

BIOGRAPHICAL SKETCH

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NAME: Fu, Ziao

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

POSITION TITLE: Postdoctoral Associate

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)	END DATE MM/YYYY	FIELD OF STUDY
Jilin University, Changchun, Jilin	B.S.	05/2012	Chemistry
Stony Brook University, Stony Brook, NY	M.S.	05/2014	Chemistry
Columbia University, New York, NY	Ph.D	05/2019	Biology
Rockefeller University, New York, NY	Postdoctoral Associate	present	Molecular Neurobiology and Biophysics

A. Personal Statement

I am a Postdoctoral Associate in Professor Roderick MacKinnon's Lab at Rockefeller University. I obtained my Ph.D. degree at Columbia University in Professor Joachim Frank's Lab. For my Ph.D. thesis work, I focused on the development and application of time-resolved cryo-electron microscopy (cryo-EM) to study short-lived intermediates during bacterial translation processes. In addition, I have also applied the conventional cryo-EM single particle analysis to study membrane protein structures. During my Ph.D., I obtained extensive training and a deep understanding of cryo-EM sample preparation, data collection and data processing. My strong background knowledge and experience earned me many opportunities to collaborate with experts in the membrane protein field. These collaborations helped to solve many important structures within the field and laid the foundation for future functional studies of the proteins. I had the opportunities to share my work at many international cryo-EM conferences, and obtained several co-first author publications. Because of the high quality and productivity of my Ph.D. work, I was awarded the 2019 Titus M. Coan Prize for Excellence in Research. My current adviser Professor Roderick MacKinnon has been working in the ion channel field for many decades. He has successfully trained 23 post-doctoral associates and 17 out of them obtained tenure-track positions. For my post-doctoral project, I aim to characterize and determine the localization of ion channels in their native environment. To accomplish these aims, I plan to learn the biochemistry of membrane proteins, purification system of ion channels, immunochemical labeling, and electrophysiological methodologies. Meanwhile, I will attend New York Structural Biology Center training sessions and learn to set up a complete workflow of studying ion channel structures in the cellular environment using correlative light electron microscopy and cryo-electron tomography. With this training, I will solve the structure of Piezo1 mechanosensitive ion channel in situ to help better understand its function and mechanism.

*indicates co-first authors

1. **Fu Z***, Indrisiunaite G, Kaledhonkar S, Shah B, Sun M, Chen B, Grassucci RA, Ehrenberg M, Frank J. The structural basis for release-factor activation during translation termination revealed by time-resolved cryogenic electron microscopy. Nat Commun. 2019 Jun 12;10(1):2579. PubMed PMID: [31189921](#); PubMed Central PMCID: [PMC6561943](#).
2. Kaledhonkar S, **Fu Z***, Caban K, Li W, Chen B, Sun M, Gonzalez RL Jr, Frank J. Late steps in bacterial translation initiation visualized using time-resolved cryo-EM. Nature. 2019 Jun;570(7761):400-404. PubMed PMID: [31108498](#); PubMed Central PMCID: [PMC7060745](#).

3. Qiu W, **Fu Z***, Xu GG, Grassucci RA, Zhang Y, Frank J, Hendrickson WA, Guo Y. Structure and activity of lipid bilayer within a membrane-protein transporter. Proc Natl Acad Sci U S A. 2018 Dec 18;115(51):12985-12990. PubMed PMID: [30509977](#); PubMed Central PMCID: [PMC6304963](#).
4. **Fu Z***, Kaledhonkar S, Borg A, Sun M, Chen B, Grassucci RA, Ehrenberg M, Frank J. Key Intermediates in Ribosome Recycling Visualized by Time-Resolved Cryoelectron Microscopy. Structure. 2016 Dec 6;24(12):2092-2101. PubMed PMID: [27818103](#); PubMed Central PMCID: [PMC5143168](#).

B. Positions and Honors

Positions and Employment

2019 - Postdoctoral Associate, Laboratory of Molecular Neurobiology and Biophysics, Rockefeller University, New York, NY

Other Experience and Professional Memberships

2012 - Member, American Chemistry Society
 2014 - Member, Biophysical Society

Honors

2018 Fisher Award, COMPPA Symposium
 2019 Titus M. Coan Prize for Excellence in Research, Columbia University
 2019 Best Poster Award, The 7th International Ion Channel Conference

