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The Effect of Random Errors on Partially Phased Fourier Maps

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Abstract

Probability methods are used to investigate the effect of random errors on partially phased Fourier maps of non-centrosymmetric structures. Two sources of error are considered: (i) inaccuracies in the atomic coordinates of the phasing model; (ii) errors in the observed structure-factor magnitudes. Expressions for both the error level in the unit cell and the peak heights at the atomic positions are derived. The results are illustrated for neutron diffraction studies of proteins.

1. Notation

$F_N \exp(i\varphi_N)$ structure factor of the complete structure (N atoms)

F_N^o observed structure-factor magnitude

$F_P \exp(i\varphi_P)$ structure factor of the P known atoms

$F_P^c \exp(i\varphi_P^c) = \sum_{p=1}^{P} b_p \exp(2\pi i \mathbf{H}.\mathbf{r}_p^c)$ calculated structure factor corresponding to inaccurate positions $\mathbf{r}_p^c$ of the P known atoms

$F_Q \exp(i\varphi_Q)$ structure factor of the Q unknown atoms

$\mathbf{r}_p$, $\mathbf{r}_q$ positions of the P and Q atoms

b_p, b_q atomic scattering factors of the P and Q atoms

$$\Sigma_P = \sum_{p=1}^{P} b_p^2, \quad \Sigma_Q = \sum_{q=1}^{Q} b_q^2,$$

$$\Sigma_N = \Sigma_P + \Sigma_Q,$$

$$\sigma_1^2 = \Sigma_P/\Sigma_N, \sigma_2^2 = \Sigma_Q/\Sigma_N.$$

2. Introduction

When part of a crystal structure is known, Fourier syntheses with coefficients $F_N^o \exp(i\varphi_P^c)$ are often used to locate the remainder of the structure. The characteristic features of partially phased Fourier maps were first discussed by Luzzati (1953) assuming error-free data [*i.e.* $F_N \exp(i\varphi_P)$]. He demonstrated that peaks representing atoms are expected to show up with weights different from their true values.

In the present paper Luzzati's probabilistic analysis is extended to include the effect of random errors in the observed structure-factor magnitudes and in the positions of the known partial structure.

Phasing models with large errors in the atomic coordinates are usually met with in the protein-structure field. In this connection it is interesting to study quantitatively how these errors affect both the maxima of the density distribution at the atomic sites and the noise level in a Fourier synthesis. Knowledge of these values is important in judging the credibility of structural features in the Fourier map. In addition, it is useful to judge the suitability of the initial trial structure before starting data collection with a given crystal.

We shall consider crystals and models which satisfy the requirements of the acentric distribution of Wilson (1949).

3. Random positional errors in the partial structure

A Fourier synthesis with the coefficients $F_N \exp(i\varphi_P^c)$ is considered. F_N is the correct structure-factor magnitude of the total structure, φ_P^c is the phase angle calculated from the inaccurate positions of the partial structure. The coordinate errors $\Delta\mathbf{r}$ are assumed to be normally distributed random vectors.

3.1. *Peak height at* $\mathbf{r}_p^c$

The average peak height of an input atom at the inaccurate position $\mathbf{r}_p^c$ may be written as the following conditional average

$$\langle \rho(\mathbf{r}_p^c) \rangle = \int_0^{H_o} \mathrm{d}^3\mathbf{H} \int_0^{\infty}\int_0^{\infty}\int_0^{2\pi} F_N \cos(2\pi\mathbf{H}.\mathbf{r}_p^c - \varphi_P^c) \times p(F_N; F_P^c, \varphi_P^c)\, p(F_P^c, \varphi_P^c; \mathbf{f}_p^c)\, \mathrm{d}\varphi_P^c\, \mathrm{d}F_N\, \mathrm{d}F_P^c, \quad (1)$$

where H_0 is the limiting radius of the reciprocal-lattice vector $\mathbf{H}$ and $\mathrm{d}^3\mathbf{H}$ is a volume element of reciprocal space.

