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No Heme-Chlorite Adduct in the Catalytic Cycle of Chlorite Dismutase: Insights From QM/MM and Dynamics Calculations

Chlorite dismutase (Cld) is one of the rare enzymes capable of forming oxygen-oxygen bonds. Cld has been identified in a very small number of anaerobic bacteria that can use perchlorate as the final electron acceptor in their electron transport/respiration chain. It has been proposed that the catalytic cycle of Cld involves the binding of chlorite to the enzyme's active site, followed by the cleavage of one of the Cl-O bonds, leading to the formation of a high-valent iron-oxo center and a ClO radical/ion, and then a reorientation to the oxygen atom bound to iron, followed by the release of chloride and molecular oxygen. However, direct experimental confirmation of the existence of a chlorite-heme adduct in Cld is still unavailable, nor is it clear what the coordination mode of chlorite is. Moreover, reaction intermediates have not been directly observed in experiments. Previous DFT calculation from us and others have concluded that hemes cannot form stable adducts with chlorite – unlike, e.g., metallacorrins such as cobalamin [1]. This paper reports the results obtained from QM/MM optimization and QM/MM molecular dynamics calculations on the catalytic cycle, revealing compelling computational evidence that a chlorite-heme adduct in Cld is unlikely to be observable experimentally.

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[1] M. Lehene, C. Zagrean-Tuza, S. Iancu, S.-R. Cosma, A. M. V. Brânzanic, R. Silaghi-Dumitrescu, B. Stoean, J. Biol. Inorg. Chem. 2024, 30, 25–34.

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