

1.6. METHODS OF SPACE-GROUP DETERMINATION

Table 1.6.4.30Reflection conditions and possible space groups with Bravais lattice cF and Laue class $m\bar{3}m$; hkl are permutable; Patterson symmetry $Fm\bar{3}m$

Reflection conditions				Space group		Space group		Space group	
hkl	$0kl$	$h \pm hl$	$h00$	group	No.	group	No.	group	No.
$h+k, h+l, k+l$	k, l	$h+l$	h	F432	209	$F\bar{4}3m$	216	$Fm\bar{3}m$	225
$h+k, h+l, k+l$	k, l	$h+l$	$h=4n$	F4₁32	210				
$h+k, h+l, k+l$	k, l	h, l	h	$F\bar{4}3c$	219	$Fm\bar{3}c$	226		
$h+k, h+l, k+l$	$k+l=4n; k, l$	$h+l$	$h=4n$	$Fd\bar{3}m$	227				
$h+k, h+l, k+l$	$k+l=4n; k, l$	h, l	$h=4n$	$Fd\bar{3}c$	228				

and have not yet enjoyed widespread distribution, use and acceptance by the community. Flack *et al.* (2011) and Parsons *et al.* (2012) give detailed information on these calculations.

1.6.5.1.2. Status of centrosymmetry and resonant scattering

The basic starting point in this analysis is the following linear transformation of $|F(hkl)|^2$ and $|F(\bar{h}\bar{k}\bar{l})|^2$, applicable to both observed and model values, to give the average (A) and difference (D) intensities:

$$A(hkl) = \frac{1}{2}[|F(hkl)|^2 + |F(\bar{h}\bar{k}\bar{l})|^2],$$

$$D(hkl) = |F(hkl)|^2 - |F(\bar{h}\bar{k}\bar{l})|^2.$$

In equation (1.6.2.1), $A(hkl)$ was denoted by $|F_{av}(hkl)|^2$. The expression for $D(hkl)$ corresponding to that for $A(hkl)$ given in equation (1.6.2.1) and using the same nomenclature is

$$D(\mathbf{h}) = \sum_{i,j} [(f_i + f'_i)f''_j - (f_j + f'_j)f''_i] \sin[2\pi\mathbf{h}(\mathbf{r}_i - \mathbf{r}_j)].$$

In general $|D(hkl)|$ is small compared to $A(hkl)$. A compound with an appreciable resonant-scattering contribution has $|D(hkl)| \approx 0.01A(hkl)$, whereas a compound with a small resonant-scattering contribution has $|D(hkl)| \approx 0.0001A(hkl)$. For centric reflections, $D_{\text{model}} = 0$, and so the values of $D_{\text{obs}}(hkl)$ of these are entirely due to random uncertainties and systematic errors in the intensity measurements. $D_{\text{obs}}(hkl)$ of acentric reflections contains contributions both from the random uncertainties and the systematic errors of the data measurements, and from the differences between $|F(hkl)|^2$ and $|F(\bar{h}\bar{k}\bar{l})|^2$ which arise through the effect of resonant scattering. A slight experimental limitation is that a data set of intensities needs to contain both reflections hkl and $\bar{h}\bar{k}\bar{l}$ in order to obtain $A_{\text{obs}}(hkl)$ and $D_{\text{obs}}(hkl)$.

The Bijvoet ratio, defined by

$$\chi = \frac{\langle D^2 \rangle^{1/2}}{\langle A \rangle},$$

is the ratio of the root-mean-square value of D to the mean value of A . In a structure analysis, two independent estimates of the Bijvoet ratio are available and their comparison leads to useful information as to whether the crystal structure is centrosymmetric or not.

The first estimate arises from considerations of intensity statistics leading to the definition of the Bijvoet ratio as a value called $\text{Friedif}_{\text{stat}}$, whose functional form was derived by Flack & Shmueli (2007) and Shmueli & Flack (2009). One needs only to know the chemical composition of the compound and the

wavelength of the X-radiation to calculate $\text{Friedif}_{\text{stat}}$ using various available software.

