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The Interpretation of Difference Maps*

By Yuen C. Leung, Richard E. Marsh and Verner Schomaker

Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California, U.S.A.

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A method is described for interpreting three-dimensional difference maps in terms of corrections to the positional and temperature-factor parameters of the input atoms and to the over-all scale parameter. The equations are somewhat more general than those previously developed by Cochran. They are similar to those derived by Cruickshank but, we believe, easier to handle in that the corrections to the temperature-factor parameters are referred to the orthogonal axes of the ellipsoid of thermal motion rather than to the crystallographic axes.

1. Introduction

The detailed interpretation of difference maps as a convenient tool for the refinement of positional and temperature-factor parameters of non-Gaussian atoms was first discussed by Cochran (1951); his derivations were based on the analogy between a difference map and a least-squares calculation in which the individual observational equations are weighted by the factor $(1/f)^2$. More recently, Cruickshank (1956) has discussed in more detail the refinement of individual temperature-factor parameters. We here give a derivation somewhat more straightforward and general than Cochran's and present the results in a form more convenient than Cruickshank's.

2. The refinement of positional parameters

The shifts in positional parameters of a given atom may be obtained from the slopes of the difference map at the assumed position of that atom. Since the measurement is restricted to a small range around the position of the atom, the influence from the neighboring atoms may, in general, be assumed to be negligible; thus, the electron density of each atom may be regarded as the Fourier transform of its atomic form factor, f, multiplied with the temperature factor, T, independently of the presence of other atoms. If the origin (0, 0, 0) is placed at the assumed position of the atom and its real position is at $(\Delta x, \Delta y, \Delta z)$, the observed and calculated electron densities of the atom are respectively

$$\varrho_o(x, y, z) = (1+\Delta K)\sum_h\sum_k\sum_l fT_0 \times \cos 2\pi[h(x-\Delta x)+k(y-\Delta y)+l(z-\Delta z)]\,, \quad (2\cdot1)$$

and

$$\varrho_c(x, y, z) = \sum_h\sum_k\sum_l fT_0 \cos 2\pi(hx+ky+lz)\,. \quad (2\cdot2)$$

The factor $(1+\Delta K)$ is introduced into the expression for ϱ_o to allow for the possibility that the scale factor K may be in error; ΔK would be zero if the observed structure factors were on the correct absolute scale. On a difference map, $D(x, y, z) = \varrho_o-\varrho_c$, the slope parallel to the **a** axis at the assumed position of the atom $(x = y = z = 0)$ is

$$\left.\frac{\delta D}{\delta x}\right)_0 = (1+\Delta K)\sum_h\sum_k\sum_l fT_0\, 2\pi h \times \sin 2\pi(h\Delta x+k\Delta y+l\Delta z)\,. \quad (2\cdot3)$$

Expanding the sine function and including only the linear terms, (2·3) becomes

$$\left.\frac{\delta D}{\delta x}\right)_0 = 4\pi^2(1+\Delta K)\sum_h\sum_k\sum_l fT_0(h^2\Delta x+hk\Delta y+hl\Delta z)\,. \quad (2\cdot4)$$

Similarly the slopes along the **b** and **c** axes may be expressed as

$$\left.\frac{\delta D}{\delta y}\right)_0 = 4\pi^2(1+\Delta K)\sum_h\sum_k\sum_l fT_0(hk\Delta x+k^2\Delta y+kl\Delta z) \quad (2\cdot5)$$

and

$$\left.\frac{\delta D}{\delta z}\right)_0 = 4\pi^2(1+\Delta K)\sum_h\sum_k\sum_l fT_0(hl\Delta x+kl\Delta y+l^2\Delta z)\,. \quad (2\cdot6)$$

