Two-Photon Spectroscopy for the Early Diagnosis of ALS: Folding and Aggregation of SOD1

Goenawan, Natasha

Mo, Ziyan

Two-photon absorption (2PA) cross-sections of dye chemically bound to proteins were used as markers to monitor the unfolding and aggregation transitions of the protein Bovine Serum Albumin (BSA) and Superoxide Dismutase 1 (SOD1). Aggregation of SOD1 is considered to be a major reason for the death of motor neurons responsible for muscle function in implicated for the familial form of Amyotrophic Lateral Sclerosis (ALS). The hypothesis behind the project is that if soluble aggregated forms of SOD1 are detected, it can lead to an early diagnostic tool for the onset of ALS disease. In search of such analytical tools, the feasibility of 2PA cross-sections of dyes bound to proteins for probing the folding and aggregation of SOD1 was investigated. The unfolding of BSA or SOD1 was carried out by varying the temperature (25-90 degrees C) and monitored by one and two-photon excited fluorescence of Fluram, a primary amine binding dye that readily binds to Lysines in proteins to give rise to color and fluorescence in the visible region, bound to the proteins. Interestingly, 2PA cross-sections (ratio of two to one photon fluorescence) are able to monitor unfolding more sensitively over other optical techniques. The mechanism is attributed to the decrease in electric fields around the dye during unfolding. The aggregation of SOD1 or BSA was studied by adding 1 M GuCl to soften the proteins and varying the temperature, and investigated with UV-Vis absorption, one and two-photon excited fluorescence, time-resolved fluorescence, and dynamic light scattering. Results indicate that 2PA cross-sections of Fluram bound to proteins can selectively monitor the aggregation of proteins and the mechanism is ascribed to the changes in local electric fields around the probe during aggregation.

Awards Won:

Spectroscopy Society of Pittsburgh: NOT ON STAGE - DO NOT ANNOUNCE&gt

Honorable Mention of $500

SPIE, the international society for optics and photonics: Second Award of $500