2. RECIPROCAL SPACE IN CRYSTAL-STRUCTURE DETERMINATION

equivalent to a Patterson with coefficients $|\mathbf{F''_h}(H)|^2$ which is proportional to $|\mathbf{F_h}(H)|^2$. Such a Patterson (Rossmann, 1961a) will have vectors between all anomalous scatterers with heights proportional to the number of anomalous electrons $\Delta f''$. This 'anomalous dispersion' Patterson function has been used to find anomalous scatterers such as iron (Smith *et al.*, 1983; Strahs & Kraut, 1968) and sulfur atoms (Hendrickson & Teeter, 1981).

It is then apparent that a Patterson with coefficients

$$\Delta F^2_{\mathrm{ANO}} = (|\mathbf{F_h}| - |\mathbf{F_{\bar h}}|)^2$$

(Rossmann, 1961a), as well as a Patterson with coefficients

$$\Delta F^2_{\mathrm{ISO}} = (|\mathbf{F}_{NH}| - |\mathbf{F}_H|)^2$$

(Rossmann, 1960; Blow, 1958), represent Pattersons of the heavy atoms. The $\Delta F^2_{\mathrm{ANO}}$ Patterson suffers from errors which may be larger than the size of the Bijvoet differences, while the $\Delta F^2_{\mathrm{ISO}}$ Patterson may suffer from partial lack of isomorphism. Hence, Kartha & Parthasarathy (1965) have suggested the use of the sum of these two Pattersons, which would then have coefficients $(\Delta F^2_{\mathrm{ANO}} + \Delta F^2_{\mathrm{ISO}})$.

However, given both SIR and anomalous-dispersion data, it is possible to make an accurate estimate of the $|\mathbf{F}_H|^2$ magnitudes for use in a Patterson calculation [Blundell & Johnson (1976, p. 340), Matthews (1966), Singh & Ramaseshan (1966)]. In essence, the Harker phase diagram can be constructed out of three circles: the native amplitude and each of the two isomorphous Bijvoet differences, giving three circles in all (Blow & Rossmann, 1961) which should intersect at a single point thus resolving the ambiguity in the SIR data and the anomalous-dispersion data. Furthermore, the phase ambiguities are orthogonal; thus the two data sets are cooperative. It can be shown (Matthews, 1966; North, 1965) that

$$F^2_N = F^2_{NH} + F^2_N \mp \frac{2}{k}(16k^2 F^2_P F^2_H - \Delta I^2)^{1/2},$$

where $\Delta I = F^{+}_{NH}{}^2 - F^{-}_{NH}{}^2$ and $k = \Delta f''/f'$. The sign in the third-term expression is $-$ when $|(\alpha_{NH} - \alpha_H)| < \pi/2$ or $+$ otherwise. Since, in general, $|\mathbf{F}_H|$ is small compared to $|\mathbf{F}_N|$, it is reasonable to assume that the sign above is usually negative. Hence, the heavy-atom lower estimate (HLE) is usually written as

$$F^2_{\mathrm{HLE}} = F^2_{NH} + F^2_H - \frac{2}{k}(16k^2 F^2_P F^2_H - \Delta I^2)^{1/2},$$

which is an expression frequently used to derive Patterson coefficients useful in the determination of heavy-atom positions when both SIR and anomalous-dispersion data are available.

2.3.5. Noncrystallographic symmetry

2.3.5.1. *Definitions*

The interpretation of Pattersons can be helped by using various types of chemical or physical information. An obvious example is the knowledge that one or two heavy atoms per crystallographic asymmetric unit are present. Another example is the exploitation of a rigid chemical framework in a portion of a molecule (Nordman & Nakatsu, 1963; Burnett & Rossmann, 1971). One extremely useful constraint on the interpretation of Pattersons is noncrystallographic symmetry. Indeed, the structural solution of large biological assemblies such as viruses is only possible because of the natural occurrence of this phenomenon. The term 'molecular replacement' is used for methods that utilize noncrystallographic symmetry in the solution of structures [for earlier reviews see Rossmann (1972) and Argos & Rossmann (1980)]. These methods, which are only partially dependent on Patterson concepts, are discussed in Sections 2.3.6–2.3.8.

