BIOGRAPHICAL SKETCH

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NAME: Mohammad R. K. Mofrad

eRA COMMONS USER NAME (credential, e.g., agency login): MMOFRAD

POSITION TITLE: Professor of Bioengineering and Mechanical Engineering, University of California Berkeley

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
Sharif University of Technology, Iran	B.Sc.	05/1991	Mechanical Engineering
University of Waterloo, Canada	M.A.Sc.	08/1994	Mechanical Engineering
University of Toronto, Canada	Ph.D.	12/1999	Mechanical Engineering
Massachusetts Institute of Technology	Post-Doc	05/2002	Biological Engineering
Massachusetts General Hospital/Harvard Medical School (joint post-doc)	Post-Doc	05/2002	

A. Personal Statement

My research program is focused on understanding the molecular basis of cell mechanics and mechanotransduction with them aim to shed light on the role of these biological processes in human disease. Our specific attention is on the role of two macromolecular systems in cellular function, namely the integrin-mediated focal adhesions at the interface between the cell and extracellular matrix (ECM) and the nuclear pore complex (NPC). Focal adhesions are the immediate sites of cell interaction with the ECM, and as such they play a key role in mechanosensing and mechanotransduction at the edge of the cell. Nuclear pores could also play a role in the overall process of cellular mechanotransduction by exquisitely controlling the material transport in and out of the nucleus, thereby regulating the gene expression and protein synthesis.

a) Mahboobi SH, Javanpour AA, **Mofrad MRK** (2015). The interaction of RNA helicase DDX3 with HIV-1 Rev-CRM1-RanGTP complex during the HIV replication cycle. PLOS One, 10(2): e0112969.
b) Golji J, **Mofrad MRK** (2014). Mechanical force can regulate the orientation of the talin dimer. Biophysical Journal. 107(8):1802-9. PMID: 25418161.
c) Mehrbod M, Trisno S, **Mofrad MRK** (2013). On the Activation of Integrin αIIbβ3: Outside-In and Inside-Out Pathways. Biophysical Journal, 2013 Sept; 105(6).
d) Moussavi-Baygi RM, Jamali Y, Karimi R, **Mofrad MRK** (2011). Biophysical Coarse-Grained Modeling Provides Insights into Transport through the Nuclear Pore Complex. Biophysical Journal. 2011; 100(6):1410-1419.

B. Positions and Honors

Positions and Employment

2002- 2004 Research Fellow, Harvard Medical School and Mass. General Hospital
2002-2003 Research Scientist, Biological Engineering, Massachusetts Institute of Technology
2003-2004 Principal Research Scientist, Biological Eng., Masaachusetts Institute of Technology
2005-2010 Assistant Professor, Department of Bioengineering, University of California Berkeley
2010-2013 Associate Professor, Department of Bioengineering, University of California Berkeley
2012-2013 Associate Professor, Department of Mechanical Engineering, University of California Berkeley
2012- Faculty Scientist, Physical Biosciences Division, Lawrence Berkeley National Lab
2013- Professor, Departments of Bioengineering and Mechanical Engineering, UC Berkeley

Other Experience and Professional Memberships

2005- Associate Editor, Journal of Molecular and Cellular Biomechanics
2012- Associate Editor, Cytotechnology
2012-2014 Chair, Bioengineering M.Eng. Program

2007- Associate Editor, Journal of Cellular & Molecular Mechanics
2009- Consulting Editor, Journal of Biomechanics
2009-2012 Chair, Education Committee, ASME Bioengineering Division
2011- Associate Editor, ASME Journal of Biomechanical Engineering
2012-2014 Faculty Co-Director, Berkeley-UCSF Master of Translational Medicine Program
2013-2015 Associate Editor, IEEE Transactions of Biomedical Engineering
2013- Academic Editor, PLoS One
2014- Associate Editor, Journal of Multiscale Modeling
2015- Guest Editor, PLoS Computational Biology

Honors

2002 Runner-up for American Society of Biomechanics Award, World Congress of Biomechanics
2003 Merit Certificate of Recognition, First US National Symposium on Frontiers of Biomechanics
2005 University of California Regents' Junior Faculty Fellow
2006 University of California Berkeley Futures
2007 Co-leader of Molecular Biomechanics Group, *Summit of Biomechanics*
2008 Hellman Faculty Award
2010 NSF CAREER Award
2012 Frontiers of Engineering, National Academy of Engineering
2012 Minner Faculty Fellowship
2014 Presidential Chair Fellowship
2015 Fellow, American Institute for Medical and Biological Engineering

C. Contribution to Science

1. **Integrin-mediated focal adhesion and mechanotransduction.** The underlying mechanics and mechanisms of mechanotransduction are not yet clearly understood. Several theories have been proposed for how the cell senses the mechanical cues from the environment and converts them to a cascade of biochemical signals that govern the cellular phenotype. One theory proposes that forces transmitted via individual proteins, either at the site of cell adhesion to its surrounding or within the stress-bearing members of the cytoskeleton, cause conformational changes that change the binding affinity of these proteins to other intracellular molecules. This altered equilibrium state can subsequently initiate biochemical signaling cascades or produce immediate structural changes. Force-induced conformational changes in mechanosensor proteins may play a critical role in initiating and controlling cell signaling pathways. Mechanosensing and adaptor proteins are capable of forming a direct linkage between the cell membrane and the actin cytoskeleton and therefore play a crucial role in transmitting and translating the mechanical forces inside the cell. Over the past 10 years, my lab has been focused on understanding mechanotransduction at the molecular level which requires detailed analysis of molecular conformational changes of cytoplasmic proteins that occur in response to mechanical forces transmitted between the extracellular matrix (ECM) and the cytoskeleton via the focal adhesion machinery that anchors the cell to ECM.

