OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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NAME: Jiang, Qiu-Xing

eRA COMMONS USER NAME (credential, e.g., agency login): jiangq9992003

POSITION TITLE: Associate Professor

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 DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Univ. Science Tech. China, Hefei, Anhui, ChinaInstitute of Biophysics, CAS, Beijing, ChinaYale University, New Haven, CTYale University, New Haven, CTYale University, New Have, CTRockefeller University, New York, NY | BSMSM. PhilPhDpostdocpostdoc | 06/199205/199503/199805/200202/200306/2007 | BiophysicsCell BiophysicsCell. Mol. Physiol.Cell. Mol. Physiol.Mol. BiophysicsMol. Neurobiology & Biophysics |

**A. Personal Statement**

My research area is in Molecular and Cellular Physiology and Molecular Biophysics. My lab has three general science directions: membrane biology, intracellular RNA-binding, and nano-scale chemical engineering and its applications to cryoEM and the first two directions. The ion channel direction is focused on two new discoveries my lab made in the past few years --- lipid-dependent gating of voltage-gated potassium (Kv) channels and new ion channels in the regulated secretory pathways. The anion channels in the regulated secretion are closely related to endocrine cancers. The second direction grew out of collaborative work and focuses on RNA-binding complexes for RNA sensing, RNAi pathway and human telomerase. The human telomerase study is closely related to cancer biology, which discovered a new dynamic control for human telomerase holoenzyme. The third direction is related to three technologies I helped initiate: random spherically constrained (RSC) reconstruction, chemically functionalized nm-thick carbon (ChemiC) films and bead-supported unilamellar membranes (bSUMs). I thus have the combined expertise in both biological investigations and technical development, and am well poised to advancing the new directions proposed in the application.

 I have been using cryo-electron microscopy (cryoEM) as a major biophysical method. RSC was first proposed when I initiated the idea of Spherical Reconstruction from cryoEM images of membrane proteins in small vesicles (paper ***a***), a method that Dr. Sigworth, my graduate adviser, and Dr. Liguo Wang has advanced significantly. It was renamed as RSC. During my postdoctoral period, I worked on two closely related problems, and made some advancement in studying the importance of phospholipids to Kv channels. After I started my own laboratory, I expended the scope of studying the lipid effects on voltage-gated potassium channels and proposed a new concept of the lipid-dependent gating hypothesis (paper ***b***). This concept has been supported by observations of mammalian Kv channels, bacterial voltage-gated sodium channels, and in the dopaminergic neurons.

 Recently, our study of ion channels in the regulated secretory pathway is a new direction which is centered around a completely new ion channel function we discovered in a granin family protein (paper in revision), which plays an important role in regulated secretion and in neuroendocrine cancers.

 I continued my technology development in my own laboratory. ChemiC was developed to overcome significant loss of samples during cryo-freezing (paper ***c***). bSUM was developed to overcome the limitation in controlling lipid composition and phase behavior as well as protein orientation in vesicles (paper ***d***). These methods form a good technical basis for developing the two new forms of supported membranes for cryoEM imaging of membrane proteins.

 I changed my research direction when I was in Dallas because of the lack of high-resolution electron microscopes when I started there. This change led me to two new directions in my own lab, and multiple new findings through collaborative studies. With the EM facilities in University of Florida and Florida State University, I am confident that we will be able to pull forward the new biological questions we discovered and the new technologies we propose to develop in the near future.

1. **Qiu-Xing Jiang**, David W. Chester, and Fred J. Sigworth. (2001) Spherical reconstruction: a method for structure determination of membrane proteins from cryo-EM images*. J. Struct. Biol*., **133:**119-131. PMID:11472084.
2. Hui Zheng, Weiran Liu, Lingyan Anderson, and **Qiu-Xing Jiang**. (2012) Lipid-dependent gating of a voltage-gated ion channel. *Nature Comm.*, **2**:250 doi:10.1038/ncomms1254. PMID:21427721 / PMCID: PMC3072105
3. Marc Llaguno, Hui Xu, Liang Shi, Nian Huang, Hong Zhang, Qinghua Liu, and **Qiu-Xing Jiang**. (2014) Chemically functionalized nanometer-thick carbon films for single molecule imaging. *J. Struct. Biol.* Jan 21. pii: S1047-8477(14)00007-0. doi: 10.1016/j.jsb.2014.01.006. PMID: 24457027
4. Hui Zheng, Sungsoo Lee, Marc Llaguno, and **Qiu-Xing Jiang**. (2016) bSUM: A bead-supported unilamellar membrane system facilitating unidirectional insertion of membrane proteins into giant vesicles. *J Gen Physiol*. **147(1):**77-93. doi: 10.1085/jgp.201511448. PMID: 26712851.

