BIOGRAPHICAL SKETCH

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NAME: Liu, Jun

eRA COMMONS USER NAME (credential, e.g., agency login): JunLiu1

POSITION TITLE: Professor of Microbial Pathogenesis and Cell Biology

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
Chengdu University of Science and Technology, Chengdu, Sichuan, China	B.S.	07/1992	Physics
Wuhan University, Wuhan, Hubei, China	M.A.	07/1995	Physics
Chinese Academy of Sciences, Beijing, China	Ph.D.	07/1998	Physics
Florida State University, Tallahassee, Florida, USA	Postdoc	05/2001	Biophysics

A. Personal Statement

My laboratory is dedicated to developing high-throughput cryo electron tomography (cryoET) pipeline in which both data collection and image analysis are streamlined and automated. Fueled by recent breakthroughs in both hardware and software that transformed cryoEM, our high-throughput cryoET pipeline has become increasingly powerful, enabling us to visualize molecular machines in their cellular context at resolutions not possible by any other technique. The *in-situ* information has been systematically utilized to gain structural insights into fundamental biological processes related to signaling transduction, flagellar assembly, protein secretion, viral infection, DNA translocation, and host-pathogen interactions. I have trained over 20 students and postdocs, two of them (Bo Hu and Jiagang Tu) started their own independent laboratories. I have published papers that are comprehensive, rigorous, and impactful.

B. Positions and Honors

Positions and Employment

2001-2006 Visiting Assistant in Research, Institute of Molecular Biophysics, Florida State University
Supervisor: Dr. Ken Taylor

2006-2007 Staff Scientist, Laboratory of Cell Biology, National Cancer Institute, National Institutes of Health
Supervisor: Dr. Sriram Subramaniam

2007-2014 Assistant Professor, Department of Pathology and Laboratory Medicine, University of Texas-Houston Medical School, Houston, TX

2014-2017 Associate Professor with tenure, Department of Pathology and Laboratory Medicine, University of Texas-Houston Medical School, Houston, TX

2008-2017 Faculty Member, Graduate School of Biomedical Sciences (GSBS) University of Texas Health Science Center, Houston, TX

2008-2017 Adjunct Professor, Department of Microbiology and Molecular Genetics, University of Texas Health Science Center, Houston, TX

2010-2017 Faculty member of the Program of Structural and Computational Biology and Molecular Biophysics, Baylor College of Medicine, Houston, TX

2017-2021 Associate Professor with tenure, Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT

2021- Professor with tenure, Department of Microbial Pathogenesis and Department of Cell Biology, Yale School of Medicine, New Haven, CT

Other Experience and Professional Memberships

2001-present Member, Biophysical Society
2001-present Member, Microscopy Society of America
2008-present Member, American Society for Microbiology
2020-2024 Member, Macromolecular Structure and Function C Study Section (MSFC), NIH, USA
***Ad hoc* reviewer** for *NIH Enabling Bioanalytical & Imaging Technologies (EBIT) Study Section,*
The Research Grants of the Medical Research Council (MRC), UK,
Fellowship grants for the Wellcome Trust and Royal Society, UK,
The Research Grants of the Swiss National Science Foundation, Switzerland.
NIH Macromolecular Structure and Function C Study Section (MSFC)
NIH special emphasis panel (ZRG1 AARR-P)
NIH Bacterial Pathogenesis Study Section (BACP)
***Ad hoc* reviewer** for *Nature, Cell, Science, Nature Communications, Journal of Structural Biology, Virology, Journal of Visualized Experiments, Biological Chemistry, Molecular Microbiology, PloS One, Journal of Virology, Journal of Bacteriology, PNAS, Cell, Nature Microbiology, PloS Pathology, Nature Methods, eLife*

2020: Invited speaker. 3rd Bacterial Cell Biology Conference, Nassau, Bahamas
2020: Invited speaker. Sensory Transduction in Microorganisms (STIM) Gordon Research Conference, USA
2019: Invited speaker. Microscopy & Microanalysis 2019 Meeting, Portland, OR, USA
2018: Co-Chair. The 2018 Kuo Symposium on 3D Cryo-EM Molecular Imaging, Hangzhou, China
2018: Discussion leader. *Gordon Research Conference on Three Dimensional Electron Microscopy, USA*
2018: Invited speaker. *Keystone Symposia on Molecular and Cellular Biology, Cryo-EM from Cells to Molecules: Multi-Scale Visualization of Biological Systems, Tahoe, California, USA*
2018: Invited speaker. *Gordon Research Conference on Bacterial Cell Surface, West Dover, VT, USA*
2018: Invited speaker. *FASEB: Virus Structure and Assembly, Steamboat Springs, CO, USA*
2016: Invited speaker. Kuo Symposium on 3D Cryo-EM Molecular Imaging, Beijing, China:
2015: Invited speaker. *Gordon Research Conference on Three Dimensional Electron Microscopy*
2014: Invited speaker. The 2014 Kuo Symposium on 3D Cryo-EM Molecular Imaging, Shanghai, China
2014: Invited speaker. Microscopy & Microanalysis 2014 Meeting, Hartford, Connecticut, USA.
2014: Invited speaker. *Spirochete, Biology of Gordon Research Conference*
2013: Invited speaker. *The 113th General Meeting of the American Society for Microbiology*
2012: Invited speaker. *Sensory Transduction in Microorganisms Gordon Research Conference*

