BIOGRAPHICAL SKETCH

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NAME: **Derya Meral**

eRA COMMONS USER NAME (credential, e.g., agency login): **N/A**

POSITION TITLE: **Postdoctoral Fellow**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Lafayette College	B.S.	05/2008	Physics
Lafayette College	B.A.	05/2008	Mathematics
Drexel University	M.S.	09/2011	Physics
Drexel University	Ph.D.	09/2015	Physics

A. Personal Statement

The main focus of my research has been the study of protein structure, dynamics, and interaction using computational techniques such as fully-atomistic and discrete molecular dynamics (MD) simulations. My work has spanned a range of scales, from the oligomerization processes of proteins to amino acid specific local order in small peptides. Under the guidance of Dr. Brigita Urbanc, my thesis work began with a study of the oligomerization pathways of a group of N-terminally truncated amyloid β-protein isoforms involved in Alzheimer's disease using an intermediate resolution discrete MD approach. This study corroborated a range of experimental results by providing structural insight into the potential causes of the relative toxicities, aggregation rates, and abundances of these peptides. My second project, which was a collaboration with Dr. Reinhard Schweitzer-Stenner's group at Drexel University, was an all-atom MD study of the effects of hydration on the conformational propensities of trialanine, alanine dipeptide, and 13 tripeptides in the GxG form. Finally, I worked on establishing a multi-scale simulation approach that combines discrete and fully atomistic MD techniques as sampling and structure refinement tools, respectively, using clustering techniques to bridge the two methods for the study of intrinsically disordered proteins.

I have recently joined the Filizola lab to conduct MD simulations of G-protein coupled receptors, such as opioid receptors, and integrins in order to elucidate their mechanisms of function and aid in the discovery of new therapeutic agents.

B. Positions and Honors

Positions and Employment

09/04-05/08 EXCEL Scholar / Research Assistant, Department of Physics, Lafayette College, Easton, PA, USA
09/08-09/15 Research Assistant / Ph.D., Department of Physics, Drexel University, Philadelphia, PA, USA
09/08-09/15 Teaching Assistant / Ph.D., Department of Physics, Drexel University, Philadelphia, PA, USA
11/15- Postdoctoral Fellow, Department of Structural and Chemical Biology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Other Experience and Professional Memberships

2015 School on Molecular Dynamics and Enhanced Sampling Methods, Temple University
2015 Biophysical Society
2015 Association for Women in Science

Honors and Awards

2012 1st place in Graduate Sciences, College of Arts and Sciences Research Day, Drexel University
2012 Graduate Research Award (Jr. Division), Department of Physics, Drexel University
2013 1st place in Computation and Bio-modeling, Research Day, Drexel University
2014 The Guoliang Yang Award for Excellence in Biophysics Research, Department of Physics, Drexel University
2015 Teaching Assistant Excellence Award Nominee, Drexel University

C. Contribution to Science

1. The amyloid β-protein (Aβ), which has been implicated in the progression of Alzheimer's disease (AD), has many variants which differ in their levels of toxicity, aggregation rates, and resistance to removal by peptidases. One particular group of isoforms, referred to as pyroglutamate Aβ (pEAβ), while significant in abundance in the AD brain, has not been studied in detail at the molecular scale despite evidence that suggests higher aggregation rates and increased toxicity compared to the wild types, Aβ[1-40] and Aβ[1-42]. Hence, to elucidate the underlying structural causes of these experimentally observed properties, I performed coarse-grained MD simulations of the oligomerization processes of the four Aβ isoforms, pEAβ[3-40/42] and pEAβ[11-40/42], and compared the resultant oligomeric structures and free energy landscapes to those of the Aβ wild types. The analysis revealed similarities between the N-terminal exposure of pEAβ[3-40/42] to those of Aβ[1-42], whose increased N-terminal exposure has been associated with higher toxicity rates as compared to Aβ[1-40]. Furthermore, the pEAβ[11-40/42] isoforms were shown to aggregate faster in aggreement with prior experimental results, in addition to forming more compact oligomers. These results present the first in depth study of the molecular structures of pEAβ. In addition to my studies of pyroglutamate isoforms of Aβ, I have also made a small contribution to a chapter on the familial Aβ mutants by providing movies of the oligomerization processes of the Arctic mutant [E22G]Aβ(1-40).

    a. Meral, D. & Urbanc, B. (2013). Discrete Molecular Dynamics Study of Oligomer Formation by N-Terminally Truncated Amyloid β-Protein. Journal of Molecular Biology, 425(12), 2260-2275.
    b. Attar, A., Meral, D., Urbanc, B., and Bitan, G. (2014). Chapter 38 - Assembly of Amyloid β-Protein Variants Containing Familial Alzheimer’s Disease-Linked Amino Acid Substitutions, In Bio-nanoimaging, edited by Uversky, V.N., and Lyubchenko, Y.L., Academic Press, Boston, 429-442.

2. There is currently a vibrant debate in the scientific community regarding the underlying mechanisms of conformational preferences of amino acid residues in the unfolded state, especially regarding the high polyproline II (pPII) and β-strand propensities observed in certain amino acid residues such as alanine. This strong preference for the pPII and β-strand conformations constitutes a significant challenge to the random coil model which fails to account for the restricted and unique Ramachandran spaces observed for individual residues. Our collaborators, Dr. Reinhard Schweitzer-Stenner's group, had previously published a wide range of data on the intrinsic conformational propensities of tripeptide systems, such as trialanine (AAA), alanine dipeptide (AdP), and numerous Glycine-x-Glycine (GxG, x = guest residue) peptides, in addition to revealing a nearly exact enthalpy-entropy compensation for the pPII ↔ β equilibria of amino acid residues near 300K, suggesting a common mechanism for the intrinsic conformational preferences of amino acid residues. Guided by these results, I performed fully atomistic MD simulations of AAA, AdP, and 15 GxG peptides, and performed a rigorous structural analysis of the water hydration shell of the central residues. For this purpose, I developed an algorithm to project the orientation of water molecules near the side chain surface onto two dimensions. This allowed us to show that the hydration shell in the β conformation is more disordered than in the pPII conformation, validating further the notion that while the pPII conformation is stabilized enthalpically, the β conformation is stabilized entropically. Furthermore, the

pPII to β hydration differences and the solvent accessible surface areas of the Cβ groups correlate strongly with experimental pPII propensities. These results led to the hypothesis that the formation of a dodecahedron-like hydrogen bond network around side chain groups of residues might be stabilizing the pPII conformation, and that the intrinsic pPII propensity of amino acid residues represents their side chain's ability to act as a template for such a water structure.

a. Toal, S., Meral, D., Schweitzer-Stenner, R., and Urbanc, B., (2013). pH-Independence of Trialanine and the Effects of Termini Blocking in Short Peptides: A Combined Vibrational, NMR, UVCD, and Molecular Dynamics Study. Journal of Physical Chemistry B, 117(14), 3689–3706.
b. Meral, D., Toal, S., Schweitzer-Stenner, R., and Urbanc, B., (2015). Water-centered interpretation of intrinsic pPII propensities of amino acid residues: In vitro-driven molecular dynamics study. Journal of Physical Chemistry B, 119(42), 13237–13251.

Complete list of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1VCH-gIo6l8Qu/bibliography/49160347/public/?sort=date&direction=ascending

D. Research Support

None.