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Metal-peptide complexes - a novel class of molecular receptors for electrochemical phosphate sensing

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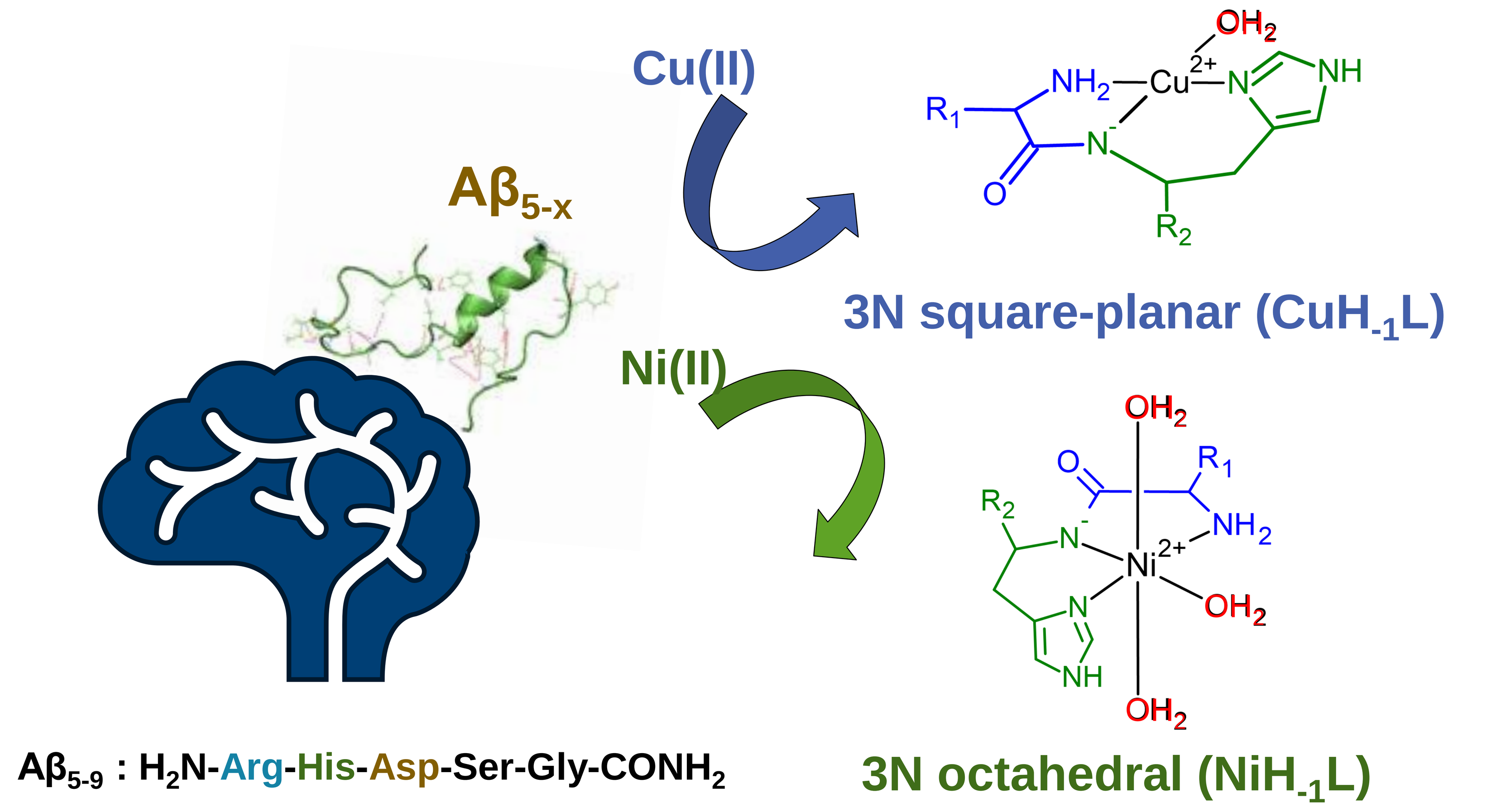
Abstract

Amyloid-β (Aβ) peptides are crucial in the pathology of Alzheimer's disease. On the other hand, their metal complexes possess distinctive coordination properties that could be of great importance in the selective recognition of (bio)analytes, such as anions.

