Rhodopsin's Ultra-Fast Activation Dynamics in Micelle and Bilayer Environments


University of Rochester Medical Center, Rochester, NY; University of Buffalo, Buffalo, NY; University of Alcalá, Alcalá de Henares, Madrid, Spain; Arizona State University, Tempe, AZ; Stockholm University, Stockholm, Sweden; LSLAC National Accelerator Laboratory, Menlo Park, CA; Deutsches Elektronen-Synchrotron DESY, Hamburg, Germany

Abstract

Dark-adapted vision in mammals starts with the absorption of a photon and the activation of rhodopsin, a G-protein-coupled receptor. The early stages of rhodopsin activation involve the cis-to-trans isomerization of the receptor’s ligand (retinal) and a relaxation process that drives the receptor through several nonequilibrium intermediates. The structural information available that describes the femtosecond-to-picossecond scale changes involved is limited. Time-resolved and wide-angle X-ray scattering with free electron lasers can provide insights into the functional protein dynamics that take place at these timescales. However, extracting structural information from scattering data is challenging. Here, we use all-atom dynamics simulations to aid in the interpretation of this type of experiment. Starting from well-equilibrated dark-state simulations of rhodopsin, we run and analyze thousands of 10 ps trajectories in two environments—micelles and bilayers—and find that dark- and light-activated models process energy in a way that suggests that the receptor is decoupled from its environment after light-excitation.

What Happens to Proteins After Being Struck by a Force?

- Proteins dissipate energy in the form of waves—proton-spike motions
- Relaxation thought to result in overdamping of global motions
- Early activation events occur at the sub-nanosecond timescale
- Limited information on ultra-fast induced changes
- Net direction of motion in light-excitation
- Protein δRpropagates as Pressure Wave

Light Excitation Induces Increase in Radius of Gyration

- Light-excitation produces an ultra-fast increase in protein's Rg
- Protein δRpropagates as Pressure Wave
- δRpropagation speed in proteins is
- Speed of sound in proteins
- Light-induced perturbation propagates at ~21 Åps
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- Light induces propagation of pressure wave
- Does retinal isomerization after correlation of residue motions?
- Liquid-crystalline state of receptor
- Light-excitation of chromophore is
- Light-induced perturbation propagates as Pressure Wave

Conclusion

- Rhodopsin relaxation occurs in an
- Photoactivation is characterized by
- Protein dynamics and environment contribute to signal
- Experimental analysis is complex
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Future Directions

- Compute scattering profiles from simulations
- Compare to experimental profiles
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- Use higher levels of detail and QM calculations to describe different states of receptor
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