MS07 Membrane Proteins

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Mammalian rhodopsin dynamics using an X-ray free-electron laser
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Abstract
Mammalian rhodopsin dynamics using an X-ray free electron laser.
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Mammalian Rhodopsin, a prototype of the largest druggable G Protein-Coupled Receptors family (GPCRs), is our light receptor for night vision. Upon photon absorption, its chromophore 11-cis retinal undergoes one of the fastest events in biology, which happens in the femtosecond range, the isomerization into the agonist form, all-trans retinal. We have developed a new crystal form of rho-dopsin in LCP, diffracting to better than 2 Å, which is suitable for room temperature time-resolved serial crystallography. At the japanese SACLA and SwissFEL X-ray free electron lasers (XFELs), we were able to collect a number of time-resolved data sets. The rhodopsin microcrystals grown in the dark are successively injected in the light of a pump laser and probed with the XFEL beam after various time-delays from femtoseconds to milliseconds (see **Figure**), revealing important insights on the detailed mechanism of rhodopsin activation, e.g. retinal isomerization, rearrangements of amino acid side chains and water molecules.
We have been able to observe how the 11-cis retinal isomerizes, undergoing a severe twist inside the tight rhodopsin binding pocket after 1 picosecond of photoactivation, followed by a thermal relaxation, which will later lead to various changes in the protein conformation. The results can be compared to those of the prokaryotic proton pump bacteriorhodopsin studied using the same method **[1-3]**, but also to spectroscopic studies and numerous computational models of rhodopsin. Time-resolved serial femtosecond crystallography on rhodopsin will not only give details on the photophysical trigger of retinal excitation upon photon absorption, but also general insights on the molecular activation of a class A GPCR.

References
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