## BIOGRAPHICAL SKETCH

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NAME: **Liang, Bo**

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

POSITION TITLE: **Co-Scientific Director and Assistant Professor of Biochemistry, Tenure Track**

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 |
|---|---|---|---|
| University of Science and Technology of China, Hefei, Anhui | B.S. | 07/2004 | Biological Science |
| University of Science and Technology of China, Hefei, Anhui | B.E. | 07/2004 | Computer Science |
| Florida State University, Tallahassee, Florida | Ph.D. | 12/2009 | Molecular Biophysics |
| Harvard Medical School, Boston, Massachusetts | Postdoctoral Fellow | 09/2016 | Structural Cell Biology and Microbiology |

### A. Personal Statement

I have the motivation, expertise, leadership, and training necessary to complete the proposed research program. As a graduate student and two-time American Heart Association predoctoral fellow with Dr. Hong Li at Florida State University, and later as a postdoctoral fellow with Drs. Stephen Harrison and Sean Whelan at Harvard Medical School, I received outstanding training in structural biology, with specific expertise in cryo-electron microscopy (cryo-EM) and x-ray crystallography and RNA biology, and virology. My current research focuses on the structures and mechanisms of macromolecules, emphasizing the viral RNA synthesis machinery and neurobiological disease-related assemblies.

As an investigator on several NIH-funded projects, I built the foundation for the proposed research by developing effective sample preparation, data acquisition, and analysis strategies. In particular, I have comprehensive experience in single-particle cryo-EM, including specimen optimization, data collection, image processing, model interpretation, and validation. Additionally, I have rigorous biochemistry and x-ray crystallography training, including protein and RNA purification, crystallization, synchrotron x-ray diffraction, data processing, model building, and refinement. I furthermore have an extensive background in RNA biology and virology.

I received a generous startup package and began my independent laboratory in the Biochemistry Department at Emory University School of Medicine in October 2016. Emory has purchased two state-of-the-art electron microscopes as part of my recruitment. Currently, I am the Co-Scientific Director of the Robert P. Apkarian Integrated Electron Microscopy Core (IEMC) at Emory. I have a dedicated mentoring committee that consists of established faculty Drs. Richard Kahn, Daniel Reines, Christine Dunham, and Anice Lowen at Emory. Drs. Stefan Sarafianos, Anita Corbett, David Steinhauer, Guido Silvestri, Jeremy Boss (former interim chair), and Eric Sundberg (Chair) also provide critical feedback. Together, these colleagues have provided (and continue to provide) invaluable guidance on staffing and acquiring funding for my laboratory, prioritizing my research efforts, and ensuring that service and teaching commitments are appropriate for my independent career.

I have successfully determined multiple high-resolution structures of the polymerases from NNS RNA viruses using single-particle cryo-EM. In particular, my lab has recently determined a 3.67 Å cryo-EM structure of the *apo* polymerase (L:P) complex of respiratory syncytial virus (RSV). We propose to extend our cryo-EM analysis to the RSV polymerase and its complex with RNA templates and RNA products and therefore request the data collection resources at NCCAT.

Ongoing and recently completed projects that I would like to highlight:

NIH/NIGMS, 1R01GM130950 09/20/2019 - 07/31/2024
**Structure and Regulation of The Respiratory Syncytial Virus Polymerase**
Role: Liang (PD/PI)

Emory University, MP3 Initiative 09/01/2020 - 08/31/2021
**Structure, function, and rational inhibitor design of the SARS-CoV-2 RNA polymerase**
Role: Liang (PD/PI), Baek Kim, Dennis Liotta (Co-PIs)

Emory University, University Research Committee Award 11/01/2020 - 10/31/2021
**Novel *in vitro* mini-nucleocapsid of respiratory syncytial virus**
Role: Liang (PD/PI)

American Lung Association, Innovation Award 07/01/2021 - 06/30/2022
**Structures and Shared Mechanisms of the RSV and SARS-CoV-2 Viral Polymerases**
Role: Liang (PD/PI)