The conditional probability density function (here-

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after p.d.f.) of F_N, given F_P^c and φ_P^c, is known to be (Srinivasan & Chandrasekaran, 1966)

$$p(F_N; F_P^c, \varphi_P^c) = \frac{2F_N}{\Sigma_N - D^2\Sigma_P} \exp\left[-\frac{F_N^2 + D^2 F_P^{c2}}{\Sigma_N - D^2\Sigma_P}\right] \times I_0\left(\frac{2DF_P^c F_N}{\Sigma_N - D^2\Sigma_P}\right), \quad (2)$$

where

$$D = \exp\left[-\frac{\pi^3}{4}\langle|\Delta\mathbf{r}|\rangle^2 H^2\right]. \quad (3)$$

$\langle|\Delta\mathbf{r}|\rangle$ is the mean positional error and I_0 is the zero-order modified Bessel function.

$p(F_P^c, \varphi_P^c; \mathbf{f}_p^c)$ is the conditional p.d.f. of F_P^c and φ_P^c, given the structure-factor contribution

$$\mathbf{f}_p^c = b_p \exp(2\pi i \mathbf{H}.\mathbf{r}_p^c).$$

From

$$p(\mathbf{F}_P^c; \mathbf{f}_p^c) = \frac{1}{\pi(\Sigma_P - b_p^2)} \exp\left[-\frac{|\mathbf{F}_P^c - \mathbf{f}_p^c|^2}{\Sigma_P - b_p^2}\right] \quad (4)$$

(Wilson, 1949) it follows that

$$p(F_P^c, \varphi_P^c; \mathbf{f}_p^c) = \frac{F_P^c}{\pi\Sigma_P} \exp\left[-\frac{F_P^{c2}}{\Sigma_P}\right] \times \left[1 + \frac{2b_p F_P^c \cos(2\pi\mathbf{H}.\mathbf{r}_p^c - \varphi_P^c)}{\Sigma_P}\right] \quad (5)$$

since

$$|\mathbf{F}_p^c - \mathbf{f}_p^c|^2 = F_P^{c2} + b_p^2 - 2b_p F_P^c \cos(2\pi\mathbf{H}.\mathbf{r}_p^c - \varphi_P^c)$$

and $\Sigma_P \gg b_p^2$.

Substitution of (2) and (5) into (1) and integration over the structure-factor variables leads to

$$\langle\rho(\mathbf{r}_p^c)\rangle = \int_0^{H_0} b_p \tau \, \mathrm{d}^3\mathbf{H} \quad (6)$$

$$\tau = \frac{1}{\sigma_1}\left[E(\sigma_A) - \frac{\sigma_B^2}{2}K(\sigma_A)\right] \quad (7)$$

with

$$\sigma_A = \sigma_1 D, \; \sigma_B = (1 - \sigma_A^2)^{1/2}.$$

$K(x)$ and $E(x)$ are the complete elliptic integrals of the first and second kinds:

$$K(x) = \int_0^{\pi/2} (1 - x^2 \sin^2\varphi)^{-1/2} \, \mathrm{d}\varphi$$

$$E(x) = \int_0^{\pi/2} (1 - x^2 \sin^2\varphi)^{1/2} \, \mathrm{d}\varphi.$$

τ is the weight by which the atomic scattering factor is modified relative to the true structure.

