

Structure and dynamics of copper(II) complexes with bioligands by EPR and NMRD methods

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Copper is an essential transition metal ubiquitously occurring in biological systems, especially in enzymes where it is included in important active sites. Copper(II) complexes with amino acids and oligopeptides are of particular interest because they serve as models for metalloproteins and transport forms of copper in living organisms. Many reports were devoted to understand coordination characteristics of such complexes and effects of the amino acid side chains on structure, conformation, and stability of amino acids, peptides, and proteins (see e.g. Ref. [1] and references therein). But so far open questions remain about effect of side chain groups and medium properties on the hydration and dynamical behavior of copper(II) amino acid and oligopeptide complexes.

In this work structural features and dynamical behavior of copper(II) complexes with amino acids and oligopeptides were investigated by combined EPR and NMR relaxation methods. Influence of salt background on the *cis-trans* isomer equilibrium of copper(II) amino acid complexes was observed by EPR. Rotational correlation times and activation energies of rotational motion were found from temperature dependences of EPR spectra and further used to simulate NMRD profiles. From NMRD data some structural and dynamical parameters of solvation shell were derived. It was found that the exchange rate constants of axial water molecules are not lower than the value k_1 (298 K) $\sim 5 \cdot 10^9 \text{ s}^{-1}$ obtained for copper(II) aqua ion [2] or even higher (as was observed for $\text{Cu}(\text{L-Asp})_2^{2-}$, $\text{Cu}(\text{L-Glu})_2^{2-}$, $\text{Cu}(\text{L-LysH})_2^{2+}$, and $\text{Cu}(\text{L-Pro})_2$). The very short 2nd coordination sphere water exchange times were obtained ($\sim 4\text{--}13 \text{ ps}$ at 298 K) for studied complexes and explained on the basis of Frank-Wen theory by quickly taking in water molecules from the 2nd coordination sphere into surrounding cavities. At the same time it was shown that carboxylic groups of aspartic and glutamic acids, alcoholic groups of serine, and ammonium groups of lysine increase the lifetimes of the 2nd coordination sphere water molecules. The same effect was observed in the case of proline probably because pyrrolidine ring of proline captures water molecules.

For confirmation of structural conclusions quantum-chemical computations of the copper(II) complexes have been performed by DFT method. On the basis of NMRD and DFT data pentacoordination of copper(II) was proposed for all complexes studied.

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1. *Amino Acids, Peptides and Proteins*. Vol. 1-38 (Specialist Periodical Reports), RSC Publishing, Cambridge, 1969-2013.
 2. A. Pasquarello, I. Petri, P. S. Salmon, O. Parisel, R. Car, È. Tòth, D. H. Powell, H. E. Fischer, L. Helm and A. E. Merbach, *Science*, 2001, **291**, 856.