C. Contribution to Science

1. Amyloid assemblies are found in many neurodegenerative pathologies including Alzheimer's, Huntington's, and prion diseases. Although much is known about the physiological consequences of these fibrils, their high-resolution structures and oligomeric precursors remained largely unexplored. I used a combination of biophysical methodologies including solid-state Nuclear Magnetic Resonance, infrared spectroscopy, fluorescence assays, electron microscopy, and atomic force microscopy to obtain the high-resolution structural information of these multimeric complexes. I also characterized two small molecule inhibitors which can disrupt the formation of these assemblies and reduce toxicity to cultured neurons.
 - a. Xu F, **Fu Z**, Dass S, Kotarba AE, Davis J, Smith SO, Van Nostrand WE. Cerebral vascular amyloid seeds drive amyloid β -protein fibril assembly with a distinct anti-parallel structure. Nat Commun. 2016 Nov 21;7:13527. PubMed PMID: [27869115](#); PubMed Central PMCID: [PMC5121328](#).
 - b. **Fu Z**, Aucoin D, Davis J, Van Nostrand WE, Smith SO. Mechanism of Nucleated Conformational Conversion of A β 42. Biochemistry. 2015 Jul 14;54(27):4197-207. PubMed PMID: [26069943](#).
 - c. **Fu Z**, Aucoin D, Ahmed M, Ziliox M, Van Nostrand WE, Smith SO. Capping of a β 42 oligomers by small molecule inhibitors. Biochemistry. 2014 Dec 23;53(50):7893-903. PubMed PMID: [25422864](#); PubMed Central PMCID: [PMC4278677](#).
 - d. Xu F, Kotarba AE, Ou-Yang MH, **Fu Z**, Davis J, Smith SO, Van Nostrand WE. Early-onset formation of parenchymal plaque amyloid abrogates cerebral microvascular amyloid accumulation in transgenic mice. J Biol Chem. 2014 Jun 20;289(25):17895-908. PubMed PMID: [24828504](#); PubMed Central PMCID: [PMC4067220](#).

2. Many interesting biological processes fall in a time range that is impossible to access by standard structural methodologies (cryo-EM single-particle analysis or X-ray). In the processes of the bacterial translation, although structural snapshots of the stable states have been solved by X-ray and cryo-EM single particle analysis, many key intermediate states are beyond capture. I applied the time-resolved cryo-EM method to solve structures of the important intermediate state in bacterial translation processes. These studies enriched our understanding of the translation process and revealed the order in which ribosomal co-factors regulate this process, how tRNA state changes, and how ribosome state transforms.
 - a. **Fu Z***, Indrisiunaite G, Kaledhonkar S, Shah B, Sun M, Chen B, Grassucci RA, Ehrenberg M, Frank J. The structural basis for release-factor activation during translation termination revealed by time-resolved cryogenic electron microscopy. *Nat Commun.* 2019 Jun 12;10(1):2579. PubMed PMID: [31189921](#); PubMed Central PMCID: [PMC6561943](#).
 - b. Kaledhonkar S, **Fu Z***, Caban K, Li W, Chen B, Sun M, Gonzalez RL Jr, Frank J. Late steps in bacterial translation initiation visualized using time-resolved cryo-EM. *Nature.* 2019 Jun;570(7761):400-404. PubMed PMID: [31108498](#); PubMed Central PMCID: [PMC7060745](#).
 - c. **Fu Z***, Kaledhonkar S, Borg A, Sun M, Chen B, Grassucci RA, Ehrenberg M, Frank J. Key Intermediates in Ribosome Recycling Visualized by Time-Resolved Cryoelectron Microscopy. *Structure.* 2016 Dec 6;24(12):2092-2101. PubMed PMID: [27818103](#); PubMed Central PMCID: [PMC5143168](#).
3. Time-resolved cryo-EM can be used to study short-lived intermediate structures. However, the images obtained often have low contrast, leading to medium resolution structures. This method requires us to spray samples onto the grid surface and immediately freeze it. I found the problem lies in the thickness of the ice layer on the cryo-EM grids, which is a result of spraying sample onto the grid surface that is required for time-resolved cryo-EM. Therefore, to improve this method, I have modified the sprayer offered by a collaborator at Columbia University to improve its performance and produce the best quality data under various conditions. I collected data after these successive optimizations and demonstrated a high-resolution structure is attainable using the spraying method.
 - a. Kaledhonkar S, **Fu Z***, White H, Frank J. Time-Resolved Cryo-electron Microscopy Using a Microfluidic Chip. *Methods Mol Biol.* 2018;1764:59-71. PubMed PMID: [29605908](#).
 - b. Feng X, **Fu Z***, Kaledhonkar S, Jia Y, Shah B, Jin A, Liu Z, Sun M, Chen B, Grassucci RA, Ren Y, Jiang H, Frank J, Lin Q. A Fast and Effective Microfluidic Spraying-Plunging Method for High-Resolution Single-Particle Cryo-EM. *Structure.* 2017 Apr 4;25(4):663-670.e3. PubMed PMID: [28286002](#); PubMed Central PMCID: [PMC5382802](#).
4. In collaboration with Professor Youzhong Guo and Professor Wayne Hendrickson, I determinate the high-resolution structure of AcrB, a membrane protein that can be extracted directly from cells surrounded by its native lipid bilayer environment using a synthetic polymer, at 3.0 Å. I found that the transmembrane part of the protein has a hollow structure filled with phospholipid bilayers. In the structure I solved, the phospholipid bilayer is composed of two layers. The lower layer is formed by the close arrangement of phospholipid molecules, while the upper layer is arranged differently. Many phospholipid molecule tails are bent and not closely packed. This is the first time the phospholipid bilayer structure has been observed directly.
 - a. Qiu W, **Fu Z***, Xu GG, Grassucci RA, Zhang Y, Frank J, Hendrickson WA, Guo Y. Structure and activity of lipid bilayer within a membrane-protein transporter. *Proc Natl Acad Sci U S A.* 2018 Dec 18;115(51):12985-12990. PubMed PMID: [30509977](#); PubMed Central PMCID: [PMC6304963](#).

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/1JMZwJ8i-JukhM/bibliography/public/>

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