# CALIFORNIA STATE SCIENCE FAIR
# 2017 PROJECT SUMMARY

**Name(s)**

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**Project Number**

**S0823**

**Project Title**

## Quantifying Binding Free Energies in Amyloid Systems Related to Alzheimer's and Enhancing Antibody Binding Affinities

**Abstract**

**Objectives/Goals**

Amyloids comprise of the amino acids that, when misfolded, are the primary cause of Alzheimer's; an antibody that binds with high affinity to the amyloid has great potential of being an improved drug candidate. Current calculations of binding energies between amyloids and antibodies remain unrefined; this project proposes a novel thermochemical and computational approach to accurately quantify the binding free energies and uses the developed model to optimize mutations for enhanced drug targeting.

**Methods/Materials**

I developed a new thermochemical and computational model using implicit solvent models and the Generalized Born equation derived from the linearized Poisson-Boltzmann equation. In this model, the energy difference between the bound and unbound state of solvated molecules were found by conducting binding energy computations in vacuum and solvating each individual step. This model was certified by comparing calculated binding energies with Gardberg's dataset of known energy values. Visualization software and molecular docking were applied to manually program the properties of each amino acid so that Autodock could predict the nature of amyloid interactions once the structure was docked. I created a machine learning algorithm to determine optimal mutations on the antibody as it interacts with the amyloid of given properties, based on the new model and looking for the absolute minimum in the energy graph. The computational results of selected antibodies were compared with nuclear magnetic resonance results from the Protein Data Bank for similarity validation.

**Results**

The results show high accuracy in numerical and structural comparisons between the simulated and actual antibody-amyloid binding mechanism. Also, >92% of optimized mutations proposed by the algorithm decreased binding energies by thousands of joules/mole (further confirmed experimentally), enhancing antibody binding affinities and specificity.

**Conclusions/Discussion**

My computational model allows me to calculate the binding Gibbs free energy of amyloid-antibody interactions. Given that binding energies can be computed, I developed an algorithm based on molecular docking and custom-programmed properties of amino acids to optimize antibody mutations. This can improve drug design by revealing the most favorable modifications of antibody receptors while reducing side effects such as mental impairment caused from lack of drug specificity.

**Summary Statement**

I developed a computational approach using implicit solvent models and the Poisson-Boltzmann equations to calculate binding energies and enhanced drug affinities through a novel machine-learning algorithm based on molecular docking.

**Help Received**

I would like to thank D'Artagnan Greene from the UCI's Biochemistry/Molecular Biology Lab for his assistance with technical issues I faced while programming. I also used UCI's supercomputers to quickly test my algorithms to expedite the debugging process