**B. Positions, Scientific Appointments, and Honors**

**Scientific Appointments**

| | |
|---|---|
| 2004-2009 | Graduate Research Assistant, Institute of Molecular Biophysics, Florida State University, Tallahassee, FL |
| 2009 | Teaching Assistant, Florida State University, Tallahassee, FL |
| 2009-2016 | Postdoctoral Research Fellow, Biological Chemistry and Molecular Pharmacology (BCMP), and Microbiology and Immunobiology (MBIB), Harvard Medical School, Boston, MA |
| 2015 | Teaching Assistant, Harvard Medical School, Boston, MA |
| 2016- | Assistant Professor of Biochemistry, Emory University School of Medicine, Atlanta, GA |
| 2018- | Co-Scientific Director, Robert P. Apkarian Integrated Electron Microscopy Core, Emory University, Atlanta, GA |

**Positions and Services**

| | |
|---|---|
| 2005-2006 | Treasurer, Students for the Effective Communication of Science, Florida State University |
| 2006-2007 | Vice President, Chinese Students and Scholars Association, Florida State University |
| 2007-2008 | President, Chinese Students and Scholars Association, Florida State University |
| 2008-2009 | Senior Consultant, Chinese Students and Scholars Association, Florida State University |
| 2010-2011 | Governing Board, HMS/HSDM Postdoctoral Association, Harvard Medical School |
| 2011-2014 | Co-Chair, HMS/HSDM Postdoctoral Association, Harvard Medical School |
| 2013-2014 | Associate Editors-in-Chief, the Journal of Postdoctoral Research |
| 2013-2016 | Trainee Committee, Biological Chemistry and Molecular Pharmacology, Harvard Medical School |
| 2014-2016 | Secretary, Harvard Medical Postdoctoral Association, Harvard Medical School |
| 2017 | Faculty Search Committee, Department of Biochemistry, Emory University School of Medicine |
| 2017- | Cryo-EM Executive Committee, Integrated Electron Microscopy Core, Emory University |
| 2017- | Editorial Board, Journal of Molecular Cell Biology |
| 2017- | Co-director, Biochemistry Departmental Seminar Program, Emory University School of Medicine |
| 2017- | Executive Committee, Microbiology and Molecular Genetics Graduate Program, Emory University |
| 2017- | Annual Graduate Course Lecturer, Virology (IBS 513), Emory University |
| 2018- | Annual Graduate Course Lecturer, Foundations of BCDB (BCDB 502), Emory University |
| 2020 - | Recruitment Committee, Biochemistry, Cell and Developmental Biology, Emory University |

2021- Editorial Board, Journal of Virology
2021- Space Committee, Department of Biochemistry, Emory University School of Medicine

**Honors**

2006 Predoctoral Fellowship, Florida/Puerto Rico Affiliate, American Heart Association
2008 Kasha Award, Florida State University
2008 Predoctoral Fellowship, Greater Southeast Affiliate, American Heart Association
2009 Protein Science Young Investigator Travel Grant, The Protein Society
2020 COVID-19 Research Award, High-Performance Computing (HPC) Consortium
2020 COVID-19 Research Award, Argonne National Laboratory
2020 RAP-c Award for COVID-19 Research, National Center for CryoEM Access and Training
2020 COVID-19 Research Award, NCI National Cryo-EM Facility
2021 Scholarly Writing and Publishing Award, Emory University
2021 Innovation Award, American Lung Association

**Professional Memberships**

Member, The Biophysical Society
Member, The RNA Society
Member, The Protein Society
Member, The American Society for Biochemistry and Molecular Biology
Member, The American Society for Microbiology
Member, The American Society of Virology
Member, The American Crystallographic Association
Member, The Microscopy Society of America

