BIOGRAPHICAL SKETCH

NAME: ATOUSA, MEHRANI

POSITION TITLE: PHD CANDIDATE

EDUCATION/TRAINING

INSTITUTE AND LOCATION	DEGREE	START DATE	COMPLETION DATE	FIELD OF STUDY
Tehran Azad University, Science and Research Branch (SRB), Iran	B.Sc.	09/2008	09/2008	Engineering Physics
Queen Mary, University of London, United Kingdom	M.Sc.	09/2012	09/2014	Biomedical Engineering
Florida State University, United States	M.Sc.	08/2016	12/2018	Biochemistry
Florida State University, United States	Ph.D. Candidate	12/2018	Present	Biochemistry

A. Personal Statement

I have a long-standing and strong interest in cryo-EM reconstruction of biological complexes. The main focus of my research is to investigate the *in-situ* role of the protein complex TFG in organizing ER exit sites in the secretory pathway by cryo-FIB milling and cryo-electron tomography. This project is performed in collaboration with Dr. Alex Noble at NYSBC. I am also involved in a number of single-particle reconstructions projects, including the structural determination of the stalled 70S ribosome and its interaction with trans-translation inhibitor. In the course of this project, I solved the structure of the 70S *E-coli* ribosome bound to a drug by single-particle reconstruction. This reconstruction achieved a resolution of 2.8 Å with well-resolved features for the ribosomal RNA and proteins. The highlights of this study will be published in the near future. However, this structure was used as supporting evidence that the DE64 camera in counting mode is capable of achieving high-resolution reconstructions. My goal is to improve my expertise in both fields of single-particle and tomographic reconstruction and to implement these methods in various aspects of biomedical science and therapeutics design.

Mendez, J.H., **Mehrani, A**., Randolph, P., Stagg, S. Throughput and Resolution with a Next Generation Direct Electron Detector. bioRxiv., DOI: https://doi.org/10.1101/620617 (recently accepted in IUCrJ)

B. Positions and Honors

Positions and Employment

2017-Present	Graduate Research Assistant	Florida State University, USA
2014-2016	Graduate Researcher	Tehran Azad University, SRB, Iran
2013-2014	Graduate Researcher	Queen Mary, University of London, UK
2011-2011	Undergraduate Researcher	Tehran Azad University, SRB, Iran

Professional Memberships

2017-Present Member, Biophysical Society
2017-2018 Member, Congress of Graduate Students, Florida State University
2017-2018 Vice President of Iranian Student Association, Florida State University

C. Contribution to Science

1. Structure of 30S methyltransferase complex

One of the aims of my research is to determine the structure of 30S subunit in conjunction with aminoglycoside-resistance 16S rRNA (m7G1405) methyltransferases. This sample was prepared in the lab of Dr. Graeme Conn at Emory University. Understanding rRNA methyltransferase-ribosome subunit interaction has relevance to both bacterial physiology as well as an antimicrobial resistance mechanism. I determined the cryo-EM structure of the 30S subunit bound to methyltransferase displaying that part of the helix 44, near the decoding center and also the head domain of the 30S is distorted in the presence of these enzymes. A high-resolution structure of the 30S: m7G1405 methyltransferase is required to precisely define the specific molecular interactions. However, these observations suggest suitable molecular targets that interfere with the action of resistance factors in bacteria.

Nosrati, M., Dey, D., **Mehrani, A**., Strassler, S. E., Zelinskaya, N., Hoffer, E. D., Stagg, S., Dunham, C. M., Conn, G., L., Critical residues in the aminoglycoside-resistance 16S rRNA (m7G1405) methyltransferase RmtC play distinct roles in 30S substrate recognition. bioRxiv., doi: https://doi.org/10.1101/712810 . (submitted to JBC)

2. Structure of 70S bound to a trans-translation inhibitor

The major part of my research centered on determining the structure of the 70S *E. Coli* ribosome together with a drug molecule that inhibits trans-translation. Trans-translation is one of the fundamental rescue mechanisms used by the stalled bacterial ribosome, which is important in many pathogenic strains. Therefore, trans-translation has been proposed as a target for the development of new antibiotics. In the lab of Dr. Ken Keiler at Penn. State University the small molecules have been synthesized that possess antibiotic properties and they inhibit rescue mechanisms in the stalled ribosomes. The action mechanism used by these drug molecules is unknown. Further, the rational improvement of these drug compounds requires detailed structural information about the target binding sites. Using single-particle cryo-EM, I have resolved the binding site of these drug molecules within *E. Coli* 70S ribosome. I have also observed a novel conformation of the ribosomal protein (L27), which may explain the function of the drug as well as the catalysis mechanism used by stalled ribosomes. The conformational change in the L27 is under further biochemistry analysis; however, the summary of the outcomes has been presented at 2019 Biophysical Society meeting.

