# Predicting X-ray diffuse scattering from translation-libration-screw structural ensembles

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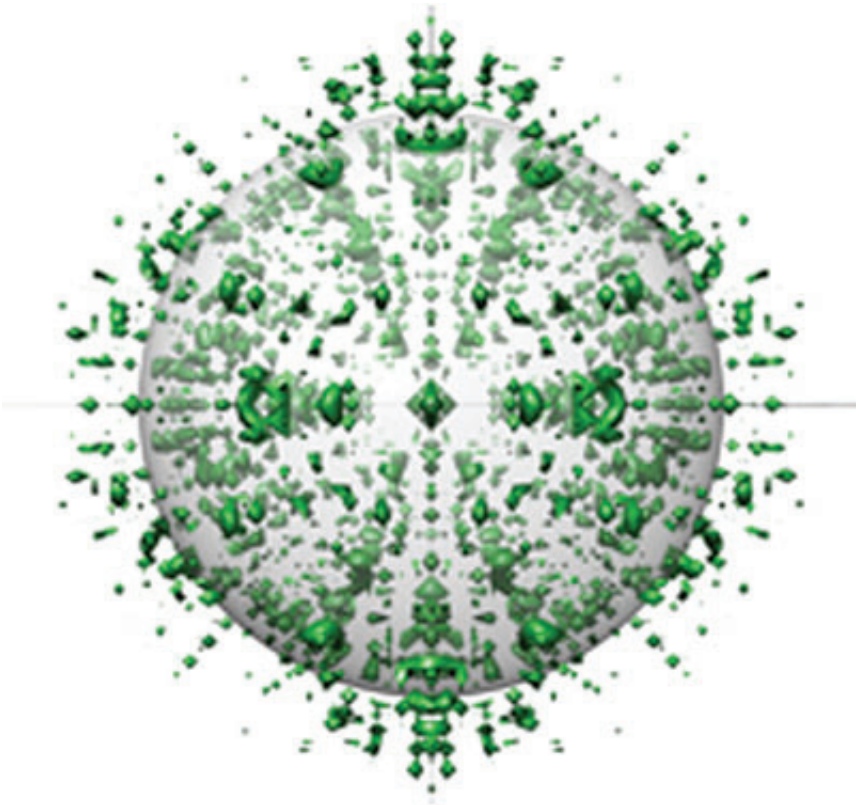

Diffuse scattering pattern. Credit: Van Benschoten et al.

Protein flexibility is essential for enzymatic turnover, signalling regulation and protein-protein interactions. The motions enabling these functions vary in length from a few angstroms to many nanometres and

include transitions between side-chain rotamers, loop openings and closings, and rigid-body subunit rotations. Multiple crystal structures are routinely compared to identify these motions and to derive hypotheses about the role of correlated motions in executing protein function. However, if only a single crystal form is available, evidence of concerted motion must be extracted from the spread in the electron density. Diffuse X-ray scattering can help by reporting on correlated atomic displacements. Although recent technological advances are increasing the potential to accurately measure diffuse scattering, computational modelling and validation tools are still needed to quantify the agreement between experimental data and different parameterizations of crystalline disorder. A new tool, phenix.diffuse, addresses this need by calculating diffuse scattering from Protein Data Bank (PDB)-formatted structural ensembles.

With the increasing availability of modelling tools, the lack of high-quality three dimensional data sets is now a key bottleneck in diffuse scattering analysis. One challenge in data collection is that long X-ray exposures can be required to reveal diffuse features. This can lead to blooming around saturated Bragg spots in diffraction images collected using commercially available charge-coupled device (CCD) area detectors, which in turn can interfere with accurate diffuse intensity measurements. Blooming can be mitigated either by reconfiguring some of the charge collection elements in each pixel as a drain to channel away excess charge (an option not currently available in commercial detectors), or by breaking single long exposures into multiple shorter exposures. Alternatively, more accurate measurements of the diffuse signal can potentially be achieved with pixel-array detectors, which possess much higher dynamic ranges as well as very small point-spread functions.

Methods for processing diffuse scattering data from raw image frames to complete a reciprocal-space map are under active development.

Because acoustic scattering is maximized at Bragg peaks, diffuse signal will be most straightforward to measure in intervening regions. These methods will be applied to new data sets of simultaneous Bragg and diffuse scattering data. Instead of being included in the background correction in estimated Bragg peak intensities, these diffuse intensities will increase the data available for refinement, enable more accurate quantification of interatomic distances and allow the simultaneous refinement of multiple coupled protein motions.

**More information:** Van Benschoten et al. (2014). *Acta Cryst.* D71, 1657-1667; DOI: 10.1107/S1399004715007415