

Combining Genetic Algorithms and Molecular Dynamics to Investigate Protein-Ligand

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The docking problem is posed as an optimization problem, where the objective is to minimize the intermolecular interaction energy between the two molecules. The number of degrees of freedom can be substantially reduced by using the low frequency normal mode (NM) space. Thus, the exploration of this space with GA, in conjunction with energy minimization or molecular dynamics using NM restraining potentials (REF) may constitute a valuable and efficient alternative in this field. The ability to solve such problems will be of great value in rational drug design; and as computing power increases, problems of protein-protein interactions and ultimately self-assembly processes can be addressed by these techniques. In this work, we are developing a applications of methods and software that combine techniques like Genetic Algorithms (GA), Molecular Dynamics (MD), Normal Mode Analysis (NMA) in order to apply them to the elucidation of docking problem, by taking into account either local or global conformational changes of the protein. We applied Genetic Algorithms with Molecular Dynamic to modeling and study the interaction among HIV Protease (PR-HIV) and the drug DMP323. In a first moment, we obtained good results using Genetic Algorithms and Rotamer Library with the backbone rigid and with the side chain flexible. The First results using GA and Rotamer Library was compared with Molecular Dynamic results and they was very interesting and very similar for this problem. Now we are combining AG and MD to make the backbone flexible.

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