## How do Signaling Photoreceptors Respond to Light?

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Signaling photoreceptors harness the energy derived from the absorption of a photon to generate a structural signal which is then transmitted to downstream partners and ultimately modulates a biological process such as phototropism in plants or swimming behavior of bacteria. To accomplish this with high efficiency, competing de-excitation pathways such as fluorescence and vibration have to be shut down (or greatly minimized). How are structural signals generated at the atomic level, by processes such as light-driven isomerization, bond breaking and bond making? We address these questions by nanosecond time-resolved crystallography, in which molecules in a single crystal of a photoreceptor are stimulated by a brief laser pulse and the subsequent structural changes probed by a synchrotron-derived, polychromatic, intense X-ray pulse. These timedependent changes are revealed over the time range from nsec to sec: molecular movies. We illustrate these experiments by considering the fully-reversible photocycles of the bacterial blue light photoreceptor, photoactive yellow protein, and the heme domain of the O<sub>2</sub>/CO sensor, fixLH. We extract by singular value decomposition the number of structurally-distinct components, identify whether a chemical kinetic mechanism characterized by a small number of distinct states exists and if so, determine the structures of these timeindependent, intermediate, short-lived states.

Keywords: time-resolved crystallography, Laue diffraction, signal transduction