Crystallographic symmetry applies to the whole of the three-dimensional crystal lattice. Hence, the symmetry must be expressed both in the lattice and in the repeating pattern within the lattice. In contrast, noncrystallographic symmetry is valid only within a limited volume about the noncrystallographic symmetry element. For instance, the noncrystallographic twofold axes in the plane of the paper of Fig. 2.3.5.1 are true only in the immediate vicinity of each local dyad. In contrast, the crystallographic twofold axes perpendicular to the plane of the paper (Fig. 2.3.5.1) apply to every point within the lattice. Two types of noncrystallographic symmetry can be recognized: proper and improper rotations. A proper symmetry element is independent of the sense of rotation, as, for example, a fivefold axis in an icosahedral virus; a rotation either left or right by one-fifth of a revolution will leave all parts of a given icosahedral shell (but not the whole crystal) in equivalent positions. Proper noncrystallographic symmetry can also be recognized by the existence of a closed point group within a defined volume of the lattice. Improper rotation axes are found when two molecules are arbitrarily oriented relative to each other in the same asymmetric unit or when they occur in two entirely different crystal lattices. For instance, in Fig. 2.3.5.2, the object A_1B_1 can be rotated by $+\theta$ about the axis at P to orient it identically with A_2B_2. However, the two objects will not be coincident after a rotation of A_1B_1 by $-\theta$ or of A_2B_2 by $+\theta$. The envelope around each noncrystallographic object must be known in order to define an improper rotation. In contrast, only the volume about the closed point group need be defined for proper noncrystallographic operations. Hence, the boundaries of the repeating unit need not correspond to chemically covalently linked units in the presence of proper rotations.

Translational components of noncrystallographic rotation elements are said to be 'precise' in a direction parallel to the axis and
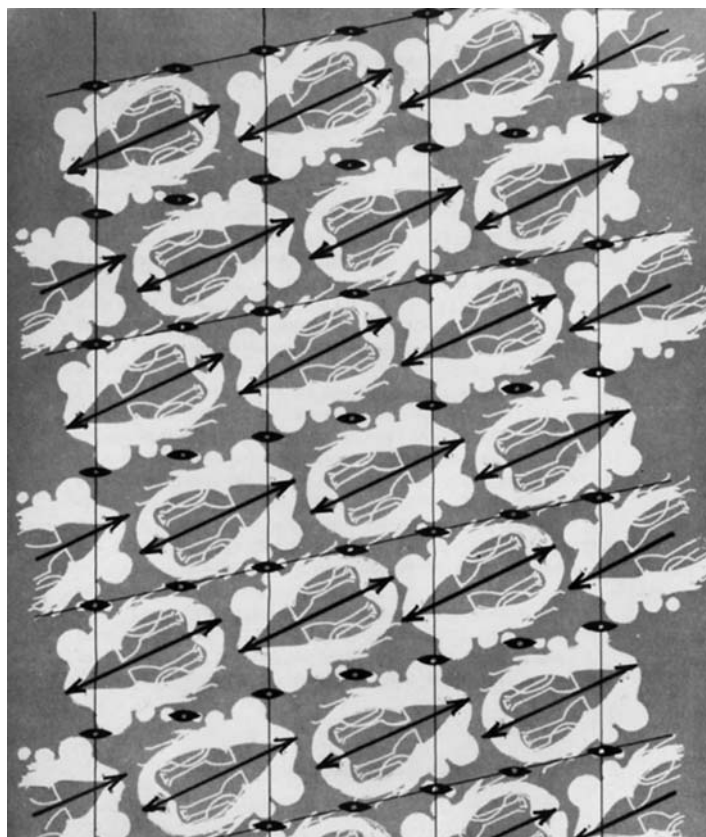

Fig. 2.3.5.1. The two-dimensional periodic design shows crystallographic twofold axes perpendicular to the page and local noncrystallographic rotation axes in the plane of the paper (design by Audrey Rossmann). [Reprinted with permission from Rossmann (1972, p. 8).]

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