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Experimental estimation of copper-ligand length precision in a model fungal LPMO under redox cycling and saccharide binding

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Lytic polysaccharide monooxygenases (LPMOs) are copper-dependent enzymes that degrade polysaccharides oxidatively, with applications in second-generation bioethanol production and as virulence factors in certain pathogens [1] [2]. They have been reclassified within the CAZy database into auxiliary activity families AA9–AA11 and AA13–AA17 [3], and their active-site histidine brace is highly conserved. The catalytic mechanism of LPMOs is complex, with the priming reaction step requiring the reduction of Cu(II) to Cu(I). Since the geometric changes associated with redox cycling—whether chemically induced or triggered by photoreduction—can be subtle, the accurate determination of bond lengths and angles is essential [4]. In this study, LsAA9A from Lentinus similis was used as a model system under various experimental conditions. Analysis of the LsAA9A_Ec and LsAA9A_Ec_Cell3 structures collected under low-dose conditions showed that, compared with other Cu-coordination distances, only the Tyr–Cu bond exhibited a statistically significant change ($p = 0.00094$ in two tailed t-test). These findings confirm that saccharide substrate binding consistently shortens the Tyr–Cu distance in LsAA9A_Ec in the Cu^{2+} state, with a measured reduction of 0.21 Å. Furthermore, experiments on LsAA9A_Ec_Asc and LsAA9A_Ec_Asc_Cell3, conducted under both low- and high-dose conditions, where Cu^{2+} can be reduced to Cu^{+} by X-ray exposure, as well as at room temperature, further probed structural responses to varying redox and experimental regimes. These findings advance the mechanistic understanding of LPMOs and offer a framework for probing subtle geometric changes in metalloenzymes.

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