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Title: Excitation energy migration to study protein oligomerization and amyloid formation.

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Keywords: Excitation energy migration

study protein oligomerization

amyloid formation

Issue Date: 2022

Publisher: Elsevier

Citation: Biophysical Chemistry, 281(1), 106719.

Abstract:

Excitation energy migration via homo-FRET (Förster resonance energy transfer) is a unique variant of traditional FRET that involves a non-radiative energy transfer between the dipoles of two or more chemical identical fluorophores in close proximity and with an overlap between its excitation and emission spectra. Such energy migrations between chemically identical fluorophores within the Förster distance having their dipoles oriented over a wide angular spread results in the depolarization of fluorescence anisotropy depending on the local density of the fluorophores. Therefore, this methodology can be employed to study protein oligomerization and amyloid fibril formation. The conceptual framework involves extracting structural information by identifying proximal and distal locations in supramolecular assemblies by monitoring the efficiency of homo-FRET between fluorophore-conjugated protein molecules within these supramolecular assemblies. This review highlights two such cases in which excitation energy migration via homo-FRET was used to characterize the formation of membrane-mediated β-sheet rich oligomers of the prion protein as well as to construct a site-specific 2D-proximity correlation map to probe interresidue proximities within the highly organized amyloid fibrils of α-synuclein. Energy migration studies will find applications in studying a wide range of biomolecular assemblies such as lipidprotein complexes, oligomers, amyloids, and phase-separated condensates.

Description: Only IISER Mohali authors are available in the record.

URI: https://doi.org/10.1016/j.bpc.2021.106719 (https://doi.org/10.1016/j.bpc.2021.106719)

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