Abstract Submitted
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Lipid-Mediated Activation of G-Protein-Coupled Receptors in Membranes[1] MICHAEL F. BROWN, UDEEP CHAWLA, SUCHITHRANGA M.D.C. PERERA, ANDREY V. STRUTS, Depts. of Chemistry and Biochemistry and Physics, University of Arizona, AZ 85721 — The role of lipid-protein interactions in membrane function is an important question in the field of lipid membrane biophysics. Lipid effects on G-protein-coupled receptors (GPCRs) are revealed by UV-visible and FTIR spectroscopic studies of rhodopsin [1]. During rhodopsin light activation, the photoreactive 11-*cis*-retinylidene chromophore is isomerized to all-*trans* leading to an equilibrium between the inactive Meta-I and active Meta-II states. Modulation of the metarhodopsin equilibrium depends on the polar head groups and acyl chain composition of the membrane lipids. A flexible surface model (FSM) describes elastic coupling of the membrane bilayer to the conformational energetics of rhodopsin. According to the FSM, membrane lipids whose spontaneous curvature stabilizes the activated state within the membrane are involved in regulating protein function. The new biomembrane model explains the effects of bilayer thickness, nonlamellar-forming lipids, and osmotic stress on protein function. An ensemble-mediated activation mechanism is proposed for rhodopsin in a natural membrane lipid environment. Bulk water is involved in the activation of rhodopsin-like GPCRs in membranes [2]. Membrane proteins and membrane-bound peptides are affected by curvature forces due to elastic deformation of the bilayer, thus giving a new paradigm for membrane lipid-protein interactions in biophysics.

[1] M. F. Brown (2012) *Biochemistry* **51**, 9782.
[2] A. V. Struts et al. (2011) *PNAS* **108**, 8263.

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