An accurate evaluation of protein-protein complex models and a simple prediction of protein-ligand complex structures

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Proteins function via interaction with other proteins or ligands. Thus, an accurate prediction of a complex of the protein with other molecules is a key to understand its functions. Recently we developed two methods which are useful in protein complex structure predictions. The first method is “evaluation with the Energy Representation method of docking generated decoys (evERdock)”. In evERdock, the binding free energy differences are calculated using a short all-atom molecular dynamics simulation with explicit solvent and solution theory in the energy representation. When the interactions at the complex interface including water mediated contacts are well optimized, the method successfully selected structures similar to the native complex structure (near-native decoys) as the lowest binding free energy structures. The second method is “Concentrated ligand Docking (ColDock)” for protein-ligand complex structure predictions. In ColDock, multiple independent MD simulations in which ligands are initially distributed randomly around the protein are conducted for relatively short time. After MD simulations, ligands which are in contact with the protein are extracted and clustered. Representatives of the populationally dominant clusters are considered as predicted ligand poses. Although the procedure is quite simple, ColDock successfully predicted complex structures in 6 out of 7 complexes which include holo structures (the protein and ligand structures were taken from the complex structures) and apo structure (the monomer structure of protein was used).