Optimization of Electrostatic Interactions in Proteins (May 2006- May 2007)

During my first summer with Dr. Alexov, I learned the basics of biophysics and applied some of the computational tools used in the lab: delphi (calculates electrostatic potentials utilizing Poisson-Boltzmann equation), profix (builds missing components of protein structure), and tinker (energy minimization and molecular dynamics). I wrote computer programs in C++ to analyze the data from the PROTCOM database and collaborated with two fellow students from SPRI, the summer research program hosting us. This allowed us to study the effects of single amino acid substitutions on the electrostatic component of binding free energy. We used a networking client to collaborate with Dr. Alexov throughout my senior year of high school.

Broader Impact: The CIO at my high school instituted a networking tool for all of the students that would allow collaboration after hearing that I was using a similar client.
Publication: Brock, K., **Talley, K.**, Coley, K., Kundrotas P.J. and Alexov, E. "*Optimization of electrostatic interactions in protein-protein complexes" Biophys*. J. (2007).

Salt Effect on Protein-Protein Interactions (May 2007- May 2008)

Dr. Alexov asked me to manage the lab and train two students from SPRI. While teaching the students how to do research in the lab, I produced programs to analyze data produced by the lab. Results were produced quickly using a distributive computing resource, Condor, with my algorithms. I developed a method to reduce the complexity of the research by introducing a common variable for different amounts of salt in the medium. The method allowed for closer study of the effects of the dielectric constant, probe radius, salt concentrations of media, and different presentations of the molecular surface on the stability of protein-protein complexes and how they can mimic the effects of conformation changes.

Broader Impact: I taught two high school students how to program in C++ and various scripting languages and how to conduct biophysics research.
Publication: Talley, K., Ng, C., Shoppell M., Kundrotas P.J. and Alexov, E. "*On the electrostatic component of protein-protein binding free energy*" PMC Biophys. (2008)

Contributions to the Binding Energy of Protein-Protein Interactions (May 2008-May 2009)

I created an empirical parameter "gamma" to measure the usefulness of computing the non-linear terms of the Poisson-Boltzmann equation in protein-protein complexes. The utilization of cluster and grid computing increased the computational power of Dr. Alexov's lab. This improved computing aided us in making predictions for an international competition, CAPRI. This increase in computational efficiency allowed me to devote additional time to develop more accurate models of protein. During this time, I also worked at Clemson's research park on high performance computing where I developed software for the Palmetto cluster which was number 85 in the TOP 500 supercomputing sites as of June 2010. By implementing these new computing resources, the computations that would have taken months, took only a week.

Broader Impact: Many other labs started to use Clemson's computational resources after hearing of our success. I helped my home high school set up its own Condor pool for computation that they still use today. My work at the research park also resulted in several manuscripts that act as tutorials for professors who are trying to set up Condor and the Palmetto cluster for their own use at Clemson.
Publication: Talley, K., Kundrotas, P.J., and Alexov, E. *"Modeling Salt Dependence of Protein-Protein Association: Linear vs Non-Linear Poisson-Boltzmann Equation"* Comm. in Computational Physics (2008)

Ab-initio Calculation for Low-Energy Elastic Scattering of Electrons from Phosphorus Atoms (June 2009 -August 2009)

During a ten week REU with Dr. Hari Saha at the University of Central Florida, my research focused on using the multi-configuration Hartree-Fock (MCHF) method to calculate scattering data for low energy electrons colliding with different atoms. The effect of polarization from the electron onto phosphorus was of particular interest. Unfortunately, there are no current experimental methods that can confirm the results we obtained. Although the work agrees with some earlier calculations for similar atoms, there is not enough data yet to verify our work. The results will be published in Physical Review A after careful internal review. This experience taught me that it is of greater importance to wait and publish strong research rather than to publish weak data. The current results were presented at an REU poster session that summer.

Broader Impact: I facilitated discussions about improving the computational resources at UCF through the implementation of a Condor pool.

pKa Calculations and pH Optimum of Activity and Stability (Sept 2009 - Present)

Dr. Alexov's lab participated in the pKa cooperative initiative. In my data analysis, the proteins were separated into two categories: (a) charged amino acids which are not buried within the protein so that the amino acids can easily access the surface where water is present and (b) charged amino acids which are buried within the protein so that the amino acid cannot easily access the surface where water is present. The structures were modified and rebuilt using *ab-initio* modeling. Through the use of MD simulations after modification, the resulting theoretical calculations of pKa were in close agreement with experimental results.

Later that year, my research focused on the correlation between the pH of optimum stability and the pH of optimum activity and other quantitative measures of proteins such as the isoelectric point, thermal stability, and molecular weight. Using the BRENDA, we found that there is significant correlation between the pH of optimum stability and pH of optimum activity.

Broader Impact: A comprehensive data table of available data used for the study from the BRENDA database was published in a more readable, user-friendly format.

Publication: Talley, K. and Alexov, E. "*On the pH-optimum of activity and stability of proteins*" Proteins: Structure, Function, and Bioinformatics. (2010)

Selective Isotope Labeling of Aminoglycoside Acetyltransferase (AAC) (June 2010-July 2010)

During an REU at the University of Tennessee, I worked with Dr. Engin Serpersu and Adrianne Norris to accomplish the following tasks: (a) culture *E. coli* and induce growth of AAC, (b) over-express and purify AAC, (c) label individual amino acids in AAC with isotopes, (d) utilize NMR to analyze AAC backbone resonance structure. This work showed me the power of combining experimental methods to supplement theoretical calculations.

Resulting Presentations:

- ACC Meeting of the Minds, May 2008 "Electrostatic Forces in Protein-Protein Interactions"
- SCJAS, March 2007 "Predicting 3D Homologous Structures and Calculating the Binding Energy of Protein Complexes"
- EUREKA! (Experiences in Undergraduate Research for Education and Knowledge Advancement) August 2007 "Effects of Using Various Models for Predictions of Protein-Protein Interactions" (Poster)