Probing Electrochemistry and Chemical Equilibria with Computational Chemistry: Corrinoids Related to Mercury Methylation

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Whether of anthropogenic or natural origin, mercury (Hg) is a highly mobile pollutant that can be transformed in the environment biotically by anaerobic bacteria and archaea and abiotically into the potent neurotoxin methylmercury ($MeHg^{+}$), which, through bioaccumulation and environmental transport mechanisms, is a global concern. We previously identified the two-gene cluster solely responsible for biotic methylation and their gene products, HgcA, a transmembrane corrinoid (i.e., B12-binding) protein, and its corresponding ferredoxin, HgcB. HgcA was predicted to bind its corrinoid cofactor tail in a "Cys-on" configuration in which a strictly conserved Cys residue from HgcA is coordinated to Co. Our previous studies support our hypothesis that the electron-rich Co–S bond facilitates unprecedented methyl carbanion ($H_3C{:}^{-}$) transfer to Hg^{II} rather than radical ($H_3C^{\bullet}$) or cation (H_3C^{+}) transfer, both of which are ubiquitous across all life. We leverage our combined expertise in computational molecular modeling and experimental spectroscopic methods to provide atomistic insights into the corrinoid–protein interactions. Expanding upon our previously developed methods for computing accurate Hg-ligand binding free energies, here we report an accurate method for computing reduction potentials and related thermochemical properties for corrinoid cofactors using density functional theory (DFT). We additionally demonstrate the robustness of our approach to calculate UV-Vis and electron-paramagnetic resonance (EPR) spectra of model corrinoids in a range of coordination environments and oxidation states. Future studies will focus on transferring our improved method to model the speciation and fate of environmental Hg and relevant redox chemistry in natural aquatic systems. Central to this end of developing a more holistic model of mercury cycling *in silico*, we are also investigating passive transport across bacterial cell membrane models with molecular dynamics (MD) simulation approaches to understand cellular Hg loading and $MeHg^{+}$ expulsion.