

2. RECIPROCAL SPACE IN CRYSTAL-STRUCTURE DETERMINATION

Table 2.3.1.1. Matrix representation of Patterson peaks

The $N \times N$ matrix represents the position \mathbf{u}_{ij} and weights w_{ij} of atomic interactions in a Patterson arising from N atoms at \mathbf{x}_i and weight w_i in the real cell.

	\mathbf{x}_1, w_1	\mathbf{x}_2, w_2	...	\mathbf{x}_N, w_N
\mathbf{x}_1, w_1	$\mathbf{u}_{11} = \mathbf{x}_1 - \mathbf{x}_1,$ $w_{11} = w_1^2$	$\mathbf{u}_{12} = \mathbf{x}_1 - \mathbf{x}_2,$ $w_{12} = w_1 w_2$...	$\mathbf{u}_{1N} = \mathbf{x}_1 - \mathbf{x}_N,$ $w_{1N} = w_1 w_N$
\mathbf{x}_2, w_2	$\mathbf{x}_2 - \mathbf{x}_1, w_2 w_1$	$0, w_2^2$...	$\mathbf{x}_2 - \mathbf{x}_N, w_2 w_N$
...
\mathbf{x}_N, w_N	$\mathbf{x}_N - \mathbf{x}_1, w_N w_1$	$\mathbf{x}_N - \mathbf{x}_2, w_N w_2$...	$0, w_N^2$

will affect the resolution of atomic peaks in the real cell as well as peaks in the Patterson cell. If U is the van der Waals volume per average atom, then the fraction of the cell occupied by atoms will be $f = NU/V$. Similarly, the fraction of the cell occupied by Patterson peaks will be $2UN(N-1)/V$ or $2f(N-1)$. With the reasonable assumption that $f \approx 0.1$ for a typical organic crystal, then the cell can contain at most five atoms ($N \leq 5$) for there to be no overlap, other than by coincidence, of the peaks in the Patterson. As N increases there will occur a background of peaks on which are superimposed features related to systematic properties of the structure.

The contrast of selected Patterson peaks relative to the general background level can be enhanced by a variety of techniques. For instance, the presence of heavy atoms not only enhances the size of a relatively small number of peaks but ordinarily ensures a larger separation of the peaks due to the light-atom skeleton on which the heavy atoms are hung. That is, the factor f (above) is substantially reduced. Another example is the effect of systematic atomic arrangements (e.g. α -helices or aromatic rings) resulting in multiple peaks which stand out above the background. In the isomorphous replacement method, isomorphous difference Pattersons are utilized in which the contrast of the Patterson interactions between the heavy atoms is enhanced by removal of the predominant interactions which involve the rest of the structure.

2.3.1.3. Modifications: origin removal, sharpening etc.

A. L. Patterson, in his first in-depth exposition of his newly discovered F^2 series (Patterson, 1935), introduced the major modifications to the Patterson which are still in use today. He illustrated, with one-dimensional Fourier series, the techniques of removing the Patterson origin peak, sharpening the overall function and also removing peaks due to atoms in special positions. Each one of these modifications can improve the interpretability of Pattersons, especially those of simple structures. Whereas the recommended extent of such modifications is controversial (Buerger, 1966), most studies which utilize Patterson functions do incorporate some of these techniques [see, for example, Jacobson *et al.* (1961), Braun *et al.* (1969) and Nordman (1980a)]. Since Patterson's original work, other workers have suggested that the Patterson function itself might be modified; Fourier inversion of the modified Patterson then provides a new and perhaps more tractable set of structure factors (McLachlan & Harker, 1951; Simonov, 1965; Raman, 1966; Corfield & Rosenstein, 1966). Karle & Hauptman (1964) suggested that an improved set of structure factors could be obtained from an origin-removed Patterson modified such that it was everywhere non-negative and that Patterson density values less than a bonding distance from the origin were set to zero. Nixon (1978) was successful in solving a structure which had previously resisted solution by using a set of

structure factors which had been obtained from a Patterson in which the largest peaks had been attenuated.

The N origin peaks [see expression (2.3.1.3)] may be removed from the Patterson by using coefficients

$$|\mathbf{F}_{\mathbf{h}, \text{mod}}|^2 = |\mathbf{F}_{\mathbf{h}}|^2 - \sum_{i=1}^N f_i^2.$$

A Patterson function using these modified coefficients will retain all interatomic vectors. However, the observed structure factors $\mathbf{F}_{\mathbf{h}}$ must first be placed on an absolute scale (Wilson, 1942) in order to match the scattering-factor term.