**B. Positions and Honors
Positions and employment**

Jul. 2007 --- Aug. 2015 Assistant Professor of Cell Biology, UT Southwestern Medical Center, Dallas, TX

Sept. 2015 --- present Associate Professor, Department of Microbiology and Cell Science, University of Florida, Gainesville, FL.

**Other Experience and Professional Memberships**

1998-- Member, American Biophysical Society

2012-- American Chemical Society

2012-- American Heart Association

2013-- American Society of Biochemistry and Molecular Biology

**Services to granting agencies**

 2010-12 NIH K99/R00

 2009-2013 AHA Study Section

 2012-2014 AHA National IRG Basic and Bioengineering Sciences, Review Committee, 2012-2014

 2013 NIH Special Emphasis Panel/SRG; 2014/01 ZRG1 MDCN-N (91) S meeting, 11/19/2013

 2015, 2018: NIH MSFB Study Section; NIH ZRG1 EMNR A(02) Special Session

 NIH F04B fellowship review: Nov., 2016; March, 2017; July, 2017; Nov. 2018; March, 2019

 NIH MSFC Study Section: June, 2017

 NIH MSFA Study Section: Feb. 2018

 NIH Review for Shared instrument grants and High-End Instrument grants (SIG and HEI): Nov., 2018

 NIH BBM Study Section: Jan. 2019

**Honors and Awards**

1993 Prize for Excellent M.S. Student, Chinese Academy of Sciences, Beijing, China

1995 President’s award for Excellent Graduate Student Chinese Academy of Sciences, Beijing, China

1995-2001 University Fellowship, Yale University, New Haven, CT

2007-2011 Endowed Scholarship, UT Southwestern Medical Center, Dallas, TX

2009-2013 EUREKA award, NIH

2011 Travel Award for Junior Faculty from GRC Molecular and Cellular Biology of Lipids.

2012-2013 National Innovative Research Award from American Heart Association

**C. Contributions to Science**

**1.** Develop new methods for cryoEM imaging of macromolecular complexes. Despite the great success of cryoEM in different frontiers, especially the instrumentation, the direct electron detectors, the algorithm for data processing and data interpretation, there is still good room for optimizing the cryoEM specimens. In the past years I have invented two different methods: spherical reconstruction and chemically functionalized nm-meter thick carbon films (ChemiC) The purpose of the first method was to obtain images of membrane proteins in membrane and I solved the first structure of the IP3R in order to get it ready for testing this method. It has been continuously developed in the Sigworth lab and by Dr. Liguo Wang’s laboratory at University of Washington. This is a method that many people in the field believe will have great potential. The ChemiC method was developed to overcome the fact that there is no selective binding directly to the carbon surface and that there was more than 99% loss of the specimens during plunge freezing using the conventional method.

For further development, I am pursuing three new ideas --- planar carbon-supported membranes and nm-bSUMs will be developed for imaging membrane proteins in membrane, and the combination of K2 Summit Detector, the ChemiC method and the Volta Phase plate in an FEI microscope will be used to image membrane proteins (or more generally many other complexes) that are <100 kDa in mass.

