CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

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Project Number

35857

Project Title

Development of Feature-Based Receptor-Ligand Docking Using POVME

Abstract

Objectives/Goals

The objective of this work was to develop an efficient receptor-ligand docking method integrated into a binding pocket analysis tool (POVME) that can potentially be used to increase the rate of drug discovery. Two major goals include the generation of uniform rotations in 3-D space and the evaluation of the accuracy of the docking and scoring functions in determining the correct position of a ligand within a receptor.

Methods/Materials

A computer with access to the Binding Database (a public, web-accessible database of measured binding affinities, focusing chiefly on the interactions of proteins considered to be drug-targets with small, drug-like molecules) was used to write and test coloring, docking, and scoring functions. Functions were written in Python and C++. Visualizations were produced using VMD.

Results

When testing methods for generating uniform rotations, point-repulsion-generated points on a sphere had the lowest standard deviation between point distances. Testing of the docking and scoring functions showed that there existed a strong negative linear association between feature scores and distance from correct ligand binding position.

Conclusions/Discussion

The low standard deviation of distances between points generated by the point repulsion method helped to fulfill design goal #1, producing more uniform and regular rotations in 3-D space. In addition, due to the strong negative linear association between feature interaction score and distance from the correct ligand orientation position, there is moderate evidence supporting that design goal #2 has been met. Overall, results show that the docking function, in a naïve case, produces scores that increase as the distance from the true ligand conformation decreases. This data suggests that the docking and scoring functions have the potential to reliably select the true ligand conformations of any given receptor and ligand maps. These advances allow accurate docking and scoring to be implemented within POVME.

Summary Statement

This work introduced binding-pocket analysis-based receptor-ligand docking and optimized scoring functions in order to expedite future drug discovery.

Help Received

Participant in BioChemCoRe program at University of San Diego, California; continued research using lab equipment from the Amaro Lab under the supervision of Mr. Jeffrey R. Wagner.