Analogous to origin removal, the vector interactions due to atoms in known positions can also be removed from the Patterson function. Patterson showed that non-origin Patterson peaks arising from known atoms 1 and 2 may be removed by using the expression

$$|\mathbf{F}_{\mathbf{h}, \text{mod}}|^2 = |\mathbf{F}_{\mathbf{h}}|^2 - \sum_{i=1}^N f_i^2 t_i^2 - 2f_1 f_2 t_1 t_2 \cos 2\pi \mathbf{h} \cdot (\mathbf{x}_1 - \mathbf{x}_2),$$

where \mathbf{x}_1 and \mathbf{x}_2 are the positions of atoms 1 and 2 and t_1 and t_2 are their respective thermal correction factors. Using one-dimensional Fourier series, Patterson illustrated how interactions due to known atoms can obscure other information.

Patterson also introduced a means by which the peaks in a Patterson function may be artificially sharpened. He considered the effect of thermal motion on the broadening of electron-density peaks and consequently their Patterson peaks. He suggested that the F^2 coefficients could be corrected for thermal effects by simulating the atoms as point scatterers and proposed using a modified set of coefficients

$$|\mathbf{F}_{\mathbf{h}, \text{sharp}}|^2 = |\mathbf{F}_{\mathbf{h}}|^2 / \bar{f}^2,$$

where \bar{f} , the average scattering factor per electron, is given by

$$\bar{f} = \sum_{i=1}^N f_i / \sum_{i=1}^N Z_i.$$

A common formulation for this type of sharpening expresses the atomic scattering factors at a given angle in terms of an overall isotropic thermal parameter B as

$$f(s) = f_0 \exp(-Bs^2).$$

The Patterson coefficients then become

$$\mathbf{F}_{\mathbf{h}, \text{sharp}} = \frac{Z_{\text{total}}}{\sum_{i=1}^N f(s)} \mathbf{F}_{\mathbf{h}}.$$

The normalized structure factors, E (see Chapter 2.2), which are used in crystallographic direct methods, are also a common source of sharpened Patterson coefficients ($E^2 - 1$). Although the centre positions and total contents of Patterson peaks are unaltered by sharpening, the resolution of individual peaks may be enhanced. The degree of sharpening can be controlled by adjusting the size of the assumed B factor; Lipson & Cochran (1966, pp. 165–170) analysed the effect of such a choice on Patterson peak shape.

All methods of sharpening Patterson coefficients aim at producing a point atomic representation of the unit cell. In this quest, the high-resolution terms are enhanced (Fig. 2.3.1.1). Unfortunately, this procedure must also produce a serious Fourier truncation error which will be seen as large ripples about each Patterson peak (Gibbs, 1898). Consequently, various techniques have been used (mostly unsuccessfully) in an attempt to balance the advantages of sharpening with the disadvantages of truncation errors.

Schomaker and Shoemaker [unpublished; see Lipson & Cochran (1966, p. 168)] used a function

2.3. PATTERSON AND MOLECULAR-REPLACEMENT TECHNIQUES

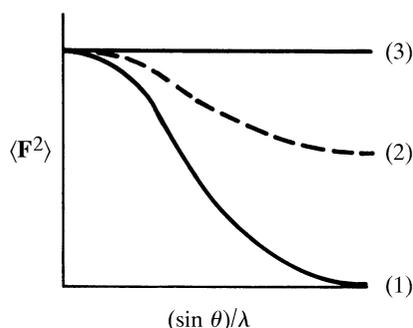


Fig. 2.3.1.1. Effect of 'sharpening' Patterson coefficients. (1) shows a mean distribution of $\langle F^2 \rangle$ values with resolution, $(\sin \theta)/\lambda$. The normal decline of this curve is due to increasing destructive interference between different portions within diffuse atoms at larger Bragg angles. (2) shows the distribution of 'sharpened' coefficients. (3) shows the theoretical distribution of $\langle F^2 \rangle$ produced by a point-atom structure. To represent such a structure with a Fourier series would require an infinite series in order to avoid large errors caused by truncation.

$$|\mathbf{F}_{h, \text{sharp}}|^2 = \frac{|\mathbf{F}_h|^2}{f^2} s^2 \exp\left[-\frac{\pi^2}{p} s^2\right],$$

in which s is the length of the scattering vector, to produce a Patterson synthesis which is less sensitive to errors in the low-order terms. Jacobson *et al.* (1961) used a similar function,

$$|\mathbf{F}_{h, \text{sharp}}|^2 = \frac{|\mathbf{F}_h|^2}{f^2} (k + s^2) \exp\left[-\frac{\pi}{p} s^2\right],$$

which they rationalize as the sum of a scaled exponentially sharpened Patterson and a gradient Patterson function (the value of k was empirically chosen as $\frac{2}{3}$). This approach was subsequently further developed and generalized by Wunderlich (1965).