Here we report a novel group of molecular receptors, metal-peptide complexes, that combines features of synthetic inorganic ligands and naturally occurring binding proteins. This approach offers the possibility of fine-tuning the receptor sensitivity and selectivity for desired applications. Thus, our research focused on the design of the receptor for phosphates consisting of the Aβ peptide and a metal ion. We analyzed how the change of metal ion center affects the coordination and redox properties of the binary Cu(II)/Ni(II)-Aβ complexes, as well as their affinity towards phosphate species.

$A\beta_{5-9}$ binary complexes



Scheme 1. Structures of a square-planar Cu(II) complex and an octahedral Ni(II) complex of the $A\beta_{5-9}$ peptide bearing a His-2 binding motif along with an amino acid sequence of the studied peptide.

POTENTIOMETRY

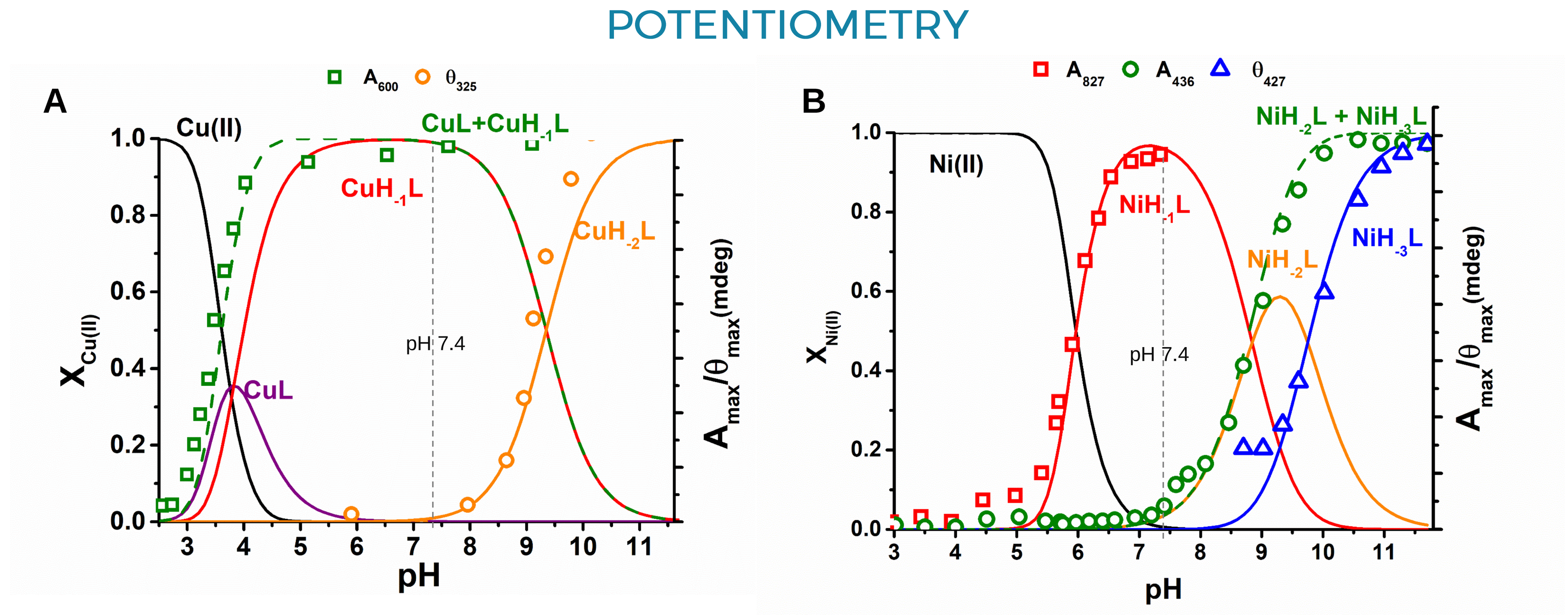


Figure 1. Species distribution calculated for Cu(II)-$A\beta_{5-9}$ (A) and Ni(II)-$A\beta_{5-9}$ (B) (metal : peptide = 0.9 mM : 1.0 mM), using stability constants determined by potentiometric titrations overlaid with results of analogous spectroscopic titrations. Diagram (A) was prepared based on our previous results [1].

