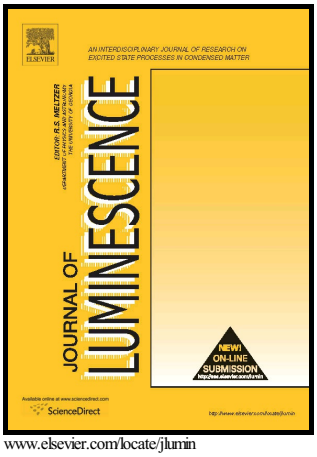

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Surface Patterns of Insulin Fibrils Revealed by Time-Resolved Spectroscopy Measurements of Fluorescent Probes

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Abstract

Amyloid fibrils are a hallmark of neurodegeneration. The structural diversity of amyloids necessitates sensitive methods and probes that can be reliably used to characterize them. Here, we study insulin fibrils and its polymorphs seeded with LVEALYL peptide in context of probing the surface patterns using Thioflavin T (ThT) and polythiophene derivative - Poly[2-(3-thienyl)ethoxy-4-butylsulfonate] (PTEBS) polymer. We investigated the dynamics and lifetimes of these two probes using time-resolved absorption and fluorescence spectroscopy. The photoluminescence emission lifetimes of the probes showed different relaxation times in the presence of structurally different amyloid fibrils. However, only PTEBS revealed sensitivity to the surface patterns of the fibrils that was explained by uneven charge distribution and exposure of different amino acids to the fibril surface where probe is interacting with the fibril. We find that PTEBS binding to distinct amyloid surfaces causes perturbation of the main chain of the polymer creating new conditions for energy distribution in the excited states that favors formation of various emitting species. The results indicate that PTEBS and ThT are comparable in terms of recognition of fibril polymorphs whereas polymer probe provides additional dimension to study fibrils surface patterns that can be revealed using time-resolved spectroscopy.

Keywords: amyloid fibrils, peptide aggregates, water soluble polythiophene, amyloid-polymer complex, time-resolved spectroscopy, fluorescence lifetimes, excited-state dynamics.

Introduction

Insulin is a hormone peptide, used by many[1] as a model system to study amyloid fibril formation. Insulin forms. Extracellular fibrils of insulin are formed at the sites of repeated insulin injection in diabetic patients[2-3], a rare medical condition which cases significantly increased since 2002[4]. Although the cause for such increase is still unknown, data suggests correlation between the injection-related cases and the production and storage of therapeutic insulin. Thus, it is critical to find methods and probes for detection of insulin amyloids. Additionally, structural studies of insulin fibrils could help find strategies to reduce amyloid fibril formation, and improve the handling and storage of therapeutic insulin.

Insulin fibrils have the characteristic for amyloids features, such as cross-β X-ray diffraction pattern[5-6], fibrilliar morphology[7], and increased quantum yield in Thioflavin T fluorescence[8]. Structural studies of insulin fibrils revealed that insulin can form different polymorphs depending on environmental factors, such as pH value, temperature, incubation time, agitation, salts, or other co-solutes[9-12].