BIOGRAPHICAL SKETCH

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NAME: Gouaux, James Eric

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

POSITION TITLE: Senior 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
Harvard College, Cambridge MA	AB	1984	Chemistry
Harvard University, Cambridge MA	PhD	1989	Physical chemistry
Harvard University, Cambridge MA	Postdoc	1989-90	Crystallography
Massachusetts Institute of Technology, Cambridge MA	Postdoc	1990-92	Membrane proteins

A. Personal Statement

My research focuses on the molecular mechanisms underpinning signal transduction at chemical synapses. To do this, I have primarily employed x-ray crystallographic methods to elucidate atomic resolution structures of crucial neurotransmitter receptors and transporters, yet I have also enthusiastically engaged and learned complimentary biochemical and biophysical methods with the ultimate aim of using all possible approaches to elaborate structure-based mechanisms. Thus, I have extensive experience in the expression, characterization and crystallization of complex neurotransmitter receptors and transporters, as well as in x-ray crystallography and electrophysiology. In addition, I have now established single particle cryo EM in my laboratory as a central method by which to elucidate neurotransmitter receptor structures. As evidence of my progress in this area, I have published multiple papers in which we have used single particle cryo-EM as the primary tool to elucidate molecular structure and, together with biochemical, electrophysiological and computational approaches have gone on to define structure-based mechanisms for important receptors and transporters. I also participate in leadership of the PNCC, an NIH-funded, national cryo-EM center.

Projects to highlight include:

NIH 2 R01 NS038631-25
Gouaux, James Eric (PI)
03/19/1999-02/28/2025
Structure and Function of Neurotransmitter Transporters

NIH 5 R01 MH070039-20
Gouaux, James Eric (PI)
07/01/2004-02/29/2024
Structure and Function of Neurotransmitter Transporters

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2015-Present	Jennifer and Bernard Lacroute Term Chair in Neuroscience Research, Portland OR
2005-Present	Senior scientist, Vollum Institute, Oregon Health and Science Univ., Portland OR
2000- Present	Investigator, Howard Hughes Medical Institute
2001-2005	Professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York NY
2000-2001	Associate professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York, NY
1996-2000	Assistant professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York NY
1993-1996	Assistant professor, Dept. Biochem. Mol. Biol., Univ. Chicago, Chicago IL

Honors

2025	Biophysical Society Lecturer
2020	National Academy of Medicine Member
2016	Anatrace Membrane Protein Award, Biophysical Society
2014	Honorary Doctorate, University of Copenhagen
2014	W. Alden Spencer Award, Columbia University
2014	Alexander M. Cruickshank Lecture, Gordon Research Conferences
2013	Physiological Society Annual Review Prize Lecture
2010	Distinguished Faculty Awards Winner for Outstanding Research
2010	National Academy of Sciences Member
2009	Medical Research Foundation Discovery Award, Oregon Health & Science University
2009	NIHMH MERIT Award
2008	NINDS Javits Investigator Award
2007	American Association for the Advancement of Science Fellow
2003	P&S Dean's Distinguished Award in the Basic Sciences, Columbia University
2000	P&S Doctor Harold & Golden Lamport Award for Excellence in Basic Science Research, Columbia University
1998	Klingenstein Research Fellow
1997	Alfred P. Sloan Research Fellow
1995	National Science Foundation Young Investigator
1994	Searle Scholar

C. Contributions to Science

My major contributions have been to provide a molecular basis for understanding the function of neurotransmitter receptor and transporters, fundamental molecular machines that mediate signal transduction at the chemical synapses of the central nervous system. We have focused on ionotropic glutamate receptors, acid sensing ion channels, ATP-gated P2X receptors and pentameric Cys-loop receptors, as well as on the transporters for glutamate and the biogenic amines. My work has not only provided insights into the three-dimensional structures of these crucial receptors and transporters, but because all of our results are deposited in the publicly accessible protein data bank, the results of my work are available to everyone throughout the world. Thus, our studies will not only inform society on the fundamental building blocks of the brain, but they will also provide a foundation for those who are devoted to developing new therapeutic agents.

