Utrafast Water Rearrangements in Phytochromes: Unveiling a Proton-Coupled Signaling Transduction Mechanism

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Photoactive proteins modulate chromophore electronic properties for efficient photosynthesis and sensing. In signaling proteins, the chromophore must transmit a conformational signal to the protein matrix, which may occur through steric interactions and, in some cases, involves proton transfer reactions of the chromophore. However, in many proteins, the mechanism of coupling between the chromophore and the protein remains to be discovered. In this study, we recorded femtosecond time-resolved serial crystallography (SX) data of the phytochrome protein derived from *D. radiodurans*.

Our data reveal an ultrafast rearrangement of a conserved hydrogen bond network that wraps around the bilin chromophore. Aided by molecular dynamics simulation and femtosecond infrared spectroscopy, we assign these changes to an ultrafast proton transfer reaction of a conserved histidine. This protonation reaction occurs very fast in less than 300 fs. Intriguingly, it occurs remotely from the photoexcited bilin chromophore and is therefore distinct from the well-studied proton-coupled electron transfer and excited state proton transfer mechanism. We suggest that this remote-controlled proton transfer may be a widely used mechanism in photoreceptor proteins to couple co-factor signals to their hosting enzymes.