Modelling Copper-Protein Backbone Binding

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The determination of the X-ray structure [1] of a complex formed by Cu^{+2} and the peptide with the (His-Gly-Gly-Gly-Trp) sequence, which is part of the prion protein octarepeat, opened a new perspective in the identification of possible copper binding sites. This structural information and that coming from further studies extended to peptides containing several octarepeat sequences and to the whole protein [2], confirmed the importance of the existence of bonds between copper and the N and O amide atoms of the peptide backbone. These bonds strongly contribute in modifying the secondary structure of the peptide and compete with the bonds between His side-chain and Cu^{+2}.

The aim of this work is at understanding of the structure of the complex Cu-(HGGG), that was proposed in the literature, in the language of quantum chemistry. The coordination chemistry of this complex is coupled with the protonation state of the peptide as well as with the distortion of the protein backbone and intramolecular hydrogen bonds. These interactions can be reasonably well described within a density functional model for the electronic structure and Car-Parrinello ab-initio molecular dynamics can be carried out through recent advances in the field [3].

[1] Burns C.S. et al., *Biochemistry*, 2002, **41**, 3991. [2] Morante S. et al., *J. Biol. Chem.*, 2004, **279**, 11753. [3] Giannozzi P. et al., *J. Chem. Phys.*, 2004, **120**, 5903.

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