Casein Kinase II (CKII) is a ubiquitous serine/threonine protein kinase involved in various cell signal transduction pathways and inhibition of CKII is a perspective for anticancer therapeutics. This work presents computer-modeling study of CKII inhibitory activity of 4-aminoquinoline and 4-aminoquinazoline derivatives based on conformations taken from molecular dynamics simulation (MD). The main point of the approach is an interpretation of multitude conformational states of the protein as a range of separated conformations and selection of the proper receptor conformations for docking. Such selection is based on grouping of the most probable (long-live) conformational states of the protein (clustering) and searching for the most optimal states by RMSD fitting. Using trajectory clustering, several perspective receptor conformations for docking of binding modes of ligands have been found. Testing of the database of 2500 4-aminoquinoline and 4-aminoquinazoline derivatives illustrated the priority of some MD snapshots for certain groups of ligands. Docking results obtained from MD snapshots were compared with docking results for the CKII crystal structure.

It was shown that implementation of receptor clustering, based on MD simulation and correct selection of optimal structures of target proteins, increases the accuracy of activity prediction for synthetic molecules in applicability to CKII.