Ligand-binding characteristics of Indoleamine 2,3-dioxygenase and Tryptophan 2,3-dioxygenase

Luciana Capece[‡], Marcelo Martí[‡], Mehrnoosh Arrar[†], and Darío A. Estrín[‡]
[‡] Departamento de Química Inorganica, Facultad de Ciencias Exactas y Naturales,
Universidad de Buenos Aires, Argentina
[†]Quantum Theory Project, University of Florida
P.O Box 118435, Gainesville, FL 32611

The first and rate-limiting step of the kynurenine pathway in which tryptophan (Trp) is converted to N-formylkynurenine can be catalyzed by two different heme-containing proteins, Indoleamine 2,3-dioxygenase (IDO) and Tryptophan 2,3-dioxygenase (TDO). Although both proteins catalyze the oxidative cleavage of the Trp indole ring, they are supposed to follow two distinct mechanisms, yet to be determined. This study utilized molecular docking methods to investigate possible binding conformations of L/D-Trp in IDO. Molecular dynamics (MD) simulations were performed on both free and substrate-bound forms of the two enzymes. Key interactions for both ligands are discussed.