

Direct phasing from Patterson syntheses by δ recycling

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The direct methods origin-free modulus sum function [Rius (1993). *Acta Cryst.* **A49**, 406–409] includes in its definition the structure factor $\mathbf{G}(\Phi)$ of the squared crystal structure expressed in terms of Φ , the set of φ phases of the normalized structure factors \mathbf{E} 's of the crystal structure of unit-cell volume V . Here the simpler sum function variant $S_P = \sum_{\mathbf{H}} E_{-\mathbf{H}} \int_V \delta_{P,\Delta}(\Phi) \exp(i2\pi\mathbf{H}\mathbf{r}) dV$ extended over all \mathbf{H} reflections is introduced which involves no \mathbf{G} 's and in which the $\delta_{P,\Delta}$ function corresponds to $\delta_P = \text{FT}^{-1}\{(E_{\mathbf{H}}^2 - \langle E^2 \rangle) \exp[i\varphi_{\mathbf{H}}(\Phi)]\}$ (where FT = Fourier transform) with all values smaller than $\Delta = 2.5\sigma_P$ equated to zero (σ_P^2 is the variance of δ_P calculable from the experimental intensities). The new phase estimates are obtained by Fourier transforming $\delta_{P,\Delta}$. This iterative phasing method (δ recycling) only requires calculation of Fourier transforms at two stages. Since $\delta_M \simeq \delta_P/2$, similar arguments are valid for $\delta_M = \text{FT}^{-1}\{(E_{\mathbf{H}} - \langle E \rangle) \exp(i\varphi_{\mathbf{H}})\}$ from which the corresponding S_M phasing function follows.

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1. Introduction

A simple way of formulating the direct methods origin-free modulus sum function is through the introduction of the δ_M^{sq} Fourier synthesis

$$\delta_M^{\text{sq}}(\mathbf{r}, \Phi) = \frac{1}{V} \sum_{\mathbf{H}} \{(G_{\mathbf{H}} - \langle G \rangle) \exp[i\psi_{\mathbf{H}}(\Phi)]\} \exp(-i2\pi\mathbf{H}\mathbf{r}) \quad (1)$$

extended over all \mathbf{H} reflections. For a $P1$ crystal structure with N equal atoms in the unit cell of volume V , the quantities involved in the δ_M^{sq} definition are as follows:

$E_{\mathbf{K}}$ and $\varphi_{\mathbf{K}}$ are the amplitude and unknown phase value of the normalized structure factor \mathbf{E} for reflection \mathbf{K} . $E_{\mathbf{K}}^2$ is directly related to the squared structure-factor amplitude $F_{\mathbf{K}}^2$ by the expression $E_{\mathbf{K}}^2 = F_{\mathbf{K}}^2 / (Nf_{\mathbf{K}}^2)$ where $f_{\mathbf{K}}$ is the atomic scattering factor affected by thermal vibration. Hence $E_{\mathbf{K}}$ can be considered the experimental E value.

$\rho(\mathbf{r}, \Phi)$ is the density distribution at an arbitrary point \mathbf{r} of the unit cell given in terms of the set Φ of phases of the \mathbf{E} 's.

$G_{\mathbf{K}}$ is the amplitude of the structure factor of the squared point-like equal-atom structure, ρ^2 , which is accessible from the experimental $E_{\mathbf{K}}$ and from the known N by means of $G_{\mathbf{K}} = E_{\mathbf{K}}/N^{1/2}$. Similarly to $E_{\mathbf{K}}$, $G_{\mathbf{K}}$ represents the experimental G . The $\langle E \rangle$, $\langle E^2 \rangle$, $\langle G \rangle$ and $\langle G^2 \rangle$ quantities appearing in the various δ Fourier syntheses described in this paper are experimental averages over the full set.

$\mathbf{G}_{\mathbf{K}}(\Phi)$ is the structure factor of $\rho^2(\mathbf{r}, \Phi)$ with amplitude and associated phase given by $G_{\mathbf{K}}(\Phi)$ and $\psi_{\mathbf{K}}(\Phi)$, respectively.

