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Departmental Seminar

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by

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SIMULATIONS OF ENZYME MECHANISMS USING QUANTITATIVELY ACCURATE DENSITY FUNCTIONAL THEORY/MOLECULAR MECHANICAL (DFT/MM) METHODS

ABSTRACT

Hybrid Quantum Mechanical/Molecular Mechanical (QM/MM) are the gold standard method for the simulation of complex enzyme reactions. A large variety of QM methods are now available to assist in the characterization and/or prediction of chemical reaction mechanisms. Yet, in order to make meaningful comparisons between computational results and experimental data, extremely demanding simulations must be performed. Often, these demands are met be resorting to approximate methods which may contain serious deficiencies in the calculation of free energy barriers and intermolecular interactions. However, with improvements in hardware, parallel programming, and simulation algorithms, the simulation of condensed phase reactions with quantitatively-accurate density functional theory (DFT) methods is still computationally demanding but attainable. In this presentation, I will provide an introduction on the construction of models for DFT/MM simulations of enzyme reactions. I will then demonstrate the use of DFT/MM methods to characterize reactions in various enzymes that include a sugar isomerase utilized for biofuel and pharmaceutical production, the inactivation of a heme-containing enzyme by hydrogen sulfide, and the re-engineering of an enzyme responsible for catalyzing the hydrolysis of deadly organophosphorus (OP) nerve agents such as Sarin and VX.

REFERENCES

Wymore, T, Field, MJ, Langan, P, Smith, JC and Parks, JM. Hydrolysis of DFP and (S)-Sarin by DFPase proceeds along two different reaction pathways: Implications for Engineering Bioscavengers. J. Phys. Chem. B, 2014, 118:4479-4489.