DATE: October 30, 2015

TO: Dr. Hang Liu

FROM: Ashton Berger
Rachel Arthur
Willie Man
Jim Corbin

SUBJECT: STC Fall 2015 Project Proposal to program a solution which would calculate the probability of inter-species ligand-receptor binding

INTRODUCTION

This proposal outlines the background of ligand-receptor pairing and the process we will execute to predict the probability of inter-species pairings. We will be attempting to accurately predict the probability of observing certain ligand-receptor pairs in a complex, multi-species ligand and multi-species receptor system using some modified statistical mechanics calculations. We will do this by constructing a computer program that will calculate these predictions quickly and accurately.

BACKGROUND

In biophysics, it has been shown that for a single species, the ligand-receptor system can be modeled to predict the probability that a ligand will bind to a receptor. We do this by using the canonical partition function which is a thermodynamic ensemble commonly used in statistical mechanics. Imagine now that there is a system with several different species of ligands and several different species of receptors, and some of the ligands possess the ability to bind to some of the receptors. The problem of interest is that we wish to know to what degree each ligand will bind to each receptor in this complex system. Given the difference in Gibb's Free Energy (dG) between a bound ligand-receptor molecule and its inversely-unbound ligand-receptor molecule, we can compute the Boltzmann factor (e^-dG/kT) for each bound ligand-receptor combination. Provided there are equal concentrations of ligands and receptors, some modifications can be made to calculate a heuristic canonical partition function solely based on these Boltzmann factors for the bound states of the ligands and receptors that do interact. By dividing the

individual Boltzmann factor for a specific ligand-receptor state by the sum of all of the other Boltzmann factors for every interacting complex in the system, we would theoretically receive a value that will represent the degree to which we can predict that a bound complex will be present in the total system. We do not know of any major publications where predictions of a multi-species ligand-receptor species have been made computationally using an application of the partition function. This leads us to believe this project has possible research merit.

APPLICATION

We have figures representing theoretical pseudo-energies for all of the ligand-receptor pairings in said systems. We would input a matrix containing the dG calculations for each possible pairing in a ligand-receptor system (i.e. a 20 ligand and 20 receptor system would have 400 possible pairings, so there would be a 20x20 matrix with each potential pairing energetic). Then, for each pairing, the unique resulting partition function would be calculated, followed by a calculated probability value. We would have to store all of the calculated values and then output the expected results in a similar matrix format as the input. To test our predictions, we have experimental data showing the actual amounts that certain ligand-receptor bound pairs are present in such systems from real world trials.

We intend to write this project in C. The high level algorithm would start by inputting the energetic value matrix. Next we would perform computations for each entry in the matrix. This part should probably be written in a way that can take advantage of parallel processing. This would be followed by an output of the predicted probability value matrix. Finally we would perform an error check with the corresponding observed probability value matrix.

CONCLUSION

Our proposal has outlined the function of ligand-receptor pairing and the value of being able to predict possible inter-species pairings in a way that has quite possibly never been attempted before. We also gave a high level overview of the algorithm we will code in the C programming language to accomplish our goals. With you approval we will begin our project immediately.