VOLTAMMETRY

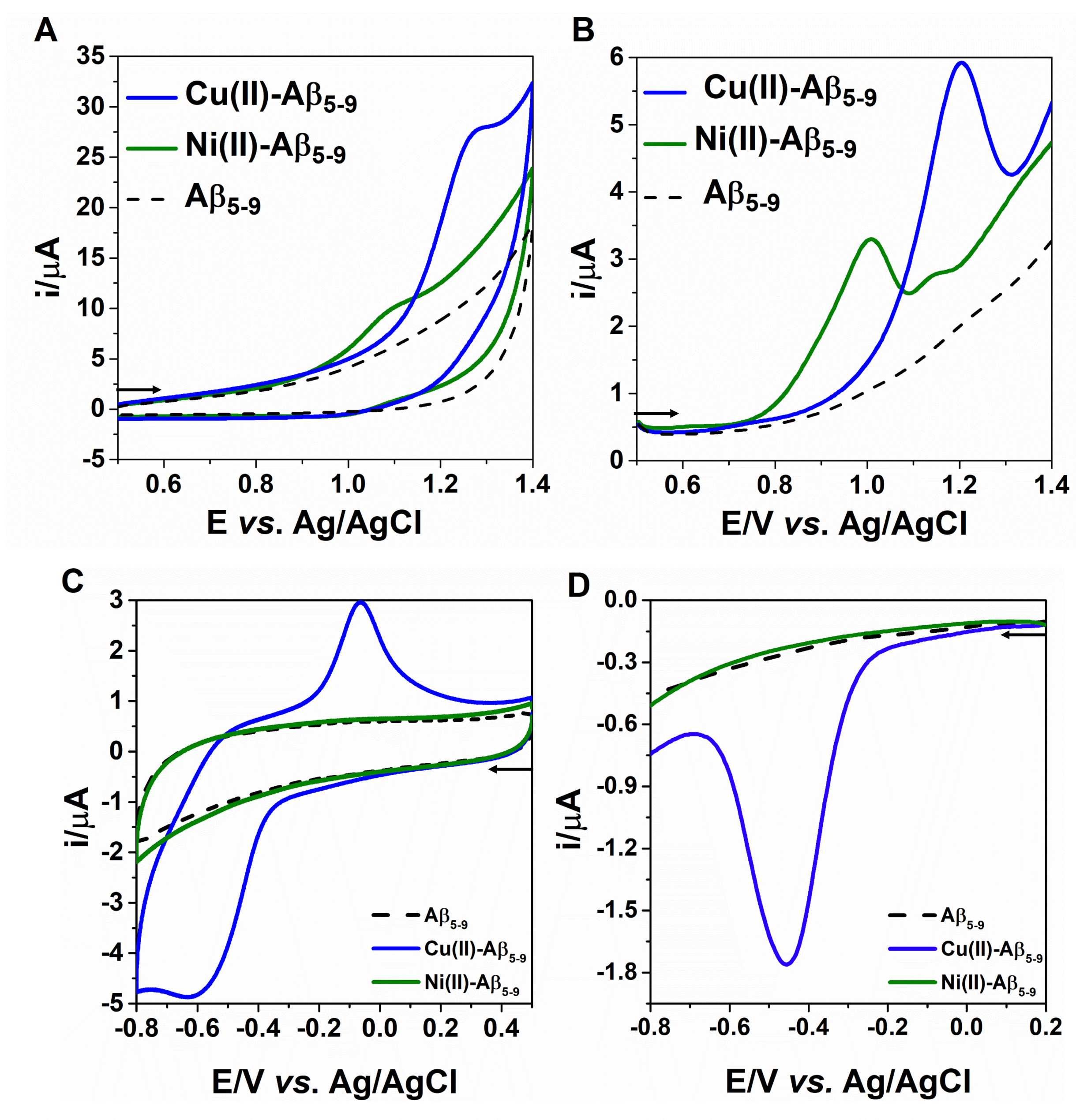


Figure 2. CV (A,C), and DPV (B,D) curves performed for 0.5 mM $A\beta_{5-9}$ in absence (black doted line) and in the presence of 0.45 mM Cu(II) [2] (blue line), or 0.45 mM Ni(II) (green line) recorded in 100 mM KNO_3 at a pH = 7.4, scan rate v = 0.1 V/s. Scanned towards possitive (A-B) and negative (C-D) potentials.