By making use of $\delta_M^{\text{sq}}(\mathbf{r}, \Phi)$, the direct methods origin-free modulus sum function (Rius, 1993; Rius *et al.*, 2007) takes the form

$$\begin{aligned} S_M &= \sum_{\mathbf{K}} E_{-\mathbf{K}} \exp(i\varphi_{-\mathbf{K}}) \\ &\quad \times \int_V \delta_M^{\text{sq}}(\mathbf{r}, \Phi) \rho(\mathbf{r}, \Phi) \exp(i2\pi\mathbf{K}\mathbf{r}) dV \\ &= \sum_{\mathbf{K}} E_{-\mathbf{K}} \exp(i\varphi_{-\mathbf{K}}) \mathbf{Q}_{\mathbf{K}}(\Phi). \end{aligned} \quad (2)$$

Phase refinement is carried out by maximizing S_M . As new $\varphi_{\mathbf{K}}$ estimates the angular parts of the corresponding $\mathbf{Q}_{\mathbf{K}}(\Phi)$ are taken. Closely related to S_M is the recently developed S_P phasing function which explores the Patterson function of the squared structure instead of the modulus function (Rius, 2011a). S_P is obtained by replacing in equation (2) δ_M^{sq} by

$$\delta_P^{\text{sq}}(\mathbf{r}, \Phi) = \frac{1}{V} \sum_{\mathbf{H}} \{(G_{\mathbf{H}}^2 - \langle G^2 \rangle) \exp[i\psi_{\mathbf{H}}(\Phi)]\} \exp(-i2\pi\mathbf{H}\mathbf{r}). \quad (3)$$

Since S_P works with intensities, it is especially well suited for dealing with powder diffraction data. The aim of this article is to investigate the possibility of refining phases with variants of S_M and S_P not using the $\psi(\Phi)$ phases of the squared structure.

2. The δ_P (δ_M) synthesis

The δ_P synthesis is defined by

$$\delta_P(\mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} [(E_{\mathbf{H}}^2 - \langle E^2 \rangle) \exp(i\varphi_{\mathbf{H}})] \exp(-i2\pi\mathbf{H}\mathbf{r}) \quad (4)$$

where the $E_{\mathbf{H}}^2 - \langle E^2 \rangle$ are the Fourier coefficients of the origin-free Patterson function (P') and where $\exp(i\varphi_{\mathbf{H}})$ are the coefficients of the phase synthesis (ρ_{φ}). According to Ramachandran & Srinivasan (1970) ρ_{φ} and ρ have peaks of similar

strength at the \mathbf{r}_j atomic positions ($j = 1, N$). Besides the peaks at atomic positions, ρ_φ also shows background peaks. Since δ_P corresponds to the convolution of ρ_φ with P' , δ_P has large maxima at \mathbf{r} values coincident with atomic vectors and a certain noise/background in the rest of the unit cell. The value of δ_P at atomic positions is [equation (23)],

$$\delta_P(\mathbf{r}_k) = \rho(\mathbf{r}_k)\langle E \rangle - f_k^2 \rho_\varphi(\mathbf{r}_k) \quad (5)$$

where f_k is the normalized scattering factor of atom k . That the negative term in equation (5) can be neglected is readily verified for an equal-atom structure. In this case f_k^2 is equal to $1/(N^{1/2})^2$ and since it is known that $\rho_\varphi(\mathbf{r}_k)$ and $\rho(\mathbf{r}_k)$ are similar, the negative term is approximately $\rho(\mathbf{r}_k)/N$, *i.e.* much smaller than the positive one. Consequently,

$$\delta_P(\mathbf{r}_k) \simeq \rho(\mathbf{r}_k)\langle E \rangle. \quad (6)$$

Similarly, the δ_M synthesis is defined by

$$\delta_M(\mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} [(E_{\mathbf{H}} - \langle E \rangle) \exp(i\varphi_{\mathbf{H}})] \exp(-i2\pi\mathbf{H}\mathbf{r}). \quad (7)$$

