Oral presentation

Ultrafast structural changes direct the first molecular events of vision

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Mammalian rhodopsin is our receptor for vision. It belongs to the highly druggable G protein-coupled receptor family. Upon light illumination, the photoreceptor binds and activates the intracellular G protein transducin, triggering a cascade of signalling events to the brain via the optic nerve within milliseconds. However, the intramolecular initial events transforming the rhodopsin resting state [1,2] (dark state) into the transducin-binding activated state [3-5] (Meta II state) are not completely understood.

Recently, we captured snapshots of the native bovine rhodopsin at room temperature using time-resolved ultrafast serial femtosecond crystallography, already successfully used for the proton pump bacteriorhodopsin [6,7], at the SACLA and SwissFEL X-ray free electron lasers (XFELs). Thousands of rhodopsin microcrystals grown in the dark were successively injected into the light of a pump laser and probed after various time-delays from femtoseconds to milliseconds using an XFEL. After correction of our diffraction data for a lattice-translocation defect, we were able to resolve the structures of dark and light-activated states [8].

Upon photon absorption, the 11-*cis* retinal chromophore of rhodopsin undergoes one of the fastest events in biology: its isomerisation into the all-trans conformation. After 1 picosecond, we observe a highly distorted all-*trans* retinal that has induced a few changes in its binding pocket while the excess photon energy dissipates anisotropically inside rhodopsin as a protein breathing motion towards the extracellular domain. Interestingly, some amino acids known to be key elements in the transduction of the signal are involved in the protein breathing motion [9].

The same type of experiment was applied at later time-delays from 100 ps to early microseconds showing a relaxation of the whole structure followed by the first major retinal conformational changes modifying its binding pocket.

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