2.3.1.4. Homometric structures and the uniqueness of structure solutions; enantiomorphic solutions

Interpretation of any Patterson requires some assumption, such as the existence of discrete atoms. A complete interpretation might also require an assumption of the number of atoms and may require other external information (*e.g.* bond lengths, bond angles, van der Waals separations, hydrogen bonding, positive density *etc.*). To what extent is the solution of a Patterson function unique? Clearly the greater is the supply of external information, the fewer will be the number of possible solutions. Other constraints on the significance of a Patterson include the error involved in measuring the observed coefficients and the resolution limit to which they have been observed. The larger the error, the larger the number of solutions. When the error on the amplitudes is infinite, it is only the other physical constraints, such as packing, which limit the structural solutions. Alternative solutions of the same Patterson are known as homometric structures.

During their investigation of the mineral bixbyite, Pauling & Shappell (1930) made the disturbing observation that there were two solutions to the structure, with different arrangements of atoms, which yielded the same set of calculated intensities. Specifically, atoms occupying equipoint set $24d$ in space group $I(2_1/a)\bar{3}$ can be placed at either $x, 0, \frac{1}{4}$ or $-x, 0, \frac{1}{4}$ without changing the calculated intensities. Yet the two structures were not chemically equivalent. These authors resolved the ambiguity by placing the oxygen atoms in question at positions which gave the most acceptable bonding distances with the rest of the structure.

Patterson interpreted the above ambiguity in terms of the F^2 series: the distance vector sets or Patterson functions of the two structures were the same since each yielded the same calculated intensities (Patterson, 1939). He defined such a pair of structures a homometric pair and called the degenerate vector set which they produced a homometric set. Patterson went on to investigate the likelihood of occurrence of homometric structures and, indeed, devoted a great deal of his time to this matter. He also developed algebraic formalisms for examining the occurrence of homometric pairs and multiplets in selected one-dimensional sets of points, such as cyclotomic sets, and also sets of points along a line (Patterson, 1944). Some simple homometric pairs are illustrated in Fig. 2.3.1.2.

Drawing heavily from Patterson's inquiries into the structural uniqueness allowed by the diffraction data, Hosemann, Bagchi and others have given formal definitions of the different types of homometric structures (Hosemann & Bagchi, 1954). They suggested a classification divided into pseudohomometric structures and homomorphs, and used an integral equation representing a convolution operation to express their examples of finite homometric structures. Other workers have chosen various means for describing homometric structures [Buerger (1959, pp. 41–50), Menzer (1949), Bullough (1961, 1964), Hoppe (1962)].

Since a Patterson function is centrosymmetric, the Pattersons of a crystal structure and of its mirror image are identical. Thus the enantiomeric ambiguity present in noncentrosymmetric crystal structures cannot be overcome by using the Patterson alone and represents a special case of homometric structures. Assignment of the correct enantiomorph in a crystal structure analysis is generally not possible unless a recognizable fragment of known chirality emerges (*e.g.* L-amino acids in proteins, D-ribose in nucleic acids, the known framework of steroids and other natural products, the right-handed twist of α -helices, the left-handed twist of successive strands in a β -sheet, the fold of a known protein subunit *etc.*) or anomalous-scattering information is available and can be used to resolve the ambiguity (Bijvoet *et al.*, 1951).

It is frequently necessary to select arbitrarily one enantiomorph over another in the early stages of a structure solution. Structure-factor phases calculated from a single heavy atom in space group $P1$, $P2$ or $P2_1$ (for instance) will be centrosymmetric and both enantiomorphs will be present in Fourier calculations based on these phases. In other space groups (*e.g.* $P2_12_12_1$), the selected heavy atom is likely to be near one of the planes containing the 2_1 axes and thus produce a weaker 'ghost' image of the opposite enantiomorph. The mixture of the two overlapped enantiomorphic solutions can cause interpretive difficulties. As the structure solution progresses, the 'ghosts' are exorcized owing to the dominance of the chosen enantiomorph in the phases.

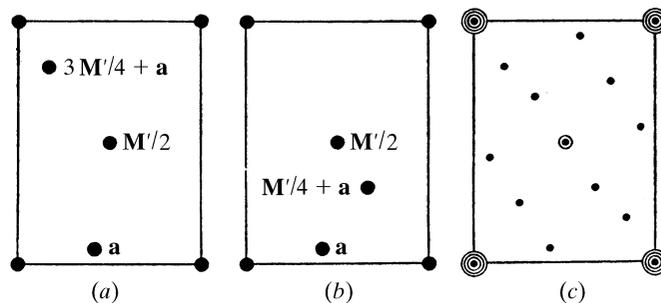


Fig. 2.3.1.2. (c) The point Patterson of the two homometric structures in (a) and (b). The latter are constructed by taking points at \mathbf{a} and $\frac{1}{2}\mathbf{M}'$, where \mathbf{M}' is a cell diagonal, and adding a third point which is (a) at $\frac{3}{4}\mathbf{M}' + \mathbf{a}$ or (b) at $\frac{1}{4}\mathbf{M}' + \mathbf{a}$. [Reprinted with permission from Patterson (1944).]