Mehrani, A., Hoffer, E.D., Goralski, T.D.P., Keiler, K.C., Dunham, Ch., Stagg, S. Investigating the structural mechanism of the stalled bacterial ribosome bound to a drug that targets trans-translation. Biophysical Journal 116(3):573a-574a · February 2019. Doi: https://doi.org/10.1016/j.bpj.2018.11.3085

3. The in-situ role of the protein complex TFG

The main aspect of my Ph.D. research is to investigate the *in situ* role of the tyrosine-receptor kinase fused gene (TFG) in organizing ER exit sites in the secretory pathway. TFG is a conserved regulator of protein secretion and its mutation is associated with oncogenesis and neurodegenerative disorders. This protein is located near the thick nucleus region of the eukaryotic cells (~ 600 nm). Therefore, cryo-FIB milling is essential to produce thin lamellae, which are detectable by cryo-EM. The RPE1 cell line containing TFG is prepared at Dr. Anjon Audhya lab at UW-Madison. I grew these cells on the TEM grids and sent them to Dr. Alex Noble in NYSBC for the FIB-milling. In the course of this project, I had an opportunity to spend a couple of days at NYSBC to gain insight into the FIB-milling procedure. The lamellae were imaged FSU where we collected a number of tilt-series, and I reconstructed the corresponding tomograms afterward. The tomograms had sufficient resolution to illustrate several organelles in the secretory pathway of the cell. However, due to the small size of the TFG proteins (~25 nm) buried in the dense sea of the surrounding molecules, a higher resolution was required to capture the TFG protein *in situ*. Further, In order to facilitate the TFG observation, I overexpressed the TFG proteins inside the cells and grew a new batch on the EM grids. The second batch was sent to Dr. Noble for the FIB-milling and data collection using an energy filter and phase plate. These improvements resulted in much higher resolution tomograms and a more notable TFG content. I have reconstructed 32 featureful tomograms, and we had been able to observe the network of TFG in some. I am currently working on segmentation and sub-tomogram averaging of TFG. In addition, the national MAG lab at FSU is equipped with the FIB-SEM instrument. In collaboration with Dr. Scott Stagg, the instrument will be outfitted with a cryo-stage in November 2019. The installation of onsite cryo_stage will accelerate the progress of this project and opens the door to more *in situ* tomography experiments in the future.

D. Additional Information: research Support and/or Scholastic Performance

During my master's degree and post-graduation, I had been involved in several research projects associated with the fabrication of micro/nanocarriers with applications in drug delivery and medical imaging. In the lab of Dr. Gleb Sukhorokov at Queen Mary, University of London, I developed skills in fabricating optical responsive polymeric microcapsules by layer-by-layer assembly technique. These microcapsules had hollow structures and could be loaded with various enzymes and drugs. By embedding by magnetic nanoparticles, these carriers could be guided to the specific site in vitro and in vivo using a magnetic field to deliver their cargoes to the site, such as cancerous cells. My role was to embed gold nanorods to the shell of these micro-carriers and observe their release mechanism under the laser irradiation.

Following this project, I got two internship positions in Iran that were involved with the fabrication of metal nanocomposites using laser ablation. Due to the optical properties, these nanocomposites are suitable to be used as contrast agents to improve the contrast and quality of the MRI imaging. Flowing that, I was involved in a research project associated with the development of the magnetic nanocarriers. These nanoparticles had a porous structure, and their surface property could be modified by various functional groups. These nanocarriers were loaded with doxorubicin (an anti-cancer drug), and their drug release mechanism was studied *in vitro*.

Mehrani, A., Dorranian, D. & Solati, E. J Clust Sci (2015) 26: 1743. Properties of Au/ZnO Nanocomposite Prepared by Laser Irradiation of the Mixture of Individual Colloids DOI: 10.1007/s10876-015-0872-z.

Mehrani, A., Ahmadvand, P., Mehdizadeh Barforushi, M. et al. J Inorg Organomet Polym (2016) 26: 226. Double Functionalized Nanoporous Magnetic Gadolinium–Silica Composite for Doxorubicin Delivery. DOI:10.1007/s10904-015-0302-6.