

This work deals with various methods of computing free energy using molecular dynamics simulations to study the inhibition of biological macromolecules and to identify potential drugs. Specifically, the possibility of using non-equilibrium methods based on Jarzynski's equality and Crooks fluctuation theorem was explored. The methods used were tested on simple systems of amino acids and a complex of ether crown with potassium. Subsequently, the tested methods were applied to complexes of adamantanes with cyclodextrins and especially to the inhibition of the main protease of SARS-CoV-2 Mpro.