

Neurodegeneration becomes one of the most commonly diagnosed dysfunction with no certain cure, which has a greater chance of affecting individuals with the age of 65 years or older. Neurodegenerative diseases are commonly associated with neuropathologically distinct amyloid plaques, neurofibrillary tangles and intracellular inclusions in the brain.

Nowadays, the main perpetrators are believed to be small mobile aggregate forms called oligomers, for example misfolded amyloid beta in the case of Alzheimer disease or  $\alpha$ -synuclein ( $\alpha$ -syn) in the case of Parkinson disease. Oligomers possess the potential to subvert several aggregation pathways and overwhelm cellular functions causing toxicity. Thus it is important to find the way for detecting the toxic oligomer species at the very early stage of their formation, so that patients can receive rapid information about their health condition and have a better outcome in the therapy.

A common and widespread method to detect protein aggregates is fluorescence. For that purpose the aggregates are stained with organic molecule named Thioflavin T (ThT) dye which is a gold standard in imaging of neurodegeneration. But fluorescence of ThT lacks the sensitivity to oligomer species.

To boost that sensitivity ThT chemical analogues will be used in the project and fluorescence will be amplified in the process of stimulated emission. In the ASE process photons emitted spontaneously by excited molecules are multiplied in the stimulated emission process when they interact with other excited molecules during their propagation through the medium (it is the physical mechanism that underlies the operation of lasers). The result is a directional emission of high intensity light with its spectrum significantly narrower than that of fluorescence.

ASE will be used to detect aggregation in vitro and in various tissues including the cerebrospinal fluid (CSF), whereby the disease-related protein recombinant is seeded with the patient's fluid. By monitoring the amplified spontaneous emission (ASE) a remarkable recognition sensitivity to pre-fibrillar oligomeric forms can be achieved. Thus, in contrast to fluorescence, ASE of ThT, can be used to detect and differentiate amyloid oligomers and evaluate the risk levels of neurodegenerative diseases to potential patients before the clinical symptoms occur.