3.2. *Peak height at* $\mathbf{r}_p$

The average peak height of an inaccurately positioned atom at its true position $\mathbf{r}_p$ may be written as

$$\langle\rho(\mathbf{r}_p)\rangle = \int_0^{H_0} \mathrm{d}^3\mathbf{H} \int_0^\infty \int_0^\infty \int_0^{2\pi} F_N \cos(2\pi\mathbf{H}.\mathbf{r}_p - \varphi_P^c) \times p(F_N; F_P^c, \varphi_P^c) p(F_P^c, \varphi_P^c; \mathbf{f}_p) \, \mathrm{d}\varphi_P^c \, \mathrm{d}F_N \, \mathrm{d}F_P^c. \quad (8)$$

The conditional p.d.f. of F_P^c, φ_P^c, given the structure-factor contribution $\mathbf{f}_p = b_p \exp(2\pi i \mathbf{H}.\mathbf{r}_p)$, can be derived from the relation

$$p(F_P^c, \varphi_P^c; \mathbf{f}_p) = \int_0^\infty \int_0^{2\pi} p(F_P^c, \varphi_P^c; F_P, \varphi_P) \times p(F_P, \varphi_P; \mathbf{f}_p) \, \mathrm{d}\varphi_P \, \mathrm{d}F_P \quad (9)$$

using the known conditional p.d.f. $p(F_P^c, \varphi_P^c; F_P, \varphi_P)$ (Luzzati, 1952). $p(F_P, \varphi_P; \mathbf{f}_p)$ is analogous to (5). The appropriate integrations yield

$$p(F_P^c, \varphi_P^c; \mathbf{f}_p) = \frac{F_p^c}{\pi\Sigma_P} \exp\left[-\frac{F_P^{c2}}{\Sigma_P}\right] \times \left(1 + \frac{2b_p DF_P^c \cos(2\pi\mathbf{H}.\mathbf{r}_p - \varphi_P^c)}{\Sigma_P}\right), \quad (10)$$

where again $b_p^2 \ll \Sigma_P$ has been taken into account.

Substitution of (2) and (10) into (8) and integration leads to

$$\langle\rho(\mathbf{r}_p)\rangle = \int_0^{H_0} b_p \chi_P \, \mathrm{d}^3\mathbf{H}, \quad (11)$$

$$\chi_P = \frac{D}{\sigma_1}\left[E(\sigma_A) - \frac{\sigma_B^2}{2}K(\sigma_A)\right]. \quad (12)$$

χ_P is the weight by which the atomic scattering factor is modified relative to the true structure.

3.3. *Peak height at* $\mathbf{r}_q$

The average peak height of an unknown atom, situated at $\mathbf{r}_q$, may be written as

$$\langle\rho(\mathbf{r}_q)\rangle = \int_0^{H_0} \mathrm{d}^3\mathbf{H} \int_0^\infty \int_0^\infty \int_0^{2\pi} F_N \cos(2\pi\mathbf{H}.\mathbf{r}_q - \varphi_P^c) \times p(F_N; F_P^c, \varphi_P^c, \mathbf{f}_q) p(F_P^c, \varphi_P^c) \, \mathrm{d}\varphi_P^c \, \mathrm{d}F_N \, \mathrm{d}F_P^c, \quad (13)$$

where $p(F_P^c, \varphi_P^c)$ is the acentric distribution (Wilson, 1949) with parameter Σ_P.

The conditional p.d.f. of F_N, given F_P^c, φ_P^c and the structure-factor contribution $\mathbf{f}_q = b_q \exp(2\pi i \mathbf{H}.\mathbf{r}_q)$, can

be readily obtained from expression (*A*7) of Srinivasan & Chandrasekaran (1966):

$$p(F_N; F_P^c, \varphi_P^c, \mathbf{f}_q) = \frac{F_N}{\pi(\Sigma_N - D^2\,\Sigma_P)} \times \int_0^{2\pi} \exp -[F_N^2 + |D\mathbf{F}_P^c + \mathbf{f}_q|^2 + 2F_N|D\mathbf{F}_P^c + \mathbf{f}_q| \cos\beta][\Sigma_N - D^2\,\Sigma_P]^{-1}\,\mathrm{d}\beta. \quad (14)$$

