

2. RECIPROCAL SPACE IN CRYSTAL-STRUCTURE DETERMINATION

larger amount of computing time required by the technique as compared to that required by the tangent formula.

(6) *Tangent techniques using simultaneously triplets, quartets, . . .*

The availability of a large number of phase relationships, in particular during the first stages of a direct procedure, makes the phasing process easier. However, quartets are sums of two triplets with a common reflection. If the phase of this reflection (and/or of the other cross terms) is known then the quartet probability formulae described in Section 2.2.5.5 cannot hold. Similar considerations may be made for quintet relationships. Thus triplet, quartet and quintet formulae described in the preceding paragraphs, if used without modifications, will certainly introduce systematic errors in the tangent refinement process.

A method which takes into account correlation between triplets and quartets has been described (Giacovazzo, 1980c) [see also Freer & Gilmore (1980) for a first application], according to which

$$\tan \varphi_h \simeq \frac{\sum_k G \sin(\varphi_k + \varphi_{h-k}) - \sum_{k,l} G' \sin(\varphi_k + \varphi_l + \varphi_{h-k-l})}{\sum_k G \cos(\varphi_k + \varphi_{h-k}) - \sum_{k,l} G' \cos(\varphi_k + \varphi_l + \varphi_{h-k-l})},$$

where G' takes into account both the magnitudes of the cross terms of the quartet and the fact that their phases may be known.

(7) *Integration of Patterson techniques and direct methods (Egert & Sheldrick, 1985) [see also Egert (1983, and references therein)]*

A fragment of known geometry is oriented in the unit cell by real-space Patterson rotation search (see Chapter 2.3) and its position is found by application of a translation function (see Section 2.2.5.4 and Chapter 2.3) or by maximizing the weighted sum of the cosines of a small number of strong translation-sensitive triple phase invariants, starting from random positions. Suitable FOMs rank the most reliable solutions.

(8) *Maximum entropy methods*

A common starting point for all direct methods is a stochastic process according to which crystal structures are thought of as being generated by randomly placing atoms in the asymmetric unit of the unit cell according to some *a priori* distribution. A non-uniform prior distribution of atoms $p(\mathbf{r})$ gives rise to a source of random atomic positions with entropy (Jaynes, 1957)

$$H(p) = - \int_V p(\mathbf{r}) \log p(\mathbf{r}) \, d\mathbf{r}.$$

The maximum value $H_{\max} = \log V$ is reached for a uniform prior $p(\mathbf{r}) = 1/V$.

The strength of the restrictions introduced by $p(\mathbf{r})$ is not measured by $H(p)$ but by $H(p) - H_{\max}$, given by

$$H(p) - H_{\max} = - \int_V p(\mathbf{r}) \log [p(\mathbf{r})/m(\mathbf{r})] \, d\mathbf{r},$$

where $m(\mathbf{r}) = 1/V$. Accordingly, if a prior prejudice $m(\mathbf{r})$ exists, which maximizes H , the revised relative entropy is

$$S(p) = - \int_V p(\mathbf{r}) \log [p(\mathbf{r})/m(\mathbf{r})] \, d\mathbf{r}.$$

The maximization problem was solved by Jaynes (1957). If $G_j(p)$ are linear constraint functionals defined by given constraint functions $C_j(\mathbf{r})$ and constraint values c_j , *i.e.*

$$G_j(p) = \int_V p(\mathbf{r}) C_j(\mathbf{r}) \, d\mathbf{r} = c_j,$$

the most unbiased probability density $p(\mathbf{r})$ under prior prejudice $m(\mathbf{r})$ is obtained by maximizing the entropy of $p(\mathbf{r})$ relative to $m(\mathbf{r})$. A standard variational technique suggests that the constrained maximization is equivalent to the unconstrained maximization of the functional

$$S(p) + \sum_j \lambda_j G_j(p),$$

where the λ_j 's are Lagrange multipliers whose values can be determined from the constraints.

Such a technique has been applied to the problem of finding good electron-density maps in different ways by various authors (Wilkins *et al.*, 1983; Bricogne, 1984; Navaza, 1985; Navaza *et al.*, 1983).

Maximum entropy methods are strictly connected with traditional direct methods: in particular it has been shown that:

(a) the maximum determinant rule (see Section 2.2.5.7) is strictly connected (Britten & Collins, 1982; Piro, 1983; Narayan & Nityananda, 1982; Bricogne, 1984);

(b) the construction of conditional probability distributions of structure factors amounts precisely to a reciprocal-space evaluation of the entropy functional $S(p)$ (Bricogne, 1984).

Maximum entropy methods are under strong development: important contributions can be expected in the near future even if a multipurpose robust program has not yet been written.

2.2.9. Some references to direct-methods packages

Some references for direct-methods packages are given below. Other useful packages using symbolic addition or multisolution procedures do exist but are not well documented.

CRUNCH: Gelder, R. de, de Graaff, R. A. G. & Schenk, H. (1993). *Automatic determination of crystal structures using Karle-Hauptman matrices*. *Acta Cryst.* **A49**, 287–293.

DIRDIF: Beurskens, P. T., Beurskens G., de Gelder, R., Garcia-Granda, S., Gould, R. O., Israel, R. & Smits, J. M. M. (1999). *The DIRDIF-99 program system*. Crystallography Laboratory, University of Nijmegen, The Netherlands.

MITHRIL: Gilmore, C. J. (1984). *MITHRIL. An integrated direct-methods computer program*. *J. Appl. Cryst.* **17**, 42–46.

MULTAN88: Main, P., Fiske, S. J., Germain, G., Hull, S. E., Declercq, J.-P., Lessinger, L. & Woolfson, M. M. (1999). *Crystallographic software: teXsan for Windows*. <http://www.msc.com/brochures/teXsan/wintex.html>.

PATSEE: Egert, E. & Sheldrick, G. M. (1985). *Search for a fragment of known geometry by integrated Patterson and direct methods*. *Acta Cryst.* **A41**, 262–268.

SAPI: Fan, H.-F. (1999). *Crystallographic software: teXsan for Windows*. <http://www.msc.com/brochures/teXsan/wintex.html>.

SnB: Weeks, C. M. & Miller, R. (1999). *The design and implementation of SnB version 2.0*. *J. Appl. Cryst.* **32**, 120–124.

SHELX97: Sheldrick, G. M. (2000a). *The SHELX home page*. <http://shelx.uni-ac.gwdg.de/SHELX/>.

SHELXS: Sheldrick, G. M. (2000b). *SHELX*. <http://www.ucg.ie/cryst/shelx.htm>.

SIR97: Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *SIR97: a new tool for crystal structure determination and refinement*. *J. Appl. Cryst.* **32**, 115–119.

XTAL3.6.1: Hall, S. R., du Boulay, D. J. & Olthof-Hazekamp, R. (1999). *Xtal3.6 crystallographic software*. <http://www.crystal.uwa.edu.au/Crystal/xtal>.