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Discovering the Mechanistic Pathway for HMG-CoA Reductase Using Time Resolved Laue Crystallography.

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HMG-CoA reductase (HMGR) converts (S)-HMG-CoA to (R)-mevalonate and is the prevalent enzyme of the mevalonate pathway. HMGR is involved in the formation of lipid components, steroids, and cholesterol for many organisms. Our laboratory studies *Pseudomonas mevalonii* and we have undertaken time resolved Laue crystallography to investigate the enzymatic reaction in HMGR crystals to enhance our understanding of the mechanistic pathway. Monochromatic experiments that will aid in deconvolution of time resolved experiments have been performed with the HMG-CoA substrate and NAD cofactor. Initial experiments done in the BioCARS 14-IDB beam line at Advanced Photon Source show the HMGR crystals to be adequate for the demanding Laue data collection. Processing of nine frames at 2.9Å resulted in a R_{merge} of 88.35%(72.56%). Photo-cleavable NAD compounds are being constructed, which are necessary to observe changes in the enzyme during the reaction. Once kinetic studies have been completed with these compounds, time-resolved studies will begin and the results will show the mechanistic pathway for the first of two hydride transfers involved in converting HMG-CoA to mevalonate.