CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

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Project Number

36860

Project Title

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

Abstract

Objectives/Goals

Fusion inhibitor proteins prevent the HIV-1 gp41 glycoprotein from binding with the receptors on the host cell. However, scientific understanding of inhibitory potencies among different inhibitors remains unclear. This project proposes a novel computational approach to investigate the protein folding mechanism, with focuses on the fusion inhibitor proteins just by looking at their amino acid sequences.

Methods/Materials

I developed a new protein folding energy function using the idea of atomic spins from the Ising model. In this new function, the atomic spins were extended into vectors to simulate the shape of the protein peptide bonds. Vector space algebra was then applied to transform the statistics-based Ising model into a deterministic form. I applied an artificial intelligence method, the Ant Colony Optimization with a deterministic searching algorithm, to solve the energy minimization based on the new folding energy function by looking for the global minimum in the energy graph. The computational results of selected fusion inhibitor examples were compared with nuclear magnetic resonance (NMR) and X-ray crystallography results for the same proteins from the Protein Data Bank for similarity validation. Similarity was validated through visualization using the 3D viewer Jmol, as well as numerical comparisons through a topological property called Relative Contact Order (RCO).

Results

The results showed high similarities in both visual and numerical comparisons between the calculated and the actual protein structures. In addition, the HIV-1 inhibitors with weaker binding strength had multiple minima in the folding energy curve and the global minimum was found at the misfolded conformation.

Conclusions/Discussion

My protein folding energy function allows me to examine both the native folded and misfolded conformations. I was able to find that for the fusion inhibitors with less inhibitory strength, the energy curve showed a global minimum at the misfolded conformation rather than at the native folded conformation. This discovery could improve drug design efficiency by contributing to the proper selection and modification of the HIV-1 fusion inhibitors, as well as other anti-virus drug design projects.

Summary Statement

I was able to develop a computational approach using vector space algebra to solve for the protein native structure by minimizing the energy through an artificial intelligence method called Ant Colony Optimization.

Help Received

I would like to thank Professor Stephen H. White from the UCI Department of Physiology and Biophysics for his mentorship by helping me narrow down my research topic and providing me with research articles. I would also like to thank my math teacher, Mr. Charles Y. Beilin, for his support in the development of