Abstract Submitted
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Theoretical study of metal binding in the Prion protein[1] JIANPING PAN, DANIEL COX, RAJIV SINGH, Department of Physics, U.C. Davis — We have used the SIESTA density functional theory code to study binding of divalent transition metal ions (Cu,Ni,Zn,Mn) to the two known types of attachment sites of the prion protein, one (I) outside the misfolded region, the other (II) within the misfolded region. Our binding energy trend for the (I) site is E_B(Cu)>>E_B(Ni)>E_B(Zn)>>E_B(Mn) in agreement with affinities measured *in vitro*. We find the Cu binding stronger in the (II) site to be stronger than that of the (I) site, in agreement with separate experiments, and propose a new structure for site (II) with bound Cu which is *incompatible* with a recently proposed β-helix structure, suggesting a possible correlation between copper deficiency and misfolding of the prion protein compatible with observations of copper depletion in infected neurons.

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