# Negative catalysis in nonheme iron enzymes, how do the enzymes trigger their chemoselectivity?

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Nonheme iron dioxygenases are versatile enzymes with vital functions for human health that include the biosynthesis of natural compounds and the detoxification of toxic metabolites.[1] These enzymes react substrate on an iron(II) center and using dioxygen and a co-substrate, such as -ketoglutarate, perform a hydroxylation reaction, which is often stereo- and regioselective. To understand details of these selectivity patterns a range of computational studies on various nonheme iron dioxygenases has been performed in my group.[2] In this presentation, I will show how second-coordination sphere effects are shown to be crucial to guide the reaction to the wanted selectivity channel. In particular, we have shown that often a regioselectivity in enzymes can be accomplished by external perturbations working on the transition state for the reaction through external charges, electric dipole moments or local electric field effects. The modelling identifies how charged groups in the substrate binding pocket influence reaction rates and selectivities dramatically. This insight can then be used to design and develop novel biomimetic models for selective hydroxylation or halogenation reactions.[3]

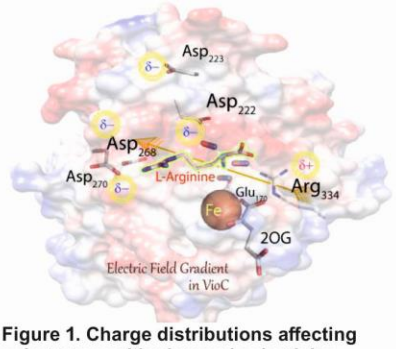


**Figure 1. Charge distributions affecting substrate positioning and selectivity.**

**References:**

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