Computational enzymology: A microscopic perspective of enzyme catalysis

Donald Hamelberg
Department of Chemistry, Georgia State University, Atlanta, GA 30302-4098

The advancement in computational chemistry has led to the development of an incredible amount of methodologies to study biological phenomena at atomistic detail. These computational methods are fast becoming indispensible in the field as a whole. Molecular dynamics is central to lots of these methods and is one of the most widely used techniques in computational chemistry due to its ability to accurately sample the energy landscape. We have used an accelerated molecular dynamics simulation method to provide detailed description of *cis-trans* isomerization of the protein peptide bond and the enzyme-assisted process. The local change of the isomeric state of the prolyl peptide bond acts as a switching mechanism in altering the conformation of proteins. A complete understanding of the mechanism of the catalyzed *cis-trans* isomerization process is still lacking, and current experimental techniques have not been able to provide a detailed atomistic picture. The role of aqueous solvent in the catalytic activity of the enzyme will also be discussed, since the landscape topology of their substrates would change upon moving from an aqueous environment into the binding site.