Understanding Cross-Talk Between Amyloid Proteins

Many neurodegenerative diseases, considered to be civilization diseases, result from assembling of proteins, or their fragments, into fibrils called amyloids. This happens as a result of partial unfolding of a protein chain, or its cutting into fragments, which reveals areas that are highly prone to connect with other protein chains exhibiting similar property. The molecules first combine into aggregates consisting of several elements, which are called oligomers. These aggregates grow, and their structures become more regular - then they are called protofibrils. Eventually, long fibrils are formed, consisting of many protein fragments. Each fibril has a very regular structure and resembles a zipper. They are very hard soluble and usually lead to cell death and a generalized disease process. Such structures have been observed in the brains of Alzheimer's disease patients, as well as in Parkinson's disease, amyotrophic lateral sclerosis, Huntington's disease, cataracts, even in type 2 diabetes, and many other diseases. There is also a group of proteins with similar properties, but more soluble, which play a useful role in organisms – they are called functional amyloids.

Some amyloids can affect aggregation of other proteins. This may occur as a result of interactions between chains with different amino acid compositions. This phenomenon is not well understood. Generally, it can be observed when interacting protein chains show some sequence similarity. However, this condition is not always met. Researchers are wondering if such interactions may lead to diseases.

The project we propose aims to address such questions. To this end, we plan to study protein chains which may be involved in such interactions and observe the characteristics of their aggregation. Based on the experimental database, a computational tool will be developed to predict the result of interactions between any pair of proteins. Bioinformatics methods will be used here. The final result will be extended experimental database, new computational methods developed and online software, made available to general public, able to predict results of such interactions.

The resulting methods will enable, among others, testing what proteins may interact with proteins involved in amyloidoses, posing a threat to accelerated development of a disease. They will also contribute to better understanding of the phenomenon of interactions between amyloid proteins.