PEPTIDES AND PROTEINS IN MEMBRANES: WHAT CAN WE LEARN VIA COMPUTER SIMULATIONS

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Membrane and membrane-active peptides and proteins play crucial role in numerous cell processes, like membrane fusion, signalling, ion conductance, and so forth. Many of them act as highly specific and efficient drugs, and therefore, attract growing pharmaceutical interest. Because of inherent experimental difficulties with characterization of spatial structure and membrane binding of such objects, essential attention is put now to molecular modeling techniques. The main difficulty here is related to correct treatment of protein-lipid interactions. Important progress achieved during the last years in molecular dynamics (MD) and Monte Carlo (MC) simulations of explicit hydrated bilayers allows atomic-resolution studies of proteins on a membrane-water interface. The questions like microscopic nature of protein-lipid interactions, protein insertion and its influence on the bilayer may be addressed only with explicit membrane models. At the same time, they are too computationally demanded and, therefore, structure and function of the bound polypeptides are assessed on relatively short time scales. Alternative possibility lies in employment of models with implicit consideration of membrane. Such models are of a special interest because of their computational efficiency and ability to account for principal trends in protein-lipid interactions. In this approximation, the bilayer is usually treated as continuum whose properties vary along the membrane thickness, and membrane insertion is simulated using either MC or MD methods. Testing against experimental data show that the calculations give good predictions both for the association state and peptide's orientation relative to the membrane surface.

The present work surveys our recent applications of explicit and implicit lipid bilayer models in computer simulations of peptides and proteins with membranes. Among the studied objects there are fusion peptides from Influeza A hemagglutinin [1] and HIV-1 gp41 coat proteins and their mutated analogs, antibacterial peptides [2], cardiotoxins from snake venoms [3], and others. Theoretical background of the membrane models is considered with examples of their applications to biologically relevant problems. Emphasis is on novel MC and MD computational protocols, on structural and/or functional information which may be obtained via molecular modeling, as well as on approximations of the models. Modeling perspectives in studies of membrane active proteins are discussed.

References.

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