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Copper Chelation in Alzheimer's Disease Protein FRISCO ROSE, MIROSLAV HODAK, JERRY BERNHOLC, NCSU - CHiPS — Alzheimer's disease (AD) is a neurodegenerative disorder affecting millions of people in the U.S. AD is primarily characterized at the cellular level by densely tangled fibrils of amyloid-β protein. These protein clusters have been found in association with elevated levels of multiple transition metals, with copper being the most egregious. Interestingly, metal chelation has shown promise in attenuating the symptoms of AD in recent clinical studies. We investigate this process by constructing an atomistic model of the amyloid-β-copper complex and profile the energetic viability in each of its subsequent disassociation stages. Our results indicate that five energetic barriers must be overcome for full metal chelation. The energy barriers are biologically viable in the presence water mediated bond and proton transfer between the metal and the protein. We model the chelation reaction using a consecutive path nudged elastic band method implemented in our *ab initio* real-space multi-grid code to obtain a viable sequence. This reaction model details a physically consistent explanation of the chelation process that could lead to the discovery of more effective chelation agents in the treatment of AD.

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