

Abstract Submitted
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Combined copper/zinc attachment to prion protein MIROSLAV HODAK, JERRY BERNHOLC, North Carolina State University — Misfolding of prion protein (PrP) is responsible for diseases such as “mad-cow disease” in cattle and Creutzfeldt-Jacob in humans. Extensive experimental investigation has established that this protein strongly interacts with copper ions, and this ability has been linked to its still unknown function. Attachment of other metal ions (zinc, iron, manganese) have been demonstrated as well, but none of them could outcompete copper. Recent finding, however, indicates that at intermediate concentrations both copper and zinc ions can attach to the PrP at the octarepeat region, which contains high affinity metal binding sites. Based on this evidence, we have performed density functional theory simulations to investigate the combined Cu/Zn attachment. We consider all previously reported binding modes of copper at the octarepeat region and examine a possibility simultaneous Cu/Zn attachment. We find that this can indeed occur for only one of the known binding sites, when copper changes its coordination mode to allow for attachment of zinc ion. The implications of the simultaneous attachment on neural function remain to be explored.

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