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Cooperative binding modes of Cu(II) in prion protein MIROSLAV HODAK, North Carolina State University, ROBIN CHISNELL, WENCHANG LU, JERRY BERNHOLC — The misfolding of the prion protein, PrP, is responsible for a group of neurodegenerative diseases including mad cow disease and Creutzfeldt-Jakob disease. It is known that the PrP can efficiently bind copper ions; four high-affinity binding sites located in the octarepeat region of PrP are now well known. Recent experiments suggest that at low copper concentrations new binding modes, in which one copper ion is shared between two or more binding sites, are possible. Using our hybrid Thomas-Fermi/DFT computational scheme, which is well suited for simulations of biomolecules in solution, we investigate the geometries and energetics of two, three and four binding sites cooperatively binding one copper ion. These geometries are then used as inputs for classical molecular dynamics simulations. We find that copper binding affects the secondary structure of the PrP and that it stabilizes the unstructured (unfolded) part of the protein.

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