begin{aligned} T(R, \psi, \zeta) = \int_{-\infty}^{+\infty} A_0 \exp\Big[2\pi i R\Big\{\sum_{u=1}^{\infty} (a_u \cos\omega\cos\psi \\ + b_u \sin\omega\cos\psi + c_u \cos\omega\sin\psi + d_u \sin\omega\sin\psi)\Big\}\Big] \\ \times \exp\Big[2\pi i\zeta\Big\{\sum_{u=1}^{\infty}(e_u\cos\omega + f_u\sin\omega)\Big\}\Big].\exp(2\pi i\varepsilon t\zeta) \\ \times \exp[2\pi i(Ra_0\cos\psi + Rc_0\sin\psi + \zeta e_0)]\, dt. \end{aligned}$$

This may be written for short

$$T(R, \psi, \zeta) = \int_{-\infty}^{+\infty} A_0 . A_R . A_\zeta . \exp(i\delta) \exp(2\pi i\varepsilon t\zeta)\, dt,$$

where $\delta = 2\pi(Ra_0\cos\psi + Rc_0\sin\psi + \zeta e_0)$ and A_R and A_ζ are the other terms involving R and ζ, respectively. A_R and A_ζ may be separated into factors, giving

$$\begin{aligned} A_R &= \exp\Big[2\pi i R \sum_{u=1}^{\infty} \tfrac{1}{2}(a_u+d_u)\cos(\omega-\psi)\Big] \\ &\quad \times \exp\Big[2\pi i R \sum_{u=1} \tfrac{1}{2}(a_u-d_u).\cos(\omega+\psi)\Big] \\ &\quad \times \exp\Big[2\pi i R \sum_{u=1}^{\infty} \tfrac{1}{2}(b_u+c_u)\sin(\omega+\psi)\Big] \\ &\quad \times \exp\Big[2\pi i R \sum_{u=1}^{\infty} \tfrac{1}{2}(b_u-c_u)\sin(\omega-\psi)\Big] \\ &= A_1 . A_2 . A_3 . A_4, \end{aligned}$$

and

$$\begin{aligned} A_\zeta &= \exp\Big[2\pi i\zeta \sum_{u=1}^{\infty} e_u \cos\omega\Big] \\ &\quad \times \exp\Big[2\pi i\zeta \sum_{u=1}^{\infty} f_u \sin\omega\Big] = A_5 . A_6. \end{aligned}$$

Each factor $A_i (i = 1, 2, \ldots, 6)$ is expressible as the limit of an infinite product of infinite summations with the aid of the relations

$$\exp(iv\cos\theta) = \sum_{m=-\infty}^{\infty} J_m(v) \exp mi(\theta + \tfrac{1}{2}\pi)$$

and

$$\exp(iv\sin\theta) = \sum_{m=-\infty}^{\infty} J_m(v) \exp mi\,\theta.$$

Thus the expressions for A_i become

$$\begin{aligned} A_1 &= \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m\{\pi i R(a_u+d_u)\} \\ &\qquad \times \exp\{im(2\pi u t/t_0 - \psi + \tfrac{1}{2}\pi)\}], \\ A_2 &= \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m\{\pi i R(a_u-d_u)\} \\ &\qquad \times \exp\{im(2\pi u t/t_0 + \psi + \tfrac{1}{2}\pi)\}], \\ A_3 &= \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m\{\pi i R(b_u+c_u)\} \\ &\qquad \times \exp\{im(2\pi u t/t_0 + \psi)\}], \\ A_4 &= \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m\{\pi i R(b_u-c_u)\} \\ &\qquad \times \exp\{im(2\pi u t/t_0 - \psi)\}], \end{aligned}$$

$$A_5 = \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m(2\pi i\zeta e_u) \exp\{im(2\pi ut/t_0+\tfrac{1}{2}\pi)\}] ,$$

and

$$A_6 = \prod_{u=1}^{\infty} \sum_{m=-\infty}^{\infty} [J_m(2\pi i\zeta f_u) \exp\{im(2\pi ut/t_0)\}] .$$

The transform of each A_i is the convolution of the transforms of the m-summations computed for every value of u; and the required transform of the product of all the factors A_i ($i = 0, 1, \ldots, 6$) is the convolution of the transform of each A_i. Evaluation is simple because every term is either constant, or periodic with repeat t_0 or t_m, and so its transform reduces to a set of Fourier coefficients. Consider A_1, for example: the integral giving the transform of one term of the summation for a particular value of u is

$$T_1(u, m) = \int_{-\infty}^{\infty} J_m\{\pi iR(a_u+d_u)\} \times \exp\{im(2\pi ut/t_0-\psi+\tfrac{1}{2}\pi)\} \exp(2\pi i\varepsilon t\zeta)\,dt$$

and is non-zero only when $\zeta+um/\varepsilon t_0 = 0$; at each such value of ζ it becomes the Fourier coefficient $F_1(u, m) = J_m\{\pi iR(a_u+d_u)\} \exp\{im(\tfrac{1}{2}\pi-\psi)\}$. Likewise, $T_0 = \int_{-\infty}^{+\infty} A_0 \exp(2\pi i\varepsilon t\zeta)\,dt$ is non-zero only when $\zeta+p/\varepsilon t_m = 0$, at which values of ζ it reduces to the Fourier coefficients $F_0 = \varrho_p$. Provided that t_0 and t_m are not incommensurable the whole structure repeats after a length $t_l = Mt_m = Nt_0$, M and N being integers having no common factor. The z-axis repeat distance is given by $c = \varepsilon t_l$, hence $um/\varepsilon t_0 = Num/c$ and $p/\varepsilon t_m = Mp/c$. The transform $T(R, \psi, \zeta)$ is then non-zero only when $\zeta = l/c$, l being an integer or zero. The structure amplitude for the layer of index l is thus given by the products of coefficients

$$F(R, \psi, l/c) = \varrho_p \prod_{i=1}^{6} \prod_{u(i)=1}^{\infty} \sum_{m(i,u)=-\infty}^{\infty} F_i(u(i), m(i, u)) \exp(i\delta) , \quad (2)$$

