The Use of Combinatorial Optimization for Phasing in Crystallography

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The knowledge about the three-dimensional structure of macromolecules is an essential base of structural biology and modern biotechnology. X-ray crystallography is actually one of the main experimental methods to determine such structures. In X-ray crystallography the aim is to build a structure model of the molecule of interest, i.e., to find a real function $\rho(r)$ describing the electron density distribution. The X-ray diffraction experiment provides only the intensities of the X-rays diffracted in different directions, whereas the information about the phase shift of the corresponding waves is lost. This so-called phase problem is an important step on the way to determine a structure model. As the information provided by the X-ray diffraction experiment is not sufficient to solve this problem, additional information about the electron density distribution has to be considered.
The *Binary Integer Programming Approach* uses that at low and middle resolution where no structural details are shown, a binary function can be used to represent a region with density values $\rho(r)$ above a certain level (Lunin et al. [2002]). At a high cut-off level $\boldsymbol{\kappa}$ the region $\Omega_{\boldsymbol{\kappa}} = \{r : \rho(r) > \boldsymbol{\kappa}\}$ is expected to consist of a small number of connected components. This is used in the *connectivity-based approach* (Lunin et al. [2000]).

The focus of my current work is the modeling of different crystallographic approaches phasing as constraint optimization problems and the development of problem specific solving strategies. A major step in the elaboration of a suitable model is the modeling of the constraints to assure that we get the right number of connected components. Therefore a modeling approach which uses a formulation based on graphs has been worked out. Currently I am working out a suitable branch-and-cut-algorithm to solve this problem.

References

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