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Watching proteins function with picosecond X-ray crystallography and molecular dynamics simulations.[1]

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Time-resolved electron density maps of myoglobin, a ligand-binding heme protein, have been stitched together into movies that unveil with $<$ 2-Å spatial resolution and 150-ps time-resolution the correlated protein motions that accompany and/or mediate ligand migration within the hydrophobic interior of a protein. A joint analysis of all-atom molecular dynamics (MD) calculations and picosecond time-resolved X-ray structures provides single-molecule insights into mechanisms of protein function. Ensemble-averaged MD simulations of the L29F mutant of myoglobin following ligand dissociation reproduce the direction, amplitude, and timescales of crystallographically-determined structural changes. This close agreement with experiments at comparable resolution in space and time validates the individual MD trajectories, which identify and structurally characterize a conformational switch that directs dissociated ligands to one of two nearby protein cavities. This unique combination of simulation and experiment unveils functional protein motions and illustrates at an atomic level relationships among protein structure, dynamics, and function.

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