1. Our studies on the ionotropic glutamate receptors have provided deep insight into their mechanism of action, showing how antagonists, agonists and allosteric modulators act on these fundamental receptors.

a. Zhao Y, Chen S, Swensen AC, Qian WJ, Gouaux E. Architecture and subunit arrangement of native AMPA receptors illuminated by cryo-EM. Science 364, 355-362 (2019). PMCID: PMC6701862
b. Zhu S. Stein RA, Yoshioka C, Lee CH, Goehring A, Mchaourab HS, Gouaux E. Mechanism of NMDA receptor inhibition and activation. Cell 165: 704-14 (2016). PMCID: PMC4914038
c. Chen S, Zhao Y, Wang Y, Shekhar M, Tajkhorshid E, Gouaux E. Activation and desensitization mechanism of AMPA receptor-TARP complex by cryo-EM. Cell 170:1234-1246 (2017). PMCID: PMC5621841

2. We have also elaborated the molecular structure of the two major classes of neurotransmitter transporters, showing how these remarkably machines carry neurotransmitter from one side of the membrane to the other.

a. Coleman JA, Yang, D, Zhao, Z, Wen, PC, Yoshioka, C, Tajkhorshid, E, Gouaux, E. Serotonin transporter ibogaine complexes illuminate mechanisms of inhibition and transport. Nature 569, 141-145 (2019). PMCID: PMC6750207
b. Coleman JA, Green EM, Gouaux E. X-ray structures and mechanism of the human serotonin transporter. Nature 532: 334-39 (2016). PMCID: PMC4898786
c. Wang KH, Penmatsa A, Gouaux E. Neurotransmitter and psychostimulant recognition by the dopamine transporter. Nature 521:322-27 (2015). PMCID: PMC4469479

3. In addition, we have elaborated the structures of other neurotransmitter receptors and ligand gated ion channels of the brain, from acid sensing ion channels and ATP-gated P2X receptors to pentameric Cys-loop receptors, thus providing the neuroscience field with molecular blueprints upon which to ground studies of mechanism and drug development.

a. Du J, Lü W, Wu S, Cheng Y, Gouaux E. Glycine receptor mechanism illuminated by electron cryo-microscopy. Nature 526:224-29 (2015). PMCID: PMC4659708
b. Baconguis I, Bohlen, CJ, Goehring A, Julius D, Gouaux E. X-ray structure of acid-sensing ion channel 1–snake toxin complex reveals open state of a sodium-selective channel. Cell 156:717-29 (2014). PMCID: PMC4190031
c. Mansoor SE, Lü W, Oosterheert W, Shekhar M, Tajkhorshid E, Gouaux E. X-ray structures define human P2X3 receptor gating cycle and antagonist action. Nature 538: 66-71 (2016). PMCID: PMC5161641.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/james.gouaux.1/bibliography/40629156/public/?sort=date&direction=ascending

FELLOWSHIP APPLICANT BIOGRAPHICAL SKETCH

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NAME OF APPLICANT: Sun, Chang

POSITION TITLE: Postdoctoral fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing. Include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	START DATE MM/YYYY	END DATE *(or expected end date)* MM/YYYY	FIELD OF STUDY
Fudan University, Shanghai, China	BS	09/2006	05/2010	Pharmacy
University of Illinois, Urbana-Champaign, IL	PhD	09/2010	05/2016	Biochemistry
University of Illinois, Urbana-Champaign, IL	Postdoc	06/2016	10/2018	Membrane protein
Oregon Health & Science University, Portland, OR	Postdoc	11/2018		Neurotransmitter receptor

A. Personal Statement

Intrigued by the myriad function membrane proteins can possess, I pursued a PhD in Biochemistry at the University of Illinois, Urbana-Champaign. I worked with a variety of membrane proteins during my graduate training under the supervision of Colin A. Wraight and Robert B. Gennis. Specifically, I studied how the protein matrix can tune the property of intermediate states during the catalytic cycle using pulsed electron magnetic resonance and optical spectroscopy. After receiving my doctoral degree in 2016, I became interested in the structure determination of membrane proteins using cryo-EM and started to collaborate with John Rubinstein's group at the University of Toronto. In 2017, I joined Emad Tajkhorshid's lab and began to model atomic structure from electron density maps and to study protein function through molecular dynamics simulation. After finishing research that culminated in a publication in Nature, I joined Eric Gouaux's group to study the structure and function of type A GABA receptors.

