

Bragg Symposium Lectures

Phasing crystals with single atoms: a century of progress

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Lawrence Bragg was able to place atoms of sodium and chlorine in rocksalt simply by looking at the diffraction pattern of a few ionic salts and using his Law to explain what he saw. Placing single atoms by logic alone had its limits however, even for Lawrence Bragg, and difference Fourier methods, Patterson methods, Direct Methods and isomorphous replacement methods were needed to meet the challenges of larger and larger structures. In macromolecular crystallography, molecular replacement has come to dominate phasing methods. The correct placement of the model structure is best found with maximum likelihood methods developed in the last decade. These methods have the strength that they can find solutions even where the models are a small fraction of the total scattering and recently molecular replacement with helical fragments has been successful in phasing whole macromolecules. This prompts the question, "How low can we go?". Statistical analysis of the likelihood function has given us insights into the answer with rather surprising results, and tells us that molecular replacement can succeed even using a single atom as a model and when the target had no atom heavier than sulphur. By using maximum likelihood rather than logic, a century on from Bragg and with targets a thousand times larger than rocksalt, we are once again placing single atoms to solve crystal structures.