

**BIOGRAPHICAL SKETCH**

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NAME: Fu, ZIAO

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

POSITION TITLE: GRADUATE STUDENT

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
JILIN UNIVERSITY, CHANGCHUN, CHINA	B.S.	2012	CHEMISTRY

**A. Personal Statement**

I have been working in the cryo-EM field for five years in Joachim Frank's lab as a graduate student. Mainly I am working on time-resolved cryo-EM method development and application. I showed a few successful cases to demonstrate the time-resolved cryo-EM method can capture short-lived intermediates which have half-life time from 10 ms to 1 s. Apart from this main project I am working on, I am also involved in a few other projects to help the researchers to succeed in solving structures using cryo-EM technique. One exciting example is a collaboration with Youzhong Guo and Wayne Hendrickson's lab on membrane protein extraction method development. Avoiding detergent in protein extraction from cell membrane, we can preserve native lipids and we observed for the native lipid bilayer directly extracted from native cell membrane. The method would help researchers working with membrane protein to gain more insight in terms of protein lipid interaction and lipid functional and structure roles.

**B. Positions and Honors**

Research Assistant 2014-2018 Columbia University.

**C. Contributions to Science**

1. The structural basis for release factor activation during translation termination revealed by time resolved cryo-EM. 2018 **Ziao Fu\***, **Gabriele Indrisiunaite\***, **Sandip Kaledhonkar\***, **Binita Shah**, **Ming Sun**, **Bo Chen**, **Robert A. Grassucci**, **Måns Ehrenberg**, **Joachim Frank** (in review)

We determined high-resolution structures of short-lived intermediates in the translation termination process using time-resolved Cryo-EM technique.

2. Real-time structural dynamics of late steps in bacterial translation initiation visualized using time-resolved cryogenic electron microscopy. 2018 **Sandip Kaledhonkar\***, **Ziao Fu\***, **Kelvin Caban\***, **Wen Li**, **Bo Chen**, **Ming Sun**, **Ruben Gonzalez Jr**, **Joachim Frank** (Nature in press)

We determined high-resolution structures of short-lived intermediates in the translation initiation process using time-resolved Cryo-EM technique.

3. Structure and Activity of Lipid Bilayer within a Membrane Protein Transporter 2018 **Weihua Qiu\***, **Ziao Fu\***, **Guoyan G. Xu**, **Robert A. Grassucci**, **Yan Zhang**, **Joachim Frank**, **Wayne A. Hendrickson**, **Youzhong Guo** Proc Natl Acad Sci U S A. 2018 Dec 18;115(51):12985-12990.  
We solved native lipid bilayer structure by Cryo-EM technique at high resolution about 3 Å.
4. A Fast and Effective Microfluidic Spraying-Plunging Method for High-Resolution Single-Particle Cryo-EM 2017 **Xiangsong Feng\***, **Ziao Fu\***, **Sandip Kaledhonkar**, **Yuan Jia**, **Binita Shah**, **Amy Jin**, **Zheng Liu**, **Ming Sun**, **Bo Chen**, **Robert A Grassucci**, **Yukun Ren**, **Hongyuan Jiang**, **Joachim Frank**, **Qiao Lin** Structure 25 (4), 663-670. e3  
We describe a spraying-plunging method for preparing cryoelectron microscopy (cryo-EM) grids with vitreous ice of controllable, highly consistent thickness using a microfluidic device. The new polydimethylsiloxane (PDMS)-based sprayer was tested with apoferritin. We demonstrate that the structure can be solved to high resolution with this method of sample preparation. Besides replacing the conventional pipetting-blotting-plunging method, one of many potential applications of the new sprayer is in time-resolved cryo-EM, as part of a PDMS-based microfluidic reaction channel to study short-lived intermediates on the timescale of 10-1,000 ms.
5. Key intermediates in ribosome recycling visualized by time-resolved cryoelectron microscopy 2016 **Ziao Fu\***, **Sandip Kaledhonkar\***, **Anneli Borg\***, **Ming Sun**, **Bo Chen**, **Robert A Grassucci**, **Måns Ehrenberg**, **Joachim Frank** Structure 24 (12), 2092-2101

We determined the structures of short-lived intermediates in the translation recycling process using time-resolved cryo-EM technique. Upon encountering a stop codon on mRNA, polypeptide synthesis on the ribosome is terminated by release factors, and the ribosome complex, still bound with mRNA and P-site-bound tRNA (post-termination complex, PostTC), is split into ribosomal subunits, ready for a new round of translational initiation. Separation of post-termination ribosomes into subunits, or “ribosome recycling,” is promoted by the joint action of ribosome-recycling factor (RRF) and elongation factor G (EF-G) in a guanosine triphosphate (GTP) hydrolysis-dependent manner. Here we used a mixing-spraying-based method of time-resolved cryo-electron microscopy (cryo-EM) to visualize the short-lived intermediates of the recycling process. The two complexes that contain (1) both RRF and EF-G bound to the PostTC or (2) deacylated tRNA bound to the 30S subunit are of particular interest. Our observations of the native form of these complexes demonstrate the strong potential of time-resolved cryo-EM for visualizing previously unobservable transient structures.

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

**Not applicable.**

**I am supported by this grant. But I don't know if I should list it here or how to describe my role in the grant.**

**Ongoing**

**RO1 GM029169 JOACHIM FRANK, PI 1994 – 2019**

**NIH NIGMS**

**STRUCTURAL ANALYSIS OF MACROMOLECULAR ASSEMBLIES**

This study explores structure and function of the ribosome actively engaged in protein synthesis, by cryo-electron microscopy (cryo-EM) and single-particle reconstruction.