The ageing of populations in developed and developing countries is becoming a challenge in many areas of human life. Among them, the currently untreatable and difficult-to-diagnose neurodegenerative diseases, typical for senior age, are becoming a serious problem due to the increase in the number of patients. Early-stage hallmarks of the neurodegenerative diseases (e.g. Parkinson's and Alzheimer's diseases, Huntington's chorea or spinal muscular atrophy) are associated with neuropathological aggregation or folding of alpha-synuclein, amyloid beta, tau protein and prions. Hence, there is a growing need to detect these processes at the earliest possible stage (before the clinical symptoms appear), particularly in a group of people at risk through genetic factors.

A common method of detecting abnormalities in human protein aggregation is fluorescence measurement preceded by dyeing of sample with Thioflavin T and rhodamine 6G fluorophores. Unfortunately, this approach is only capable for the observation of advanced hallmarks of neuropathological protein folding, remaining insensitive to detecting the early-stage oligomers.

An important step in the early-stage diagnosis of neurodegenerative diseases was made at the University of Warsaw, where amplified spontaneous emission and laser action has been observed for illuminated Thioflavin T. Contrary to the standard fluorescence measurements, in lasing spectroscopy the signal is amplified, enabling a generation of a narrow-band laser beam. Lasing spectroscopy involves irradiating thin biolayers, droplet resonator, or dye solutions with peptides confined between two mirrors (resonant cavity). The high dye content enables population inversion associated with the detection of oligomeric forms for selected markers of neurodegenerative diseases. Unfortunately, this approach contains a number of drawbacks. The resonance cavity is suitable and engineered for one kind of dye. The changing of sample requires that cavity have to disassembled and reassembled each time is associated with keeping of a high level of parallelism between the mirrors and a short distance between them. The bonding nature of the Thioflavin T dye to the peptide in the liquid is not sufficient to slow molecular movement, and thus the signals obtained are weak. Hence, viscous solvents to slowdown the molecular movement of the dye are required.

The project will focus on the detection of aggregates (oligomers) with increasing size and typical of the early-stage form of Parkinson's (GA, GVATVA, GGAVVT, and alpha-synuclein) and Alzheimer's (diphenylalanine, KLVFFA, and amyloid beta) diseases using lasing spectroscopy simultaneously eliminating the abovementioned drawbacks and giving new value to the neurodegenerative-diseases diagnosis. A proposed alternative to thin biolayers, droplet resonators and fluid inside resonant cavity is the adaptation of nanoporous anodic alumina as a membrane. The membranes will be surface-functionalised in order to efficiently immobilise the stained peptides in the pores. The absence of a liquid phase in the membrane will enable strong laser signals to be obtained during sample irradiation, while at the same time the surface functionalisation will prevent dye-peptide aggregation as was observed for thin biofilm. The pore diameter of the membrane will be varied periodically, allowing the formation of internal light-scattering centers to amplify the laser signal. In addition, the anodic alumina membranes have a tunable photonic bandgap, enabling the bonding of peptides with different dyes (Thioflavin T and rhodamine 6G), and extending the analytical capabilities of lasing spectroscopy. Application (spotting), sample-lifetime and handling of the stained material will be greatly improved in respect of existing approaches.