During my training in the Gouaux lab, I have learned advanced molecular biology techniques, antibody engineering, native protein purification, and cryo-EM grid preparation. I have also received one-on-one training from PNCC staff on microscope operation. Given my already strong understanding of membrane proteins, the opportunity to continue to learn from Dr. Gouaux, and the excellent research environment in the Gouaux lab, I am confident to advance our understanding of the structure and function ligand-gated ion channels.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	END DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Postdoc	06/16	10/18	Membrane protein	University of Illinois, Urbana-Champaign, IL	Emad Tajkhorshid
Postdoc	11/18		Neurotransmitter receptor	Oregon Health & Science University, Portland, OR	Eric Gouaux

Academic and Professional Honors

2016 Travel Award for the 17th International Congress on Photosynthesis, Maastricht, Netherlands
2014 Robert L. Switzer Award for Teaching, University of Illinois, Urbana-Champaign, IL
2010 Scholarship of Hui-Chun Chin and Tsung-Dao Lee Chinese Undergraduate Research Endowment, Fudan University, Shanghai, China

C. Contributions to Science

1. My early research focused on characterizing membrane proteins with optical spectroscopy. Depending on the instrumental setup, optical spectroscopy can probe reactions with a time resolution ranging from picosecond to second. My studies on the photosynthetic reaction centers demonstrated the modulation on the electron transfer kinetic from an auxiliary protein subunit.
    a. Sun C, Carey AM, Gao BR, Wraight CA, Woodbury NW, Lin S. (2016). Ultrafast electron transfer kinetics in the LM Dimer of bacterial photosynthetic reaction center from *Rhodobacter sphaeroides*. *J. Phys. Chem. B*., 120, 5395-404.
    b. Sun, C. (2017). Removal of the H subunit results in enhanced exposure of the semiquinone sites in the LM dimer from *Rhodobacter sphaeroides* to oxidation by ferricyanide and by O_2. *Photosynth. Res.*, 133, 371-377.

2. I also used pulsed magnetic resonance spectroscopy and crystallography to study the interactions between the protein matrix and the quinone cofactor.
    a. Sun, C. *et al.* (2015). Regulation of the primary quinone binding conformation by the H subunit in reaction centers from *Rhodobacter sphaeroides. J. Phys. Chem. Lett.*, 6, 4541-4546.
    b. Sun, C. *et al.* (2016). Q-Band electron-nuclear double resonance reveals out-of-plane hydrogen bonds stabilize an anionic ubisemiquinone in cytochrome bo_3 from *Escherichia coli*. *Biochemistry*, 55, 5714-5725.
    c. Schieferstein, J. M. *et al.* (2017). X-ray transparent microfluidic chips for high-throughput screening and optimization of in meso membrane protein crystallization. *Biomicrofluidics*, 11, 024118.

3. During my postdoc study at the University of Illinois, I started to work on molecular modeling with cryo-EM data and solved the first structure of a membrane protein prepared with a styrene maleic acid copolymer.
    a. Sun, C. *et al.* (2018). Structure of the alternative complex III in a supercomplex with cytochrome oxidase. *Nature*, 557, 123-126.

4. At the Gouaux lab, I elucidated the architecture and molecular pharmacology of GABA A receptors in the rodent brain using a combination of single-particle cryo-EM and native protein isolation.
    a. Sun, C., Zhu, H., Clark, S. & Gouaux, E. (2023) Cryo-EM structures reveal native GABAA receptor assemblies and pharmacology. *Nature*, 622, 195–201.

Complete list of my published work:
https://scholar.google.com/citations?user=GAoInH0AAAAJ&hl=en

D. Scholastic Performance

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
2006	General Chemistry	B	2006	Experiments in General Chemistry	A-
2006	General Physics B	A	2007	Organic Chemistry	A
2007	Introduction to Modern Biological Science	A	2007	Fundamentals of Medicine	A-
2008	Pharmacology	A-	2008	Molecular Biology	A-
2008	Natural Products Chemistry I	A	2009	Medicinal Chemistry I	A-
2009	Pharmaceutical Analysis I	A-	2009	Drug Design	A-
2010	Physical Chemistry	A	2011	Physical Chemistry II	A
2011	Electric Circuit	A			