The only difference between δ_P and δ_M is the substitution of $E^2 - \langle E^2 \rangle$ by $E - \langle E \rangle$, *i.e.* the introduction of the coefficients of the origin-free modulus function, M' . Both M' and P' contain, each one, $N^2 - N$ peaks at the ends of the $\mathbf{r}_k - \mathbf{r}_l$ interatomic vectors ($k \neq l$). The respective approximate peak strengths are $f_k f_l / 2$ and $f_k f_l$, so that one may assume $P'(\mathbf{r}) \simeq 2M'(\mathbf{r})$ (Ramachandran & Srinivasan, 1970). In view of this result and by expressing δ_P as the convolution of ρ_φ with P' , the mathematical relationship between δ_P and δ_M at an arbitrary \mathbf{r} is

$$\begin{aligned} \delta_P(\mathbf{r}) &= \int_V \rho_\varphi(\mathbf{u}) P'(\mathbf{r} - \mathbf{u}) \, d\mathbf{u} \\ &\simeq 2 \int_V \rho_\varphi(\mathbf{u}) M'(\mathbf{r} - \mathbf{u}) \, d\mathbf{u} = 2\delta_M(\mathbf{r}). \end{aligned} \quad (8)$$

Combining equation (8) with equation (6) yields the value of δ_M at the k atomic position,

$$\delta_M(\mathbf{r}_k) \simeq \rho(\mathbf{r}_k) \frac{\langle E \rangle}{2}. \quad (9)$$

2.1. Variance of δ_P (δ_M)

The variance of a given $\eta(\mathbf{r})$ density function with structure-factor amplitudes $C_{\mathbf{H}}$ is (see Appendix B)

$$\sigma_\eta^2 = \frac{1}{V^2} \sum_{\mathbf{H} \neq 0} C_{\mathbf{H}}^2. \quad (10)$$

Replacement of $C_{\mathbf{H}}$ by $E^2 - \langle E^2 \rangle$ in the case of δ_P and by $E - \langle E \rangle$ for δ_M leads to the respective variances

$$\sigma_P^2 = \frac{1}{V^2} \sum_{\mathbf{H} \neq 0} (E_{\mathbf{H}}^2 - \langle E^2 \rangle)^2 = \frac{N_{\mathbf{H}}}{V^2} ((E^4) - \langle E^2 \rangle^2), \quad (11)$$

$$\sigma_M^2 = \frac{1}{V^2} \sum_{\mathbf{H} \neq 0} (E_{\mathbf{H}} - \langle E \rangle)^2 = \frac{N_{\mathbf{H}}}{V^2} ((E^2) - \langle E \rangle^2) \quad (12)$$

from which the experimental σ_P/σ_M value can be derived. For a P1 equal-atom structure the calculated σ_P/σ_M quotient is

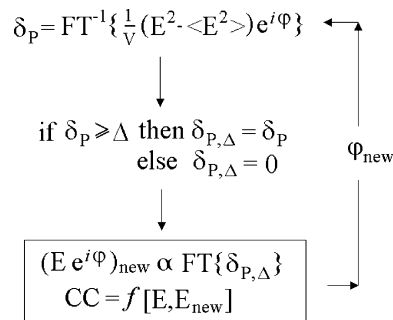


Figure 1

Phase refinement by δ_P recycling. (Top) Initial (or updated) phase estimates are used to compute δ_P ; (middle) δ_P values are compared with $\Delta = 2.5\sigma_P$ to impose positivity, thus leading to the constrained $\delta_{P,\Delta}$; (bottom) new structure-factor estimates are obtained by Fourier transforming $\delta_{P,\Delta}$. CC measures the correlation between observed and new amplitudes. Refinement continues until convergence is reached. This algorithm is also valid for δ_M , the principal difference being substitution of $E^2 - \langle E^2 \rangle$ by $E - \langle E \rangle$.

2.16, since $\langle E^4 \rangle = 2$, $\langle E^2 \rangle = 1$ and $\langle E \rangle = 0.886$ from the theory of intensity statistics. Notice that σ_P^2 and σ_M^2 are phase independent. In this connection it should be mentioned that Giacovazzo & Mazzone (2011) and Giacovazzo *et al.* (2011) have recently shown how to calculate the variance of a map at different stages of the phasing process.

