doi 10.18699/bgrs2024-3.1-33

“Dynamic molecular portrait” approach in computational structural biology of membrane proteins

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Key words: protein structure and dynamics; molecular dynamics; protein-membrane interactions; computational molecular modeling

Understanding at the molecular level the structure, dynamics, and mechanisms of functioning of membrane proteins (MPs) is important both from a fundamental and applied point of view – for the development of new drugs and therapies for a number of socially significant diseases. Traditionally, of particular interest in recent years has been the study of receptors and ion channels. In this work, we make focus on two families from these classes of MPs – receptor tyrosine kinases (RTKs) and transient receptor potential (TRP) ion channels. This is due to the presence of experimentally determined models of the spatial structure of a number of these MPs in various functional states. Computer modeling provides important information about the features of MPs, allowing, on the basis of experimentally obtained models, to evaluate the fine details of their conformational dynamics, analyze the evolution of their physicochemical properties, assess the integral membrane effects and the role of individual bound lipids, etc. The results of calculations contribute to the identification at the atomic level of the relationship of these characteristics of MPs of different types with the parameters of their action in the cell. The report presents the results of in silico modeling of a number of proteins from the RTK and TRP family that were taken in several functional states and embedded in hydrated lipid bilayers mimicking the cell membrane. Calculations of molecular dynamics in the all-atom presentation, as well as original computer technologies for mapping and visualization of physicochemical properties of protein-membrane systems were used as the main methods of computational experiment. Special attention was paid to application of our original “dynamic molecular portrait” technology, which permits detailed assessment and pictorial visualization of the combination of structural, dynamic, hydrophobic, electric, and other properties of MPs calculated with high spatial and temporal resolution. The results obtained significantly supplement the information obtained using standard experimental techniques.
Funding: The study is supported by the Russian Science Foundation (grant No. 23-14-00313).