subject to the conditions

$$l+Mp+N\sum_{i=1}^{6} \sum_{u(i)=1}^{\infty} u(i)m(i, u) = 0 . \quad (3)$$

The coefficients are

$$\left.\begin{aligned}
F_1(u(1), m(1, u)) &= J_{m(1,u)}\{\pi iR(a_{u(1)}+d_{u(1)})\} \times \exp\{im(1, u)(\tfrac{1}{2}\pi-\psi)\} ,\\
F_2(u(2), m(2, u)) &= J_{m(2,u)}\{\pi iR(a_{u(2)}-d_{u(2)})\} \times \exp\{im(2, u)(\tfrac{1}{2}\pi+\psi)\} ,\\
F_3(u(3), m(3, u)) &= J_{m(3,u)}\{\pi iR(b_{u(3)}+c_{u(3)})\} \times \exp(im(3, u)\psi) ,\\
F_4(u(4), m(4, u)) &= J_{m(4,u)}\{\pi iR(b_{u(4)}-c_{u(4)})\} \times \exp(-im(4, u)\psi) ,\\
F_5(u(5), m(5, u)) &= J_{m(5,u)}(2\pi i(l/c)e_{u(5)}) \times \exp(im(5, u)\tfrac{1}{2}\pi) ,\\
F_6(u(6), m(6, u)) &= J_{m(6,u)}(2\pi i(l/c)f_{u(6)}) .
\end{aligned}\right\} \quad (4)$$

Each order m and harmonic u has been tagged, as shown in equations (2), (3) and (4), in order that the terms contributing to a given layer may be identified. The coefficients ϱ_p will in general be complex. Two special cases of interest are (i), electron density constant along the wire, in which case all ϱ_p are zero except ϱ_0, and equation (3) reduces to

$$l+\sum_{i=1}^{6} \sum_{u(i)=1}^{\infty} u(i)m(i, u) = 0;$$

and (ii), electron density concentrated in points spaced t_m apart, one such point being at $t = t_1$, in which case $\varrho_p = C \exp(-2\pi ipt_1/t_m)$, where C is a constant.

Expression (2) gives the structure amplitude for one convoluted chain. If the structure contains different types of convoluted chains their scattering amplitudes must be calculated separately. A simpler procedure may be employed when all the chains are similar; in this case a common parameter t may be used for all chains and the Fourier coefficients a, b, etc. will remain unchanged if the periodic variations of the x, y and z coordinates of the jth chain are expressed as Fourier series in $t-t_j$. Additional generality and convenience are obtained if the equations (1) are put in the form

$$\left.\begin{aligned}
x &= x_j+\sum_{u=1}^{\infty}[a_u \cos(2\pi ut/t_0-\varphi_{uj}) + b_u \sin(2\pi ut/t_0-\varphi_{uj})] ,\\
y &= y_j+\sum_{u=1}^{\infty}[c_u \cos(2\pi ut/t_0-\varphi_{uj}) + d_u \sin(2\pi ut/t_0-\varphi_{uj})] ,\\
z &= \varepsilon t+z_j+\sum_{u=1}^{\infty}[e_u \cos(2\pi ut/t_0-\varphi_{uj}) + f_u \sin(2\pi ut/t_0-\varphi_{uj})] .
\end{aligned}\right\} \quad (5)$$

The coefficients $F_1, \ldots, F_6$ given by equations (4) must now be multiplied by $\exp(-im\varphi_{uj})$, and the phase factor in equation (2) becomes $\exp(i\delta_j)$ with $\delta_j = 2\pi(Rx_j \cos\psi+Ry_j \sin\psi+(l/c)z_j)$.

As an example of application of the foregoing theory, the structure amplitudes for a discontinuous coiled coil may be calculated, using Crick's (1953*a*) model. The coordinates of the major helix are

$$\left.\begin{aligned}
x &= r_0 \cos(\omega_0 t+\varphi_0) ,\\
y &= r_0 \sin(\omega_0 t+\varphi_0) ,\\
z &= P(\omega_0 t/2\pi)+z_0 ;
\end{aligned}\right\} \quad (6)$$

and those of the minor helix in its own rotating frame of reference are

$$\left.\begin{aligned}
x' &= r_1 \cos(\omega_1 t+\varphi_1) ,\\
y' &= r_1 \sin(\omega_1 t+\varphi_1) ,\\
z' &= 0 .
\end{aligned}\right\} \quad (7)$$

The major helix, which is right-handed, makes N_0 turns while the minor helix (left-handed) makes N_1 turns in its own frame of reference, in the same z-distance c. This condition makes $-\omega_1/\omega_0 = N_1/N_0$.

There are M point atoms in the repeat c, thus $t_t = t_0 = Mt_m$. One atom is at $t=t_1$, so $\varrho_p = C\exp(-ip\varphi_M)$ where $\varphi_M = 2\pi Mt_1/t_0$. The coiled-coil coordinates are

$$\begin{aligned} x &= r_0\cos(\omega_0 t+\varphi_0) \\ &\quad +\bar{r}_1\cos[\omega_0 t(N_1/N_0-1)t-\varphi_0-\varphi_1] \\ &\quad +\Delta\cos[\omega_0 t(N_1/N_0+1)+\varphi_0-\varphi_1], \\ y &= r_0\sin(\omega_0 t+\varphi_0) \\ &\quad -\bar{r}_1\sin[\omega_0 t(N_1/N_0-1)t-\varphi_0-\varphi_1] \\ &\quad +\Delta\sin[\omega_0 t(N_1/N_0+1)+\varphi_0-\varphi_1], \\ z &= P(\omega_0 t/2\pi)+z_0+r_1\sin\alpha\sin[\omega_0 t(N_1/N_0)-\varphi_1], \end{aligned}$$

in which $\tan\alpha = 2\pi r_0/P$, $\bar{r}_1 = \frac{1}{2}r_1(1+\cos\alpha)$, and $\Delta = \frac{1}{2}r_1(1-\cos\alpha)$. Identifying the above coordinates with the general coordinates of equations (5) enables the Fourier coefficients a_u, b_u, c_u, etc. to be written down by inspection. It is seen first that $\varepsilon \equiv \omega_0 P/2\pi$, $c \equiv N_0 P$ and $t_0 \equiv 2\pi N_0/\omega_0$, so that $2\pi ut/t_0$ becomes $\omega_0 ut/N_0$. Only four harmonics are active: these are $u = N_0$, N_1-N_0, N_1, and N_1+N_0. It is convenient to tabulate the coefficients as shown (Table 1).