2.2. Evolution of δ/σ with data resolution

Of practical interest is the evolution of the δ_P/σ_P ratios at different data resolutions. The ratio at the peak centre \mathbf{r} of an arbitrary k atom may be estimated with

$$\frac{\delta_P(\mathbf{r}_k)}{\sigma_P} \simeq \frac{\langle E \rangle}{(\langle E^4 \rangle - \langle E^2 \rangle^2)^{1/2}} \left(\frac{N_{\mathbf{H}}}{N} \right)^{1/2}, \quad (13)$$

which follows from equations (6) and (11) under consideration of the well known expression, $\rho(\mathbf{r}_k) = (1/N^{1/2})(N_{\mathbf{H}}/V)$. Similarly, in view of equations (9) and (12), the ratio for δ_M becomes

$$\frac{\delta_M(\mathbf{r}_k)}{\sigma_M} \simeq \frac{\langle E \rangle}{2(\langle E^2 \rangle - \langle E \rangle^2)^{1/2}} \left(\frac{N_{\mathbf{H}}}{N} \right)^{1/2}. \quad (14)$$

Since the left factors in equations (13) and (14) are both close to 1, the respective δ/σ ratios are similar.

2.3. Application of the positivity constraint

It has been shown that δ_P essentially corresponds to the $\langle E \rangle \rho$ product and that its variance, σ_P^2 , only depends on the amplitudes derived from experiment. The simplest way to impose the positivity condition on δ_P is by equating to zero all δ_P values below $\Delta = 2.5\sigma_P$. Hereafter, to distinguish between constrained and unconstrained δ_P , the former will be denoted $\delta_{P,\Delta}$. The same arguments hold for δ_M , and the corresponding constrained function will be called $\delta_{M,\Delta}$.

It is clear that the positivity condition cannot be applied to δ_P if ρ contains positive and negative scatterers. In such cases,

Table 1

Relevant parameters of δ_P (δ_M) synthesis at three different data resolutions specified by the smallest d spacing, d_{\min} .

N_H : number of reflections; σ_P (σ_M): standard deviation of the δ synthesis; δ_P (δ_M): (a) theoretical δ value at atomic positions and (b) refined value of largest δ peak; δ_P/σ_P (δ_M/σ_M): experimental ratio derived from equation (13) [equation (14)]; CC_P (CC_M): correlation coefficient computed with equation (17).

d_{\min} (Å)	N_H	σ_P (Å ⁻³)	δ_P (a)	δ_P (b)	δ_P/σ_P	CC_P
0.85	7526	0.08707	0.807	0.867 (45)	9.27	0.900 ± 2
1.00	4624	0.06559	0.501	0.565 (45)	7.64	0.893 ± 3
1.15	3050	0.05334	0.331	0.397 (36)	6.20	0.874 ± 4

d_{\min} (Å)	N_H	σ_M (Å ⁻³)	δ_M (a)	δ_M (b)	δ_M/σ_M	CC_M
0.85	7526	0.03849	0.403	0.419 (49)	10.45	0.894 ± 4
1.00	4624	0.02915	0.250	0.269 (16)	8.59	0.897 ± 3
1.15	3050	0.02360	0.165	0.194 (12)	7.01	0.875 ± 4

the possibility still exists to impose the peaked nature of ρ by equating to zero all absolute values of δ_P smaller than Δ .

3. The $S_{P'}$ ($S_{M'}$) sum function: the δ recycling method

The proposed variant of the direct methods sum function

$$S'_P = \sum_{\mathbf{H}} [E_{-\mathbf{H}} \exp(i\varphi_{-\mathbf{H}})] \int_V \delta_{P,\Delta}(\mathbf{r}) \exp(i2\pi\mathbf{H}\mathbf{r}) dV \quad (15)$$

results from replacing in S_P the $\rho\delta_P^{\text{sq}}$ product by the $\delta_{P,\Delta}$ function. Similarly to S_P or S_M , phase refinement is carried out maximizing S'_P , i.e. the angular part of the Fourier transform

Table 2

Direct phasing by δ_P and δ_M recycling of several sets of intensity data.

