Computational Study of the Structure of Lactoperoxidase and its Active Site

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Poster Presentation Abstract:

Lactoperoxidase (LPO) is an enzyme that fights in the first line of defense against infection. LPO catalyzes the formation of oxidizing chemicals that indiscriminately kill foreign microbes and viruses caught in the mucous membranes of vulnerable body parts, namely of the eyes and upper airways. Because of its importance for the immune system, the molecular structure and efficacy of native forms of LPO against various pathogens have been studied for potential applications in medical therapies. Despite its frequency in research, the mechanism by which LPO converts common ions, such as chloride, into antimicrobial agents has not been resolved in atomistic detail. Thus, we seek to determine catalytic mechanism of LPO using the methods of computational chemistry, which incorporates classical and quantum mechanics to simulate chemical phenomena.

To start, we examined various three-dimensional structures of LPO taken from the Protein Data Bank to estimate the variability and flexibility of the active site and the overall protein. An active-site structural model was then constructed to compute the spatial distribution and strength of intermolecular forces at play in the LPO active site using a force field specially optimized for proteins. The resulting implications to substrate binding and catalysis were analyzed. This allows us to progress to the next stage, where quantum chemical methods will be used to ultimately elucidate the catalytic mechanism of LPO.

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