Table 1. *Fourier coefficients of coiled coil.*

	$u =$	N_0	N_1-N_0	N_1	N_1+N_0
Coefficient F_1:	a_u+d_u	$2r_0$	—	—	2Δ
Coefficient F_2:	a_u-d_u	—	$2\bar{r}_1$	—	—
Coefficient F_3:	b_u+c_u	—	—	—	—
Coefficient F_4:	b_u-c_u	—	—	—	—
Coefficient F_5:	e_u	—	—	—	—
Coefficient F_6:	f_u	—	—	$r_1\sin\alpha$	—
Phase:	φ_u	$-\varphi_0$	$(\varphi_1+\varphi_0)$	φ_1	$(\varphi_1-\varphi_0)$

Substituting the coefficients from Table 1 in equations (4) the series become,*

$$\Sigma F_1 = \sum_{m(N_0)=-\infty}^{\infty} J_{m(N_0)}(2\pi Rr_0)\exp[im(N_0)(\tfrac{1}{2}\pi-\psi+\varphi_0)] \times \sum_{m(N_1+N_0)=-\infty}^{\infty} J_{m(N_1+N_0)}(2\pi R\Delta) \times\exp[im(N_1+N_0)(\tfrac{1}{2}\pi-\psi-\varphi_1+\varphi_0)],$$

$$\Sigma F_2 = \sum_{m(N_1-N_0)=-\infty}^{\infty} J_{m(N_1-N_0)}(2\pi R\bar{r}_1) \times\exp[im(N_1-N_0)(\tfrac{1}{2}\pi+\psi-\varphi_1-\varphi_0)],$$

and

$$\Sigma F_6 = \sum_{m(N_1)=-\infty}^{\infty} J_{m(N_1)}(2\pi(l/c)r_1\sin\alpha)\exp[-im(N_1)\varphi_1].$$

The phase factor $\exp(i\delta)$ is $\exp(2\pi ilz_0/c)$. In order to bring the notation into line with Crick's put $p = m'$, $m(N_0) = -p$, $m(N_1-N_0) = -q$, $m(N_1) = -s$, and $m(N_1+N_0) = -d$. The expression for the structure amplitude then becomes

$$\begin{aligned} F(R,\psi,l/c) = C \sum_{p=-\infty}^{\infty}\sum_{q=-\infty}^{\infty}\sum_{s=-\infty}^{\infty}\sum_{d=-\infty}^{\infty} & J_p(2\pi Rr_0) \\ \times J_q(2\pi R\bar{r}_1)J_s(2\pi(l/c)r_1\sin\alpha)J_d(2\pi R\Delta) & \\ \times\exp[ip(\psi-\varphi_0+\tfrac{1}{2}\pi)+iq(-\psi+\varphi_0+\varphi_1+\tfrac{1}{2}\pi) & \\ +is(\pi+\varphi_1)+id(\psi+\varphi_1-\varphi_0+\tfrac{1}{2}\pi)-im'\varphi_M+2\pi ilz_0/c], & \end{aligned} \tag{8}$$

subject to the conditions

$$N_0p+(N_1-N_0)q+N_1s+(N_1+N_0)s = l+Mm'. \tag{9}$$

These equations are identical with Crick's equations (13) and (14) if the constant C is put equal to unity, except for the phase angles multiplied by q, s and d. The discrepancy in the latter has been traced to an error in Crick's derivation of his coiled-coil coordinates from the major and minor helix coordinates (6) and (7).*

It is thus seen that if the x, y and r coordinates of the convoluted structure can be expressed in such a way that the various multiples of the fundamental periodicity can be readily picked out, the expression for the structure amplitudes on any layer can be written down without further calculation.

Approximate theory for coiled coils

If the α-helices in α-keratin are coiled into super-helices it is unlikely that the angle between the α-helix axis and the super-helix axis (i.e. the fibre axis) is large: the diffraction evidence suggests that it is about 10°. This angle, denoted by α, has been termed by Crick the 'pitch angle'. However, in the conventional description of helices, such as screw-threads, the term 'pitch angle' is used for the angle made by a tangent to the helix with the plane normal to the helix axis, and is thus the complement of α. With α-keratin, where α is small, no confusion is likely to arise, but this is not the case with structures in which the α-helices are coiled into relatively flat super-helices. It is therefore here proposed that the angle α, which measures the instantaneous angle of tilt of the minor helix axis away from the major helix axis, be called the 'tilt-angle'.

The most detailed diffraction patterns of α-keratin available show discrete reflexions only on the equator and in the meridional and near-meridional region. On the equator itself (but not in the near-equatorial region) an adequate calculation of the diffraction pattern of coiled coils may be made with the assumption of cylindrical symmetry. The restriction of the remainder of the diffraction pattern of interest to the near-meridional region, together with the basic notion that the α-helix is but little distorted when it is deformed into a coiled coil, provide the physical justification of the approximate diffraction theory described below.

* Note that according to the notation adopted above in equations (2), (3), (4), $m(N_1-N_0)$, say, does not signify $m\times(N_1-N_0)$, but that the m belongs to the series whose harmonic u is N_1-N_0.

* The writer wishes to thank Dr Crick for the loan of his original calculations.

It will be assumed that all the α-helices are of the same sense and that they try to pack together so that side-chains of one helix fit into spaces between side-chains of another helix. This is the concept of 'knobs' fitting into 'holes' as proposed by Crick (1952, 1953*b*). In the general case, if the number of residues per turn of the α-helix is not exactly $\frac{1}{2}n$, where n is an integer, the α-helices will have to deform themselves into coiled coils in order for fitting to occur. It is to be expected that several coiled-coils will combine to form a multi-strand cable. How is this deformation best described geometrically? Consider the simple case of a pair of α-helices of the same sense (left-handed) and having 3·6 residues per turn. Part of one turn of each α-helix is represented schematically in Fig. 1(*a*), (*b*),

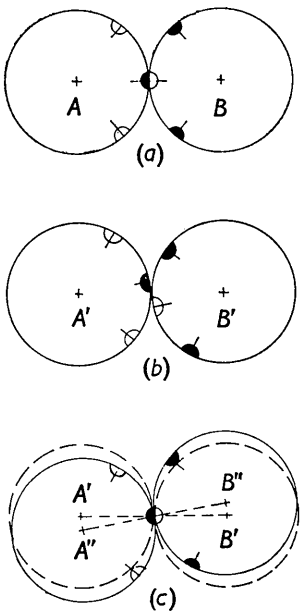

Fig. 1. The deformation of α-helices into coiled coils. (*a*) A level with knob–hole fitting; (*b*) one turn higher, no deformation and no fit; (*c*) the same level as (*b*), with the deformation required to give knob–hole fitting.

