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In search of a viable reaction pathway in the chelation of a metallo-protein FRISCO ROSE, MIROSLAV HODAK, JERRY BERNHOLC, CHiPS / NCSU — Misfolded metallo-proteins are potential causal agents in the onset of neuro-degenerative diseases, such as Alzheimer's and Parkinson's Diseases (PD). Experimental results involving metal chelation have shown significant promise in symptom reduction and misfolding reversal. We explore, through atomistic simulations, potential reaction pathways for the chelation of Cu^{2+} from the metal binding site in our representation of a partially misfolded α-synuclein, the protein implicated in PD. Our *ab initio* simulations use Density Functional Theory (DFT) and nudged elastic band to obtain the minimized energy coordinates of this reaction. Our simulations include *ab initio* water at the interaction site and in its first solvation shells, while the remainder is fully solvated with orbital-free DFT water representation [1]. Our ongoing studies of viable chelation agents include nicotine, caffeine and other potential reagents, we will review the best case agents in this presentation.

[1] Hodak M, Lu W, Bernholc J. Hybrid ab initio Kohn-Sham density functional theory/frozen-density orbital-free density functional theory simulation method suitable for biological systems. J. Chem. Phys. 2008 Jan;128(1):014101-9.

Frisco Rose
CHiPS / NCSU

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