

Abstract Submitted
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Ensemble Activation of G-Protein–Coupled Receptors Revealed by Small-Angle Neutron Scattering XIANG-QIANG CHU, Wayne State University, SUCHITHRANGA PERERA, University of Arizona, UTSAB SHRESTHA, Wayne State University, UDEEP CHAWLA, ANDREY STRUTS, University of Arizona, SHUO QIAN, Oak Ridge National Laboratory, MICHAEL BROWN, University of Arizona — Rhodopsin is a G-protein–coupled receptor (GPCR) involved in visual light perception and occurs naturally in a membrane lipid environment. Rhodopsin photoactivation yields *cis-trans* isomerization of retinal giving equilibrium between inactive Meta-I and active Meta-II states. Does photoactivation lead to a single Meta-II conformation, or do substates exist as described by an ensemble-activation mechanism (EAM)? We use small-angle neutron scattering (SANS) to investigate conformational changes in rhodopsin-detergent and rhodopsin-lipid complexes upon photoactivation. Meta-I state is stabilized in CHAPS-solubilized rhodopsin, while Meta-II is trapped in DDM-solubilized rhodopsin. SANS data are acquired from 80% D₂O solutions and at contrast-matching points for both DDM and CHAPS samples. Our experiments demonstrate that for detergent-solubilized rhodopsin, SANS with contrast variation can detect structural differences between the rhodopsin dark-state, Meta-I, Meta-II, and ligand-free opsin states. Dark-state rhodopsin has more conformational flexibility in DDM micelles compared to CHAPS, which is consistent with an ensemble of activated Meta-II states. Furthermore, time-resolved SANS enables study of the time-dependent structural transitions between Meta-I and Meta-II, which is crucial to understanding the ensemble-based activation.

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