

2. RECIPROCAL SPACE IN CRYSTAL-STRUCTURE DETERMINATION

Table 2.3.2.3. Position of Harker sections within a Patterson

Symmetry element	Form of $P(x, y, z)$
(a) Harker planes	
Axes parallel to the b axis:	
(i) 2, 3, $\bar{3}$, 4, $\bar{4}$, 6, $\bar{6}$	$P(x, 0, z)$
(ii) 2 ₁ , 4 ₂ , 6 ₃	$P(x, \frac{1}{2}, z)$
(iii) 3 ₁ , 3 ₂ , 6 ₂ , 6 ₄	$P(x, \frac{1}{3}, z)$
(iv) 4 ₁ , 4 ₃	$P(x, \frac{1}{4}, z)$
(v) 6 ₁ , 6 ₅	$P(x, \frac{1}{6}, z)$
(b) Harker lines	
Planes perpendicular to the b axis:	
(i) Reflection planes	$P(0, y, 0)$
(ii) Glide plane, glide = $\frac{1}{2}a$	$P(\frac{1}{2}, y, 0)$
(iii) Glide plane, glide = $\frac{1}{2}c$	$P(0, y, \frac{1}{2})$
(iv) Glide plane, glide = $\frac{1}{2}(a + c)$	$P(\frac{1}{2}, y, \frac{1}{2})$
(v) Glide plane, glide = $\frac{1}{4}(a + c)$	$P(\frac{1}{4}, y, \frac{1}{4})$
(vi) Glide plane, glide = $\frac{1}{4}(3a + c)$	$P(\frac{3}{4}, y, \frac{1}{4})$
(c) Special Harker planes	
Axes parallel to or containing body diagonal (111), valid for cubic space groups only:	
Equation of plane $lx + my + nz - p = 0$	
(i) 3	$l = m = n = \cos 54.73561^\circ = 0.57735$ $p = 0$
(ii) 3 ₁	$l = m = n = \cos 54.73561^\circ = 0.57735$ $p = \sqrt{3}/3$
Rhombohedral threefold axes produce analogous Harker planes whose description will depend on the interaxial angle.	

quality of the data. A useful rule of thumb is that the ratio

$$r = \frac{\sum_{\text{heavy}} Z^2}{\sum_{\text{light}} Z^2}$$

should be near unity if the heavy atom is to provide useful starting phase information (Z is the atomic number of an atom). The condition that $r > 1$ normally guarantees interpretability of the Patterson function in terms of the heavy-atom positions. This 'rule', arising from the work of Luzzati (1953), Woolfson (1956), Sim (1961) and others, is not inviolable; many ambitious determinations have been accomplished *via* the heavy-atom method for which r was well below 1.0. An outstanding example is vitamin B₁₂ with formula C₆₂H₈₈CoO₁₄P, which gave an $r = 0.14$ for the cobalt atom alone (Hodgkin *et al.*, 1957). One factor contributing to the success of such a determination is that the relative scattering power of Co is enhanced for higher scattering angles. Thus, the ratio, r , provides a conservative estimate. If the value of r is well above 1.0, the initial easier interpretation of the Patterson will come at the expense of poorly defined parameters of the lighter atoms.

A general strategy for determining heavy atoms from the Patterson usually involves the following steps.

- (1) List the number and type of atoms in the cell.
- (2) Construct the interaction matrix for the heaviest atoms to predict the positions and weights of the largest Patterson vectors. Group recurrent vectors and notice vectors with special properties, such as Harker vectors.

(3) Compute the Patterson using any desired modifications. Placing the map on an absolute scale [$P(000) = \sum Z^2$] is convenient but not necessary.

(4) Examine Harker sections and derive trial atom coordinates from vector positions.

(5) Check the trial coordinates using other vectors in the predicted set. Correlate enantiomorphic choice and origin choice for independent sites.

(6) Include the next-heaviest atoms in the interpretation if possible. In particular, use the cross-vectors with the heaviest atoms.

(7) Use the best heavy-atom model to initiate phasing.

Detailed and instructive examples of using Pattersons to find heavy-atom positions are found in almost every textbook on crystal structure analysis [see, for example, Buerger (1959), Lipson & Cochran (1966) and Stout & Jensen (1968)].