Now, insert

$$|D\mathbf{F}_P^c + \mathbf{f}_q|^2 = D^2 F_P^{c2} + b_q^2 + 2b_q DF_P^c \cos(2\pi\mathbf{H}.\mathbf{r}_q - \varphi_P^c)$$

into (14) and expand the exponential function ($b_q^2 \ll \Sigma_N - D^2\,\Sigma_P$). Substitution of (14) into (13) and integration leads to

$$\langle\rho(\mathbf{r}_q)\rangle = \int_0^{H_0} b_q\,\chi_Q\,\mathrm{d}^3\mathbf{H}, \quad (15)$$

$$\chi_Q = \frac{1}{2\sigma_A}[E(\sigma_A) - \sigma_B^2\,K(\sigma_A)]. \quad (16)$$

3.4. *Error in the Fourier map*

The mean-square difference between a Fourier map based on $\mathbf{F}_N$ and that based on $F_N \exp(i\varphi_P^c)$ is given by

$$\langle(\Delta\rho)^2\rangle = 2V^{-2}\sum_{\mathbf{H}} F_N^2[1 - \cos(\varphi_N - \varphi_P^c)] = 2(\Sigma_N/V) \times \int_0^{H_0} (1 - \langle F_N^2 \cos(\varphi_N - \varphi_P^c)\rangle/\Sigma_N)\,\mathrm{d}^3\mathbf{H}, \quad (17)$$

where V = unit-cell volume. Substitution of the average value

$$\langle F_N^2 \cos(\varphi_N - \varphi_P^c)\rangle = \Sigma_N \frac{1}{2\sigma_A} \times [(1 + \sigma_A^2)\,E(\sigma_A) - \sigma_B^2\,K(\sigma_A)] \quad (18)$$

(see Appendix*) into (17) yields an *a priori* formula for $\langle(\Delta\rho)^2\rangle$.

The mean-square bias due to the systematic reduction and enhancement of the peak heights may be expressed as

$$\delta^2 = V^{-2}\sum_{\mathbf{H}} \{(1 - \chi_Q)^2\,\Sigma_Q + (1 - \chi_P)^2\,\Sigma_P\} = (\Sigma_N/V)\int_0^{H_0} \{(1 - \chi_Q)^2\,\sigma_2^2 + (1 - \chi_P)^2\,\sigma_1^2\}\,\mathrm{d}^3\mathbf{H} \quad (19)$$

* The Appendix has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38549 (4 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

(Luzzati, 1953) assuming non-overlapping atoms.

The variance $\sigma^2(\rho)$ is related to the mean-square error and bias by

$$\sigma^2(\rho) = \langle(\Delta\rho)^2\rangle - \delta^2. \quad (20)$$

Substitution of the above expressions into (20) provides an *a priori* estimate for the mean noise level of the partially phased Fourier map.

3.5. *Discussion*

For a rigorous evaluation of the average peak heights the H dependence of both the atomic scattering factors (including the temperature factor) and the weights has to be taken into account.

As an example we consider in Fig. 1 the variation of the peak height of unknown hydrogen atoms in a neutron Fourier map ($b_H = -3{\cdot}8$ fm) as a function of the resolution d_{min} ($=H_0^{-1}$) for different fixed values of $\langle|\Delta\mathbf{r}|\rangle$. The thermal parameter and the fractional partial structure contribution have been assigned to $B = 10$ Å^2 and $\sigma_1^2 = 0{\cdot}7$. These values are typical for neutron diffraction studies of proteins where initial phases are calculated from a structural model determined from X-ray diffraction. It is seen that errors in the model up to about 0·2 Å affect the peak height only slightly. For large positional errors, however, the peak strength has approached a constant value already at moderate resolution. Hence, it does not pay to collect neutron data at very high resolution ($d_{min} < 1{\cdot}4$ Å) unless one can resort to a sufficiently refined X-ray model of the protein. This result is not unexpected since

