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Transition-metal prion protein attachment: Competition with copper MIROSLAV HODAK, JERRY BERNHOLC, North Carolina State University — Prion protein, PrP, is a protein capable of binding copper ions in multiple modes depending on their concentration. Misfolded PrP is implicated in a group of neurodegenerative diseases, which include "mad cow disease" and its human form, variant Creutzfeld-Jacob disease. An increasing amount of evidence suggests that attachment of non-copper metal ions to PrP triggers transformations to abnormal forms similar to those observed in prion diseases. In this work, we use hybrid Kohn-Sham/orbital-free density functional theory simulations to investigate copper replacement by other transition metals that bind to PrP, including zinc, iron and manganese. We consider all known copper binding modes in the N-terminal domain of PrP. Our calculations identify modes most susceptible to copper replacement and reveal metals that can successfully compete with copper for attachment to PrP.

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