Inspection of the table indicates that both δ_P and δ_M recycling procedures show similar behaviour. CC_P and CC_M measure the correlation between observed and refined amplitudes. n_T specifies the trial at which the solution has been found with the elapsed time (min) in parentheses (DELL Precision PWS390 PC, Intel core CPU, 6700 @ 2.66 GHz and 2.00 GB RAM). Number of refinement cycles per trial is always 100 except for SUOA (200).

Compound code	Space group	Atoms in asymmetric unit (no H)	d_{\min} (Å)	CC_P	(δ_P) n_T (min)	CC_M	(δ_M) n_T (min)
Tval ^a	<i>P1</i>	256	0.85	0.90	1 (0.5)	0.90	1 (0)
Rubredoxin ^b	<i>P2</i> ₁	452 + 1Fe	1.00	0.88	1† (8.5)	0.88	1† (9)
Winter2 ^c	<i>P2</i> ₁	82 + 2Cl	0.84	0.88	1 (1)	0.89	1 (0.5)
Tpala ^d	<i>P2</i> ₁	39	0.85	0.87	1 (0)	0.89	1 (0.5)
Goldman2 ^e	<i>Cc</i>	56	0.76	0.90	2 (1)	0.89	3 (2.5)
Munich1 ^f	<i>C2</i>	40	0.89	0.90	26 (4.5)	0.90	13 (2.5)
App ^g	<i>C2</i>	300 + 1Zn	0.99	0.88	1† (2)	0.87	1† (3)
Hov1 ^h	<i>C2/m</i>	Pr ₇ Ni ₄ Si _{4.5}	0.78	0.88	1 (0.5)	0.90	1 (0.5)
Bed ⁱ	<i>I4</i>	34	1.00	0.88	2 (1.5)	0.90	2 (1)
Hops ^j	<i>R3</i>	27	0.84	0.90	1 (0.5)	0.90	2 (1.5)
Tur10 ^k	<i>P6</i> ₃ 22	17	0.89	0.87	1 (1)	0.89	1 (1)
Azet ^l	<i>Pca</i> 2 ₁	46 + 2Cl	1.01	0.84	1 (0.5)	0.85	1 (1)
No55 ^m	<i>Fdd</i> 2	24	0.84	0.89	1 (1)	0.86	2 (3)
Cortison ⁿ	<i>P2</i> ₁ 2 ₁ 2 ₁	26	0.89	0.89	2 (0.5)	0.90	1 (0)
Loganin ^o	<i>P2</i> ₁ 2 ₁ 2 ₁	27	0.75	0.90	4 (1)	0.90	1 (0)
Suoa ^p	<i>P2</i> ₁ 2 ₁ 2 ₁	47	0.84	0.91	28 (32)	0.90	62 (75)

† Only one trial is required to develop the structure due to the scattering power of the fixed metal atom. References: (a) Smith *et al.* (1975); (b) Sheldrick *et al.* (1993); (c) Butters *et al.* (1981); (d) Smith *et al.* (1981); (e) Irngartinger *et al.* (1981); (f) Szeimies-Seebach *et al.* (1978); (g) Glover *et al.* (1983); (h) Hovestreydt *et al.* (1983); (i) Sheldrick *et al.* (1978); (j) Jones *et al.* (1992); (k) Braekman *et al.* (1981); (l) Colens *et al.* (1974); (m) Sheldrick & Trotter (1978); (n) Declercq *et al.* (1972); (o) Jones *et al.* (1980); (p) Oliver & Strickland (1984).

$$\varphi_{\mathbf{H}}^{\text{new}} = \text{phase of } \left[\int_V \delta_{P,\Delta}(\mathbf{r}) \exp(i2\pi\mathbf{H}\mathbf{r}) dV \right] \quad (16)$$

is taken as the new phase estimate (Rius *et al.*, 2007).