[1] N. E. Wezynfeld, A. Tobolska, M. Mital, U. E. Wawrzyniak, M. Z. Wiloch, D. Plonka, K. Bossak-Ahmad, W. Wróblewski, W. Bal, Inorg. Chem. 2020, 59, 14000-14011.
[2] A. Tobolska, N. E. Wezynfeld, U. E. Wawrzyniak, W. Bal, W. Wróblewski, Dalton Trans. 2021, 50, 2726-2730.

Interaction with phosphate anions

SENSITIVITY OF PHOSPHATE RECOGNITION

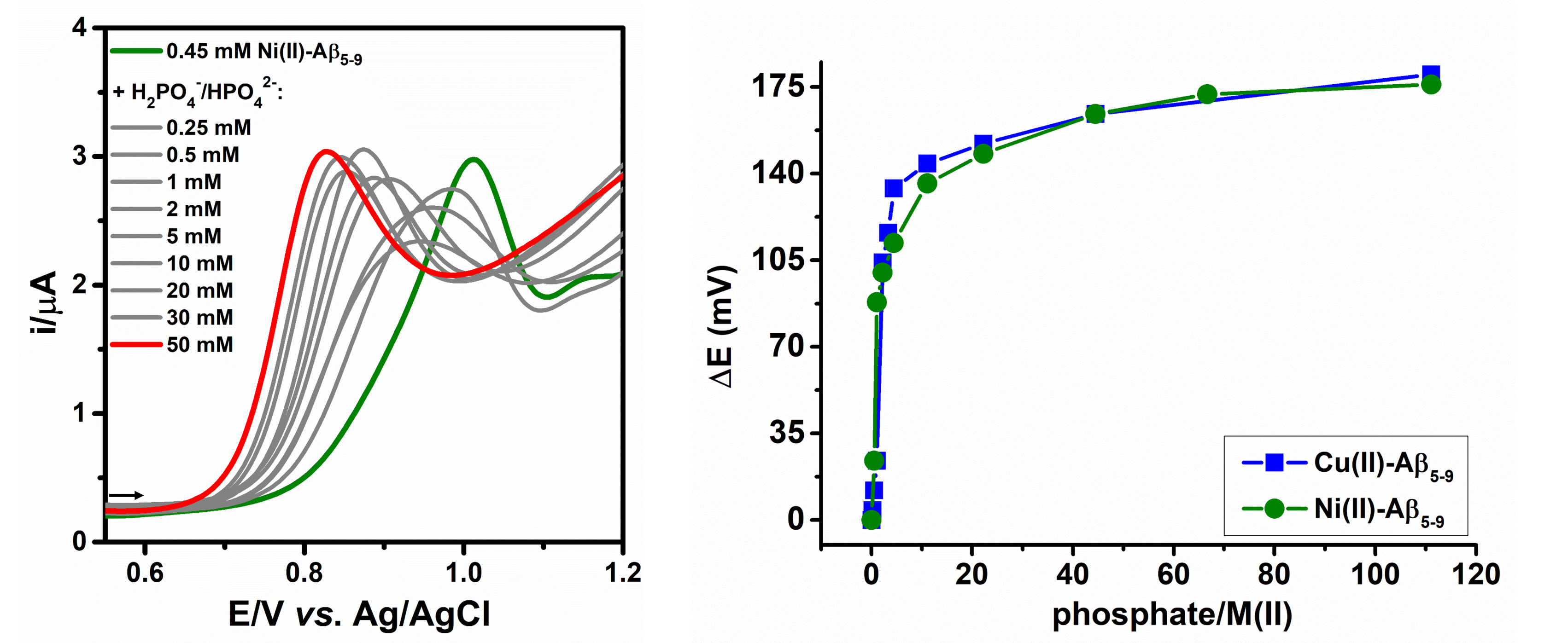


Figure 3. Left: DPV curves of the titration of Ni(II)-$A\beta_{5-9}$ (0.9 : 1.0 molar ratio) with NaH_2PO_4/Na_2HPO_4 recorded in 100 mM KNO_3 (pH 7.4). **Right**: Dependence of ΔE on the phosphate to metal ion ratio for $A\beta_{5-9}$ complexes with Cu(II) [2] (blue curve) and Ni(II) (green curve). ΔE is the change of the potential of Cu(II)/Ni(II) oxidation for the binary complex and the respective ternary systems.

