In 2020, there were about 50 million people in the world suffering from Alzheimer's disease. It is estimated that by 2050 this number will increase to 152 million. As a result of this debilitating disorder, memory and thinking abilities as well as social skills are significantly reduced. Because of that, ill people require constant care, which leads to a significant burden on the healthcare system, even in the wealthiest countries.

In the brain tissue of Alzheimer's patients, so-called amyloid plaques are observed. The plaques result from the pathological aggregation of the amyloid-β (Aβ) protein. According to one of the hypotheses, the presence of amyloid plaques causes a progressive neurodegeneration leading to the death of neurons. Despite of extensive studies the molecular mechanisms of the abnormal aggregation of amyloids are not fully explained. Thus, it is not possible to develop effective therapeutic strategies. According to current scientific reports, the process of Aβ aggregation is a phenomenon closely related to changes in the secondary structure of a protein.

In order to follow secondary structure changes occurring upon the abnormal aggregation an experimental methodology that allows investigation into the secondary structure of individual aggregates has to be applied. Amyloids samples are very heterogeneous and consist of many aggregates at various stages of fibrillation. Conventional analytical techniques deliver only averaged information from many molecules because they are not sensitive enough to track changes in chemical structure at the individual aggregate level. Therefore, I propose to use nanospectroscopic techniques that combine the high resolution of scanning probe microscopy (SPM) and the chemical selectivity of vibrational spectroscopy (infrared spectroscopy, Raman spectroscopy). Its high sensitivity and spatial resolution allow for simultaneous imaging with a scan step of several nanometers, allowing the visualization of individual Aβ structures and the detection of chemical changes of the secondary structure of individual aggregates.

Various chemical compounds that can inhibit Aβ aggregation are currently intensively investigated. One of them is epigallocatechin gallate (EGCG), which is present in green tea. It can interact with the Aβ aggregates, by forming hydrogen bonds with individual amino acids. It results in blocking the formation of the β-sheet secondary structure and thus preventing fibrillation. Despite numerous studies, the exact mechanism of the EGCG-Aβ interaction with Aβ is still not fully understood. In this project, I propose the use of infrared nanospectroscopic approach (nanoFTIR and AFM-IR) to study the inhibition of Aβ aggregation in a rat protein model. The aggregation process will be examined for several protein fragments. Applied methods will allow me to determine the effect of EGCG on the inhibition of aggregation. Conducting measurements for the investigated fragments will allow a better understanding of the nature of the interaction between EGCG and Aβ at the single-molecule level.

In this project, I will perform a comprehensive study of Aβ aggregation, which will provide a better understanding of the interaction of EGCG with various types of Aβ protein fragments. To reduce the risk of this ambitious project, I propose to optimize several experimental procedures including: measurements of Aβ macroscopic samples using conventional spectroscopic techniques (Raman, ATR-FTIR) and AFM imaging. The obtained results will enable a better understanding of the aggregation of Aβ in Alzheimer's disease, and will be helpful in the development of therapeutic strategies inhibiting the pathological aggregation of Aβ.