Emma Bernstein

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During the the 2017 summer, I will be working 30 hours/week as a UROP for the Tidor Lab at MIT CSAIL. My project will focus on Ketol-acid Isomeroreductase (KARI), which is a key enzyme in the biosynthesis of amino acids. We are focusing on this particular enzyme because it is thought to be the rate limiting step in the isomerization and NADPH reduction reaction that converts pyruvate into Valine and Isoleucine. By using Transition State Theory (TST) to determine reactant mutants with below average activation energy, as well as Transition Path Sampling (TPS) to study reaction pathways there is potential to find a path of least resistance for the reaction. Targeting the factors that increase the rate of the reaction would enable researchers to move the entire reaction more quickly

My primary goal for this project is to determine why certain features of any particular reaction, such as distance between atoms, bond angles, etc. influences the reaction rate. To do this I will analyze the electronic structure of the enzyme and substrate using quantum calculations to look for changes in factors such as partial charges given alterations to various nearby features. In addition I will also analyze transition states to determine which reaction pathways have the lowest activation energies with the goal of determining ideal conditions to run the reaction. Finally, I will seek to build a framework which outlines how to ask questions about facilitating enzymatic reactions for future work by determining which factors are most influential in reducing the activation energy of the enzyme.