SELECTIVITY OF PHOSPHATE RECOGNITION

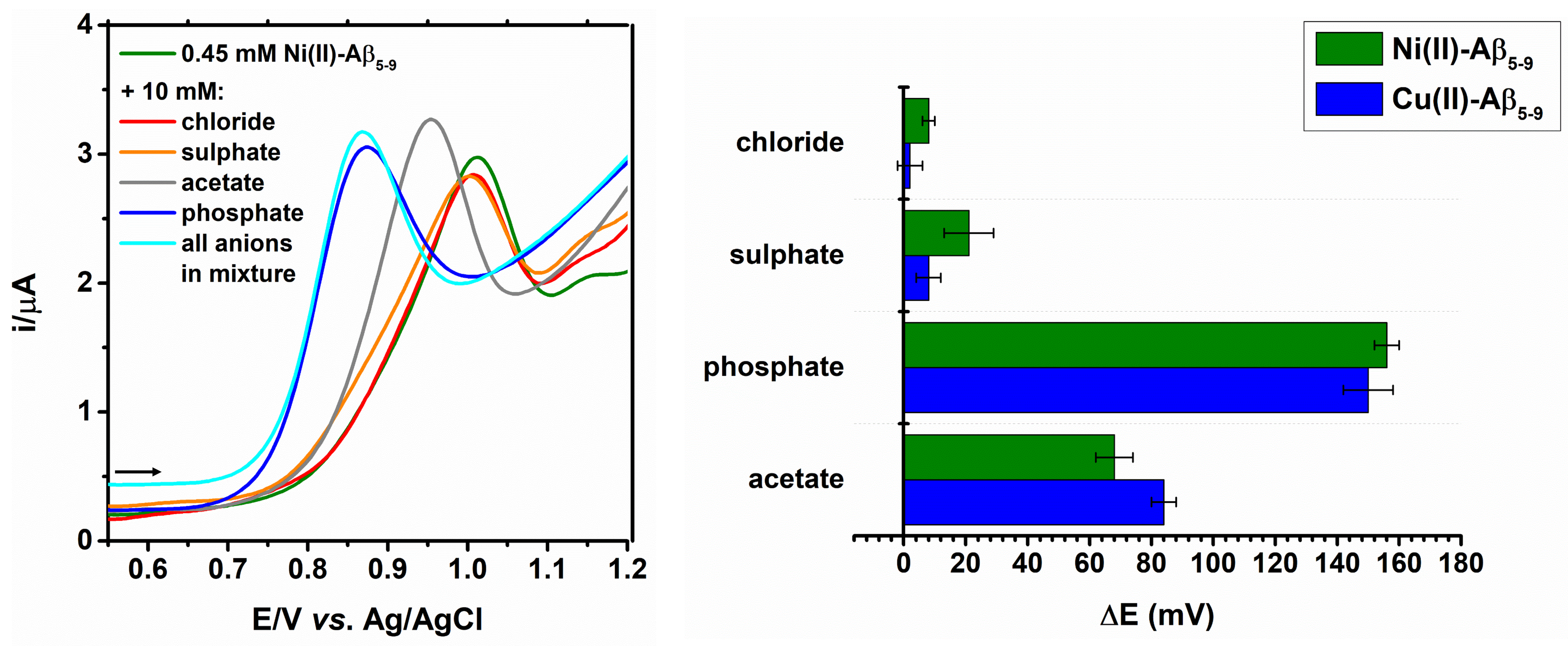
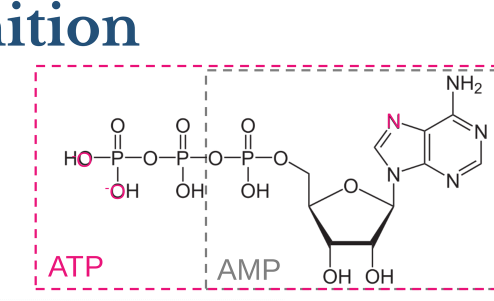


Figure 4. Left: DPV curves obtained for Ni(II) complexes with $A\beta_{5-9}$ (0.9 : 1.0 molar ratio) after addition of 10 mM selected anions performed at pH 7.4 in 100 mM KNO_3. **Right**: Column diagram showing changes in the Cu(II)/Ni(II)-$A\beta_{5-9}$ oxidation signal position after anion addition.

