Hyper-Restraints: Improving Supercell Approximation Refinements of an Incommensurately Modulated Protein

Jeffrey J. Lovelace[1], Garib Murshudov[2], Václav Petříček[3], Gloria E. O. Borgstahl[1]

[1]*Eppley Institute for Research in Cancer, Omaha, NE, USA*

[2]*MRC Laboratory of Molecular Biology, Cambridge, UK*

[3]*Institute of Physics of the Czech Academy of Sciences, Prague, Czech Republic*

gborgstahl@unmc.edu

Crystals grown from a complex of profilin and actin (PA) can be incommensurately modulated[1]. For PA, the modulation can be described using a (3+1)D superspace. Here, (3+1)D superspace refers to a space with a higher dimension than three but one that encompasses only a small subset of the total 4D space. The modulation manifests itself in the diffraction data as main reflections with associated satellite reflections near the main but with typically lower intensity. Modulations come in two varieties: commensurate and incommensurate. Commensurate modulations can be dealt with by constructing a supercell that correctly indexes the satellites and solved using standard approaches. Incommensurate data must be handled using superspace methods[2,3] resulting in indexing that has a q-vector to describe the satellite positions relative to the main. In superspace, atoms are described as lines that follow a periodic path described by an atomic modulation function (AMF).

One option for incommensurately modulated data is to treat the reflections with a supercell approximation and solve the approximation. As long as the q-vector for the approximation and the q-vector for the incommensurate data are close (~10%) and the AMFs are smooth, the refined positions in the supercell should be a reasonable representation of the positions that would be described by the AMFs. From theory[4], higher order satellites (distance from main) have a rapid decrease in intensity (quickly become undetectable) for sinusoidal modulations. For the PA crystals, only first order satellites are observed which leads to the conclusion that the AMFs must be smoothly varying (close to sinusoidal). By plotting the atomic positions from supercell refinements for the PA data in higher dimensional space it was clear that the atoms were not following a smoothly varying function, which would be expected based on the single order satellites. This lead to the idea of restraining the motion of the atoms in the higher dimension to be sinusoidal as a first guess. This was accomplished by creating an R script to restrain the atomic motions between cycles of refinement by Refmac. By restraining the atoms in (3+1)D space more favorable R to R_{free} refinements were observed. Although this approach was created specifically to improve the refinement of an incommensurate approximation the idea may be useful for other supercell cases.

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