The second estimate of the Bijvoet ratio, $\text{Friedif}_{\text{obs}}$, is obtained from the observed diffraction intensities. One problematic point in the evaluation of $\text{Friedif}_{\text{obs}}$ arises because A and D do not have the same dependence on $\sin\theta/\lambda$ and it is necessary to eliminate this difference as far as possible. A second problematic point in the calculation is to make sure that only acentric reflections of any of the noncentrosymmetric point groups in the chosen Laue class are selected for the calculation of $\text{Friedif}_{\text{obs}}$. In this way one is sure that if the point group of the crystal is centrosymmetric, all of the chosen reflections are centric, and if the point group of the crystal is noncentrosymmetric, all of the chosen reflections are acentric. The necessary selection is achieved by taking only those reflections that are general in the Laue group. To date (2015), the calculation of $\text{Friedif}_{\text{obs}}$ is not available in distributed software. On comparison of $\text{Friedif}_{\text{stat}}$ with $\text{Friedif}_{\text{obs}}$, one is able to state with some confidence that:

- (1) if $\text{Friedif}_{\text{obs}}$ is much lower than $\text{Friedif}_{\text{stat}}$, then the crystal structure is either centrosymmetric, and random uncertainties and systematic errors in the data set are minor, or noncentrosymmetric with the crystal twinned by inversion in a proportion close to 50:50;
- (2) if $\text{Friedif}_{\text{obs}}$ is close in value to $\text{Friedif}_{\text{stat}}$, then the crystal is probably noncentrosymmetric and random uncertainties and systematic errors in the data set are minor. However, data from a centrosymmetric crystal with large random uncertainties and systematic errors may also produce this result; and
- (3) if $\text{Friedif}_{\text{obs}}$ is much larger than $\text{Friedif}_{\text{stat}}$ then either the data set is dominated by random uncertainties and systematic errors or the chemical formula is erroneous.

Example 1

The crystal of compound Ex1 (Udupa & Krebs, 1979) is known to be centrosymmetric (space group $P2_1/c$) and has a significant resonant-scattering contribution, $\text{Friedif}_{\text{stat}} = 498$ and $\text{Friedif}_{\text{obs}} = 164$. The comparison of $\text{Friedif}_{\text{stat}}$ and $\text{Friedif}_{\text{obs}}$ indicates that the crystal structure is centrosymmetric.

Example 2

The crystal of compound Ex2, potassium hydrogen (2R,3R) tartrate, is known to be enantiomerically pure and appears in space group $P2_12_12_1$. The value of $\text{Friedif}_{\text{obs}}$ is 217 compared to a $\text{Friedif}_{\text{stat}}$ value of 174. The agreement is good and allows the deduction that the crystal is neither centrosymmetric, nor twinned by inversion in a proportion near to 50:50, nor that the

1. INTRODUCTION TO SPACE-GROUP SYMMETRY

Table 1.6.5.1

R_{merge} values for Ex2 for the 589 sets of general reflections of mmm which have all eight measurements in the set

R_{merge} (%)	mmm	$2mm$	$m2m$	$mm2$	222
R_A	1.30	1.30	1.30	1.30	1.30
R_D	100.0	254.4	235.7	258.1	82.9

data set is unsatisfactorily dominated by random uncertainty and systematic error.

Example 3

The crystals of compound Ex3 (Zhu & Jiang, 2007) occur in Laue group $\bar{1}$. One finds $\text{Friedif}_{\text{stat}} = 70$ and $\text{Friedif}_{\text{obs}} = 499$. The huge discrepancy between the two shows that the observed values of D are dominated by random uncertainty and systematic error.

1.6.5.1.3. Resolution of noncentrosymmetric ambiguities

It was shown in Section 1.6.5.1.2 that under certain circumstances it is possible to determine whether or not the space group of the crystal investigated is centrosymmetric. Suppose that the space group was found to be noncentrosymmetric. In each Laue class, there is one centrosymmetric point group and one or more noncentrosymmetric point groups. For example, in the Laue class mmm we need to distinguish between the point groups 222, $2mm$, $m2m$ and $mm2$, and of course between the space groups based on them. We shall show that it is possible in practice to distinguish between these noncentrosymmetric point groups using intensity differences between Friedel opposites caused by resonant scattering.

An excellent intensity data set from a crystal (Ex2 above) of potassium hydrogen ($2R$, $3R$) tartrate, measured with a wavelength of 0.7469 Å at 100 K, was used. The Laue group was assumed to be mmm . The raw data set was initially merged and averaged in point group 1 and all special reflections of the Laue group mmm (i.e. $0kl$, $h0l$, $hk0$, $h00$, $0k0$, $00l$) were set aside. The remaining data were organized into sets of reflections symmetry-equivalent under the Laue group mmm , and only those sets (589 in all) containing all 8 of the mmm -symmetry-equivalent reflections were retained. Each of these sets provides 4 A_{obs} and 4 D_{obs} values which can be used to calculate R_{merge} values appropriate to the five point groups in the Laue class mmm . The results are given in Table 1.6.5.1. The value of 100% for R_{merge} in a centrosymmetric point group, such as mmm or $2/m$, arises by definition and not by coincidence. The R_D of the true point group has the lowest value, which is noticeably different from the other choices of point group.