1. **Qiu-Xing Jiang**, David W. Chester, and Fred J. Sigworth. (2001) Spherical reconstruction: a method for structure determination of membrane proteins from cryo-EM images*. J. Struct. Biol*., **133:**119-131. PMID:11472084.
2. Hui Zheng, Sungsoo Lee, Marc Llaguno, and **Qiu-Xing Jiang**. (2016). bSUM: A bead-supported unilamellar membrane system facilitating unidirectional insertion of membrane proteins into giant vesicles. *J Gen Physiol*. **147(1):**77-93. doi: 10.1085/jgp.201511448. PMID: 26712851.
3. **Qiu-Xing Jiang**, Edwin C. Thrower, David W. Chester, Barbara E. Ehrlich, and Fred J. Sigworth. (2002) Three-dimensional structure of Type 1 inositol 1,4,5-trisphosphate receptor at 24 Å resolution. *EMBO J.*, **21(14):**3575-3581. PMID:12110570 / PMCID:PMC126125.
4. Marc Llaguno, Hui Xu, Liang Shi, Nian Huang, Hong Zhang, Qinghua Liu, and **Qiu-Xing Jiang**. (2014) Chemically functionalized nanometer-thick carbon films for single molecule imaging. *J. Struct. Biol.* Jan 21. pii: S1047-8477(14)00007-0. doi: 10.1016/j.jsb.2014.01.006. PMID: 24457027.

**2.** Structural study of a Kv channel that leads to a new concept of lipid-dependent gating. When I started to work on the voltage-gating in 2003, there was a controversy about the biophysical mechanism for the voltage-sensing process because of the un-natural conformation seen in the KvAP/Fab crystal structure. We used the cryo-negative stain EM and obtained a 10.5 Å structure of the channel in the apparently open (inactivated) state with the voltage sensor domains in an activate state. Our structure was of a pretty good resolution for a 300-kDa complex at that time. It demonstrated the first structure for the activated state of the voltage sensor. It also indicated that the phosphate groups in the lipid bilayer might be important to the ion channel. l later advanced the concept of lipid-dependent gating and developed the bSUM for quantify the lipid-dependent gating effects There was an observation of the ring-like voltage sensor structure in the cryo-negative-stain structure (in an inactivated state) and we had a lot of biochemical data consistent with it, instead of the current model, which was proposed by others in *Shaker* K channel around 2004. However, due to technical difficulties in our collaboration with Dr. Tamir Gonen (HHMI Janelia Farm Research Campus) on the KvAP 2D crystals, we have been developing new ChemiC-based methods in order to avoid the slow-progressing electron crystallography and use single particle cryoEM to reveal the structural basis for lipid-dependent gating. We recently made progress in this direction and found new evidence for the rearrangement of the VSDs that is responsible for lipid-dependent gating and the possible peripheral accessibility of the S4 (paper in revision).

1. Hui Zheng, Weiran Liu, Lingyan Anderson, and **Qiu-Xing Jiang**. (2012) Lipid-dependent gating of a voltage-gated ion channel. *Nature Comm.*, **2**:250 doi:10.1038/ncomms1254. PMID:21427721 / PMCID: PMC3072105.
2. Daniel Schmidt\*, **Qiu-Xing Jiang**\*, and Roderick MacKinnon. (2006). Phospholipids and the origin of cationic gating charges in voltage sensors. *Nature* **444**:775-779. (\* equal contribution). PMID:17136096.
3. Qiu-Xing Jiang. (2018) Lipid-dependent gating of ion channels. In: Protein-lipid interactions by Angel Catala (editor). Nova Science Publisher, Inc.

<https://www.researchgate.net/publication/322159809_Lipid-dependent_gating_of_ion_channels>

1. Hui Zheng, Sungsoo Lee, Marc Llaguno, and **Qiu-Xing Jiang**. (2016) bSUM: A bead-supported unilamellar membrane system facilitating unidirectional insertion of membrane proteins into giant vesicles. *J Gen Physiol*. **147(1):**77-93. doi: 10.1085/jgp.201511448. PMID: 26712851.

**3.** Through collaborative studies, we discovered the structural mechanism for the innate-immune response by the human C-type lectin. It was the first helical reconstruction I did using the single particle method. It reveals that the oligomerization and membrane insertion of the C-type lectin makes it possible to assemble into a hexamer whose central opening is broad enough for releasing intracellular materials from the cell and killing the *G+* bacteria. The common idea is that the oligomerization in membrane introduces protein-protein interactions and protein-lipid interactions, which overcomes the entropy loss and the energetic cost of dehydration and protein insertion into the lipid bilayer. After this study, a few other membrane inserting proteins came into our attention, including the VopQ and the CHGB.

