My Personal Statement

I studied in China Pharmaceutical University from 2003 to 2007 as an undergraduate, majoring in pharmacy. During this period of time, I gained a great deal of hands-on experience in drug synthesis and analysis. In my last undergraduate year, I was involved in the synthesis of silybin analogues. Silybin has antioxidant and anti-inflammatory properties and could potentially be used to treat chronic tissue damage. However, its low water solubility is one of its major deficits. With the help of Professor Li Chen, I successfully synthesized some novel 7-hydroxyl and 20-hydroxyl derivatives of silybin which are much more soluble in water. These analogues could be used as intermediates for more biological active molecules. At that time, the intensive synthesis training made me think that I would be a synthesist.

I was first introduced by the concept of Computer Aided Drug Design in my computer science class in 2004. I was impressed by this technology but didn't have much idea about how this technology could help the development of the pharmaceutical industry and the life sciences. I just thought it was up-to-date and very fancy. When I came to California State University, Long Beach (CSULB) in 2007, I was intrigued by Dr. Sorin's recruit poster. It showed that computational simulation could help solve problems with protein folding, RNA folding and drug targeting/binding affinity, etc. I joined the Sorin group because I thought it was a great opportunity for me to i) gain more knowledge about the life sciences ii) develop new ideas from a physical chemist's perspective in this field iii) develop a solid understanding of how physics work in biological systems, and iv) learn computer science and other technologies that help the development of the life sciences. Since I was an organic synthesist and was far from an expert about the applications of computational chemistry, I had a tough time adjusting in becoming a physical-computational chemist at the beginning of my study in the Sorin lab. After a few months of leaning bio-physics theories, computational methodologies, programming skills, and software usages, I became confident in dealing with computational problems as well as capable of learning from these problems.

When I picked my project in 2008, I selected computational study on cholinesterases folding and inhibition. Both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) are involved in the progress of Alzheimer's disease (AD). I was interested in studying the fundamental folding property of cholinesterases, especially the fluctuation of crucial residues in the active gorge as well as the conformational changes of some key parts within the gorge. Since some experimental papers suggested that AChE undergoes substantial folding at the microsecond to millisecond level, I decided to carry out a ten microsecond simulation to investigate the folding mechanism for cholinesterases. Cholinesterase inhibition is one of the current approaches that are approved by FDA to treat Alzheimer's disease. We set up a cooperation work team with Dr. Acey and Dr. Nakayama at CSULB in an effort to discover some potent inhibitors as potential AD drugs. My plan was to apply both docking and molecular dynamics (MD) simulation to study the binding affinity of drug candidates and dynamics of the enzyme-inhibitor complex. Our discovery concerning binding mechanism may help provide guidelines for drug synthesis.

In 2008, I was awarded the University Provost's Summer Research Scholarship for my proposed computational research. Starting with docking research, I tested a novel series of Diakyl Phenyl Phosphates, calculated their binding scores, and studied their binding modes. Then I extended my docking research to a library of novel bivalent Diakyl Phenyl Phosphates linked by multi-methylene spacers. In spring 2009 I started MD simulation for both enzymes. I compared the effect of different force fields on protein folding/unfolding first. Then, I started to use a distributed computation system named folding@home to collect simulation data from all over the world. I have collected a 14μs trajectory for BChE and a 15μs trajectory for AChE. I have analyzed some key aromatic residues, especially the ones in the peripheral site, focusing on structural fluctuation, conformational change, and hydrogen bonding/unbonding. More detailed analyses will be done soon. In the meantime, I will put the enzyme-inhibitor complex simulations on folding@home to compare inhibitory activities for different drugs and enzymes.

Not only have I made tremendous progress in my research ability during my time at CSULB, but I have also learned to teach basic chemistry working as a teaching assistant. In fall 2008 I taught Chem101 labs for science majors; in spring and fall 2009 I taught Chem140 labs and seminars for nursing majors. From my teaching experience, I understand that although the ease of homework and exams do matter to students, they also value clarity and helpfulness from an instructor. I tried to help the students as much as possible with both conceptual understanding and problem solving skills and I got 4.7/5.0 from two of my Chem140 classes which was higher than the mean scores of both the dept and the college. Besides teaching entry level chemistry, I helped my advisor to develop, teach, and grade a new course project for his physical chemistry class (Chem377A). Because most of the students in this class are biology or biochemistry majors, we decided to set up a docking project using ICM-pro to address some applications of physical chemistry to biological systems. I believe the teaching and course designing experience makes me a better Ph.D student candidate.

My insatiable desire to study the mechanisms of cholinesterase inhibition and its implications for Alzheimer's disease and the satisfying experiences I have already had propels me to apply for graduate school. My goals for graduate school are to strengthen my independent research ability and to further investigate my research interests with in-depth studies into the application of computational chemistry in the life sciences. For my graduate study, I am most interested in continuing research on how the cholinesterase inhibition can affect the function of both AChE and BChE and possibly, on how to rationally design drugs that could cure Alzheimer's by inhibiting these two drugs with efficacy. I strongly believe that XXX is an ideal place for me to continue my research training.