Honors

2016: McGovern Scholar Award

C. Contribution to Science

1. Cryo electron tomography (cryoET) has emerged as the most powerful technique for high resolution structure determination of large macromolecular complex *in situ*. I am fortunate enough to have 20-year experience in cryoET by working with Dr. Kenneth Taylor (2008-2006) and Dr. Sriram Subramaniam (2006-2007) and then at my own laboratory (2007-present). I had an opportunity to push the cryoET envelope and determine the first 2.0 nm structure of myosin-V in inactive state (*Liu et al., Nature 2006*). Then I applied the technique from *in vitro* myosin-V assemblies to native HIV-1 Env trimer and its interactions with CD4 and antibodies at 2.0 nm resolution (*Liu et al., Nature 2008*). In my own laboratory, high-throughput cryoET has been effectively utilized to study many important but challenging biological processes: such as viral infection (*Hu, et al., Science 2013*), flagellar assembly (*Zhao, et al., PNAS 2013*), protein secretion (*Hu, et al., Cell 2018*), and host-pathogen interaction (*Park, et al., eLife 2018*). These studies are among the best-known cryoET applications, and have profound impacts on the exciting field.
    a. **Liu J**, Taylor DW, Krementsova EB, Trybus KM, Taylor KA: Three-dimensional structure of the myosin V inhibited state by cryoelectron tomography. ***Nature*** 2006, 442:208-211. PMID: 16625208
    b. **Liu J**, Bartesaghi A, Borgnia M, Sapiro G, Subramaniam S: Molecular architecture of native HIV-1 gp120 trimers. ***Nature*** 2008, 455:109-113. PMCID: PMC2610422
    c. Hu B, Lara-Tejero M, Kong Q, Galán JE, **Liu J**: *In situ* molecular architecture of the *Salmonella* type III secretion machine, ***Cell*** 2017 Mar 9;168(6):1065-1074.e10. PMCID: PMC5393631
    d. Park D, Lara-Tejero M, Waxham MN, Li W, Hu B, Galán JE, **Liu J**: Visualization of the type III secretion mediated *Salmonella*-host cell interface using cryo-electron tomography, ***Elife***. 2018 Oct 3;7. pii: e39514. doi: 10.7554/eLife.39514. PMCID: PMC6175578