The Fourier transforms can be calculated simultaneously by means of the fast Fourier transform (FFT) algorithm. However, if the atomicity condition applies, a combination of $\delta_{M,\Delta}$ peak search with subsequent structure-factor calculation constitutes a fast and efficient alternative. This second procedure is the one that has been employed in the test calculations for obtaining the new φ values. The updated Φ is then used for calculating the new $\delta_P(\Phi)$ and $\delta_{P,\Delta}(\Phi)$ syntheses. This cyclic process (δ recycling) continues until the correlation coefficient between experimental and calculated amplitudes,

$$CC = \left\{ \frac{[\sum_{\mathbf{H}} E_{\mathbf{H}} \times E_{\mathbf{H}}(\Phi)]^2}{\sum_{\mathbf{H}} E_{\mathbf{H}}^2 \times \sum_{\mathbf{H}} E_{\mathbf{H}}(\Phi)^2} \right\}^{1/2}, \quad (17)$$

indicates that convergence is reached (Fig. 1). By analogy to S'_P , the corresponding sum function based on $\delta_{M,\Delta}$,

$$S'_M = \sum_{\mathbf{H}} [E_{-\mathbf{H}} \exp(i\varphi_{-\mathbf{H}})] \int_V \delta_{M,\Delta}(\mathbf{r}) \exp(i2\pi\mathbf{H}\mathbf{r}) dV, \quad (18)$$

can be introduced, which can be maximized by applying the tangent formula

$$\varphi_{\mathbf{H}}^{\text{new}} = \text{phase of } \left[\int_V \delta_{M,\Delta}(\mathbf{r}) \exp(i2\pi\mathbf{H}\mathbf{r}) dV \right] \quad (19)$$

embedded in the δ recycling method described in Fig. 1.

4. Test calculations

In Table 1 the theoretical and experimental values of some relevant parameters of the δ_P and δ_M syntheses are compared. To this purpose MBH2, a nearly equal-atom crystal structure representing the ideal case, was selected (unit-cell contents $C_{45}H_{72}O_9$, i.e. $N = 54$; $V = 1106.2 \text{ \AA}^3$; space-group symmetry *P1*) (Poyser *et al.*, 1986). The measured single-crystal intensity data reach atomic resolution (minimum d spacing = 0.85 \AA , $N_H = 7526$ reflections) and the corresponding experimental $\langle E^4 \rangle$, $\langle E^2 \rangle$ and $\langle E \rangle$ values are 2.233, 1 and 0.871, respectively. The results listed in Table 1 confirm that:

(i) The (δ/σ) ratios decrease with decreasing data resolution. In general (δ/σ) ratios higher than 6 for P' or 7 for M' are necessary for successful δ recycling of purely organic compounds. This corresponds to a minimum d spacing of 1.15 \AA . At this resolution a slight degradation of the CC figure of merit begins to occur.

(ii) The value of δ_P is approximately two times that of δ_M at atomic peak positions.

(iii) σ_P and σ_M are related by a factor close to 2.2.

Table 2 summarizes the application of δ recycling to intensity data of several crystal structures. Rather than being an exhaustive test, the purpose of these calculations is to show the viability of δ recycling as a phasing method. For simplicity, all refinements were carried out in *P1*, although, in principle, nothing prevents us from using the space-group symmetry of the compound as a constraint. All calculations were carried out with a modified version of *XLENS* (Rius, 2011*b*) starting from random phase values. Inspection of Table 2 clearly indicates that both δ_P and δ_M recycling are efficient phasing procedures. In most cases the number of necessary trials is rather modest.

APPENDIX A

The value of δ_P at atomic positions

Let equation (4) be written in the form

$$\delta_P(\mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} \frac{E_{\mathbf{H}}^2 - \langle E^2 \rangle}{E_{\mathbf{H}}} E_{\mathbf{H}} \exp(-i2\pi\mathbf{H}\mathbf{r}). \quad (20)$$

