

# Optimization model for density modification based on single-crystal X-ray diffraction data

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## Overview

Finding 3-dimensional structures of molecules is important in the understanding of structure-property relations, reaction kinetics and dynamics, and drug design. A variety of techniques have been developed for molecular structure elucidation, including X-ray diffraction, NMR spectroscopy, and electron spectroscopy. In the area of protein structures, in particular, more than 85% of structures present in the Protein Data Bank have been solved using X-ray diffraction methods [2].

After bombarding a crystal with X rays, a detector provides the intensities of diffracted rays. These measurements are then to be used to determine the phases of the diffracted rays. Once phases and intensities are at hand, a map of electron density provides the location of the atoms in space. Several approaches have been devised over almost a century now for determining the phases from intensity measurements. Calculation of the phases from intensity measurements is a very challenging problem. Various post-processing techniques are often required as existing algorithms often fail to locate the optimal phase solution, a significant obstacle, particularly in the presence of low-resolution data. One such post-processing technique, density modification, has been shown to significantly improve phases and structure quality [1, 3, 6]. In [5, 4], the reader can find an introduction to several optimization models used in phasing and density modification calculations from X-ray diffraction data. Here, we present a density modification model recently developed in [4]. An MINLP model as well as two MILP models are described. At the time of this writing, none of these models has been solved to global optimality, although several good quality solutions have been obtained.

## References

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