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*A novel method in modelling diffuse scattering in protein crystallography*

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Protein molecules can perform their specific functions only because of their evolutionary-tailored three-dimensional atomic structures. The dynamic behaviour of atoms or groups of atoms is also important for the function and efficiency of a protein molecule.

X-ray diffraction experiments measure the space and time averaged crystal structure from Bragg reflections. Atomic displacements, either caused by dynamic mobility or static disorder, give rise to diffuse scattering in-between Bragg reflections. If correlations between the displacements exist at length scales larger than the unit cell dimensions, features such as streaks can be observed. Short range correlations between groups atoms within the unit cell, show up as cloudy diffuse scattering, and therefore such scattered intensity can be used to derive the dynamic behaviour of protein molecules.

The type of motion that gives rise to this class of diffuse scattering has been debated for over 20 years. In 1992, synchrotron data were collected from tetragonal lysozyme crystals. A liquid-like model that represents internal motion of the lysozyme molecules was used to reproduce the diffuse scattering[1]. In 1996 the experiment was repeated, but the authors used rigid body translations and rotations of independent lysozyme molecules in the crystal to model to the diffuse data, thus opposing the above mentioned model[2] .

Both interpretations yielded similar diffuse scattering; the source of the diffuse signal from tetragonal lysozyme thus remained an open question. Diffuse scattering has recently become a subject of interest again, mostly due to advances in detector technology, allowing noise free read out of images, and computational power.

Here we present a general method for calculating diffuse scattering from atomic models of motion in the crystal unit cell, thereby making it possible to test the different hypotheses described above (liquid-like and rigid-body). Following the original formulation of Guinér[3] we calculate the diffuse scattering as the difference between the total scattering and the Bragg scattering, at and in between Bragg positions in reciprocal space.

We can model both correlated rigid body (TLS-like) motions, and liquid-like motions by generating ensembles of molecules and conformations. We will use this method to investigate which type of motion is responsible for diffuse (cloudy) scattering.

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[2] Pérez, J., et al. (1996). Acta Crystallogr. Sect. D Biol. Crystallogr. 52, 722–729.
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