**a)** Sohini Mukherjee, Hui Zheng, Mehabaw Derebe, Keith Callenberg, Carrie L. Partch, Darcy Rollins, Daniel C. Propheter, Josep Rizo, Michael Grabe, **Qiu-Xing Jiang**\*, and Lora V. Hooper\*. (2014) Antibacterial membrane attach by a pore-forming C-type lectin. *Nature*, 505(7481) : 103-7. (\*co-senior authors). PMID: 24256734.

**b)** Anju Sreelatha,Terry L. Bennett, Hui Zheng, **Qiu-Xing Jiang**, Kim Orth, and Vincent J. Starai. (2013) *Vibrio parahaemolyticus* Effector VopQ forms agated,outward rectifying channel that disrupts host ion homeostasis. *PNAS.* 9;110(28):11559-64. PMID:2379844 / PMCID: PMC3710849.

**c)** Gaya P Yadav, Hui Zheng, Qing Yang, Lauren G Douma, Linda B Bloom, Qiu-Xing Jiang. Secretory granule protein chromogranin B (CHGB) forms an anion channel in membranes. (2018). *Life Sci. Alliance*. 24 September 2018. DOI: 10.26508/lsa.201800139.

<http://www.life-science-alliance.org/content/1/5/e201800139>

**4)** Through collaboration, we identified the prion-like filament of MAVS that serves as a signal amplification platform in the intracellular RIG-I/MAVS pathway that launches innate immune response against RNA viruses. Using helical reconstruction, we were able to resolve the structures of the filaments in C3 symmetry and the ones in C1 symmetry. The heterogeneity in the specimens originally led to the selection of the C3 symmetry, and later, a new dataset from low-salt treated specimens and a new sorting mechanism led to a stable solution of C1 symmetry. When we compared the C1 map with the raw data from denatured and renatured specimens by Wu et al (2014), the total power spectrum of the raw data does not agree with the summed power spectrum of the C1 model. The average power spectrum from the C3 model has the layer lines 4 and 5 of comparable intensity, whereas that of the C1 model has the layer line 5 significantly weaker (almost invisible) than the layer line 4. Such a difference is not sensitive to out-of-plane tilting, suggesting that the dataset from the Harvard group be as heterogeneous as our dataset. *The open question is in vivo which one of the two filaments or both are used for signal amplification because biochemical and histochemical studies in cells all failed to detect co-localization of RIG-I and MAVS in RNA-virus-infected cells, which goes against the molecular imprinting model suggested by the matching between the C1 map and the tetrameric RIG-I CARD model.*A review is written to discuss structural variability and high-sensitivity detection with a newly discovered adaptor protein.

**a)** Fajian Hou, Lijun Sun, Hui Zheng, Brian Skaug, **Qiu-Xing Jiang** and Zhijian J. Chen. (2011) MAVS Forms Functional Prion-Like Aggregates To Activate and Propagate Antiviral Innate Immune Response. *Cell* **146(3):**448-461. PMID: 22398450 / PMCID: PMC3343696

**b)** Hui Xu, Xiaojing He, Hui Zheng, Lily J. Huang, Fajian Hou, Zhiheng Yu, M. Jason de la Cruz, Brian Borkowski, Xuewu Zhang\*, Zhijian J. Chen\* and **Qiu-Xing Jiang\***. (2014) Structural basis for the prion-like MAVS filaments in antiviral innate immunity. *eLife*. 3:e01489. doi: 10.7554/eLife.01489. PMID: 24569476. A correction was issued to account for a small fraction of MAVS C1 filaments in our original dataset and resolve its structure at 4.18 Å, which settled a controversy in the field.

**c)** Cai X, Chen J, Xu H, Liu S, **Jiang QX**, Halfmann R, Chen ZJ. (2014) [Prion-like Polymerization Underlies Signal Transduction in Antiviral Immune Defense and Inflammasome Activation.](http://www.ncbi.nlm.nih.gov/pubmed/24630723) *Cell*. 156(6) : 1207-22. PMID: 24630723.

**d) Qiu-Xing Jiang**. (2018) Structural variability in the RLR-MAVS pathway and sensitivity detection of viral RNAs. *Med. Chem.* (Bentham Science). In press.

