Undoubtedly, neurodegenerative diseases are one of the most serious diseases in modern society. Understanding the general mechanism underlying these diseases is an enormous problem, but on the other hand, also a challenge for young scientists. It is necessary to understand the current state of knowledge at the molecular level and the impact of metal binding on the pathogenesis of the diseases. Unfortunately, up to date most of these mechanisms are based only on hypothesis and conjectures.

The knowledge about neurodegenerative diseases is mainly based on the pathology and accumulation of abnormal forms of amyloidogenic proteins in the brain. Prion disease are group of fatal neuronal, and to some extent infectious disorders, characterized by progressive brain degeneration. Prion diseases are associated with protein infectious agents called prions (proteinaceous infectious particles) that cause the conversion of the normal cellular prion protein form (PrP^{C}) into the abnormal scrapie prion protein (PrP^{Sc}). The two forms of PrP have an identical primary structure, but differ in their secondary structure and in their physicochemical properties. Unlike PrP^{C}, PrP^{Sc} is highly insoluble and highly prone to aggregate. Protein aggregation and formation of pathological deposits are associated with elevated β-sheet content in PrP^{Sc}.

It has been shown that the N-terminal domain of the prion protein contains in its structure the amino acid sequences capable of binding to copper ions, and responsible for the neurotoxic properties of the protein (the ability to easily form fibrils/deposits/protein aggregates in the brain). The aim of the project is the understanding of the bioinorganic chemistry of biologically significant copper complexes of the N-terminal domain of the human prion protein (hPrP), in the presence of micelles, which mimic the lipid bilayer, to which the hPrP is anchored to in vivo. Due to the presence of a hydrophobic domain in amyloidogenic fragment of human prion protein and the ability of the prion protein to interact with the lipid bilayer, the physiochemical research is carried out in the presence of surfactants mimicking the membrane environment *in vitro*. The use of surfactants in the proposed project is extremely important to explore the impact of the presence of biological membranes on the specific metal ion binding modes. The coordination abilities of the proposed ligands in the absence and presence of a surfactant will be compared to each other. The relevant aim of the research is to receive information if the presence of a membrane environment has influence on conformational changes of the investigated peptide fragments and their copper complexes.

To achieve the proposed aims, it is necessary to use a variety of different thermodynamics and spectroscopies techniques useful to (i) determine the thermodynamic parameters of copper binding, (ii) identify donor atoms and coordination geometry species, (iii) study the stoichiometry of copper-ligand complex formation and (iv) determine three-dimensional structure of ligands and their copper complexes. Moreover, Atomic force microscopy (AFM) is very useful technique, which will allow us to understand prion protein folding that can lead to aggregation and influence metal ions on the conformational state of PrP. The obtained result lead to get the answer for question: Does the addition of metal ions has influence on the accumulation of the pathological form of prion protein, and maybe the presence of biological membranes favor this process?

The proposed project involves basic research aiming to determine the binding mode and properties of formed complexes with peptide fragments of the human prion protein N-terminal domain. The project will provide important information about the bioinorganic chemistry of this protein. The research in membrane-mimicking environment will increase the knowledge about biological/cellular processes concerning interactions of prion proteins with membrane cells. Neurodegenerative diseases are still based on huge number of hypothesis, therefore it is important to find out the mechanism which leads to the pathogenic process. The overall view of neurodegenerative diseases is not remotely optimistic because no effective drugs are available to cure or stop the progression of these diseases. No drugs can cure or relieve the symptoms of prion disease. The rarity of this disease (one person per million) means that developing drugs and conducting clinical trials is even more complicated than that for other neurodegenerative diseases.