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A Neutron View of Proteins in Lipid Bilayers[1]

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Despite the growing number of atomic-resolution membrane protein structures, direct structural information about proteins in their native membrane environment is scarce. This problem is particularly relevant in the case of the highly-charged S1-S4 voltage- sensing domains responsible for nerve impulses, where interactions with the lipid bilayer are critical for the function of voltage-activated potassium channels. We have used neutron diffraction, solid-state nuclear magnetic resonance spectroscopy, and molecular dynamics simulations to investigate the structure and hydration of bilayer membranes containing S1-S4 voltage-sensing domains. Our results show that voltage sensors adopt transmembrane orientations, cause a modest reshaping of the surrounding lipid bilayer, and that water molecules intimately interact with the protein within the membrane. These structural findings reveal that voltage sensors have evolved to interact with the lipid membrane while keeping the energetic and structural perturbations to a minimum, and that water penetrates into the membrane to hydrate charged residues and shape the transmembrane electric field.

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