**5**) New anion channels in the regulated secretory pathway. By serendipity, we discovered that the amphipathic proteins, chromogranin B in the secretory granules, are able to become tightly associated with membranes and form an anion channel that is required for normal granule acidification and maturation. This serves the long-sought anion channel that has been missing for forty years. In collaboration with Dr. Jerry Shay and Dr. Woodring Wright’s lab, we discovered a new ON-OFF control of the human telomerase holoenzyme. A manuscript is under review.

 **a)** Gaya P Yadav, Hui Zheng, Qing Yang, Lauren G Douma, Linda B Bloom, Qiu-Xing Jiang. (2018) Secretory granule protein chromogranin B (CHGB) forms an anion channel in membranes. Life Science Alliance. 24 September 2018. DOI: 10.26508/lsa.201800139.

 **b)** Gaya Yadav, Hui Zheng, Qing Yang, Lauren Douma, Mani Annamalai, Sutonuka Bhar, Linda Bloom, Clayton Mathews, **Qiu-Xing Jiang**. (2018) Novel organelle anion channels formed by chromogranin B drive normal granule maturation in endocrine cells. bioRxiv: [http://biorxiv.org/cgi/content/short/302828v1](https://urldefense.proofpoint.com/v2/url?u=http-3A__biorxiv.org_cgi_content_short_302828v1&d=DwMFaQ&c=pZJPUDQ3SB9JplYbifm4nt2lEVG5pWx2KikqINpWlZM&r=P2JY4Ggp34jCrKsRhFNcaQ&m=nAo6Z_aWEuYybCN0Pkr4aQVAomWtmvUTFIYevD0gybE&s=4vmgPiZuWZ2_tvxDjDrK9qgcX4ykDjLfF7L-FQ3qgnI&e=)

(First part of this preprint was paper a, and the second part is another paper under review)

A complete list of publications by the PI can be found in the Pubmed.

[https://www.ncbi.nlm.nih.gov/sites/myncbi/qiu-xing.jiang.1/bibliography/43623440/public/?sort=date&direction= descending](https://www.ncbi.nlm.nih.gov/sites/myncbi/qiu-xing.jiang.1/bibliography/43623440/public/?sort=date&direction=%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20%20descending)

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

**Active:**

R01 GM111367  Jiang (PI #2, Dr. Q. Liu as PI #1) 04/01/2015 – 07/31/2019 2.4 calendar

NIGMS only three-year support to the Jiang lab due to lab relocation

Title: "Molecular Mechanisms of the RNAi/MicroRNA Pathways"

The goal is to understand the structural basis for the molecular players involved in the RNAi pathway.

JIANG15G0 Jiang (PI) 04/01/2015 --- 03/31/2019 2.4 calendar

CF Foundation two-year support, and in NCE due to lab relocation.

Title: “ A chemical strategy for cryoEM studying CFTR structure in membrane”

The goal is to use the new chemical engineering method developed in the PI’s lab to reconstitute functional CFTR proteins into membranes for 3D cryoEM imaging and reconstruction.

1U24GM116788 Jiang (co-PI, Dr. K. Taylor as contact PI) 07/18/2016 – 06/30/2020 0.36 calendar

NIGMS (no fund to the Jiang lab; 6 days of scope time)

Title: “The Southeastern Consortium for Microscopy of MacroMolecular Machines”.

This consortium grant will help fund outside users of the Titan Krios at Florida State University for high-resolution electron microscopy. 6-days of use will be available to the PI’s group.

**Recently Completed:**

R01GM093271 Jiang (PI) 6/1/2010 --- 5/31/2017

NIH / NIGMS Only funded for four years with reduced budget and two years of NCE due to lab relocation

Title: “Structural study of a Kv channel in different conformations in membranes”

The goal is to understand how the voltage-gating works in membranes, especially in light of the recent finding that the phospholipid bilayer plays an indispensible role in the conformational change of the voltage sensor.

SECIM Pilot Project 2016: Jiang (co-PI, Dr. H. Ghayee as PI) 07/01/2016—06/30/2017

SECIM at UF

Title: “Metabolic Analysis of Human PCC/PGL Cancer Cells Reveals the Importance of Chromogranin-mediated Deacidification in Cancer Survival”

The purpose is to support the metabolomics analysis of 40 different samples of cancer cells under different conditions.