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Developing Serial Diffraction and Microdroplet Beams for Protein Structure Determination¹

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The first protein structure to be measured was that of myoglobin, in 1958 by John Kendrew, who then remarked “Perhaps the most remarkable features of the molecule are its complexity and lack of symmetry.” Indeed, it is this complexity that allows a protein to distinguish a specific molecular species from the thousands with which it might interact. Accordingly, protein structure can offer great insight into protein function but is very challenging to measure. As “lensless imaging” techniques are developed to extract real space structural information from nonperiodic diffraction measurements, serial diffraction of both electrons and x-rays become viable candidates for high-throughput measurement of protein structure. Both probe species require a vacuum environment and hence a means of injecting proteins from solution into vacuum while maintaining the protein in a hydrated form (water soluble proteins) or micellular form (membrane proteins) at all times. Microdroplet beams of the form proposed by Rayleigh in the 1880’s offer the ideal tool. This talk will deliver a brief overview of protein structure, discuss the inversion of serial diffraction measurements by “phase retrieval,” and then present the requirements, challenges, and various experimental schemes currently directed towards protein structure determination by use of microdroplet beams.

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