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 NS038631-24
Gouaux, James Eric (PI)
03/19/1999-02/28/2025
Structure and Function of Neurotransmitter Transporters

NIH 5 R01 MH070039-19
Gouaux, James Eric (PI)
07/01/2004-02/29/2024
Structure and Function of Neurotransmitter Transporters

NIH 5 R01 GM100400-08
Gouaux, James Eric (PI)
06/01/2012-03/31/2022
Structural biology of neurotransmitter ion channels

HHMI (no number)
Gouaux, James Eric (PI)
09/01/2010-08/31/2027
Molecular Studies of Synapses

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

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

BIOGRAPHICAL SKETCH

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NAME: Kim, Junhoe

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

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. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Korea University, Seoul, Republic of Korea	B.S.	02/2012	Life Sciences
Korea University, Seoul, Republic of Korea	Ph.D.	02/2019	Structural biology
Korea University, Seoul, Republic of Korea	Postdoc	06/2019	Structural biology
Oregon Health and Science University, Oregon	Postdoc	Ongoing	Structural biology

A. Personal Statement

I majored Life Sciences during undergraduate at Korea University and earned a B.S. degree with top graduating by ranking 1 out of 193 students. Since I started my research experience at Prof. Hyun Kyu Song's laboratory in the same university as an undergraduate research assistant, I have been constantly developing my skills toward structural determination and biochemical characterization of proteins. During the Ph.D. course, I focused on the elucidation of structure and function of core autophagy-related proteins using multidisciplinary approaches including biophysical methods, such as X-ray crystallography and small-angle X-ray scattering, as well as cellular expression of mutant proteins to prove physiological effects. As a result of these experience, I am aware of the importance of finding biological meaning from structural information. With appreciation of the research originality and prospects, I awarded a National Research Foundation-funded fellowship during Ph.D. course for five years. After receiving the doctoral degree, I was interested in the structure determination of membrane protein using cryogenic electron microscopy (cryo-EM). To pursue this, I joined Dr. Eric Gouaux's lab at Oregon Health and Science University as a postdoctoral fellow to study structures and mechanisms of neurotransmitter receptors. In this lab, I successfully developed research idea for structural study of native proteins from rodent brain tissues and produced several promising preliminary results. I have been trained with state-of-the-art microscope, which is crucial for conducting this research project, to become an independent operator. Now I have the expertise, experience, training, and motivation necessary to successfully carry out the proposed research project.

B. Positions, Scientific Appointments, and Honors

Positions

07/2010-02/2012 Undergraduate research assistant in Prof. Hyun Kyu Song's lab, Korea University, Seoul, Korea

03/2012-02/2019 Ph.D. candidate in Prof. Hyun Kyu Song's lab, Korea University, Seoul, Korea

03/2012-06/2012 Teaching assistant for 'General Chemistry Laboratory' course, Korea University, Seoul, Korea
03/2019-06/2019 Postdoctoral fellow in Prof. Hyun Kyu Song's lab, Korea University, Seoul, Korea
08/2019-present Postdoctoral fellow in Dr. Gouaux's lab, Vollum Institute, OHSU, Portland, OR

Honors

09/2005 College specialization support project scholarship, Korea University ($1,050)
03/2009 Best honors scholarship, Korea University (tuition covered)
09/2009 Scholarship, OH HYUNHO FOUNDATION (tuition covered)
02/2010 Scholarship, OH HYUNHO FOUNDATION (tuition covered)
09/2010 Scholarship, LOTTE FOUNDATION (tuition covered)
03/2011 Scholarship, LOTTE FOUNDATION (tuition covered)
09/2011 Scholarship, LOTTE FOUNDATION (tuition covered)
03/2012-02/2017 PI of Global Ph.D. Fellowship, National Research Foundation, Korea ($25,000/y, 5 yrs)
- Title: Structural studies of core autophagic proteins for autophagosomal formation

06/2017-05/2018 Co-PI of EAPSI program (East Asia and Pacific Summer Institutes for U.S. Graduate Students), National Science Foundation, US
- PI-Shelby Brooks (The University of Alabama)
- Title: Crystallization of mutant N-demethylase enzymes

02/2012 Presidential award, Korean Society for Biochemistry and Molecular Biology
03/2012 Teaching assistant scholarship, Korea University (tuition covered)
12/2013 Poster award, Asian Crystallographic Association
01/2015 Presentation award, Department of Life Sciences, Korea University
02/2016 Presentation award, Department of Life Sciences, Korea University
02/2019 Outstanding paper award, Korea University