## C. Contributions to Science

- **Illustrated the molecular basis of key assembly stages of a novel family of RNA-guided RNA modification enzyme.** My interest in ribonucleoprotein (RNP) machinery began with my graduate studies in Professor Hong Li's laboratory, where I focused on box H/ACA RNPs that are essential for ribosome and spliceosome maturation. Box H/ACA RNPs utilize the same four proteins, Cbf5, Nop10, Gar1, and L7Ae, which are also core components of the telomerase, and a set of non-coding guide RNAs to capture ribosomal RNAs and snRNAs for chemical modification. My primary contribution was to illustrate the molecular basis of key assembly stages of the box H/ACA RNP assembly and function with a set of crystal structures, including one complex of Cbf5:Nop10:Gar1 (2.1 Å), one substrate-bound (2.87 Å), and one functional (2.35 Å) box H/ACA RNP. I also devised a fluorescence assay to dissect the accurate placement of the substrate RNA and analyzed the impact of chemical substitutions with biochemical and structural approaches and dynamic simulations. These findings, as papers cited below, collectively had a significant impact on understanding the multistep and multicomponent-mediated enzyme activity of the box H/ACA RNP.
  - **Liang B.**, Zhou J., Kahen E., Terns R. M., Terns M. P., Li H. Structure of a functional ribonucleoprotein pseudouridine synthase bound to a substrate RNA. ***Nat Struct Mol Biol*** 16, 740-746 (**2009**) | PMC5706466.
  - **Liang B.**, Kahen E. J., Calvin K., Zhou J., Blanco M., Li H. Long-distance placement of substrate RNA by H/ACA proteins. ***RNA*** 14, 2086-2094 (**2008**) | PMC2553744.
  - **Liang B.**, Xue S., Terns R. M., Terns M. P., Li H. Substrate RNA positioning in the archaeal H/ACA ribonucleoprotein complex. ***Nat Struct Mol Biol*** 14, 1189-1195 (**2007**) | 10.1038/nsmb1336.
  - Rashid R., **Liang B.**, Baker D. L., Youssef O. A., He Y., Phipps K., Terns R. M., Terns M. P., Li H. Crystal structure of a Cbf5-Nop10-Gar1 complex and implications in RNA-guided pseudouridylation and dyskeratosis congenita. ***Mol Cell*** 21, 249-260 (**2006**) | 10.1016/j.molcel.2005.11.017.

- **Determined the first structure of the multifunctional L protein of a non-segmented negative-strand RNA virus with cryo-EM.** My subsequent work in the laboratories of Professors Stephen Harrison and Sean Whelan at Harvard Medical School directly visualized the atomic structure of the multifunctional RNA polymerase of vesicular stomatitis virus (VSV), a model non-segmented negative-sense (NNS) RNA virus. NNS RNA viruses are a group of viruses containing many significant human pathogens, including Ebola,

rabies, and respiratory syncytial virus (RSV). The RNA synthesis by the RNA polymerase of these viruses is central to their life cycle. The RNA polymerase, constituted of the large protein (**L**) and the phosphoprotein (**P**), contains multiple distinct activities of RNA-dependent RNA polymerase, polyribonucleotidyl transferase, and RNA methyltransferase. I have successfully prepared and biochemically characterized the L complexes. My colleagues and I obtained the first architectures of L alone and its complexes using negative-stain EM. Importantly, I obtained a 3.8 Å cryo-EM structure of VSV L and performed the *de novo* model building of this 2109-residue polypeptide. Two significant contributions resulted from this work: 1) the determination of the first atomic structure of an asymmetric protein of less than 250 kDa using cryo-EM; 2) the first atomic view of the RNA polymerase of NNS RNA viruses. Further, I have successfully expressed and purified the L protein of rabies virus (RABV) and adapted an *in vitro* transcription assay from VSV to RABV.

