

## DO 'STANDARD' DIRECT METHODS STILL HAVE A ROLE TO PLAY IN XRPD STRUCTURE DETERMINATION OF MOLECULAR SOLIDS?

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Direct methods (DM) are an extremely powerful and reliable way of solving crystal structures when high-resolution single-crystal X-ray diffraction data are available. In the case of X-ray powder diffraction (XRPD), they are, in general, much less successful because of the well-known limitations of the diffraction data. As such, they have been somewhat eclipsed the global optimisation methods now widely implemented in programs such as FOX, DASH, Powdersolve and Topas, although DM continue to develop apace in the form of the EXPO suite. Nevertheless, when an accurate and complete set of structure factors is available to near atomic resolution, DM remain the methods of choice for structure determination, as they do not require *a-priori* knowledge of chemical connectivity. The challenge for XRPD is in obtaining such a dataset and we have recently been investigating the use of differential thermal expansion (DTE) to collect more 'single-crystal-like' diffraction data collected from powder samples both in the laboratory and at beamline ID31 at the ESRF.

This presentation will show the advantages and limitations of experiments designed to produce 'single-crystal-like' data using XRPD and will address amongst other things:

- practical problems in implementing DTE, especially at the synchrotron where sample degradation in the beam can be a severe impediment to long data collections
- problems in processing the diffraction data to yield a single set of structure factors and quantification of the improvement in the quality of the resultant structure factors
- the use of standard DM packages (i.e. SHELXS-97 and SIR-92) in solving structures from the DTE-derived structure factors

It will also draw comparisons between the DM and global optimisation approaches and highlight their respective relevance to structure determination of pharmaceuticals.