1.3. FOURIER TRANSFORMS IN CRYSTALLOGRAPHY

The explicitly three-dimensional approach to the factorization of the DFT and the use of symmetry offers the possibility of richer and more versatile data structures. For instance, the use of 'decimation in frequency' in real space and of 'decimation in time' in reciprocal space leads to data structures in which real-space coordinates are handled by blocks (thus preserving, at least locally, the three-dimensional topological connectivity of the maps) while reciprocal-space indices are handled by parity classes or their generalizations for factors other than 2 (thus making the treatment of centred lattices extremely easy). This global three-dimensional indexing also makes it possible to carry symmetry and multiplicity characteristics for each subvector of intermediate results for the purpose of automating the use of the orbit exchange mechanism.

Brünger (1989) has described the use of a similar three-dimensional factoring technique in the context of structure-factor calculations for the refinement of macromolecular structures.

1.3.4.4. Basic crystallographic computations

1.3.4.4.1. Introduction

Fourier transform (FT) calculations play an indispensable role in crystallography, because the Fourier transformation is inherent in the diffraction phenomenon itself.

Besides this obligatory use, the FT has numerous other applications, motivated more often by its mathematical properties than by direct physical reasoning (although the latter can be supplied after the fact). Typically, many crystallographic computations turn out to be convolutions in disguise, which can be speeded up by orders of magnitude through a judicious use of the FT. Several recent advances in crystallographic computation have been based on this kind of observation.

1.3.4.4.2. Fourier synthesis of electron-density maps

Bragg (1929) was the first to use this type of calculation to assist structure determination. Progress in computing techniques since that time was reviewed in Section 1.3.4.3.1.

The usefulness of the maps thus obtained can be adversely affected by three main factors:
(i) limited resolution;
(ii) errors in the data;
(iii) computational errors.

Limited resolution causes 'series-termination errors' first investigated by Bragg & West (1930), who used an optical analogy with the numerical aperture of a microscope. James (1948*b*) gave a quantitative description of this phenomenon as a convolution with the 'spherical Dirichlet kernel' (Section 1.3.4.2.1.3), which reflects the truncation of the Fourier spectrum by multiplication with the indicator function of the limiting resolution sphere. Bragg & West (1930) suggested that the resulting ripples might be diminished by applying an artificial temperature factor to the data, which performs a further convolution with a Gaussian point-spread function. When the electron-density map is to be used for model refinement, van Reijen (1942) suggested using Fourier coefficients calculated from the model when no observation is available, as a means of combating series-termination effects.

Errors in the data introduce errors in the electron-density maps, with the same mean-square value by virtue of Parseval's theorem. Special positions accrue larger errors (Cruickshank & Rollett, 1953; Cruickshank, 1965*a*). To minimize the mean-square electron-density error due to large phase uncertainties, Blow & Crick (1959) introduced the 'best Fourier' which uses centroid Fourier coefficients; the associated error level in the electron-density map was evaluated by Blow & Crick (1959) and Dickerson *et al.* (1961*a,b*).

Computational errors used to be a serious concern when Beevers–Lipson strips were used, and Cochran (1948*a*) carried out a critical evaluation of the accuracy limitations imposed by strip methods. Nowadays, the FFT algorithm implemented on digital computers with a word size of at least 32 bits gives results accurate to six decimal places or better in most applications (see Gentleman & Sande, 1966).

1.3.4.4.3. Fourier analysis of modified electron-density maps

Various approaches to the phase problem are based on certain modifications of the electron-density map, followed by Fourier analysis of the modified map and extraction of phase information from the resulting Fourier coefficients.

1.3.4.4.3.1. Squaring

Sayre (1952*a*) derived his 'squaring method equation' for structures consisting of equal, resolved and spherically symmetric atoms by observing that squaring such an electron density is equivalent merely to sharpening each atom into its square. Thus

$$F_{\mathbf{h}} = \theta_{\mathbf{h}} \sum_{\mathbf{k}} F_{\mathbf{k}} F_{\mathbf{h}-\mathbf{k}},$$

where $\theta_{\mathbf{h}} = f(\mathbf{h})/f^{\mathrm{sq}}(\mathbf{h})$ is the ratio between the form factor $f(\mathbf{h})$ common to all the atoms and the form factor $f^{\mathrm{sq}}(\mathbf{h})$ for the squared version of that atom.

Most of the central results of direct methods, such as the tangent formula, are an immediate consequence of Sayre's equation. Phase refinement for a macromolecule by enforcement of the squaring method equation was demonstrated by Sayre (1972, 1974).

1.3.4.4.3.2. Other nonlinear operations

A category of phase improvement procedures known as 'density modification' is based on the pointwise application of various quadratic or cubic 'filters' to electron-density maps after removal of negative regions (Hoppe & Gassmann, 1968; Hoppe *et al.*, 1970; Barrett & Zwick, 1971; Gassmann & Zechmeister, 1972; Collins, 1975; Collins *et al.*, 1976; Gassmann, 1976). These operations are claimed to be equivalent to reciprocal-space phase-refinement techniques such as those based on the tangent formula. Indeed the replacement of

$$\rho(\mathbf{x}) = \sum_{\mathbf{h}} F_{\mathbf{h}} \exp(-2\pi i \mathbf{h} \cdot \mathbf{x})$$

by $P[\rho(\mathbf{x})]$, where P is a polynomial

$$P(\rho) = a_0 + a_1 \rho + a_2 \rho^2 + a_3 \rho^3 + \dots$$

yields

$$P[\rho(\mathbf{x})] = a_0 + \sum_{\mathbf{h}} \left[a_1 F_{\mathbf{h}} + a_2 \sum_{\mathbf{k}} F_{\mathbf{k}} F_{\mathbf{h}-\mathbf{k}} \right.$$
$$\left. + a_3 \sum_{\mathbf{k}} \sum_{\mathbf{l}} F_{\mathbf{k}} F_{\mathbf{l}} F_{\mathbf{h}-\mathbf{k}-\mathbf{l}} + \dots \right] \exp(-2\pi i \mathbf{h} \cdot \mathbf{x})$$

and hence gives rise to the convolution-like families of terms encountered in direct methods. This equivalence, however, has been shown to be rather superficial (Bricogne, 1982) because the 'uncertainty principle' embodied in Heisenberg's inequality (Section 1.3.2.4.4.3) imposes severe limitations on the effectiveness of any procedure which operates *pointwise* in *both* real and reciprocal space.

In applying such methods, sampling considerations must be given close attention. If the spectrum of ρ extends to resolution Δ and if the pointwise nonlinear filter involves a polynomial P of

references