However, since at $x = y = z = 0$

$$\varrho''_{xx} = \left.\frac{\delta^2\varrho_o}{\delta x^2}\right)_0 = 4\pi^2(1+\Delta K)\sum_h\sum_k\sum_l fT_0h^2\,, \quad (2\cdot7)$$

$$\varrho''_{xy} = \left.\frac{\delta^2\varrho_o}{\delta x\delta y}\right)_0 = 4\pi^2(1+\Delta K)\sum_h\sum_k\sum_l fT_0hk\,, \text{ etc.,} \quad (2\cdot8)$$

the equations (2·4), (2·5), and (2·6) become

$$\delta D/\delta x)_0 = \varrho''_{xx}\Delta x+\varrho''_{xy}\Delta y+\varrho''_{xz}\Delta z\,, \quad (2\cdot9)$$

$$\delta D/\delta y)_0 = \varrho''_{xy}\Delta x+\varrho''_{yy}\Delta y+\varrho''_{yz}\Delta z\,, \quad (2\cdot10)$$

$$\delta D/\delta z)_0 = \varrho''_{xz}\Delta x+\varrho''_{yz}\Delta y+\varrho''_{zz}\Delta z\,. \quad (2\cdot11)$$

The shifts in positional parameters may be obtained by solving the above set of simultaneous equations,

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substituting, if more convenient, the calculated curvatures $\delta^2\varrho_c/\delta x^2$, etc., for the observed ones. If the problem is referred to the three mutually perpendicular principal axes of the ellipsoidal atom, the cross terms of the second derivatives vanish, and the shifts in atomic coordinates reduce to the expressions derived by Cochran:

$$\Delta x = \frac{\delta D/\delta x)_0}{\varrho''_{xx}}, \quad \Delta y = \frac{\delta D/\delta y)_0}{\varrho''_{yy}}, \quad \Delta z = \frac{\delta D/\delta z)_0}{\varrho''_{zz}}.$$

3. The refinement of scale and temperature factors

In treating anisotropic thermal vibrations we consider only the case in which the electron density of an atom may be assumed to be ellipsoidal; the major and minor axes of the ellipsoid are along the maximum and minimum vibration directions, respectively. The scattering factor of such an atom may be expressed as

$$f(\mathbf{h}) = f_0 T \exp\left[\tfrac{1}{4}(\Delta B_1 h_1^2 + \Delta B_2 h_2^2 + \Delta B_3 h_3^2)\right], \quad (3\cdot1)$$

in which f_0 is the scattering factor for the atom at rest, $T\ (= \exp[-B_0 \sin^2\theta/\lambda^2])$ is the assumed isotropic temperature factor, ΔB_1, ΔB_2, ΔB_3 are the anisotropic corrections on the same scale as B_0, and h_1, h_2, h_3 are the components of the reciprocal vector $\mathbf{h}\,(|\mathbf{h}| = h = 2\sin\theta/\lambda)$ along the three principal axes of the ellipsoids.

The observed electron density of the atom may then be expressed as

$$\varrho_o(\mathbf{r}) = (1+\Delta K)\int_0^{h_0} f_0 T \exp\left[\tfrac{1}{4}(\Delta B_1 h_1^2 + \Delta B_2 h_2^2 + \Delta B_3 h_3^2)\right] \times \exp[-2\pi i \mathbf{h}.\mathbf{r}]\, dV_h. \quad (3\cdot2)$$

If the assumed temperature factor is isotropic, the calculated electron density is spherically symmetric:

$$\varrho_c(\mathbf{r}) = \int_0^{h_0} f_0 T \exp[-2\pi i \mathbf{h}.\mathbf{r}]\, dV_h. \quad (3\cdot3)$$

In equations (3·2) and (3·3), h_0 is the cut-off limit of h, beyond which no reflections are observed, and the integration is carried over the whole volume within this sphere of reflection.

From (3·2), it follows that the peak height at the center of the atom ($\mathbf{r} = 0$) is

$$\varrho_o(0) = (1+\Delta K)\int_0^{h_0} f_0 T \times \exp\left[\tfrac{1}{4}(\Delta B_1 h_1^2 + \Delta B_2 h_2^2 + \Delta B_3 h_3^2)\right] dV_h. \quad (3\cdot4)$$

Expansion of (3·4) gives

$$\varrho_o(0) = (1+\Delta K)\,\varrho_c(0) + \sum_i \frac{\delta\varrho_c(0)}{\delta B_i}\Delta B_i, \quad (3\cdot5)$$

with

$$\varrho_c(0) = 4\pi\int_0^{h_0} h^2 f_0 T\, dh, \quad (3\cdot6)$$

and

$$\frac{\delta\varrho_c(0)}{\delta B_i} = \frac{\pi}{3}\int_0^{h_0} h^4 f_0 T\, dh. \quad (3\cdot7)$$