(*c*). An opaque semi-circle represents a knob, an open semi-circle, a hole. In Fig. 1(*a*), a knob on the helix whose axis is A fits into a hole of the helix whose axis is B. Now consider the fit at one helix-repeat higher. As shown in Fig. 1(*b*), a knob–hole match no longer occurs. A good fit may be restored by giving each turn of each helix a small *translation without rotation*. A' is translated to A'', and B' to B'', the angle between $A'B'$ and $A''B''$ being approximately 10°. The deformation given to each turn may be considered either as a small shear on horizontal planes, in a direction normal to the line joining the minor to the major helix axis (which in this case is the mid-point of AB), or as a tilt of individual turns so that their axes follow AA'' rather than AA', and BB'' rather than BB', at this particular level. The latter description is more convenient. It implies a discontinuous deformation of the α-helix once per turn; whereas, if the deformation takes place by rotation about the α-carbon-atom bonds, which can be regarded as forming a universal joint connecting the planar residues, it is distributed over 3·6 points per turn of the helix, and thus approaches a continuous deformation. The difference between these two models is not significant since the deformation is small. In the model adopted here, each turn, with its 3·6 residues, retains its physical identity and orientation in space except for the introduction of the small tilt. This model has the advantage over Crick's model involving two coordinate systems in that it permits a smooth passage from an α-helix with straight axis to either a right-handed or left-handed coiled coil, depending upon whether there are more or fewer than 3·5 residues per turn, respectively.

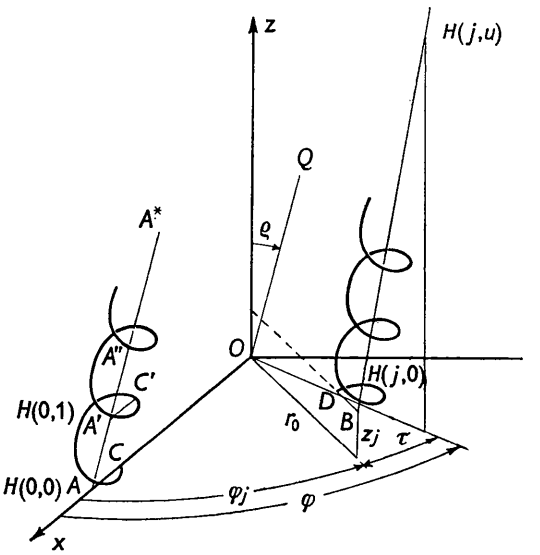

Fig. 2. Cartesian and cylindrical-polar coordinate systems for coiled coils.

In the case considered here of a coiled coil formed of a left-handed minor helix and a right-handed major helix, it can be seen that when the minor helix crosses the line joining the minor helix axis to the major helix axis its slope is at a minimum, and its projection on the major helix axis has maximum density. It is convenient to take the origin of the major helix at one such node. Thus, referring to Fig. 2, if Oz is the axis of the major helix AA^*, the axis Ox is chosen so that A, C and O lie on the same straight line, AC pointing towards O. The turn of the minor helix to which C belongs is designated $H(0, 0)$ and its scattering power considered lumped at its origin A. Similarly the scattering power of the next minor helix above, $H(0, 1)$, is considered concentrated at A'; $AA' = A'A''$, etc. The point C' is one turn of the minor helix up from C, and $A'C'$ lies in a vertical plane parallel to AC. The radius of the major helix is $AO = r_0$. Consider, next, another coiled coil. Assume that this has the same axis

Oz, radius r_0 and tilt-angle α. It is desirable to choose its origin at a recognizable physical feature of one turn of its minor helix, i.e. a node. Let this origin be at the point B, where BD lies on the perpendicular from Oz. If this is the jth coiled coil with Oz as axis the minor helix whose scattering is considered concentrated at B may be designated $H(j, 0)$. The coordinates of $H(j, 0)$ are (r_0, φ_j, z_j). Let the assemblage of coiled-coils have a z-axis repeat distance c. If P is the vertical repeat of a major helix and p that of a minor helix (i.e. AA' projected on Oz), then $c = np = NP$, where n and N are integers with no common factor. The scattering power of the uth minor helix of the jth major helix, concentrated at the point $H(j, u)$, may be denoted by $A(j, u)$. The coordinates of $H(j, u)$ are

$$x_u = r_0 \cos \varphi = r_0 \cos (\tau+\varphi_j) ,$$
$$y_u = r_0 \sin \varphi = r_0 \sin (\tau+\varphi_j) ,$$
$$z_u = z_j+up, \quad \text{where} \quad \tau = 2\pi upN/c .$$

The structure amplitude at the reciprocal-lattice point (ξ, η, ζ) due to the n minor helices of the jth major helix contained in the z-axis repeating unit is

$$F(j) = \sum_{u=0}^{u=n-1} A(j, u) \exp [2\pi i(x_u\xi+y_u\eta+z_u\zeta)] .$$

In this expression one may put $\zeta = l/c$, l being zero or an integer, since spectra occur only at these values of ζ. It is convenient to introduce the reciprocal-lattice polar angle ϱ, where $\zeta \tan \varrho = (\xi^2+\eta^2)^{\frac{1}{2}}$, and azimuthal angle ψ, where $\tan \psi = \eta/\xi$. Then the expression for the structure amplitude on layer l becomes, on substituting for x_u, y_u and z_u,

$$F(j, l) = \sum_u A(j, u) \exp [2\pi i (l/c) (r_0 \tan \varrho \cos (\psi-\varphi)+z_j+up)] .$$

Since $\tan \alpha = 2\pi r_0 N/c$, the above expression may be written

$$F(j, l) = \sum_u A(j, u) \exp (2\pi i l z_j/c) \exp (2\pi i l u p/c) \exp (i(l/N) \tan \alpha \tan \varrho \cos (\psi-\varphi)) .$$

