Maximum likelihood refinement of Macromolecular structures against data from twinned crystals

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Twinning is a crystal growth phenomenon where two or more individual crystal exists together. Usually (but not always) it happens when lattice symmetry is higher than that of crystal. As a result two or more crystals contribute to the intensities of Bragg reflections.
Analysis of the PDB (Lebedev et al, 2006) shows that there is a non-negligible number of cases when twinning have not been noticed. It usually happens when non-crystallographic symmetry is close to twinning symmetry. Although on average neglecting twinning do not seem to affect electron density interpretation, there are number of cases where it may have resulted some model inaccuracies. These analyses show that it is necessary to implement an automatic procedure to deal with this type of crystal peculiarities.
In this talk an automatic procedure to recognise and refine twinning will be presented. The procedure consists of the following steps: 1) Automatic recognition of twinning operators; 2) Reorganisation of the experimental data to take into account the relation between twin related reflections; 3) Building a joint conditional probability distribution (that is proportional to the likelihood function) of intensities of reflections related by twin operators given the model parameters; 4) Multidimensional integration to calculate derivatives of the likelihood function with respect to individual atomic (positional, thermal and occupancy) and overall parameters; 6) Refinement using these derivatives; 7) Calculation of map coefficients that are the expected values of unknown complex structure factors from a single crystal.
The developed data organisation is able to account for such cases as split crystals, (non-)merohedral twinning, unmerged intensities.. Calculations of derivatives of the likelihood function and “best” electron density map coefficients require multidimensional (currently maximum 48) integration. The integration is considerable speeded up by employing Laplace approximation. Twinning will be available in future REFMAC (Murshudov et al, 1997) versions.
It seems the developed data organisation and likelihood function could further be generalised and adapted for refinement against data produced by powder diffraction techniques.

Lebedev AA, Vagin AA, Murshudov GN “Intensity statistics in twinned crystals with examples from the PDB” Acta Crystallographica D62: 83-95;2006
Murshudov GN, Vagin AA, Lebedev A, Wilson KS, Dodson EJ. Efficient anisotropic refinement of macromolecular structures using FFT. *Acta Cryst*. 1999;D55:247-255