   a) Golji J, **Mofrad MRK** (2013). The Interaction of Vinculin with Actin. PLoS Computational Biology, 2013 Apr;9(4):e1002995.
   b) Shams H, Golji J, **Mofrad MRK** (2012). A molecular trajectory of α-actinin activation. Biophys J.
      a. 103(10):2050-9. PMCID: PMC3512038
   c) Golji J, Wendorff TJ, **Mofrad MRK** (2012). Phosphorylation Primes Vinculin for Activation. Biophysical Journal, 2012 May; 102:2022-2030.
   d) Yoon SH, Chang J, Lin L, **Mofrad MRK**. A biological breadboard platform for cell adhesion and detachment studies. Lab on a Chip, 2011; 11(20):3555-62[highlighted in Lab Chip Research Highlights, December 21, 2011, 11(24):4141-3].

2. **Mechanics of the Nuclear Pore.** The nucleus is the pivotal defining feature of eukaryotes, compartmentalizing the flow of information from DNA to protein by requiring that mRNA be exported to the cytoplasm prior to translation into proteins. RNA is exported across nuclear pore complexes (NPCs), mega-Dalton multi-protein assemblies embedded in the nuclear envelope, bridging the nucleoplasm and cytoplasm. While the underlying mechanism for nucleocytoplasmic transport is not thoroughly understood,

several studies have attempted to dissect the NPC and various transport models have been hypothesized. Yet, the selective gating mechanism of the NPC is a matter of extensive debate. While the entire process of nucleocytoplasmic transport is in the order of several milliseconds, the underlying individual transient interactions within the NPC are only nanosecond-long. Hence, currently available experimental techniques are unable to capture the dynamics of the transport mechanisms. What adds to this complexity is the confined geometry of the NPC's central channel, which is at the heart of the nuclear pore and believed to be the chief location where the selective gating process happens. Putatively, the channel is filled and/or lined with numerous natively disordered phenylalanine-glycine (FG) repeat domains of specific Nups, called FG-Nups. There is almost no doubt that FG-Nups, cooperatively, are essential players of the selectivity mechanism in that their interactions with the nuclear transport receptor somehow allow the cargo-complex to travel across the NPC and reach the cytoplasm or the nucleus. The natively unfolded FG-repeat domains are highly dynamic and lack any structure, and this makes it even more challenging to explore the transport mechanism at high enough spatiotemporal resolutions both in vivo and in vitro. As a result, the behavior of these unstructured domains within the confined geometry of the central channel is highly debated. Currently, only computational techniques can elucidate the detailed nucleocytoplasmic traffic events with a refined spatiotemporal resolution to account for transient interactions between NTRs and FG-repeats. To gain insight into this phenomenon, we are investigating the NPC at three different scales with computational approaches: continuum finite element, coarse-grained (microscale), meso-scale and all-atom models. Multiple scales will help us to find the essential features for the function of NPC. Furthermore, they complement each other by feeding the right parameters at different hierarchies. For example, even a simple continuum model can shed light on the vibrational modes of the NPC, which may affect the transport. On the other hand, a meso-scale model may be sufficient to investigate a transport regime dominated by rather static bonding sites.

a) Azimi M, Bulat E, Weis K, **Mofrad MRK** (2014). An agent-based model for mRNA export through the nuclear pore complex. Molecular Biology of the Cell, 2014 Nov 5;25(22):3643-53.
b) Zhao C, Mahboobi SH, Moussavi-Baygi R, **Mofrad MRK** (2014). The Interaction of CRM1 and the Nuclear Pore Protein Tpr. PLoS One, April 2014, Volume 9 | Issue 4 | e93709.
c) Azimi M, **Mofrad MRK** (2013). Higher Nucleoporin-Importinβ Affinity at the Nuclear Basket Increases Nucleocytoplasmic Import. PLoS One. 2013 Nov 25;8(11):e81741.
d) Moussavi-Baygi RM, Jamali Y, Karimi R, **Mofrad MRK**. Brownian Dynamics Simulation of Nucleocytoplasmic Transport: A Coarse-Grained Model for the Functional State of the Nuclear Pore Complex. PLoS Computational Biology. 2011 June; 7(6): e1002049.

3. **Multiscale Models of the Aortic Heart Valve Mechanics: Applications in Disease and Surgery.** A long-term goal of my research program is to develop multiscale biomechanical models to understand the role of mechanics and mechanotransduction in cardiovascular diseases, in particular calcific aortic stenosis and arterial atherosclerosis.
   a) Weinberg EJ, Mack PJ, Schoen FJ, Garcia-Cardena G, **Kaazempur Mofrad MR** (2010). Hemodynamic environments from opposing sides of human aortic valve leaflets evoke distinct endothelial phenotypes in vitro. Cardiovasc Eng. 10(1):5-11.
   b) Weinberg EJ, Schoen FJ, **Mofrad MR** (2009). A computational model of aging and calcification in the aortic heart valve. PLoS One. 4(6):e5960.
   c) Weinberg EJ, **Kaazempur Mofrad MR** (2008). A multiscale computational comparison of the bicuspid and tricuspid aortic valves in relation to calcific aortic stenosis. J Biomech. 41(16):3482-7.
   d) Weinberg EJ, **Kaazempur Mofrad MR** (2007). Transient, three-dimensional, multiscale simulations of the human aortic valve. Cardiovasc Eng. 7(4):140-55.

Complete List of Published Work in My Bibliography:
http://biomechanics.berkeley.edu/publications