Examples of the direct phasing of protein structures with high solvent contents

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The phase problem in X-ray crystallography is a fundamental problem where the phases required to obtain an image of the electron density in the crystal are not directly recorded with the diffraction intensities and must be deduced by other means. Traditionally, in protein crystallography, the phases have come from MIR, MAD/SAD (where differences in intensity due to a subset of added or natively present heavier or anomalously scattering atoms are exploited) or molecular replacement (which requires a similar known structure be placed in the cell to obtain starting phases). While these techniques have been very successful, the phasing of new structures without sufficiently close homologs and for cases where it can be difficult to obtain heavy atom or anomalous scattering substitutions remains a problem.

In the case of crystals with high solvent content, there has been progress using iterative transform phasing algorithms that have been developed in the fields of astronomy, coherent diffraction imaging and transmission electron microscopy. Several groups have had success starting from a low resolution protein masks. He & Su (2015, *Acta Crystallogr*. **A71**:92) reported the successful *de novo* phasing of a couple of structures with high solvent content using a hybrid input-output algorithm combined with a dynamically adjusted protein mask. Here we report on some of our on-going trials with this method and prospects to extend it to lower solvent contents.

This material is based upon work supported by the STC Program of the National Science Foundation through BioXFEL under Agreement No. 1231306, the Texas Center for Superconductivity and the Robert A. Welch Foundation (E-1070).