The determination of the crystal structure of cholesteryl iodide by Carlisle & Crowfoot (1945) provides an example of using the Patterson function to locate heavy atoms. There were two molecules, each of formula C₂₇H₄₅I, in the $P2_1$ unit cell. The ratio $r = 2.8$ is clearly well over the optimal value of unity. The $P(x, z)$ Patterson projection showed one dominant peak at $\langle 0.434, 0.084 \rangle$ in the asymmetric unit. The equivalent positions for $P2_1$ require that an iodine atom at x_1, y_1, z_1 generates another at $-x_1, \frac{1}{2} + y_1, z_1$ and thus produces a Patterson peak at $\langle 2x_1, \frac{1}{2}, 2z_1 \rangle$. The iodine position was therefore determined as 0.217, 0.042. The y coordinate of the iodine is arbitrary for $P2_1$ yet the value of $y_1 = 0.25$ is convenient, since an inversion centre in the two-atom iodine structure is then exactly at the origin, making all calculated phases 0 or π . Although the presence of this extra symmetry caused some initial difficulties in the interpretation of the steroid backbone, Carlisle and Crowfoot successfully separated the enantiomorphic images. Owing to the presence of the perhaps *too heavy* iodine atom, however, the structure of the carbon skeleton could not be defined very precisely. Nevertheless, all critical stereochemical details were adequately illuminated by this determination. In the cholesteryl iodide example, a number of different yet equivalent origins could have been selected. Alternative origin choices include all combinations of $x \pm \frac{1}{2}$ and $z \pm \frac{1}{2}$.

A further example of using the Patterson to find heavy atoms will be provided in Section 2.3.5.2 on solving for heavy atoms in the presence of noncrystallographic symmetry.

2.3.2.4. Superposition methods. Image detection

As early as 1939, Wrinch (1939) showed that it was possible, in principle, to recover a fundamental set of points from the vector map of that set. Unlike the Harker–Buerger implication theory (Buerger, 1946), the method that Wrinch suggested was capable of using all the vectors in a three-dimensional set, not those restricted to special lines or sections. Wrinch's ideas were developed for vector sets of points, however, and could not be directly applied to real, heavily overlapped Pattersons of a complex structure. These ideas seem to have lain dormant until the early 1950s when a number of independent investigators developed superposition methods (Bevers & Robertson, 1950; Clastre & Gay, 1950; Garrido, 1950a; Buerger, 1950a).

A Patterson can be considered as a sum of images of a molecule as seen, in turn, for each atom placed on the origin (Fig. 2.3.2.3). Thus, the deconvolution of a Patterson could proceed by superimposing each image of the molecule obtained onto the others by translating the Patterson origin to each imaging atom. For instance, let us take a molecule consisting of four atoms $ABCD$ arranged in the form of a quadrilateral (Fig. 2.3.2.3). Then the Patterson consists of the images of four identical quadrilaterals with atoms A, B, C and D placed on the origin in turn. The Pattersons can then be

2.3. PATTERSON AND MOLECULAR-REPLACEMENT TECHNIQUES

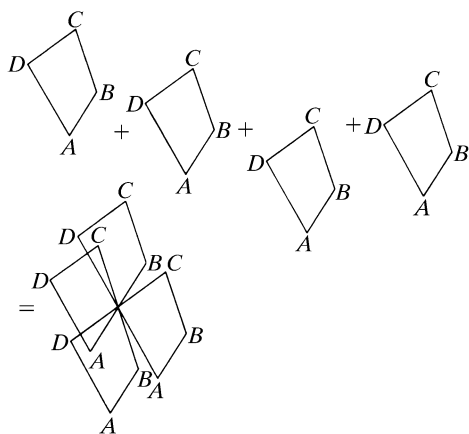


Fig. 2.3.2.3. Atoms $ABCD$, arranged as a quadrilateral, generate a Patterson which is the sum of the images of the quadrilateral when each atom is placed on the origin in turn.

deconvoluted by superimposing two of these Pattersons after translating these (without rotation) by, for instance, the vector \mathbf{AB} . A further improvement could be obtained by superimposing a third Patterson translated by \mathbf{AC} . This would have the additional advantage in that ABC is a noncentrosymmetric arrangement and, therefore, selects the enantiomorph corresponding to the hand of the atomic arrangement ABC [cf. Buerger (1951, 1959)].

A basic problem is that knowledge of the vectors \mathbf{AB} and \mathbf{AC} also implies some knowledge of the structure at a time when the structure is not yet known. In practice 'good-looking' peaks, estimated to be single peaks by assessing the absolute scale of the structure amplitudes with Wilson statistics, can be assumed to be the result of single interatomic vectors within a molecule. Superposition can then proceed and the result can be inspected for reasonable chemical sense. As many apparently single peaks can be tried systematically using a computer, this technique is useful for selecting and testing a series of reasonable Patterson interpretations (Jacobson *et al.*, 1961).

