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Automated Identification of Cholesterol Interaction Sites on G-protein Coupled Receptors[1] ERIC ROUVIERE, CLEMENT ARNAREZ, EDWARD LYMAN, Univ of Delaware — G-protein coupled receptors (GPCRs) are transmembrane proteins responsible for transmitting signals from the extracellular region into the cytoplasm of the cell. It is known that cholesterol molecules present in the cell membrane affect the stability and the function of many GPCRs by interacting with the protein surface. Cholesterol, however, does not interact uniformly over the surface of the protein. Certain areas on the protein (that we report as interaction sites) are more favorable to cholesterol binding. The goal of this work is to develop a robust method to locate and analyze these interaction sites to guide experimental tests. To achieve this goal, we used a coarse-grained model (Martini) and molecular dynamic simulations of an Adenosine A_{2a} receptor (A2AR) in a lipid bilayer embedding cholesterol molecules to identify the key residues involved in the A2AR/cholesterol interactions. Our simulations show that cholesterol is most likely to bind in three distinct areas on the surface of the protein. We identify the most important residues for each of the three interaction sites and compare them to published experimental and simulation data. Based on these results, future paths for the development of the method are discussed.

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