Military service

05/2006-08/2008 Republic of Korea Air Force, Sergeant, Honorable discharge

C. Contributions to Science

1. Including the period of an undergraduate research assistant, my early research during Ph.D. course was focused on the structural study of core autophagic machinery proteins, which are mammalian ATG5, ATG16L1, and TECPR1 using X-ray crystallography. These proteins has been known to drive autophagosome maturation via lysosomal fusion but there was a controversy whether they can make a triple complex or exclusive one to another. I revealed that they bind exclusively to ATG5 using same binding motif which sequence is highly conserved in other eukaryotes and suggested a model of their swapping mechanism based on local pH change. I served as the primary investigator in all of these studies.
    a. **Kim, J.H.**, Hong, S.B., Lee, J.K., Han, S., Roh, K.H., Lee, K.E., Kim, Y.K., Choi, E.J. & Song, H.K. Insights into autophagosome maturation revealed by the structures of ATG5 with its interacting partners. *Autophagy* 11:1, 75-87 (2015) (*Cover illustration*)
    b. **Kim, J.H.** & Song, H.K. Swapping of interaction partners with ATG5 for autophagosome maturation. *BMB Rep.* 48(3): 129-130 (2015)

2. To broaden the comprehensive understanding of autophagy mechanism, I also collaborated on other projects in the lab by helping purify proteins and conducting biochemical experiment. These works were including structural studies of Atg10 the autophagic ubiquitin E2 enzyme, xenophagy-related NDP52-galectin8 complex, Atg13-Atg101 the upstream autophagy signaling complex, and LC3B complexed Legionella effector protein RavZ.
    a. Hong, S.B., Kim, B.W., **Kim, J.H.** & Song, H.K. Structure of the autophagic E2 enzyme Atg10. *Acta Crystallog. D Biol Crystallogr.* 68, 1409-17 (2012).
    b. Kim, B.W., Hong, S.B., **Kim, J.H.**, Kwon D.H. & Song, H.K. Structural basis for recognition of autophagic receptor NDP52 by the sugar receptor galectin-8. *Nat. Commun.* 4, 1613 (2013)

c. Kim, B.*, Jin Y.*, Kim, J.*, **Kim, J.H.***, Jung, J., Kang, S., Kim, I.Y., Kim, J., Cheong, H., & Song, H.K. The C-terminal region of ATG101 bridges ULK1 and PtdIns3K complex in autophagy initiation. *Autophagy* 14(12):2104-2116 (2018)
***Contributed equally**

d. Kwon, D.H., Kim, L., Kim, B., **Kim, J.H.**, Roh, K.H., Choi, E.J. & Song, H.K. A novel conformation of the LC3-interacting region motif revealed by the structure of a complex between LC3B and RavZ. *Biochem Biophys Res Commun.* 26;490(3):1093-1099 (2017)

3. As a methodology development, I joined a project making a prediction system of the orientation of coiled-coil (CC) oligomer. The major oligomeric state of CCs is dimer, which can be either parallel or antiparallel. Even the orientation of each α-helix in a CC domain is critical for the molecular function of CC-containing proteins, but cannot be determined easily by sequence-based prediction. I contributed to develop the biochemical method for assessing differences between parallel and antiparallel CC homodimers, by purifying proteins and confirming their structures using X-ray crystallography and small angle X-ray scattering.
    a. Kim, B., Jung, Y.O., Kim, M.K., Kwon, D.H., Park, S.H., **Kim, J.H.**, Kuk Y.B., Oh, S.J., Kim, L., Kim, B.H., Yang, W.S., & Song, H.K. ACCORD: an assessment tool to determine the orientation of homodimeric coiled-coils. *Sci Rep.* 7:43318 (2017)

4. At the second half of my Ph.D. course, I studied the structures and mechanism of N-demethylases from Pseudomonas putida which enable to live them by using caffeine as a sole carbon and nitrogen source. In addition to solve the structures, I also figured out the exact oligomeric states of the enzymes in solution using small-angle X-ray scattering and, from following HPLC analysis, I identified their heteromeric complexation enhances the entire caffeine degradation efficiency. By elucidating complex structures with real substrates and complex structure with thioredoxin of the electron transport system, I provided insights of detailed molecular mechanism of the caffeine degradation pathway by bacterial enzymes which is potentially useful for application studies. I served as the primary investigator in this study.
    a. **Kim, J.H.**, Kim, B.H., Brooks, S., Kang, S.Y., Summers, R.M., & Song. H.K., Structural and Mechanistic Insights into Caffeine Degradation by the Bacterial N-Demethylase Complex. *J Mol Biol.* Sep 6;431(19):3647-3661 (2019).