2. In collaboration with Drs. Steven Norris, Md Motaleb, Chunaho Li, and Nyles Charon, we utilized the Lyme disease spirochete as a model system to study the structure and function of bacterial flagella by combining genetics with cryoET. We provided the first structural blueprint of the assembly process of the bacterial flagella in intact cells. We made important progress in dissecting mechanisms underlying flagellar torque generation, directional switching, and protein secretion.
    a. **Liu J**, Lin T, Botkin DJ, McCrum E, Winkler H, Norris SJ: Intact Flagellar Motor of *Borrelia burgdorferi* Revealed by Cryo-Electron Tomography: Evidence for Stator Ring Curvature and Rotor/C Ring Assembly Flexion, ***J Bacteriol*** 191(16):5026-36, 2009. PMCID: PMC2725586
    b. Zhao X, Zhang K, Boquoi T, Hu B, Motaleb MA, Miller K, James M, Charon NW, Manson MD, Norris SJ, Li C, **Liu J**: Cryo-Electron Tomography Reveals the Sequential Assembly of Bacterial Flagella in *Borrelia burgdorferi*. ***Proc Natl Acad Sci U S A***, 110(35):14390-5, 2013. PMCID: PMC3761569
    c. Qin Z, Tu J, Lin T, Norris SJ, Li C, Motaleb MA, **Liu J**: Cryo-electron tomography of periplasmic **flagella** in *Borrelia burgdorferi* reveals a distinct cytoplasmic ATPase complex. ***PLoS Biol*** 2018 Nov 9;16(11):e3000050. PMCID: PMC6248999
    d. Chang Y, Zhang K, Carroll B, Zhao X, Charon NW, Norris SJ, Motaleb MA, Li C, **Liu J**: Molecular mechanism for rotational switching of the bacterial flagellar motor ***NSMB*** 2020 Nov 27 (11):1041-1047. PMCID: PMC8129871
3. In collaboration with Drs. William Margolin and Ian Molineux, we genetically engineered bacteria to generate tiny minicells from parental cells. The minicells as small as 0.2 μm in diameter have been successfully utilized as host cells for *in situ* structural characterization of bacteriophage infection initiation. Our studies provided new insights into the mechanisms by which tailed phages overcome the multiple barriers of the bacterial envelope and to deliver their genetic materials into the host cell cytoplasm.
    a. Hu B, Margolin W, Molineux IJ, **Liu J**: The bacteriophage T7 virion undergoes extensive structural remodeling during infection, ***Science*** 339(6119):576-9, 2013. PMCID: PMC3873743
    b. Hu B, Margolin W, Molineux IJ, **Liu J**: Structural remodeling of bacteriophage T4 and host membranes during infection initiation, ***Proc Natl Acad Sci U S A***. 2015 Sep 1;112(35):E4919-28. PMCID: PMC4568249
    c. Farley M, Tu J, Kearns DB, Molineux IJ, **Liu J**: Ultrastructural analysis of bacteriophage Φ29 during infection of *Bacillus subtilis*. ***J Struct Biol***, 2016, S1047-8477(16)30167-8. PMCID: PMC5272854
    d. Wang C, Tu J, **Liu J**, Molineux IJ: Structural dynamics of bacteriophage P22 infection initiation revealed by cryo-electron tomography, ***Nat Microbiol***, 2019, 4(6): 1049-1056, PMCID: PMC653319
4. In collaboration with Drs. Jorge Galán, Craig Roy, and Bill Picking, we used cryoET to determine bacterial secretion machine structures in situ at high resolution, providing new insights into molecular mechanisms underlying protein secretion and bacterial pathogenesis.
    a. Hu B, Morado DR, Margolin W, Rohde JR, Arizmendi O, Picking WL, Picking WD, **Liu J**: Visualization of the type III secretion sorting platform of *Shigella flexneri.* ***Proc Natl Acad Sci U S A*** 2015, 112(4):1047-1052. PMCID: PMC4313800
    b. Hu B, Lara-Tejero M, Kong Q, Galán JE, **Liu J**: *In situ* molecular architecture of the *Salmonella* type III secretion machine, ***Cell*** 2017 Mar 9;168(6):1065-1074.e10. PMCID: PMC5393631
    c. Chetrit D, Hu B, Christie PJ, Roy CR, **Liu J**: A Unique Cytoplasmic ATPase Complex Defines the Legionella pneumophila Type IV Secretion Channel, ***Nat Microbial*** 3(6):678-686, 2018. PMCID: PMC5970066
    d. Park D, Lara-Tejero M, Waxham MN, Li W, Hu B, Galán JE, **Liu J**: Visualization of the type III secretion mediated *Salmonella*-host cell interface using cryo-electron tomography, ***Elife***. 2018 Oct 3;7. pii: e39514. doi: 10.7554/eLife.39514. PMCID: PMC6175578

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/jun.liu.2/bibliography/40516970/public/?sort=date&direction=descending

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

Ongoing Research Support

R01 AI087946 (NIH/NIAID) Liu (PI) 02/15/2010 - 12/31/2025

Structure-Function Relationships in the Spirochetal Flagellar Motor

The goal of this study is to characterize flagellar motor structure using a combination of cryo-electron microscopy, biophysical, and genetic approaches.

Role: PI

R01 GM110243 (NIH/NIGMS) Liu, Molineux (multi-PI) 05/01/2014-11/30/2024
Structural Basis of Phage Infection and DNA Ejection
The objective of this study is to understand conformational rearrangements during phage infection by combining high throughput cryo-electron tomography with molecular genetics of both phage and host.
Role: PI

R01 GM124378-01 (NIH/NIGMS) Molineux (PI) 09/01/2017 - 05/31/2022 (NCE)
Initiation of Phage Infection
The overall objective of the proposal is to provide new molecular insights into the mechanistic pathways leading to phage P22 infection.
Role: co-I

R01 AI132818-01A1 (NIH/NIAID) Motaleb (PI) 05/01/2018 - 04/30/2022
Delineation of Unique Flagellar Proteins in Spirochetes
The proposal aims to understand how the periplasmic flagella are assembled in spirochetes.
Role: co-I

R01 AI150560 (NIH/NIGMS) Mothes, Liu (multi-PI) 07/01/2019 - 06/30/2023
HIV-1 Env Structure and Function assessed by paralled smFRET and cryoET
The proposal aims to understand the HIV-1Env structure and function in native virion.
Role: multi-PI

R01 AI152421 (NIH/NIAID) Liu, Roy (multi-PI) 09/16/2020-08/30/2025
Functional and Structural Analysis of the Dot/Icm Type IVB Secretion Machine
The gold of the proposal is to dissect structure and function of the *Legionellae* T4SS machines.
Role: co-PI

Completed Research Support
R01 GM107629 (NIH/NIGMS) Liu (PI) 09/30/2014-08/31/2019
Structural basis of signaling between bacterial chemoreceptors and flagella
The overall objective of this proposal is to correlate structural changes in the chemoreceptor complex and the flagellar motor of cells in different signaling states.
Role: PI