

13. MOLECULAR REPLACEMENT

13.1. Noncrystallographic symmetry

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13.1.1. Introduction

Excellent reviews of noncrystallographic symmetry exist. The subject is also discussed in Volume B of this series (Rossmann & Arnold, 2001). Other important reviews include those by Rossmann (1990), Lawrence (1991) and Rossmann (1995). A volume produced for a Daresbury Study Weekend (Dodson *et al.*, 1992) has many interesting chapters.

In this introductory chapter, effort has been made to cite some of the earliest work which initiated the methods which have now become familiar.

13.1.2. Definition of noncrystallographic symmetry

13.1.2.1. Standard noncrystallographic symmetry

The standard cases of noncrystallographic symmetry arise when *there is more than one similar subunit in the crystallographic asymmetric unit*.

The phrase 'noncrystallographic symmetry' is used because the operation required to superimpose one subunit on another is similar to a symmetry operation, but it operates only over a local volume, and the symmetry is inexact because the subunits are in different environments.

The 'subunit' can be a molecular aggregate, a single molecule, a monomer unit of an oligomeric molecule, or a fragment of a molecule.

The word 'similar' is used because protein subunits in different environments are never identical. At the very least, surface side chains are differently ordered, and solvation is different because of different interactions with adjacent subunits.

If noncrystallographic symmetry exists, methods are available to define the operation required to superimpose one unit on another (Rossmann & Blow, 1962; Rossmann *et al.*, 1964). When this has been done, new information is available to improve the accuracy of structural results (Rossmann & Blow, 1963).

Table 13.1.2.1 presents different types of symmetry situations which may arise when noncrystallographic symmetry exists. It is frequently observed that the local symmetry corresponds or

approximates to point-group symmetry. This arises very often because a natural molecular form is a symmetric oligomer whose symmetry is not fully expressed in the crystal symmetry [cases (1) and (3)]. Helical symmetry or pseudo-helical symmetry is also common [case (2)], especially in biological materials, but it cannot always be exploited crystallographically because the specimens are often noncrystalline fibres.

13.1.2.2. Generalized noncrystallographic symmetry

Crystallographic methods similar to those which exploit standard noncrystallographic symmetry can often be applied to a more general situation, where *similar subunits exist in different crystals* (Scouloudi, 1969; Tollin, 1969) or *where the structure of a subunit is already predictable* (Hoppe, 1957; Lattman & Love, 1970). The types of relationship which may arise are summarized in the right-hand column of Table 13.1.2.1.

13.1.2.3. Exploitation of noncrystallographic symmetry

In order to draw structural information from noncrystallographic symmetry, the different classes of subunit must provide different information. Cases of pseudo-crystallographic symmetry, where subunits are *almost* in an arrangement of higher crystallographic symmetry, are difficult to exploit by the techniques discussed in this chapter. Typically only weak reflections (those which would be forbidden by the higher symmetry if it were exact) provide extra information. This situation often arises in case (6), Table 13.1.2.1. Similarly in cases (7) and (8), comparison of crystals whose cell dimensions or contents are only slightly altered gives little new information.

13.1.3. Use of the Patterson function to interpret noncrystallographic symmetry

13.1.3.1. Rotation operations

The first step towards identifying and exploiting noncrystallographic symmetry is to find the operation that is required to

Table 13.1.2.1. *Noncrystallographic symmetry in crystals*

| | Relationships within the same crystal | Relationships between different crystals |
|---------------------------------|--|--|
| Symmetry relations | (1) Symmetry of a noncrystallographic point group (<i>e.g.</i> 532) (2) Infinite non-closed symmetry (helix) (3) Crystallographic point-group symmetry, not incorporated into lattice | (6) Simple crystallographic relationship between two crystal forms |
| Relations not forming a group | (4) Similar subunits without systematic relationship | (7) Polymorphism (identical molecules crystallize differently) |
| Partial structural relationship | (5) Similar subunits account for only a part of unit-cell contents | (8) Crystals of different but similar molecules (9) Crystals containing similar molecules, with other scattering material |