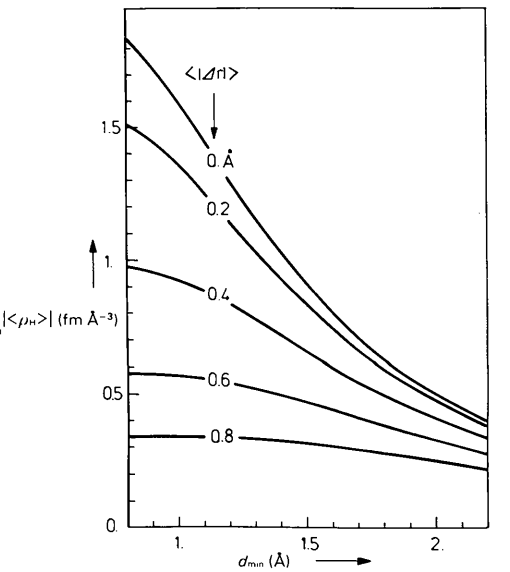

Fig. 1. Average peak height at the position of a hydrogen atom ($B = 10$ Å^2) in a Fourier map based on neutron diffraction data as a function of the resolution for $\sigma_1^2 = 0{\cdot}7$ and different values of $\langle|\Delta\mathbf{r}|\rangle$.

the effects of coordinate errors are more important at high resolution where the d spacings become comparable to the magnitudes of the errors.

Fig. 1 should be compared with Fig. 2 which shows the standard deviation $\sigma(\rho)$ evaluated from (20) with the same parameters used above. Σ_N/V has been assigned to 2·71 fm^2 Å^{-3} (partially deuterated myoglobin).

In order to get some feeling for the variation of the peak heights it is convenient to consider the average over reciprocal space

$$\bar{X} = 3H_0^{-3} \int_0^{H_0} XH^2 \, dH, \qquad (21)$$

where X stands for τ, χ_P or χ_Q. $\bar{X}$ are the weights which correspond to point atoms (neutron-diffraction case) at rest. $\bar{X}$ may be seen to depend on both σ_1 and the product $H_0\langle|\Delta\mathbf{r}|\rangle$. In general, (21) has to be evaluated by numerical integration. Only for a perfectly accurate partial structure ($D = 1$) are the relative peak heights independent of H_0 (Luzzati, 1952; Nixon & North, 1976).

The variation of the average values $\bar{\tau}$, $\bar{\chi}_P$ and $\bar{\chi}_Q$ as a function of $H_0\langle|\Delta\mathbf{r}|\rangle$ for different values of σ_1^2 are shown in Fig. 3. It is apparent that peaks at inaccurate positions are only slightly suppressed; the decrease in peak strength is much more pronounced at the positions $\mathbf{r}_p$ and $\mathbf{r}_q$.

The theory presented here does not account for features due to atomic overlap resulting either from the positional errors or from a limited resolution. The influence of adjacent atoms on one another is de-

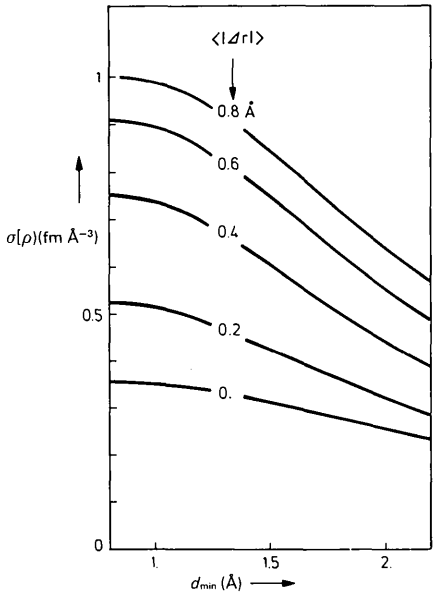

Fig. 2. Average standard deviation in a neutron Fourier map as a function of the resolution calculated with the parameters from Fig. 1 ($\Sigma_N/V = 2{\cdot}71$ fm^2 Å^{-3}).

