Mechanism and dynamics of fatty acid photodecarboxylase

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Light is important for organisms from all domains of life, serving as an energy resource or carrier of information initiating intra- or intercellular signaling. Photosensitive proteins, endowed with a light-absorbing chromophore, enable this. Detailed insights, including the initial events on the ultrafast time scale, can be obtained by various forms of spectroscopy and computation. However, direct structural information necessary to understand the underlying molecular mechanisms has been inaccessible until recently. The unique properties of X-ray free electron lasers open the sub-ps time domain for time-resolved crystallography using small crystals that can be efficiently photolyzed, thus providing access to the long sought-after excited state and intermediate structures. Photodecarboxylation is a well-established reaction in chemistry; however, no photo-enzymatic equivalent was known until the discovery of Fatty Acid Photodecarboxylase (FAP), a flavin containing photoenzyme [1].The enzymatic mechanism was investigated in detail by a large interdisciplinary consortium [2]: decarboxylation occurs directly upon reduction of the photo-excited flavin by the fatty acid substrate. Along with flavin reoxidation by the alkyl radical intermediate, a major fraction of the cleaved carbon dioxide unexpectedly transforms in 100 ns into another species, assigned to be bicarbonate based on IR-spectroscopy performed on cryogenic samples. Despite a great deal of insight into the catalytic mechanism and the role of two strictly conserved residues for substrate stabilization and functional charge transfer [2], a number of questions remain. To address these, including the nature of the transiently generated CO_2-derivative we performed a follow-up time-resolved serial femtosecond crystallography experiment at SwissFEL spanning time-delays from ns to ms after photoexcitation. The results will be discussed.

[1] Sorigué et al An algal photoenzyme converts fatty acids to hydrocarbons, Science 357: 903-907 (2017)
[2] Sorigué et al Mechanism and dynamics of fatty acid photodecarboxylase, Science 372, eabd5687 (2021)