Nucleotide recognition



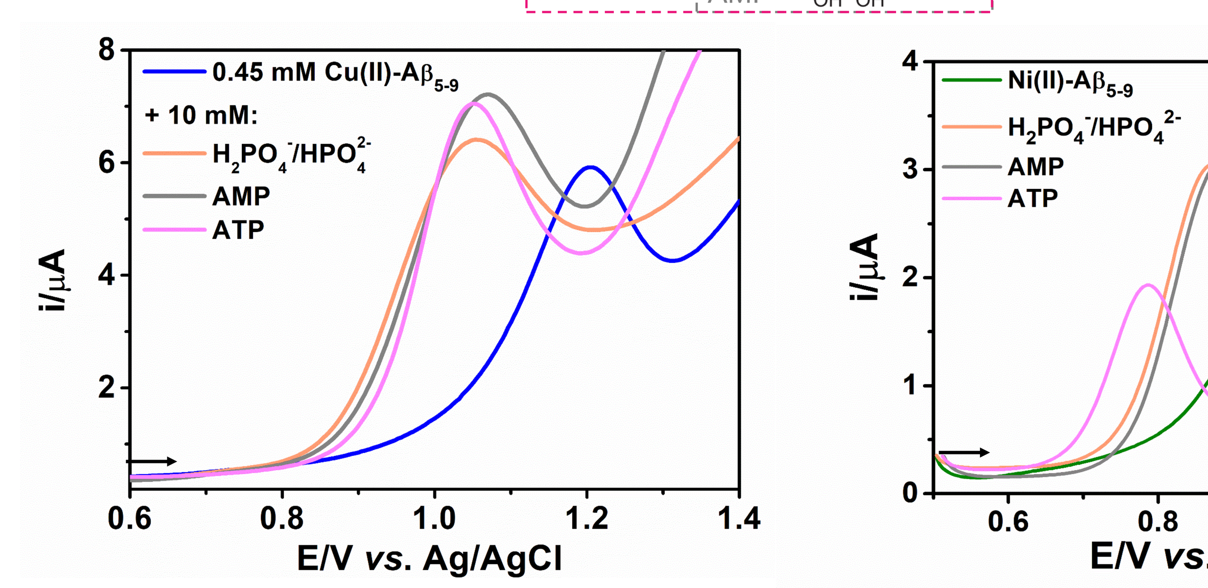


Figure 5. DPV curves obtained for Cu(II) (**left**) [2] and Ni(II) (**right**) complexes with $A\beta_{5-9}$ (0.9 : 1.0 molar ratio) after addition of 10 mM $H_2PO_4^-/HPO_4^{2-}$, Adenosine 5'-monophosphate (AMP), Adenosine 5'-triphosphate (ATP) performed at pH 7.4 in 100 mM KNO_3.

Summary and conclusion

The change of the metallic center in the peptide complex significantly influences its coordination properties and redox activity.

- At pH 7.4 Cu(II)-$A\beta_{5-9}$ complex is square-planar when Ni(II)-$A\beta_{5-9}$ is rather octahedral (Scheme 1 and Fig. 1).
- Significant differences in redox behavior were observed: (i) facilitated oxidation process, (Fig 2. A-B) (ii) lack of reduction process (Fig. 2 C-D) for Ni(II) complexes.
- Altering the metal center from Cu(II) to Ni(II) does not change the sensitivity of the complex toward phosphate anions (Fig. 3).
- Smaller changes of oxidation peak potential in the presence of interfering anions were observed for Cu(II)-$A\beta_{5-9}$ (Fig. 4). Nevertheless, both complexes show good selectivity for phosphate anions.
- The signal in the DPV curves for Ni(II)-$A\beta_{5-9}$ occurs at different potentials in the presence of AMP and ATP in contrast to Cu(II)-$A\beta_{5-9}$ (Fig. 5).

Obtained results could lead to development of a novel group of redox-active compounds for phosphate recognition and bring a new perspective on the design of peptide-based receptors for electrochemical biosensors.

Acknowledgements

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