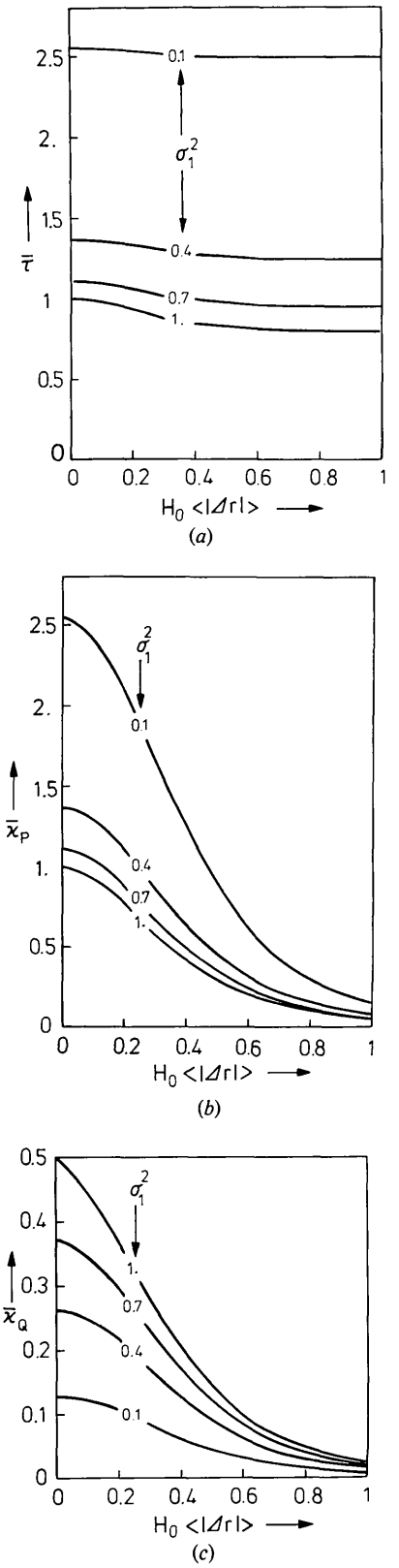

Fig. 3. Overall values of the fractional peak heights at (*a*) $\mathbf{r}_p^c$, (*b*) $\mathbf{r}_p$ and (*c*) $\mathbf{r}_q$ as a function of the product $H_0\langle|\Delta\mathbf{r}|\rangle$ for different values of σ_1^2.

creased in difference Fourier maps to which the above results also apply.

It is interesting to note that the expressions for the peak heights are closely related to some correlation functions discussed by Srinivasan & Parthasarathy (1976, p. 111):

$$\tau = \Sigma_P^{-1}\langle F_N F_P^c\rangle, \tag{22}$$

$$\chi_Q = \tfrac{1}{2}\langle\cos(\varphi_N - \varphi_P^c)\rangle. \tag{23}$$

4. Random errors in the structure-factor magnitudes

A Fourier synthesis with the coefficients $F_N^o \exp(i\varphi_P)$ is considered. F_N^o is the observed structure factor magnitude, φ_P is the phase angle calculated from the correct positions of the partial structure.

It will be assumed that $\mathbf{F}_N^o$ follows a normal distribution of variance σ_F^2 around $\mathbf{F}_N$

$$p(F_N^o, s; F_N) = (2\pi\sigma_F^2)^{-1/2} \times \exp[-(F_N^{o2} + F_N^2 - 2sF_N^o F_N)/2\sigma_F^2] \tag{24}$$

with $s = \pm 1$ according as $F_N^o \gtrless F_N$. The conditional p.d.f. of F_N^o, given F_N, is obtained by summation over the two values of s:

$$p(F_N^o; F_N) = (2/\pi\sigma_F^2)^{1/2} \exp[-(F_N^{o2} + F_N^2)/2\sigma_F^2] \times \cosh(F_N^o F_N/\sigma_F^2). \tag{25}$$

4.1. *Peak height at* $\mathbf{r}_p$

An expression for the average peak height of a known atom follows from (1) by replacing the set $(F_N, F_P^c, \varphi_P^c, \mathbf{r}_p^c)$ by the set $(F_N^o, F_P, \varphi_P, \mathbf{r}_p)$.