If f_j designates the normalized scattering factor of an arbitrary j atom and if ρ_φ and P' are expressed in terms of their respective peak distributions with j, k and l going from 1 to N , then

$$\begin{aligned} \delta_P(\mathbf{r}) &= \frac{1}{V} \sum_{\mathbf{H}} \sum_j f_j(E_{\mathbf{H}})^{-1} \sum_k \sum_{l \neq k} f_k f_l \\ &\quad \times \exp[i2\pi\mathbf{H}(\mathbf{r}_j + \mathbf{r}_k - \mathbf{r}_l - \mathbf{r})] \\ &= \sum_k \frac{f_k}{V} \sum_{\mathbf{H}} (E_{\mathbf{H}})^{-1} \exp[i2\pi\mathbf{H}(\mathbf{r}_k - \mathbf{r})] \\ &\quad \times \sum_j \sum_{l \neq k} f_j f_l \exp[i2\pi\mathbf{H}(\mathbf{r}_j - \mathbf{r}_l)] \\ &= \sum_k \frac{f_k}{V} \sum_{\mathbf{H}} \exp[i2\pi\mathbf{H}(\mathbf{r}_k - \mathbf{r})] \\ &\quad \times [E_{\mathbf{H}} - f_k \exp(-i2\pi\mathbf{H}\mathbf{r}_k) \exp(i\varphi_{\mathbf{H}})]. \quad (21) \end{aligned}$$

Consequently, the δ_P value for an arbitrary \mathbf{r}_k atomic vector is given by

$$\delta_P(\mathbf{r}_k) = \frac{f_k N_{\mathbf{H}}}{V} \langle E \rangle - \frac{f_k^2}{V} \sum_{\mathbf{H}} \exp(i\varphi_{\mathbf{H}}) \exp(-i2\pi\mathbf{H}\mathbf{r}_k) \quad (22)$$

where $N_{\mathbf{H}}$ is the total number of reflections in the \mathbf{H} sum. Since it is known that the value of ρ at the location of an atomic centre is $\rho(\mathbf{r}_k) = f_k N_{\mathbf{H}}/V$, substitution of $\rho(\mathbf{r}_k)$ and $\rho_\varphi(\mathbf{r}_k)$ in equation (22) yields

$$\delta_P(\mathbf{r}_k) = \rho(\mathbf{r}_k) \langle E \rangle - f_k^2 \rho_\varphi(\mathbf{r}_k), \quad (23)$$

from which the value of δ_P at \mathbf{r}_k can be estimated.

APPENDIX B

Variance of a density function expressed as Fourier synthesis

If $\eta(\mathbf{r})$ is a real continuous density function given by the Fourier synthesis

$$\eta(\mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} C_{\mathbf{H}} \exp(i\alpha_{\mathbf{H}}) \exp(-i2\pi\mathbf{H}\mathbf{r}), \quad (24)$$

where $C_{\mathbf{H}}$ and $\alpha_{\mathbf{H}}$ are, respectively, the amplitude and associated phase of the \mathbf{H} Fourier term, the corresponding variance can be computed with the expression

$$\begin{aligned} \sigma_\eta^2 &= \frac{1}{V} \int_V \eta(\mathbf{r})^2 dV - \left[\frac{1}{V} \int_V \eta(\mathbf{r}) dV \right]^2 \\ &= I_1 - I_2^2. \quad (25) \end{aligned}$$

By Parseval's identity, integral I_1 is equal to

$$I_1 = \frac{1}{V^2} \sum_{\mathbf{H}} C_{\mathbf{H}}^2. \quad (26)$$

On the other hand, integral I_2 can be worked out to

$$I_2 = \frac{1}{V^2} \sum_{\mathbf{H}} C_{\mathbf{H}} \exp(i\alpha_{\mathbf{H}}) \int_V \exp(-i2\pi\mathbf{H}\mathbf{r}) dV, \quad (27)$$

wherein the integral vanishes for $\mathbf{H} \neq 0$ and is equal to V for $\mathbf{H} = 0$, so that

$$I_2^2 = \frac{1}{V^2} C_{\mathbf{H}=0}^2. \quad (28)$$

Finally, by making $I_1 - I_2^2$, it follows that

$$\sigma_\eta^2 = \frac{1}{V^2} \sum_{\mathbf{H} \neq 0} C_{\mathbf{H}}^2. \quad (29)$$

The variance of η is given by equation (29) and only depends on the squared amplitudes.

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