Similarly, the curvatures of the observed electron density at $r = 0$ along each of the three principal axes of the ellipsoid are

$$\frac{\delta^2\varrho_o(0)}{\delta r_i^2} = -4\pi^2(1+\Delta K)\int_0^{h_0} h_i^2 f_0 T \times \exp\left[\tfrac{1}{4}(\Delta B_1 h_1^2 + \Delta B_2 h_2^2 + \Delta B_3 h_3^2)\right] dV_h \quad (i = 1, 2, \text{ or } 3). \quad (3\cdot8)$$

Expansion of (3·8) gives

$$\frac{\delta^2\varrho_o(0)}{\delta r_i^2} = (1+\Delta K)\left(\frac{\delta^2\varrho_c(0)}{\delta r_i^2}\right) - \sum_j \frac{\delta}{\delta\Delta B_j}\left(\frac{\delta^2\varrho_c(0)}{\delta r_i^2}\right)\Delta B_j, \quad (3\cdot9)$$

with

$$\frac{\delta^2\varrho_c(0)}{\delta r_i^2} = -4\pi^2\int_0^{2\pi}\int_0^{\pi}\int_0^{h_0} h^2\cos^2\theta f_0 T h^2 dh \sin\theta\, d\theta\, d\varphi = -\frac{16\pi^3}{3}\int_0^{h_0} h^4 f_0 T\, dh \quad (3\cdot10)$$

and

$$\frac{\delta}{\delta B_j}\left(\frac{\delta^2\varrho_c(0)}{\delta r_i^2}\right) = \pi^2\int_0^{2\pi}\int_0^{\pi}\int_0^{h_0} f_0 T h_i^2 h_j^2 h^2 dh \sin\theta\, d\theta\, d\varphi = \begin{cases} \tfrac{4}{5}\pi^3\int_0^{h_0} h^6 f_0 T\, dh & \text{if } i = j, \\ \tfrac{4}{15}\pi^3\int_0^{h_0} h^6 f_0 T\, dh & \text{if } i \neq j. \end{cases} \quad (3\cdot11)$$

If we write

$$I_n = \int_0^{h_0} h^n f_0 T\, dh$$

and express the height and curvatures measured from the difference Fourier map as $D(0)$ and $D_i''(0)$ respectively, the following set of equations is obtained:

$$D(0) = \varrho_o(0) - \varrho_c(0) = 4\pi I_2\Delta K - \frac{\pi}{3}I_4(\Delta B_1 + \Delta B_2 + \Delta B_3), \quad (3\cdot12)$$

$$D_1''(0) = -\tfrac{16}{3}\pi^3 I_4\Delta K + \tfrac{4}{15}\pi^3 I_6(3\Delta B_1 + \Delta B_2 + \Delta B_3), \quad (3\cdot13)$$

$$D_2''(0) = -\tfrac{16}{3}\pi^3 I_4\Delta K + \tfrac{4}{15}\pi^3 I_6(\Delta B_1 + 3\Delta B_2 + \Delta B_3), \quad (3\cdot14)$$

$$D_3''(0) = -\tfrac{16}{3}\pi^3 I_4\Delta K + \tfrac{4}{15}\pi^3 I_6(\Delta B_1 + \Delta B_2 + 3\Delta B_3). \quad (3\cdot15)$$

These four expressions are analogous to the seven equations (2·8) derived by Cruickshank (1956); however, in Cruickshank's treatment second derivatives of the difference map (including the cross terms) are measured along the crystallographic axes, whereas in the present treatment curvatures are measured along the directions of the principal axes of the ellipsoid of thermal motion. Two of the principal axes of the ellipsoid are in the directions of the maximum and minimum curvatures observed on the difference map; the third must be normal to these two.