The function $p(F_N^o; F_P, \varphi_P)$ can be obtained from the relation

$$p(F_N^o; F_P, \varphi_P) = \int_0^\infty p(F_N^o; F_N)\, p(F_N; F_P, \varphi_P)\, \mathrm{d}F_N \tag{26}$$

using the conditional p.d.f.'s from (25) and (2) [with $\mathbf{F}_P^c \equiv \mathbf{F}_P, D = 1$].

It is possible to carry out the integrations over F_N^o, F_P, φ_P analytically, leading to

$$\tau = \sigma_2^4\, \sigma_1^{-1}\, \pi^{1/2} \int_0^\infty x^2 \exp(-x^2)\, {}_1F_1(\tfrac{3}{2}; 1; \sigma_1^2 x^2)\, g\, \mathrm{d}x \tag{27}$$

with

$$g = \mathrm{erf}\left(\frac{x}{\sqrt{2\psi}}\right) + \frac{\sqrt{2\psi}}{\sqrt{\pi}x}\exp(-x^2/2\psi), \tag{28}$$

where $x = F_N/\Sigma_Q^{1/2}$, $\psi = \sigma_F^2/\Sigma_Q$ and ${}_1F_1$ is the confluent hypergeometric function.

In the limiting case that $\sigma_F^2 = 0$ the function g equals unity and integration reduces (27) to (12). Direct evaluation of (27) shows that the error function may be replaced by the asymptotic formula

$$\mathrm{erf}(z) \simeq 1 - \pi^{-1/2}\exp(-z^2)/z \tag{29}$$

(Abramowitz & Stegun, 1965) without appreciable error. Equation (29) implies $g \simeq 1$. Therefore, τ is practically independent of σ_F^2.

4.2. *Peak height at* $\mathbf{r}_q$

Correspondingly, the weight of an unknown atom is obtained as

$$\chi = \sigma_1\, \sigma_2^2\, \pi^{1/2} \int_0^\infty x^4 \exp(-x^2)\, {}_1F_1(\tfrac{3}{2}; 2; \sigma_1^2 x^2)\, g\, \mathrm{d}x - \frac{\sigma_1^2}{\sigma_2^2}\tau \tag{30}$$

with τ and g as defined by (27) and (28). Just as above, with $g \simeq 1$ (30) reduces to (16), and χ is almost independent of the magnitude of the experimental errors.

Hence, errors due to an imperfect model and experimental errors manifest themselves in different ways. Namely, experimental errors introduce background fluctuations in the Fourier map but do not affect the average atomic peak heights.

4.3. *Discussion*

It has been repeatedly pointed out (*e.g.* Lipson & Cochran, 1968) that for small values of σ_2^2 accuracy of measurement is the limiting factor for the resolution of the unknown rest structure. A suitable criterion for the limitation of the method is provided by the following signal-to-noise ratio

$$\mu = [\langle\rho_Q^2\rangle/\sigma^2(\rho)]^{1/2} \tag{31}$$

(Nixon & North, 1976). $\langle\rho_Q^2\rangle$ is the mean-square value of the average unknown density, written as a sum of non-overlapping atomic densities

$$\langle\rho_Q^2\rangle = V^{-1}\int_V \left[\sum_{q=1}^{Q}\langle\rho(\mathbf{r}_q)\rangle\right]^2 \mathrm{d}^3\mathbf{r} = V^{-2}\chi^2\sum_{\mathbf{H}} F_Q^2. \tag{32}$$

