Description for the general public

The growing problem of bacteria resistance to conventional antibiotics is a huge challenge facing medicine of the twenty-first century. Diseases that are easily cured, such as sore throats and ear infections may soon become immune to antibiotics. In many bacterial strains, virulence has increased as a result of the acquired drug resistance. The World Health Organization reports that more than ten thousand people are annually infected and die in U.S. hospitals because of lack of effective antibiotics.

Another equally serious health problem for people living in the twenty-first century are incurable so far neurodegenerative diseases, including Alzheimer's and Parkinson's disease. About 24 million people worldwide have dementia mostly associated with AD (50-60% of cases). The prevalence of dementia is <1% in the aged 60-64 years, but shows a dramatic increase with age reaching 33% of prevalence in people aged 85 years or older.

Membrane-active peptides (MAPs), including **antymicrobial peptides** (AMPs) and **amyloid peptides** (APs), on the one hand are a promising class of **therapeutics**, which are able to kill multidrug-resistant bacteria but, on the other, they can act as toxins for human cells inducing very serious neurodegenerative diseases.

AMPs are able to kill multidrug-resistant bacteria. They are components of the innate immune system of all living organisms, such as bacteria, fungi, insects, tunicates, amphibians, crustaceans, birds, fish, mammals, and human beings. Currently available antibiotics interact strongly with specific target molecules, usually proteins. In contrast, most antimicrobial peptides act by a nonspecific mechanism and often induce cell death by disrupting the plasma membrane. As a result, the bacteria do not become resistant to the antimicrobial peptides. Despite that AMPs have been studied for many years, their mechanism of activity is still under debate. Understanding of the AMP membrane disruption mechanisms by different peptides in many different types of membranes is necessary to elucidate factors determining the activity of a peptide in a particular membrane environment and to design therapeutic peptides with the desired potency and selectivity.

The presence of fibrillary plaques in the brain of the Alzheimer’s and Parkinson’s patients directed scientists to focus on the fibrillary state as a central to disease progression. However, the latest study proved that the monomers or oligomers of APs are the primary toxic species, which triggers pathological processes that lead to disease. Currently available treatment can only alleviate symptoms of these diseases. Therefore, there is a need to improve the understanding of pathogenesis to design new therapeutics.

A common feature of AMPs and APs is their ability to bind to biological membranes. A similar structure, sequence, and biological activity suggests that the mechanism of action of these peptides is governed by similar physico-chemical phenomena. The mechanism of AMPS and APs action is based on the disintegration of the cell membrane by creating channels, depolarization or fragmentation of the membrane.

The research goal of the project is to study interactions of different membrane-active peptides and selected therapeutic with model biological membranes with the use of electrochemical, spectroscopic, and surface imaging techniques. The techniques proposed will allow "looking" deep into the pores formed by the peptides and fully characterize the studied modeled biological systems in conditions similar to the natural. Our research will provide a fundamental understanding, at the molecular level, how biologically active peptides disintegrate model cell membranes. This knowledge will contribute to the development of new pharmaceuticals, alternative to currently available antibiotics as well as effective drugs for neurodegenerative diseases. In addition, our research will determine the durability of phospholipid bilayers in different conditions. This information can be used in a wide range of biomedical research, such as the drugs delivery, biocompatibility of the implant, cell adhesion, etc.