Title:	Short-Range Backbone Dihedral Rotations Modulate Internal Friction in Intrinsically Disordered Proteins
Authors:	Das, Debapriya (/jspui/browse?type=author&value=Das%2C+Debapriya) Arora, Lisha (/jspui/browse?type=author&value=Arora%2C+Lisha) Mukhopadhyay, Samrat (/jspui/browse?type=author&value=Mukhopadhyay%2C+Samrat)
Keywords:	Dihedral Rotations Modulate Intrinsically Disordered Proteins
Issue Date:	2022
Publisher:	ACS Publications
Citation:	Journal of the American Chemical Society, 144(4), 1739-1747.
Abstract:	Protein folding and dynamics are governed by an intricate interplay of thermal and viscosity-mediated effects. The solvent viscosity contributes to the frictional drag in protein dynamics. In addition to this viscosity-dependent effect, there is also an intriguing viscosity-independent component that represents the intrinsic resistance of the polypeptide chain to changing its conformation. This solvent-independent component is termed internal friction. A longstanding question is what is the fundamental molecular origin of internal friction in highly solvated and rapidly fluctuating intrinsically disordered proteins (IDPs) devoid of any persistent intrachain interactions? Here, we present a unique case to directly demonstrate that sequence-specific backbone dihedral barriers control local internal friction in an archetypal IDP, namely, α-synuclein. We performed site-directed fluorescence depolarization kinetics using picosecond time-resolved fluorescence anisotropy measurements to directly observe the directional decorrelation arising due to short-range backbone torsional fluctuations in the dihedral space. A linear viscosity-dependent model of the dihedral relaxation time yielded a finite zero-viscosity intercept that corresponds to internal friction. Our site-specific dynamic readouts were able to detect localized sequence-specific frictional components that are otherwise skewed in viscosity-dependent long-range chain fluctuations. Our results revealed the presence of low internal friction in nonproline sequence segments. In contrast, a proline introduces torsional stiffness in the segment exhibiting high internal friction that can be compensated by a conformationally flexible glycine. Such an intriguing interplay of local dihedral dynamics can modulate sequence-dependent internal friction in a wide range of IDPs involved in a myriad of important events including folding, binding, assembly, and phase transitions.
Description:	Only IISERM authors are available in the record.
URI:	https://doi.org/10.1021/jacs.1c11236 (https://doi.org/10.1021/jacs.1c11236) http://hdl.handle.net/123456789/4956 (http://hdl.handle.net/123456789/4956)
Appears in Collections:	Research Articles (/jspui/handle/123456789/9)

Files in This Item:

File	Description	Size	Format

Need to add pdf (1).docx (/jspui/bitstream/123456789/4956/1/Need%20to%20add%20pdf%20%281%29.docx)	9.74 kB	Microsoft Word XML	View/Open (/jspui/bitstrea

Show full item record (/jspui/handle/123456789/4956?mode=full)

(/jspui/handle/123456789/4956/statistics)