Title:	Discerning Dynamic Signatures of Membrane-Bound α-Synuclein Using Site-Specific Fluorescence Depolarization Kinetics
Authors:	Bhasne, K. (/jspui/browse?type=author&value=Bhasne%2C+K.) Jain, N. (/jspui/browse?type=author&value=Jain%2C+N.) Karnawat, R. (/jspui/browse?type=author&value=Karnawat%2C+R.) Arya, S. (/jspui/browse?type=author&value=Arya%2C+S.) Majumdar, A. (/jspui/browse?type=author&value=Majumdar%2C+A.) Singh, Anubhuti (/jspui/browse?type=author&value=Singh%2C+Anubhuti) Mukhopadhyay, S. (/jspui/browse?type=author&value=Mukhopadhyay%2C+S.)
Keywords:	Binding energy Fluorescence depolarization Membrane-Bound α-Synuclein
Issue Date:	2020
Publisher:	American Chemical Society
Citation:	Journal of Physical Chemistry B 124(5-6), pp.708-717.
Abstract:	α-Synuclein is an intrinsically disordered protein that adopts an α-helical structure upon binding to the negatively charged lipid membrane. Binding-induced conformational change of α-synuclein plays a crucial role in the regulation of synaptic plasticity. In this work, we utilized the fluorescence depolarization kinetics methodology to gain the site-specific dynamical insights into the membrane-bound α-synuclein. We took advantage of the nonoccurrence of Cys in α-synuclein and created single-Cys variants at different sites for us to be able to label it with a thiol-active fluorophore. Our fluorescence depolarization results reveal the presence of three dynamically distinct types of motions of α-synuclein on POPG (1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-(1′-rac-glycerol)) small unilamellar vesicles (SUVs): (i) the (local) wobbling-in-cone motion of the fluorophore on the subnanosecond timescale, (ii) the backbone segmental mobility on the nanosecond timescale, and (iii) a slow depolarization component with a characteristic long rotational correlation time (~60 ns) that is independent of the residue position. This characteristic timescale could potentially arise due to global tumbling of the protein-membrane complex, the global reorientation of only the protein within the membrane, and/or the translation diffusion of the protein on the curved membrane surface that could result in fluorescence depolarization due to the angular displacement of the transition dipole. In order to discern the molecular origin of the characteristic long rotational correlation time, we then carried our depolarization experiments varying the curvature of the membrane and varying the binding affinity by changing the lipid headgroup. These experiments revealed that the long rotational correlation time primarily arises due to the translational diffusion of α-synuclein on the curved membrane surface with a diffusion coefficient of ~8.7 × 10-10 m2/s. The site-specific fluorescence depolarization methodology will find broad application in quantifying diffusion of a wide range of membrane-associated proteins involved in functions and diseases.
URI:	https://pubs.acs.org/doi/10.1021/acs.jpcb.9b09118 (https://pubs.acs.org/doi/10.1021/acs.jpcb.9b09118) http://hdl.handle.net/123456789/3398 (http://hdl.handle.net/123456789/3398)
Appears in Collections:	Research Articles (/jspui/handle/123456789/9)

Files in This Item:

File	Description	Size	Format	
Need to add pdf.odt (/jspui/bitstream/123456789/3398/1/Need%20to%20add%20pdf.odt)		8.63 kB	OpenDocument Text	View/Open (/jspui/bitstream/12345

Show full item record (/jspui/handle/123456789/3398?mode=full)

(/jspui/handle/123456789/3398/statistics)