

THEORETICAL STUDIES OF ENZYMATIC REACTIONS

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In recent years, it has become possible to model chemical reactions in large biomolecules using combined quantum mechanical / molecular mechanical (QM/MM) methods. After a general outline of the theoretical background and the chosen strategy [1,2], the lecture will describe some of our recent work on biocatalysis by enzymes, in particular cytochrome P450cam [3-8]. Topics include the electronic structure of P450cam intermediates, two-state reactivity in the oxygenation reaction, the biocatalytic role of single water molecules, revised mechanisms for the formation of the Compound I intermediate, and the competition between coupling and uncoupling reactions in the wild-type enzyme and several mutants. P450cam will thus serve as an example of the chemical insights and the improved mechanistic understanding that can be provided by QM/MM calculations. Time permitting, the lecture will also address theoretical studies that rationalize the improved enantioselectivity of lipase mutants generated by directed evolution in our institute [9].

References:

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