BIOGRAPHICAL SKETCH

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NAME: Chen, Muyuan

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

POSITION TITLE: Staff Scientist

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
Southeast University, Nanjing, Jiangsu, China	B.Eng.	06/2013	Biomedical Engineering
Baylor College of Medicine, Houston, TX, USA	Ph.D.	10/2017	Quantitative and Computational Biosciences
Baylor College of Medicine, Houston, TX, USA	Postdoctoral	06/2019	Biochemistry

A. Personal Statement

Since the start of my graduate study, my research has been focused on developing computational methods to handle cryo-electron microscopy (CryoEM) data and study the 3D structure and dynamics of macromolecules. With a strong computational background, I work on adapting machine learning algorithms to process the extremely noisy images produced by CryoEM and extract biologically meaningful information. My work covers a wide range of CryoEM applications, including methods for resolving macromolecular structural variability for single particle analysis, *de novo* modeling tools for CryoEM density maps at near-atomic resolution, and a complete workflow for tomography data processing that allows high-resolution structure determination inside cells. My software has been used by research groups around the world, and I routinely provide support for users. I am also involved in many collaborative projects in which data processing expertise is necessary to provide insights for fundamental biological questions.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2019-2022 Instructor, Department of Biochemistry and Molecular Biology, Baylor College of Medicine
2022- Staff scientist, SLAC National Accelerator Laboratory, Stanford University

Other Experience and Professional Memberships

2015- Biophysical Society
2017- Microscopy Society of America

Honors

2018 Ruth McLean Bowman Bowers Excellence in Research Award, Baylor College of Medicine, Department of Biochemistry and Molecular Biology

C. Contributions to Science

1. Software development for CryoEM/CryoET image processing. In the past few years, one of my major contributions to the CryoEM filed is introducing machine learning algorithms to CryoEM data processing. With

my effort, deep learning techniques have been adapted to automate previously labor-intensive steps like particle picking and feature annotation in cellular tomograms. Recently, my focus has shifted more to CryoET, with the development of a complete data processing pipeline spanning from raw tilt series to high-resolution averaged structures. The pipeline brings more automation to the entire process, routinely achieving significantly better structures with much less human intervention than existing protocols.

- **M. Chen**, J. M. Bell, X. Shi, S. Y. Sun, Z. Wang, S. J. Ludtke (2019). A complete data processing workflow for CryoET and subtomogram averaging. *Nature Method.* 2019. PMC5623144
- **M. Chen**, W. Dai, S. Y. Sun, D. Jonasch, C. Y. He, M. F. Schmid, W. Chiu, S. J. Ludtke (2017). Convolutional Neural Networks for Automated Annotation of Cellular Cryo-Electron Tomograms. *Nature Methods*. 14, 983–985 (2017). PMC5623144
- J. M. Bell, **M. Chen**, P. R. Baldwin, S. J. Ludtke (2016). High Resolution Single Particle Refinement in EMAN2.1. *Methods (San Diego, Calif.)*, 100, 25-34. PMC4848122.

2. Modeling the structure and dynamics of proteins from CryoEM datasets. Advanced data processing techniques are not only necessary for generating high resolution structures from noisy CryoEM images, but also key to interpreting those structures, turning those density maps into meaningful molecular models. Indeed, modeling of CryoEM maps has been one of my research focuses since my early days of graduate school. In addition to building molecular model for static structures, recently with the help of deep neural network methods, I put forward computational tools that resolve the structural variability of proteins using a similar pseudo-atom representation. My work integrated the molecular model representation of proteins into the CryoEM refinement pipeline, providing a new way of exploring the dynamics of macromolecular systems.

- **M. Chen**, B. Toader, R. Lederman (2023). Integrating Molecular Models into CryoEM Heterogeneity Analysis Using Scalable High-resolution Deep Gaussian Mixture Models. *Journal of Molecular Biology*, 435 (9), 168014. PMC10164680
- **M. Chen**, S. J. Ludtke (2021). Deep learning based mixed-dimensional GMM for characterizing variability in CryoEM. *Nature Method*, 18, 930–936. PMC8363932
- **M. Chen**, P. R. Baldwin, S. J. Ludtke, M. L. Baker (2016). De Novo Modeling in Cryo-EM Density Maps with Pathwalking. *Journal of Structural Biology*, 196(3), 289-298. PMC5118137

3. In situ structure characterization with CryoET. While standard data processing protocols exist for single particle reconstruction of purified samples, when studying with protein complexes inside cells using CryoET, specialized algorithms are often needed to interpret the tomograms and build biological stories from the data. In collaborative projects with different research groups, I studied interactions between proteins and their surrounding environment, performed statistical analysis on protein distribution throughout cells, and characterized unidentified protein densities from cellular tomograms. Those biological projects also drive further development of computational methods that are integrated into software packages that are available to other researchers.

- S. Y. Sun*, L. Segev-Zarko*, **M. Chen***, G. D. Pintilie, M. F. Schmid, S. J. Ludtke, J. C. Boothroyd, W. Chiu (2022) Cryo-ET of Toxoplasma parasites gives sub-nanometer insight into novel tubulin-based structures. *P.N.A.S.* PMC8832990
- X. Shi*, **M. Chen***, Z. Yu, J. M. Bell, H. Wang, I. Forrester, H. Villarreal, J. Jakana, D. Du, B. F. Luisi, S. J. Ludtke, Z. Wang (2019). *In situ* structure and assembly of the multidrug efflux pump AcrAB-TolC*. Nature Communication*. 10, 2635. PMC6570770
- O. Levitan*, **M. Chen***, X. Kuang*, K. Y. Cheong, J. Jiang, M. Banal, N. Nambiar, M. Y. Gorbunov, S. J. Ludtke, P. G. Falkowski, W. Dai (2018). Structural and Functional Analyses of Photosystem II in Thylakoid Membranes of a Marine Diatom. *P.N.A.S.*, 116 (35), 17316-17322. PMC6717305