Hot And Bothered: Perturbing Protein Dynamics with Temperature-Jump for Time-Resolved Crystallography Experiments

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Understanding and controlling protein motion at atomic resolution is a hallmark challenge for structural biologists and protein engineers because conformational dynamics are essential for complex functions such as enzyme catalysis and allosteric regulation. Time- resolved crystallography offers a window into protein motions, yet without a universal perturbation to initiate conformational changes the method has been limited in scope. To overcome this challenge, we have developed the use of infrared laser-induced temperature- jump (T-jump) as a rapid perturbation for time-resolved crystallography. I will present the results of initial experiments, in which we used T-jump crystallography to map structural motions in lysozyme, a dynamic enzyme, demonstrating the feasibility of the technique.

Next, I will describe ongoing efforts to apply T-jump crystallography beyond model systems such as lysozyme. I will show how we are using T-jump to understand the complex catalytic mechanism of soybean lipoxygenase, and share how we are developing instrumentation for T-jump experiments across both synchrotron and XFEL beamlines. Because T-jump is a universal method for perturbing molecular motion, the method demonstrated here is broadly applicable for studying protein dynamics.