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**Time-resolved X-ray scattering of proteins in solution: a new method for probing biomolecular structure and function<sup>1</sup>**  
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X-ray scattering patterns from proteins in solution exhibit a radial intensity distribution that is sensitive to protein size, shape, and structure. When acquired in a time-resolved fashion, these ‘fingerprints’ unveil conformational changes that occur as a protein executes its designed function. We recently developed the infrastructure required to record X-ray scattering snapshots with ~100-ps time resolution on the BioCARS beamline at the Advanced Photon Source in Argonne, IL. This methodology was used to probe structural changes in hemoglobin after photodissociating a bound ligand. Remarkably, the scattering fingerprint exhibited changes at the earliest times resolved, evidently corresponding to small amplitude tertiary structure changes. On longer time scales, the allosteric quaternary structure transition was resolved. These scattering fingerprints provide robust constraints for structural models of intermediates and their dynamics, which are crucial to develop a detailed understanding of biophysical processes.

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