Determining the Protein Structure from Ant Colony Optimization Using Energy Minimization Derived From the Ising Model

Xu, Michelle

Fusion inhibitors prevent the HIV-1 protein gp41 from binding with the receptors on the host cell. However, scientific understanding of inhibitory potencies among different inhibitors is yet to be discovered. This project proposes a novel computational approach to investigate the protein folding mechanism, especially for the fusion inhibitor proteins. Many existing protein folding algorithms are based on atomic force fields and focus only on a protein's native folding conformation. This project develops a new protein energy function based on the Ising model that can solve both the native folded and the misfolded conformations through energy minimization. The magnetic dipole moments of atomic spins in the Ising model were replaced with 3D vectors to represent protein structures. The protein structure was then simulated and solved using a swarm intelligence method called Ant Colony Optimization. The computational results of selected fusion inhibitor examples were compared with nuclear magnetic resonance and X-ray crystallography results for the same proteins from the Protein Data Bank for similarity validation. This project revealed that for a particular inhibitor which exhibits a weaker potency than others, the global minimum of the folding energy was found at the misfolded conformation, not the native conformation. This discovery would contribute to drug design efficiency for the HIV-1 fusion inhibitor, as well as other anti-virus drug designs in general.

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