Putting $B = (1/N) \tan \alpha \tan \varrho$, and making use of the expansion

$$\exp (ilB \cos (\psi-\varphi)) = \sum_{\nu=-\infty}^{\infty} J_\nu(lB) \exp [i\nu(\psi-\varphi+\tfrac{1}{2}\pi)] ,$$

there is obtained

$$F(j, l) = \sum_{u=0}^{n-1} \sum_{\nu=-\infty}^{\infty} A(j, u) \exp (2\pi i l z_j/c) \times \exp (2\pi i l u p/c) J_\nu(lB) \exp [i\nu(\psi-\varphi+\tfrac{1}{2}\pi)] .$$

Since $\varphi = 2\pi upN/c+\varphi_j$, this may be written

$$F(j, l) = \sum_u \sum_\nu A(j, u) \exp (2\pi i l z_j/c) J_\nu(lB) \times \exp [2\pi i (up/c)(l-\nu N)] \exp [i\nu(\psi-\varphi_j+\tfrac{1}{2}\pi)] .$$

The quantity $A(j, u)$ is evaluated in the following way. Consider reflection by a plane whose normal is OQ (Fig. 2). In space reciprocal to one turn of the minor helix (reciprocal coordinate axes $O\xi'$, $O\eta'$, $O\zeta'$) the plane normal OQ makes not the polar angle ϱ, but an angle greater or less than this depending upon the orientation of the minor helix axis with respect to OQ (Fig. 3). As one turn of the major helix is

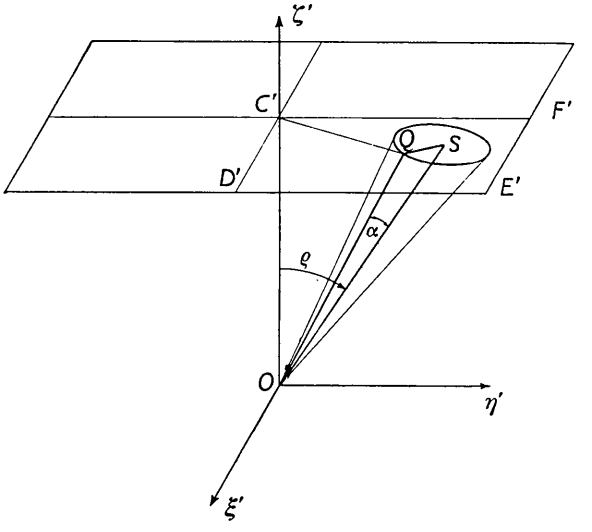

Fig. 3. The reciprocal-lattice construction in α-helix reciprocal space.

described, OQ will precess about the direction OS, where OS has polar angle ϱ and the angle between OS and OQ is α. The expression for the form factor at reciprocal-lattice layer heights corresponding to the minor helix repeat-spacing and submultiples thereof is given by the simple formula of Cochran, Crick & Vand (1952). The effect of the major helix modulation is to split each layer into bands of closely spaced layers. In practice only the first band is of importance in the α-keratin pattern, i.e. that centred at $\zeta = n/c$. Since the minor helix transform varies slowly and smoothly with ζ in this region, the convenient approximation is employed of using the form factor of the minor helix first level to calculate the amplitudes of all components of the band. The form-factor values used are those lying round the curve traced out by Q as it precesses about OS on the first level $C'D'E'F'$ of the minor helix transform. Since the variation of the form factor is cyclic, with a fundamental period corresponding to one turn of the major helix, it can be represented by a Fourier series periodic in τ. The point Q describes an ellipse on $C'D'E'F'$ but at small values of ϱ it may be regarded simply as a circle centred at S. This circle will be referred to as the precession circle. Its radius for the case of $\varrho = 0$ is $(n/c) \sin \alpha$. The above construction is equivalent to considering the axis $O\zeta'$ as fixed, parallel to $O\zeta$, and

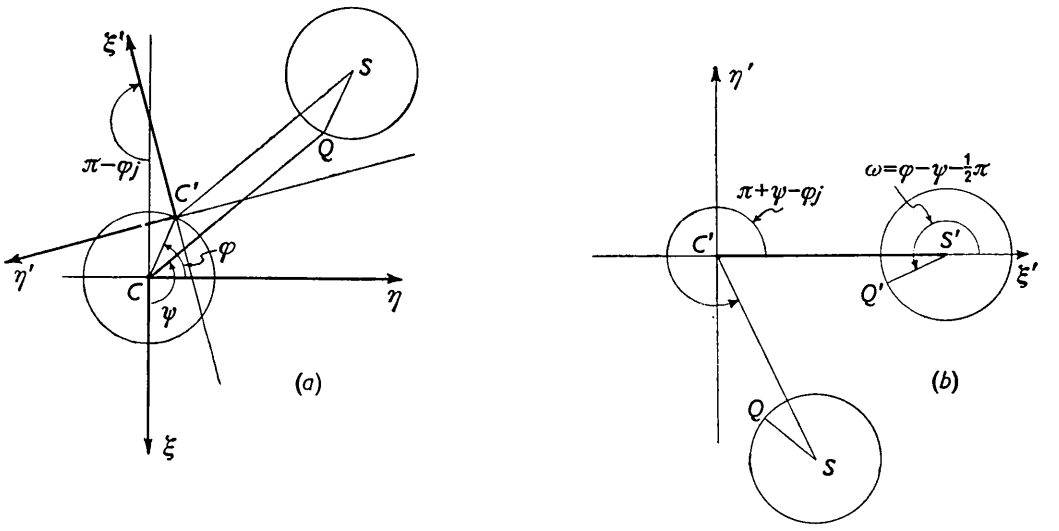

Fig. 4. (*a*) The relative orientation of reciprocal-lattice layers of the coiled coil (0), and of one turn $H(j, u)$ of the minor helix of the coiled coil (j). (*b*) The rotation of S into S'.

the plane normal OQ as varying in polar angle and azimuth.

