

Abstract Submitted
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Concentration-dependent Cu(II) binding to prion protein

MIROSLAV HODAK, NC State U, WENCHANG LU, JERRY BERNHOLC, NC State U and ORNL — The prion protein plays a causative role in several neurodegenerative diseases, including mad cow disease in cattle and Creutzfeldt-Jakob disease in humans. The normal function of the prion protein is unknown, but it has been linked to its ability to bind copper ions. Experimental evidence suggests that copper can be bound in three distinct modes depending on its concentration, but only one of those binding modes has been fully characterized experimentally. Using a newly developed hybrid DFT/DFT method [1], which combines Kohn-Sham DFT with orbital-free DFT, we have examined all the binding modes and obtained their detailed binding geometries and copper ion binding energies. Our results also provide explanation for experiments, which have found that when the copper concentration increases the copper binding mode changes, surprisingly, from a stronger to a weaker one. Overall, our results indicate that prion protein can function as a copper buffer. 1. Hodak, Lu, Bernholc, JCP, in press.

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