The crystal of Ex1 above (space group $P2_1/c$) was treated in a similar manner. Table 1.6.5.2 shows that R_D values display no preference between the three point groups in Laue class $2/m$.

Intensity measurements comprising a full sphere of reflections are essential to the success of the R_{merge} tests described in this section.

1.6.5.1.4. Data evaluation after structure refinement

There is an excellent way in which to evaluate both data measurement and treatment procedures, and the fit of the model to the data, including the space-group assignment, at the completion of structure refinement. This technique is applicable both to noncentrosymmetric and to centrosymmetric crystals. A scattergram of D_{obs} against D_{model} , and $2A_{\text{obs}}$ against $2A_{\text{model}}$

Table 1.6.5.2

R_{merge} values for Ex1 for the 724 sets of general reflections of $2/m$ which have all four measurements in the set

R_{merge} (%)	$2/m$	m	2
R_A	1.29	1.29	1.29
R_D	100.0	98.3	101.7

pairs are plotted on the same graph. All (D_{obs} , D_{model}) pairs are plotted together with those ($2A_{\text{obs}}$, $2A_{\text{model}}$) pairs which have $2A_{\text{obs}} < |D_{\text{obs}}|_{\text{max}}$. The range of values on the axes of the model and of the observed values should be identical. For acentric reflections, for both A and D , a good fit of the observed to the model quantities shows itself as a straight line of slope 1 passing through the origin, with some scatter about this ideal straight line. For an individual reflection, $2A$ and D are, respectively, the sum and the difference of the same quantities and they have identical standard uncertainties. It is thus natural to select $2A$ and D to plot on the same graph. In practice one sees that the spread of the $2A$ plot increases with increasing value of $2A$. Fig. 1.6.5.1 shows the $2AD$ plot for Ex2 of Example 2 in Section 1.6.5.1.2, which is most satisfactory and confirms the choice of point group from the use of R_{merge} . The conventional R value for all reflections is 3.1% and for those shown in Fig. 1.6.5.1 it is 10.4%. The R value for all D values is good at 51.1%. Fig. 1.6.5.2 shows the $2AD$ plot for Ex1 of Example 1 in Section 1.6.5.1.2. The structure model is centrosymmetric so all D_{model} values are zero. The conventional R value on A for all reflections is 4.3% and for those shown in Fig. 1.6.5.2 it is 9.1%. The R value on all the D values is 100%.

1.6.5.2. Space-group determination in macromolecular crystallography

For macromolecular crystallography, succinct descriptions of space-group determination have been given by Kabsch (2010a,b, 2012) and Evans (2006, 2011). Two characteristics of macromolecular crystals give rise to variations on the small-molecule procedures described above.

The first characteristic is the large size of the unit cell of macromolecular crystals and the variation of the cell dimensions from one crystal to another. This makes the determination of the Bravais lattice by cell reduction problematic, as small changes of cell dimensions give rise to differences in the assignment. Kabsch (2010a,b, 2012) uses a ‘quality index’ from each of Niggli’s 44 lattice characters to come to a best choice. Grosse-Kunstleve *et al.* (2004) and Sauter *et al.* (2004) have found that some commonly used methods to determine the Bravais lattice are susceptible to numerical instability, making it possible for high-symmetry Bravais lattice types to be improperly identified. Sauter *et al.* (2004, 2006) find from practical experience that a deviation δ as high as 1.4° from perfect alignment of direct and reciprocal lattice rows must be allowed to construct the highest-symmetry Bravais type consistent with the data. Evans (2006) uses a value of 3.0° . The large unit-cell size also gives rise to a large number of reflections in the asymmetric region of reciprocal space, and taken with the tendency of macromolecular crystals to decompose in the X-ray beam, full-sphere data sets are uncommon. This means that confirmation of the Laue class by means of values of R_{int} (R_{merge}) are rarer than with small-molecule crystallography, although Kabsch (2010b) does use a ‘redundancy-independent R factor’. Evans (2006, 2011) describes methods very similar to those given as the second stage in Section 1.6.2.1. The conclusion of Sauter *et al.* (2006) and Evans (2006) is that R_{int} values as high