Thus, substituting for $A(j, u)$ the series

$$\sum_{k=-\infty}^{\infty} a(j, k) \exp(-ik\tau),$$

the expression for the structure amplitude becomes

$$F(j, l) = \exp(2\pi i z_j(l/c)) \sum_u \sum_v \sum_k a(j, k) J_v(lB) \times \exp[2\pi i u(p/c)(l-Nv-Nk)] \exp[iv(\psi-\varphi_j+\tfrac{1}{2}\pi)].$$

This summation is non-zero only when

$$(l-Nv-Nk)(p/c) = m,$$

where m is an integer or zero, i.e. $l = mn+Nv+Nk$. Introducing the integer μ defined by $\mu = v+k$, the structure amplitude contributed by the jth compound helix to the layer $l = mn+N\mu$ is given by the expression

$$F(j, mn+N\mu) = n \exp[2\pi i(mn+N\mu)z_j/c] \sum_{v=-\infty}^{\infty} \{a(j, \mu-v) \times J_v[(mn+N\mu)B] \exp[iv(\psi-\varphi_j+\tfrac{1}{2}\pi)]\}. \quad (10)$$

Hence, if the Fourier coefficients applicable to the jth compound helix have been found, the value of F is readily calculated by summing appropriate products of these with Bessel coefficients. In the region of the 5·18 Å meridional arc, $m = 1$. The argument of the Bessel coefficient may be alternatively expressed. Since $\tan\alpha = 2\pi r_0 N/c$ and $\tan\varrho = Rc/(mn+N\mu)$, we have $(mn+N\mu)B = 2\pi r_0 R$; and so computation is simplified if F is calculated along lines of constant R rather than constant ϱ. It remains to show how the coefficients $a(j, \mu-v)$ are derived from a Fourier series independent of j.

Fig. 4(*a*) represents a plan of a layer, axes $C\xi$ and $C\eta$, of the compound-helix reciprocal lattice, together with the corresponding layer of the transform of the minor helix $H(j, u)$ in the correct relative orientation. From the definition of the origin of the jth compound helix it follows that $C'\xi'$ is directed along BD (Fig. 2) and so makes an angle $\pi-\varphi_j$ with $C\xi$. According to the construction shown in Fig. 3, when $C'\xi'$ and $C'\eta'$ are regarded as fixed in space, the point Q moves round the precession circle centre S. Alternatively, when $C\xi$ and $C\eta$ are considered fixed, C' moves round the precession circle having its centre at C, SQ and $C'C$ being equal and parallel. Fig. 4(*b*) shows $C'S$ rotated backwards about C' so that it comes into the position $C'S'$, lying along $C'\xi'$, i.e. $C'S$ rotated through the angle $-(\pi+\psi-\varphi_j)$. Suppose $T(Q')$ is the value of the form factor of the minor helix at Q' and suppose that this has been expressed as a Fourier series periodic in ω,

$$T(Q') = \sum_{k=-\infty}^{\infty} b_k \exp(-ik\omega).$$

The form factor at Q, $T(Q)$, (which is in fact $A(j, u)$) is required in terms of a Fourier series periodic in τ. Now let $\mathscr{R}(\pi+\psi-\varphi_i)$ be the factor by which $T(Q')$ has to multiplied in order to obtain $T(Q)$. In the case of the first-order helix-repeat layer of a *left-handed* helix of radius r, $T(R', \psi') = J_1(2\pi R'r) \exp i(\frac{1}{2}\pi-\psi')$, by Cochran *et al.* (1952), and so $\mathscr{R}(\pi+\psi-\varphi_j)$ is $\exp[-i(\pi+\psi-\varphi_j)]$. From Fig. 4(*a*) and (*b*) it is seen that $\omega = \varphi-\psi-\frac{1}{2}\pi = \tau+\varphi_j-\frac{1}{2}\pi-\psi$. The two Fourier series are thus related by the identity

$$\sum_k a(j, k) \exp(-ik\tau) \equiv \mathscr{R}(\pi+\psi-\varphi_j) \sum_k b_k \exp(-ik\omega);$$

hence $a(j, k) = b_k \exp[i(k-1)(\psi-\varphi_j+\frac{1}{2}\pi)] \exp(-\frac{1}{2}\pi)$.

This value of $a(j, k)$ may now be substituted in

equation (10) to find the structure amplitude in the band $m = 1$ due to j compound helices in which the minor helixes are left-handed: there is obtained

$$F(n+N\mu) = \sum_j \sum_\nu n \exp[2\pi i(n+N\mu)z_j/c] b_{\mu-\nu} \times J_\nu[(n+N\mu)B] \exp[i(\mu-1)(\psi-\varphi_j+\tfrac{1}{2}\pi)] \exp(-\tfrac{1}{2}\pi). \quad (11)$$

As a simple illustration of the above formula one may calculate the intensity on the meridian at 5·18 Å. All J_ν are zero except $J_0(nB)$, which is equal to unity. The point S' is coincident with C', $\psi' = \omega$, $Q'S' = (n/c)\sin\alpha$, and so $T(Q') = J_1(2\pi r(n/c)\sin\alpha)\exp[i(\tfrac{1}{2}\pi-\omega)]$. Thus the only coefficient b_k active is $b_1 = J_1(2\pi r(n/c)\sin\alpha) \times \exp(i\tfrac{1}{2}\pi)$. Hence $\mu = 1$ only, and diffracted intensity is observed on the single layer $n+N$, the structure amplitude being

$$F(n+N) = \sum_j n J_1(2\pi r(n/c)\sin\alpha) \times \exp[2\pi i(n+N)z_j/c]. \quad (12)$$

This equation contains, as to be expected, no phase factor involving ψ or φ_j. Since $(n+N)/c$ may be written $(1/p+1/P)$ the factor containing z_j just expresses the manner in which the degree of reinforcement of the component compound helices depends upon how their origin nodes are distributed over a vertical distance which is the z-axis repeat between nodes of any one compound helix. As pointed out above, the node is a definite physical feature and so the z_j coordinates of any model are easily found.

