SS03-6 Molecular simulations on protein-complex and drug design

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To understand molecular recognition in proteins has been one of the most fundamental issues in protein science. In early studies, the lock and key model has been proposed to explain ligand bindings in proteins or enzymes. Recent experimental studies including NMR also suggest the importance of protein conformational dynamics and/or protein-solvent interactions in the ligand bindings in proteins. The induced fit or population shift models are two of the most popular ones proposed from such experimental studies. In the induced fit model, proteins or enzymes change their conformations eventually upon ligand binding processes, whereas the population shift model proposes the existence of large conformational fluctuations in the ligand-free states. In this model, the liganded conformation is included in the fluctuations and its population increases upon the ligand binding. To elucidate molecular mechanisms underlying such ligand-binding, computational analysis including molecular dynamics (MD) simulations or integral equation theory (3d-RISM) become useful tools recently. In this talk, we show our recent results on LILR/HLA-G complex formations analyzed by MD simulations and ligand mapping analysis in proteins using 3d-RISM theory and discuss about the applicability of computational analysis in drug design.