Three major methods have been used for the detection of molecular images of superimposed Pattersons. These are the sum, product and minimum 'image seeking' functions (Raman & Lipscomb, 1961). The concept of the sum function is to add the images where they superimpose, whereas elsewhere the summed Pattersons will have a lower value owing to lack of image superposition. Therefore, the sum function determines the average Patterson density for superimposed images, and is represented analytically as

$$S(\mathbf{x}) = \sum_{i=1}^N P(\mathbf{x} + \mathbf{u}_i),$$

where $S(\mathbf{x})$ is the sum function at \mathbf{x} given by the superposition of the i th Patterson translated by \mathbf{u}_i , or

$$S(\mathbf{x}) = \sum_{\mathbf{h}} \left\{ F_{\mathbf{h}}^2 \exp(2\pi i \mathbf{h} \cdot \mathbf{x}) \left[\sum_{i=1}^N \exp(2\pi i \mathbf{h} \cdot \mathbf{u}_i) \right] \right\}.$$

Setting

$$m \exp(i\varphi_{\mathbf{h}}) = \sum_{i=1}^N \exp(2\pi i \mathbf{h} \cdot \mathbf{u}_i)$$

(m and $\varphi_{\mathbf{h}}$ can be calculated from the translational vectors used for the superposition),

$$S(\mathbf{x}) = \sum_{\mathbf{h}} F_{\mathbf{h}}^2 m \exp(2\pi i \mathbf{h} \cdot \mathbf{x} + \varphi_{\mathbf{h}}).$$

Thus, the sum function is equivalent to a weighted 'heavy atom' method based on the known atoms assumed by the superposition translation vectors.

The product function is somewhat more vigorous in that the images are enhanced by the product. If an image is superimposed on no image, then the product should be zero.

The product function can be expressed as

$$Pr(\mathbf{x}) = \prod_{i=1}^N P(\mathbf{x} + \mathbf{u}_i).$$

When $N = 2$ (\mathbf{h} and \mathbf{p} are sets of Miller indices),

$$Pr(\mathbf{x}) = \sum_{\mathbf{h}} \sum_{\mathbf{p}} F_{\mathbf{h}}^2 F_{\mathbf{p}}^2 \exp[2\pi i (\mathbf{h} + \mathbf{p}) \cdot \mathbf{x}] \\ \times \exp[2\pi i (\mathbf{h} \cdot \mathbf{u}_1 + \mathbf{p} \cdot \mathbf{u}_2)].$$

Successive superpositions using the product functions will quickly be dominated by a few terms with very large coefficients.

Finally, the minimum function is a clever invention of Buerger (Buerger, 1950b, 1951, 1953a,b,c; Taylor, 1953; Rogers, 1951). If a superposition is correct then each Patterson must represent an image of the structure. Whenever there are two or more images that intersect in the Patterson, the Patterson density will be greater than a single image. When two different images are superimposed, it is a reasonable hope that at least one of these is a single image. Thus by taking the value of that Patterson which is the minimum, it should be possible to select a single image and eliminate noise from interfering images as far as possible. Although the minimum function is perhaps the most powerful algorithm for image selection of well sharpened Pattersons, it is not readily amenable to Fourier representation.

The minimum function was conceived on the basis of selecting positive images on a near-zero background. If it were desired to select negative images [*e.g.* the $(\mathbf{F}_1 - \mathbf{F}_2)^2$ correlation function discussed in Section 2.3.3.4], then it would be necessary to use a maximum function. In fact, normally, an image has finite volume with varying density. Thus, some modification of the minimum function is necessary in those cases where the image is large compared to the volume of the unit cell, as in low-resolution protein structures (Rossmann, 1961b). Nordman (1966) used the average of the Patterson values of the lowest 10 to 20 per cent of the vectors in comparing Pattersons with hypothetical point Pattersons. A similar criterion was used by High & Kraut (1966).

Image-seeking methods using Patterson superposition have been used extensively (Beevers & Robertson, 1950; Garrido, 1950b; Robertson, 1951). For a review the reader is referred to *Vector Space* (Buerger, 1959) and a paper by Fridrichsons & Mathieson (1962). However, with the advent of computerized direct methods (see Chapter 2.2), such techniques are no longer popular. Nevertheless, they provide the conceptual framework for the rotation and translation functions (see Sections 2.3.6 and 2.3.7).

2.3.2.5. Systematic computerized Patterson vector-search procedures. Looking for rigid bodies

The power of the modern digital computer has enabled rapid access to the large number of Patterson density values which can serve as a lookup table for systematic vector-search procedures. In the late 1950s, investigators began to use systematic searches for the placement of single atoms, of known chemical groups or fragments and of entire known structures. Methods for locating single atoms were developed and called variously: vector verification (Mighell & Jacobson, 1963), symmetry minimum function (Kraut, 1961; Simpson *et al.*, 1965; Corfield & Rosenstein, 1966) and consistency functions (Hamilton, 1965). Patterson superposition techniques using stored function values were often used to image the structure