

## 13. MOLECULAR REPLACEMENT

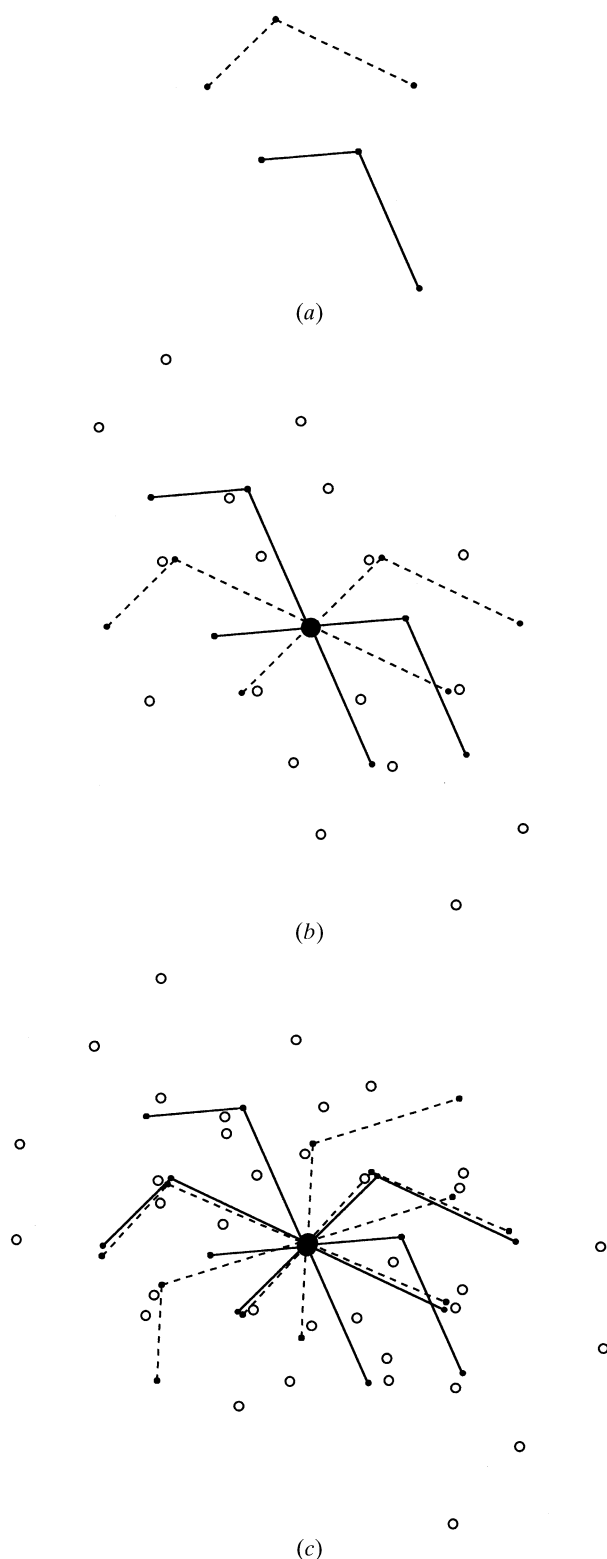


Fig. 13.1.3.1. (a) A dimer in which the two subunits are related by arbitrary rotation and translation. One member of the dimer is indicated by dashed lines joining its atoms. (b) The vector set representing the Patterson function of this dimer. The intra-subunit vectors of each subunit are indicated by filled circles linked by lines; the inter-subunit vectors are shown as open circles. (c) A second copy of the Patterson function has been rotated over the original. Intra-subunit vectors of the original Patterson function are indicated by full lines; the rotated intra-subunit vectors are distinguished by dashed lines. The rotation is almost the same as the rotation of one subunit to make it parallel to the other. When the rotation is exactly correct, half of the intra-subunit vectors of one Patterson will superimpose onto the other. None of the inter-subunit vectors superimpose.

superimpose one subunit upon another. Superposition of one asymmetric rigid body upon a similar one requires in general that it be rotated and translated. A general rotation in three-dimensional space requires three variables to specify it: these can be the latitude and longitude of a rotation axis and the angle of rotation ( $\kappa, \psi, \varphi$ ), or they can be the Euler angles. These rotational systems are presented in *IT B* (Rossmann & Arnold, 2001) and are discussed in detail in Chapter 13.2 by Navaza. Similarly, a general three-dimensional translation is specified by three variables. The operation to superimpose subunits therefore requires six variables to define it. Surveys or searches in six-dimensional functions are overwhelmingly laborious, though they have long been possible (Milledge, 1962; Kayushina & Vainshtein, 1965) and are now becoming easier (Kissinger *et al.*, 1999; Sheriff *et al.*, 1999).

The Patterson function, a function directly calculable from observed diffraction intensities, is a function which defines its own origin. Being a function in vector space, its origin is necessarily at a point representing a vector of zero length. It is this special property of the Patterson function which allows its use to factorize the six-dimensional problem into two three-dimensional ones. It is available without information about the phases of the diffraction data. Even when structural data are available, it is usually easier to make a three-dimensional rotation search based on the Patterson function than to carry out a full six-dimensional search using the known structure.

The Patterson function of a crystal may be considered to have two components: vectors between scattering centres in the same subunit, and those between different subunits. The intra-subunit vectors are necessarily shorter than the maximum subunit dimension. Inter-subunit vectors, though a few may be short, are clustered about the distances separating different subunits in the crystal, so they are mostly of the magnitude of the subunit dimensions or longer. By considering the region closer to the origin of the Patterson function, it is possible to include a high proportion of intra-subunit vectors.

Fig. 13.1.3.1 shows how the relation between the set of intra-subunit vectors of one subunit and the intra-subunit vectors of a similar subunit defines a rotation operation. This rotation is identical to the rotational part of the operation required to superimpose the subunits. If the whole Patterson function is rotated in this way, and then superimposed upon itself, one set of intermolecular vectors of the rotated Patterson function is superimposed upon a set of intermolecular vectors of the original (Fig. 13.1.3.1c). The self-rotation function (Rossmann & Blow, 1962) searches for correlations between a rotated Patterson function and the original.

By working with Patterson-function vectors, there is no dependence on the relative positions of the two subunits. Relative rotations can be determined in the standard case (Rossmann & Blow, 1962) or in the generalized case (Prothero & Rossmann, 1964; Lattman & Love, 1970). Methods for using the Patterson function to identify the rotation operation are detailed in Chapter 13.2.

## 13.1.3.2. Translation operations

When the rotation operation has been identified, the translation between the two differently oriented subunits needs to be determined (see Chapter 13.3 by Tong). The translation can only be defined in relation to an assigned origin of the subunit. It is possible to define the translation vector relative to the 'centres of gravity' (more precisely, the centres of scattering density) of the subunits. In this way, a translation may be defined between subunits of unknown structure. This approach, based only on information in the Patterson function, is the only available method if no phase information is available, but has several difficulties – it only applies