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# Ensemble Docking Simulation for $\beta_2$ Adrenergic Receptor Using Elastic Network Model

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G protein-coupled receptors (GPCRs) are membrane proteins involved in signal transduction pathways, and so many of them are target molecules for drug discovery of various human diseases. Although more and more crystal structures of GPCRs have been determined with particular agonists and antagonists, it is now widely known that drug docking simulations based on such rigid crystal structures do not always succeed because of their very flexible structural features. Therefore, we adopted an ensemble docking method to take into account the protein flexibility in drug docking and screening.

In an ensemble docking method, each compound in the library including drug candidates is docked at the pockets of the individual receptor conformations, which were produced by molecular simulations. Molecular Dynamics (MD) simulation now becomes standard for producing putative different conformations of GPCRs, but the dynamic aspects of GPCRs can be captured by a much simpler model such as an elastic network model (ENM).

In this study, we generated the conformation polymorphism of $\beta_2$ adrenergic receptor by ENM with the successive Normal Mode Analysies (NMA), based on the X-ray crystal structure (PDBID: 2RH1). Various structual models were built by moving the atom positions following several representative modes, which were calculated by ENM-NMA. Then, docking simulations were made for those virtual models. The models based on the selected particular five modes showed the best scores for agonist and antagonist screenings. Compared to the initial crystal structure, virtual model provided 20% better screening efficiency.