- Jenni S., Bloyet L. M., Diaz-Avalos R., **Liang B.**, Whelan S. P. J., Grigorieff N., Harrison S. C. Structure of the Vesicular Stomatitis Virus L Protein in Complex with Its Phosphoprotein Cofactor. ***Cell Rep*** 30, 53-60 e55 (**2020**) | PMC7049099.
- Morin B., **Liang B.**, Gardner E., Ross R. A., Whelan S. P. J. An *In Vitro* RNA Synthesis Assay for Rabies Virus Defines Ribonucleoprotein Interactions Critical for Polymerase Activity. ***J Virol*** 91, (**2017**) | PMC5165209.
- **Liang B.**, Li Z., Jenni S., Rahmeh A. A., Morin B. M., Grant T., Grigorieff N., Harrison S. C., Whelan S. P. J. Structure of the L Protein of Vesicular Stomatitis Virus from Electron Cryomicroscopy. ***Cell*** 162, 314-327 (**2015**) | PMC4557768.
- Rahmeh A. A., Morin B., Schenk A. D., **Liang B.**, Heinrich B. S., Brusic V., Walz T., Whelan S. P. Critical phosphoprotein elements that regulate polymerase architecture and function in vesicular stomatitis virus. ***Proc Natl Acad Sci U S A*** 109, 14628-14633 (**2012**) | PMC3437890.

- **Illustrated the structure and regulation of the respiratory syncytial virus RNA synthesis machine.** After being independent, I switched the focus to the structure and regulation of the RNA synthesis machine of RSV, a pathogenic NNS RNA virus. The **L** protein and an essential tetramer of **P** constitute the polymerase that acts on the viral genome, which is a complex of genomic RNA tightly coated by nucleoprotein (**N**). In some cases, additional viral proteins (VP30 in Ebola and **M2-1** in RSV) are necessary for full polymerase processivity. Thus far, (**1**) We adapted and set up the RSV RNA polymerization assay in the lab and provided new mechanistic insights into the initiation and elongation of RSV RNA synthesis. (**2**) We have determined a 3.67 Å cryo-EM structure of the *apo* RSV polymerase (L:P) complex. (**3**) We established a protocol to obtain RNA-free N protein ($N^0$) and successfully demonstrated the *in vitro* trackable assembly of N with RNA into nucleocapsid-like particles (NCLPs) for in-depth mechanistic analyses. (**4**) We determined a 2.7 Å co-crystal structure of RSV M2-1 bound to a short RNA oligo and provided a structural basis for recognizing RNA by M2-1.
  - Cao D., Gao Y., Roesler C., Rice S., D'Cunha P., Zhuang L., Slack J., Antonova A., Romanelli S., **Liang B.*** *In vitro* primer-based RNA elongation and promoter fine mapping of the respiratory syncytial virus. ***J Virol*** 95, (**2020**) | 10.1128/JVI.01897-20 | PMC7737744.
  - Gao Y., Cao D., Pawnikar S., John K., Ahn H. M., Ha J. M., Parikh P., Ogilvie C., Yang A., Bell A., Salazar A., Miao Y.*, **Liang B.*** Structure of the human respiratory syncytial virus M2-1 protein in complex with a short positive-sense gene-end RNA. ***Structure*** 28, 979-990 e974 (**2020**) | PMC7484405.
  - Cao D., Gao Y., Roesler C., Rice S., D'Cunha P., Zhuang L., Slack J., Domke M., Antonova A., Romanelli S., Keating S., Forero G., Juneja P., **Liang B.*** Cryo-EM structure of the respiratory syncytial virus RNA polymerase. ***Nat Commun*** 11, 368 (**2020**) | PMC6969064.
  - Gao Y., Cao D., Ahn H. M., Swain A., Hill S., Ogilvie C., Kurien M., Rahmatullah T., **Liang B.*** *In vitro* trackable assembly of RNA-specific nucleocapsids of the respiratory syncytial virus. ***J Biol Chem*** 295, 883-895 (**2020**) | PMC6970927.

**Complete Publication List:**
https://www.ncbi.nlm.nih.gov/myncbi/bo.liang.2/bibliography/public/