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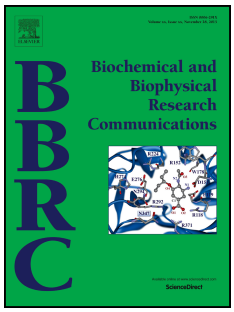

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Predicting ligand binding poses for low-resolution membrane protein models: Perspectives from multiscale simulations

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Abstract

Membrane receptors constitute major targets for pharmaceutical intervention. Drug design efforts rely on the identification of ligand binding poses. However, the limited experimental structural information available may make this extremely challenging, especially when only low-resolution homology models are accessible. In these cases, the predictions may be improved by molecular dynamics simulation approaches. Here we review recent developments of multiscale, hybrid molecular mechanics/coarse grained (MM/CG) methods applied to membrane proteins. In particular, we focus on our in-house MM/CG approach. This is especially tailored for G-protein coupled receptors, the largest membrane receptor family in humans. We show that our MM/CG approach is able to capture the atomic details of the receptor/ligand binding interactions, while keeping a low computational cost by representing the protein frame and the membrane environment in a highly simplified manner. We close this review by discussing ongoing improvements and challenges of the current implementation of our MM/CG code.