

## Space group determination

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Crystal symmetry is an abstract concept that is applied to experimental data. 65 space groups compatible with chiral crystal lattices in which macromolecules are usually crystallized are determined in a hierarchical manner. During data processing, a metric symmetry that provides 14 possible Bravais lattices is selected and merging will select one of 24 possible Patterson symmetries. However, the symmetry of diffraction intensities may not follow the metric symmetry, which may represent accidental coincidences of unit cell parameters.

The determination of space group symmetry requires analysis of systematic absences, which may arise from screw axes but may also be a consequence of lattice centering or of non-crystallographic pseudo-symmetry. To determine whether the screw axis is present along an analyzed direction, one needs to measure a subset of reflections and check whether the pattern of intensities is consistent with the presence of the selected symmetry element. The interpretation of such systematic absences is always uncertain, as sometimes the intensity measurements needed for such analysis are missing, or are affected by non-Bragg scattering, which leads to absent reflections with non-zero intensity. In some cases, the presence of pseudotranslational symmetry may generate misleading patterns. For enantiomorphic space groups and the space group pair  $I222$  and  $I2_12_12_1$ , one cannot determine the space group symmetry during scaling and merging. For this reason, space group determination is concluded only after successful phasing in one of the possible symmetries.

However, even in the case of approximate (broken) symmetries, the best choice of how to proceed is often not obvious. Non-intuitively, choosing higher symmetry is often advantageous for multiple reasons and this applies to finding substructures, phase extension, molecular replacement, and model-building and deposit.

I will discuss how to determine symmetry and how to make an informed decision in difficult cases.