

Abstract Submitted  
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**Copper attachment to a non-octarepeat site in prion protein**

MIROSLAV HODAK, North Carolina State University, Raleigh, NC, JERRY BERNHOLC, NC State U and ORNL — Prion protein, PrP, plays a causative role in several neurodegenerative diseases, including mad cow disease in cattle and Creutzfeldt-Jakob disease in humans. The PrP is known to efficiently bind copper ions and this ability has been linked to its function. PrP contains up to six binding sites, four of which are located in the so-called octarepeat region and are now well known. The binding sites outside this region are still largely undetermined, despite evidence of their relevance to prion diseases. Using a hybrid DFT/DFT, which combines Kohn-Sham DFT with orbital-free DFT to achieve accurate and efficient description of solvent effects in ab initio calculations, we have investigated copper attachment to the sequence GGGTH, which represents the copper binding site located at His96. We have considered both NNNN and NNNO types of copper coordination, as suggested by experiments. Our calculations have determined the geometry of copper attachment site and its energetics. Comparison to the already known binding sites provides insight into the process of copper uptake in PrP.

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