An iterative algorithm for crystal structure factors from fluctuation x-ray scattering data.

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Crystallography is the quintessential method for determining the atomic structure of protein crystals, however, it is limited by the requirements for large, single crystal samples [1]. This creates challenges in using crystallography in the structure determination of ensembles of nanocrystals, which are ideal samples for a variety of applications. Studying chemically induced structural changes in protiens, such as in ezymatic catalysis, is not condusive of large single crystals, as the triggering molecule takes time to diffuse through the crystal [2]. Greater temporal resolution in the changes could be achieved if we studied the changes on an ensemble of nanocrystal samples. Membrane proteins are nortoriusly hard to crystallize into large cyrstals, as the molecular species contains hydrophilic and hydrophobic regions. Membrane proteins also comprise up to 30% of the human genome, and 50% of small molecule drug targets, despite making up only 10% of the known sturctures in the protein data bank [3]. As such, we require a novel method of structure determination that is less stringent on size and number of crystals being used. Furthermore, by studying the crystal growth and neucleation of proteins [1], we could understand how to grow better crystals for traditional crystallography experiments. This would only be possible by studying an ensemble of small nanocrystals. Powder diffraction has previously been used for structure determination of ensembles of small crystals [4], however, this method is challengeing with large crystal unit cells, as is the case for protein crystals. Modern x-ray sources such and x-ray free electron lasers are also equiped to study ensembles of crystals, as seen with the latest serial femtosecond crystallography experiments [5]. Hence, there is a need for novel structural determaination methods for ensembles of nanocrystal samples, that can faccilitate experiments for crystal growth studies, chemically induced structural changes in proteins, and for membrane protein crystals that are hard to grow to study with traditional crystalographic methods. Fluctuation X-ray Scattering (FXS) is a diffraction analysis method that measures the correlations of scattered intensities from ensembles of randomly orientated but identical particles [6]. It has been used to study a variety of materials, such as self assembled lipid crystals [7], amorphous materials [8], and protein crystal structure [9]. With FXS, there are less stringent experiment requirements such as particle size, or number of particles in an ensemble [6], and as such, FXS is well suited to the demands of modern crystallography experiments with nanocrystal samples [9]. In this presentation, we present an iterative algorithm for extracting crystal structure factors from fluctionation x-ray scattering data. Through the use of this method, we could leverage existing structure refinement techniques observed in crystallography, onto novel samples and experiment conditions.

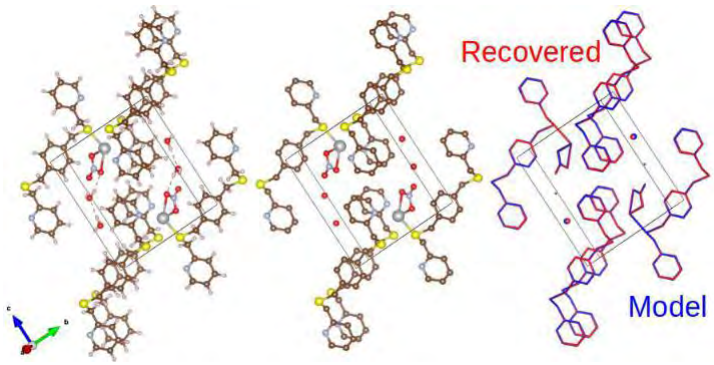

Figure 1. Recovered crystal structure using the iterative algorithm from FXS data. Left, the original crystal structure. Middle, the structure generated from the recovered structure factors from FXS data. Right, an overlay of the original and recovered structure.

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