

Peptides and proteins play numerous important roles in living organisms. Their biological activity depends, among others, on the ability to bind metal ions. Metal ion coordination by peptides and proteins leads to various properties of the resulting complexes, which has positive or negative effects on the living organism functions. The negative impact of such complexes can contribute to the development of disorders and disease.

Metal complexes with peptide called β -amyloid ($A\beta$) are crucial in the pathology of Alzheimer's disease – a chronic brain disorder that results in a progressive loss of memory and cognitive functions. $A\beta$ peptides have a strong aggregation tendency, additionally induced by the binding of copper(II) ions, and accumulate in the brain as senile plaques. This process causes irreversible neuron damage, and according to one of the popular hypotheses, complexes of metal ions with $A\beta$ promote the generation of the reactive oxygen species (ROS), which may lead to oxidative cell damage.

The complexes of amyloid β are well-known for neurotoxicity. However, $A\beta$ peptides also have distinctive coordination properties enabling selective recognition i.e. specific interactions with bioanalytes, such as negatively charged molecules (anions). Anions are molecules of great concern to human and environmental health. Among them, phosphate anions, which are involved in ATP synthesis, protein phosphorylation, skeletal mineralization, as well as are related to the proper functions of muscle and nervous system, deserve special attention. Monitoring of phosphate concentration, e.g. in blood, allows the diagnosis of bone, kidney, and thyroid diseases. Therefore, the development of new methods for the quantitative analysis (determination) of these anions is an important scientific goal. Chemical sensors are a good alternative to classic analytical methods due to high selectivity and sensitivity, but their construction requires the synthesis of appropriate receptors selectively binding the analyte.

The project aims to develop a novel redox-active class of molecular receptors – metal-peptide complexes, selective for phosphate species in physiological conditions. The studies are focused on metal complexes of peptides, based on N-truncated amyloid β sequence $A\beta_{5-9}$. The presence of metal ion allows to use simple electrochemical techniques to investigate the interactions between the analyte and receptor molecule, and in the future, enables the construction of electrochemical biosensors. The distinguishing feature of the proposed class of recognition compounds is the possibility of fine-tuning their sensitivity and selectivity, by altering the amino acid sequence and the metal ion center.

The implementation of the project is significant in the perspective of designing novel molecular receptors selective for biologically relevant anion species. The obtained results may contribute to the development of modern analytical methods, in particular peptide-based electrochemical sensors, which are simple, portable devices enabling the rapid determination of an analyte in complex samples. In addition, the conducted research could be interesting due to the possibility of describing the interactions between peptide/protein metal complexes and phosphates (or other biologically active molecules) occurring in the body. Therefore, the results may lead to better understanding of many pathologies and to the establishment of new therapeutic targets or even to the design of innovative drugs.