Method of computation

Formula (11) enables the diffraction pattern to be calculated in a number of steps which are independent both from the physical and computational point of view. The form factor of the α-helix (with or without side chains) is calculated once and for all and plotted graphically. When the value of α has been decided upon, a number of precession circles are drawn at various values of R, and harmonic analysis of the variation of $T(Q')$ round the circles is made by a method such as that described below. Bessel coefficients and Fourier coefficients are conveniently inserted in spaces in a table of the form indicated (Table 2); this makes clear which products contribute to a given layer line. For example, the sole product

Table 2. *Values of* $\mu-\nu$

Layer \ ν	−4	−3	−2	−1	0	1	2	3	4
$mN+4$					4	3	2	1	0
$mN+3$				4	3	2	1	0	−1
$mN+2$			4	3	2	1	0	−1	−2
$mN+1$		4	3	2	[1]	0	−1	−2	−3
mN	4	3	2	1	0	−1	−2	−3	−4
$mN-1$	3	2	1	0	−1	−2	−3	−4	
$mN-2$	2	1	0	−1	−2	−3	−4		
$mN-3$	1	0	−1	−2	−3	−4			
$mN-4$	0	−1	−2	−3	−4				

contributing to the 5·18 Å meridional arc is enclosed in a square. The table is drawn for a case when no values of μ or $\mu-\nu$ need be considered outside the range −4 to +4.

The procedure for harmonic analysis used by the writer is illustrated in Fig. 5. The continuous curve

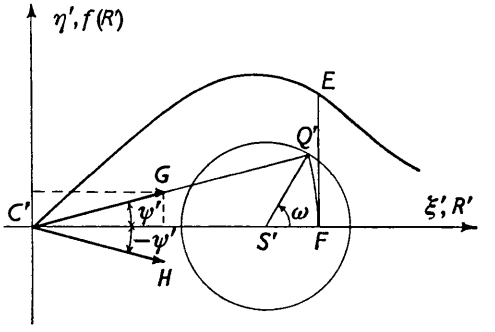

Fig. 5. Graphical method for finding real and imaginary parts of $f(R')$.

gives the calculated numerical value of the α-helix form factor, $f(R')$, plotted against R', (R' and ξ' being on the same scale). The α-helix is thus replaced by a single effective helix whose form factor is

$$T(Q') = T(R', \psi') = f(R') \exp[i(\tfrac{1}{2}\pi-\psi')].$$

The harmonic analysis is most conveniently performed on the quantity $T'(Q') = f(R')\exp(-i\psi')$; hence all the coefficients derived from this must be multiplied by i. The real and imaginary parts of $T'(Q')$ are found by reading from the graph the value of $f(R')$ at $R' = C'F = C'Q'$, marking off $C'G$ along $C'Q'$ equal to $EF = f(R')$ and noting its ξ' and η' components. Actually it is the vector $C'H$ which represents $T'(Q')$, but $C'G$ may be used if the negative of the η' reading is taken. The point Q' is one of a number which regularly divide the upper half of the precession circle. A division into fifteen sections gives ample resolution for the analysis of the slowly changing quantity $T'(Q')$, and has been found convenient to use since the computation has been done with Beevers–Lipson strips according to the method of Stokes (1948). If c' and d' are the cosine and sine coefficients of the real part of $T'(Q')$, and c'' and d'' the cosine and sine coefficients of the imaginary part of $T'(Q')$, then, remembering that $T(Q') = iT'(Q')$, the required coefficients b_k are given by

$$b_k = -\tfrac{1}{2}(c_k''+d_k') + \tfrac{1}{2}i(c_k'-d_k'')$$

and

$$b_{-k} = \tfrac{1}{2}(d_k'-c_k'') + \tfrac{1}{2}i(c_k'+d_k''),$$

k being positive or zero.

In the present case all d' and all c'' are zero so the above reduce to

$$b_k = \tfrac{1}{2}i(c_k'-d_k''), \quad b_{-k} = \tfrac{1}{2}i(c_k'+d_k'').$$

Comparison of approximate and exact theories

It is of interest to see how the value of F derived from the approximate formula (11) differs from that given by the general formula (2). A comparison made when the structure is a simple coiled-coil will clearly be valid for the case of a composite minor helix, such as an α-helix. Using Crick's description of the coiled coil, the general formula takes the form of equations (8) and (9). The Fourier coefficients to be inserted in the approximate formula (11) can in this case be found exactly by integration. For the band $m = 1$, the form factor is given by

$$T(Q') = J_1(2\pi r_1 R') \exp [i(\tfrac{1}{2}\pi - \psi')] ,$$

r_1 being the minor helix radius; and

$$b_k = \frac{1}{2\pi}\int_0^{2\pi} T(Q') \exp (ik\omega) d\omega .$$

It is seen from Fig. 5 that $C'Q' = R'$, $C'S' = R$ and, taking the precession-circle radius as constant, $S'Q' = (n/c) \sin \alpha$, $= a$, say. Substitute $\chi = \pi - \omega$, $z = 2\pi r_1 a$, and $Z = 2\pi r_1 R$; the geometry of triangle $C'Q'S'$ then shows that $2\pi r_1 R' = (Z^2 + z^2 - 2Zz \cos \chi)^{\frac{1}{2}}$. Hence the expression for b_k becomes

$$b_k = \frac{1}{2\pi}\int_0^{2\pi} J_1[(Z^2+z^2-2Zz \cos \chi)^{\frac{1}{2}}] \exp (-i\psi') \times \exp (-ik\chi) \exp (ik\pi) \exp (-\tfrac{1}{2}i\pi) d\chi .$$

By means of Neumann's addition theorem the expansion may be made:

$$\exp (-i\psi') J_1[(Z^2+z^2-2Zz \cos \chi)^{\frac{1}{2}}] = \sum_{m=-\infty}^{\infty} J_{1+m}(Z) J_m(z) \exp [-im\chi] .$$

The integral

$$b_k = \frac{1}{2\pi}\int_0^{2\pi} \sum_m J_{1+m}(Z) J_m(z) \times \exp [-i\chi(k+m)] \exp (ik\pi) \exp (-\tfrac{1}{2}i\pi) d\chi$$

is non-zero only when $m+k = 0$. Thus the Fourier coefficients are given simply by

$$b_k = J_{1-k}(Z) J_k(z) \exp (-\tfrac{1}{2}i\pi) .$$

Inserting these in equation (11) gives

$$F(n+N\mu) = \sum_j \sum_\nu n \exp [2\pi i(n+N\mu) z_j/c] \times J_\nu(2\pi r_0 R) J_{1-\mu+\nu}(2\pi r_1 R) J_{\mu-\nu}(2\pi r_1 (n/c) \sin \alpha) \times \exp [i(\mu-1)(\psi - \varphi_j + \tfrac{1}{2}\pi) + i\pi] .$$

