MS07-P12 | ENZYMATIC CONTROL OF O2 REACTIVITY AND FUNCTIONALIZATION OF THE FLAVIN COFACTOR

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The chemical reactions of enzymes and cofactors with gaseous molecules such as dioxygen (O_2) are demanding to study and remain a contentious field in biochemistry. Until now, it remains partially cryptic how enzymes steer their reactions with O_2, as exemplified by the ubiquitous flavoenzymes that mostly facilitate redox reactions such as the oxygenation of organic substrates. We employed O_2-pressurized X-ray crystallography and quantum mechanical calculations to reveal how particular positioning of O_2 within flavoenzyme active sites enables the regiospecific formation of covalent flavin-N5-oxygen adducts that may serve as oxygen transferring agent (e.g.the flavin-N5-oxide) by mimicking a critical transition state. This study establishes how flavoenzymes may control the O_2 functionalization of an organic cofactor as prerequisite for oxidative catalysis. Our work thus illustrates how O_2 reactivity can be harnessed in an enzymatic environment and provides important knowledge for future rational design of O_2-reactive enzymes.