Following the arguments of Luzzati (1953) the mean variance in the unit cell can be expressed as

$$\sigma^2(\rho) = V^{-2}\sum_{\mathbf{H}}(F_N^2 + \sigma_F^2 - \tau^2 F_P^2 - \chi^2 F_Q^2), \tag{33}$$

again assuming non-overlapping atoms. Hence, in terms of normalized variables,

$$\mu = \chi\sigma_2/[1 + \varepsilon^2 - \tau^2\sigma_1^2 - \chi^2\sigma_2^2]^{1/2} \tag{34}$$

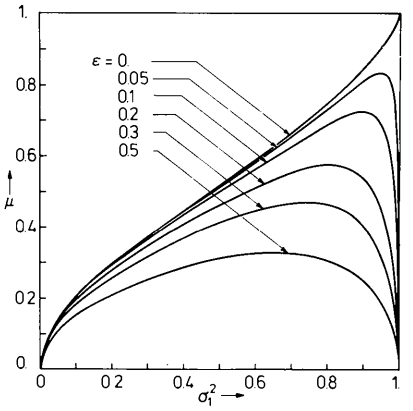

Fig. 4. Signal-to-noise ratio as a function of σ_1^2 for different accuracies of measurement.

with

$$\varepsilon^2 = \langle \sigma_F^2 \rangle / \Sigma_N.$$

Fig. 4 shows the variation of μ as a function of σ_1^2 for different values of the mean normalized error ε. It demonstrates the loss of structural information for finite ε as $\sigma_1^2 \to 1$. There occurs an optimum signal-to-noise ratio for $\sigma_1^2 \simeq 1 - \varepsilon$.

Assume the critical value of μ for the statistical significance of the features in the map to be 0·5 corresponding to $\sigma_1^2 \simeq 0{\cdot}5$ for the error-free data. This implies that data with $\varepsilon = 0{\cdot}1$ should allow a structure completion from inspection of difference maps up to $\sigma_1^2 \simeq 0{\cdot}98$. With $\varepsilon = 0{\cdot}05$ the corresponding value of σ_1^2 is even greater than 0·99. Hence, in general, accuracy of measurement should not be a very critical factor.

A similar result is obtained from another argument. The observed data should meet the condition

$$\langle |F_N - F_P| \rangle > \langle \sigma_F^2 \rangle^{1/2}, \qquad (35)$$

which can be rewritten in terms of the residual $R(F)$ $(=\langle |F_N - F_P| \rangle / \langle F_N \rangle)$ as

$$\frac{\sqrt{\pi}}{2} R(F) > \varepsilon \qquad (36)$$

since $\langle F_N \rangle = (\sqrt{\pi}/2)\Sigma_N^{1/2}$ (Wilson, 1949), Now, using the theoretical expression for $R(F)$ (Srinivasan, Raghupathy Sarma & Ramachandran, 1963) we find, for example, ε $(\sigma_1^2 = 0{\cdot}97) < 0{\cdot}1$ and ε $(\sigma_1^2 = 0{\cdot}99) < 0{\cdot}06$. The case that σ_2^2 is small occurs especially in protein crystallography when difference Fourier maps are used to reveal small molecules added to the protein (Henderson & Moffat, 1971).

Equation (25) implies a preponderance of positive errors, *i.e.* $F_N^o > F_N$. The resulting bias in the density, however, is quite small. The average height of an atomic peak in an $F_N^o \exp(i\varphi_N)$ map is obtained as $(1 + \varepsilon^2)/(1 + 2\varepsilon^2)^{1/2}$ times the true height.

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A Varying-Step Algorithm for Numerical Integration of Takagi–Taupin Equations

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Abstract

The numerical integration of the Takagi–Taupin equations using a constant step of integration does not allow the simulation of traverse topographs since the accuracy of the computation is rather poor. A new algorithm is described in which the step of integration varies inside the crystal, following the oscillations of the amplitudes of the wavefields. The precision becomes good enough to simulate either section topographs, taking into account the real width of the incident beam, or traverse topographs. Moreover in most cases the

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