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Prediction of Protein-ligand Binding Affinities Using Molecular Simulations

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Accurately predicting the binding affinities of small-molecule ligands to target proteins is one of the ultimate goals of structure-based drug design. A variety of computational methods have been developed and tested in reproducing experimental binding data for different target systems. The computational methods range from molecular docking to free energy calculations using molecular dynamics (MD) simulations.

In this study, we have studied the calculation of protein–ligand binding affinities by using MD simulations with external perturbations. Especially we focused on the steered MD simulations[1-3]. Steered MD simulation induces unbinding of ligand and conformational changes in protein on time scales accessible to the simulations. Time-depepndent external forces are applied to a system, and the responses of the system are analyzed. We have validated the conditions of steered MD simulations toward the practical use of the drug discovery.

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