The integrals I_2, I_4, and I_6 may be calculated from the atomic scattering factor f_0, the assumed isotropic temperature factor T, and the cut-off limit h_0. As an example, the following table contains the values of these integrals for carbon, nitrogen and oxygen, using McWeeny's form factors (1951) and temperature factor $T = \exp[-3{\cdot}2 \sin^2 \theta/\lambda^2]$ up to the limit of data taken with Cu $K\alpha$ radiation ($h_0 = 1{\cdot}297$ Å^{-1})

	I_2 (e.Å^{-3})	I_4 (e.Å^{-5})	I_6 (e.Å^{-7})
C	0·70	0·50	0·51
N	0·86	0·59	0·59
O	1·05	0·70	0·68

The values of these integrals are very sensitive to h_0, since the values of the coefficients $h^n f_0 T$ are usually large even at high angles. This sensitivity reflects the fact that the high-ordered reflections have a large influence on the determination of the temperature factors.

For a structure with N atoms in one asymmetric unit, $4N$ independent observed equations of the type (3·12)–(3·15) may be obtained which may be solved for $3N+1$ unknowns (three ΔB's for each of the N atoms and one ΔK); because of the symmetry of these equations, however, it is simpler to solve first for a value of ΔK for each atom. An average value of ΔK may be chosen and the three quantities, ΔB_1, ΔB_2, and ΔB_3 for each atom may then be obtained from the four simultaneous equations, (3·12)–(3·15).

In solving these four equations for the three temperature-factor corrections, an appropriate weighting scheme may be introduced. Thus, equation (3·12) may be given a low weight if it is felt that extinction effects or the neglect of light atoms may affect the accuracy of the low-order reflections and hence lead to uncertainty in the values of $D(0)$; on the other hand, equations (3·13)–(3·15) may be given low weight if it is felt that there are uncertainties in the measured curvatures.

If the scale factor is assumed to be correct and if equation (3·12) is assigned zero weight, equations (3·13)–(3·15) give the temperature-factor corrections as

$$\Delta B_1 = \frac{3}{8\pi^3 I_6}(4D_1''(0) - D_2''(0) - D_3''(0)) . \qquad (3{\cdot}16)$$

This expression is equivalent to Cochran's result

$$u_j = \frac{3V[4(\delta^2 D/\delta r_1^2)_j - (\delta^2 D/\delta r_2^2)_j - (\delta^2 D/\delta r^2)_j]}{8\pi^2 \sum_n f_j s^4} ,$$

the factor $\sum_n fs^4/V$ in Cochran's expression being equivalent to

$$\int_0^{h_0} h^4 f dV_h = \int_0^{2\pi}\int_0^{\pi}\int_0^{h_0} h^4 f h^2 dh \sin\theta d\theta d\varphi = 4\pi I_6 .$$

The coefficients $\alpha, \beta, \gamma, \delta, \eta$, and ε in the general expression for anisotropic temperature factor $\exp(-\alpha h^2 - \beta k^2 - \gamma l^2 - \delta hk - \eta hl - \varepsilon kl)$ may be obtained from ΔB_1, ΔB_2, and ΔB_3 and the direction cosines of the principal axes of the ellipsoid in a straightforward manner (see, for example, Rollett & Davies, 1955).

The method of deriving anisotropic temperature-factor corrections described above applies only when the input electron densities are spherically symmetric, that is, when the calculated structure factors in the coefficients of the difference Fourier contain only isotropic temperature factors. In practice it has been found that the application of this method leads to anisotropic temperature-factor corrections which are accurate within, perhaps, 20%; further small adjustments, if necessary, may be estimated.

It should be pointed out that, in cases of acentric structures, the temperature-factor corrections derived by this or any similar method should be corrected by an n-shift analogous to that used in the refinement of positional parameters (Shoemaker, Donohue, Schomaker & Corey, 1950). The value chosen for n depends in a rather complicated manner upon the particular structure in question. Thus, if all atoms within the structure vibrate in the same direction and with equal magnitude, the value of n should be 1; on the other hand, if the atoms are vibrating at random with respect to one another, the value of n should be that proposed by Shoemaker *et al.* for corrections to positional parameters. In the case of leucyl-prolyl-glycine (Leung & Marsh, 1957), where most of the atoms are vibrating in the same direction but with varying magnitudes, the value 4/3 was chosen for n, and the resulting anisotropic temperature-factor corrections proved to be very nearly correct.

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