Putting $\nu = p$, $1-\mu+\nu = q$ and $u-\nu = s$, the above may be written

$$F(R, \psi, l/c) = \sum_j \sum_p \sum_q \sum_s n J_p(2\pi r_0 R) J_q(2\pi r_1 R) \times J_s(2\pi (n/c) r_1 \sin \alpha) \exp [ip(\psi - \varphi_j + \tfrac{1}{2}\pi) + iq(\varphi_j - \psi + \tfrac{1}{2}\pi) + is\pi + 2\pi i l z_j/c] , \quad (13)$$

where

$$l = Np + nq + (n+N)s . \quad (14)$$

These equations may now be compared with equations (8) and (9) as applied to continuous coiled coils. The phase factors become identical upon putting $\varphi_0 = \varphi_j$ and $\varphi_1 = 0$. Equation (14) is seen to impose the same restrictions on p, q and s as equation (9), since the relation between the periodicities in Crick's geometrical description of a coiled-coil and that adopted here is $N_0 = N$, and $(N_1 - N_0) = n$. Formula (13) does not differentiate between r_1 and $\bar{r}_1$, and omits the series involving Δ, but these differences are of quite negligible importance. Thus, the only significant difference is the use of n/c rather than l/c in the argument of J_s, and the effect of this vanishes at the centre of the band. The approximate reciprocal-lattice construction for calculating $A(j, u)$, as illustrated in Fig. 3, and used with a constant radius of precession circle, is seen to be justified. It is somewhat surprising that the results of the approximate and exact calculations correspond so closely, and in particular that they do not diverge with increasing R.

An application of the approximate theory

Consider, for example, the three-strand cable, shown schematically in Fig. 6. One turn of each α-helix is

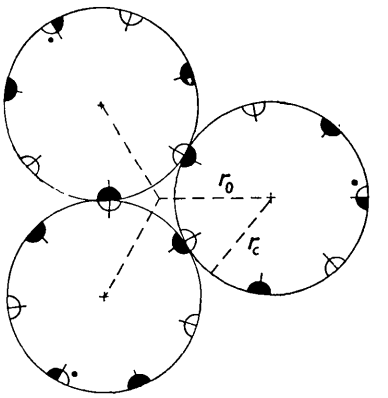

Fig. 6. Schematic representation of the three-strand cable.

shown, projected along its axis. Opaque half circles represent knobs, clear half-circles represent holes. In the divided location the quadrant marked with the dot is one turn higher (i.e. above the plane of the diagram) than that not so marked. For simplicity the number of locations on each circle is made exactly seven in the drawing. For perfect packing of the three α-helices along their lines of contact, knobs and holes opposing each other should be at the same height. This condition is fulfilled and the three knob–hole pairs surrounding the central axis are all at the same height when $\alpha = 10°$ and the contact radius r_c is 4·8 Å. The major helix radius r_0 is then r_c sec 30° and equals approximately 5·5 Å. With these values of r_0 and α

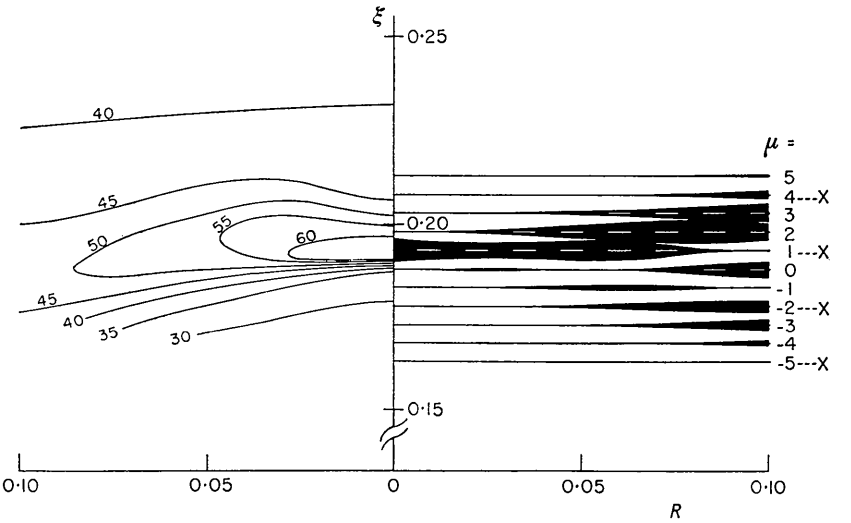

Fig. 7. Calculated and observed intensities near the 5·18 Å meridional arc of the α-keratin diffraction pattern.

the z-axis repeat is 197 Å. This coincides with the value of c which permits all the meridional reflections to be indexed satisfactorily. The 5·18 Å arc is the 38th order of 197 Å, so the value of n is 37.

The coordinates used for the α-helix and βC atoms were those listed by Pauling & Corey (1951*b*) with the βC in position 2. No account was taken of the rest of the side chain. Harmonic analysis of the first-layer form factor was made with Beevers–Lipson strips at $R = 0{\cdot}025$, 0·050, 0·075 and 0·010. It was found that the only Fourier coefficients having appreciable values were b_0, b_1 and b_{-1}, except at $R = 0{\cdot}025$ where b_2 and b_{-2} had to be included. The calculated intensities for the band from $\mu = -5$ to $\mu = +5$ are shown on the right side of Fig. 7, the width of the layer lines being proportional to intensity. On the left are experimentally observed intensity contours taken from diffractometer measurements on Canadian porcupine quill. A single coiled-coil will give the complete band pattern, but if coiled-coils are packed together in a regular way many of the band components will be extinguished. In the case of the three-strand cable, $\varphi_j = 2\pi/3$ and all z_j are zero. Hence the condition $\mu - 1 = 3r$ is imposed, r being an integer or zero. The band components appearing with this restriction are marked by crosses. It is seen that the 5·18 Å meridional reflection is accounted for satisfactorily; the side-chains would be expected to produce some redistribution of intensity on the layer $\mu = 1$ which would increase the intensity at $R = 0$. The restriction on the values of μ required if the structure consisted solely of three-strand cables with perfect knob–hole packing of the three component helices would appear to be rather too stringent. However, the rapid fade-out of the observed pattern away from the meridian makes difficult the comparison with calculated intensities other than in the region near $R = 0$.

The author wishes to thank Dr O. S. Duffendack, Director, Philips Laboratories, for his interest in this work.

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