BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Farzad Jalali-Yazdi

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

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology	B.S.	08/2004	06/2008	Chemical Biological Engineering
Massachusetts Institute of Technology	B.S.	08/2004	06/2008	Biology
University of Southern California	Ph.D.	08/2010	08/2015	Chemical Engineering
Oregon Health and Science University	Postdoc	09/2016	Ongoing	Structural Biology

A. Personal Statement

I started my undergraduate career at MIT, where I earned a B.S. degree in biology and another in chemical-biological engineering. There, I joined a joint research project between Prof. Langer's lab in the chemical engineering department and Prof. Cima's lab in the material science department, focusing on the development of an implantable cancer monitoring device capable of measuring the concentration of the cancer marker hCG. The multidisciplinary approach implemented in this project allowed me to develop varied skillsets while familiarizing myself with the process of collaborative research in academic settings. After my graduation, I worked for two years at BioScale, Inc., a startup company developing an ultrasensitive, high-throughput diagnostic device. I led the antibody quantitation project and developed an immunoassay capable of measuring the concentration of antibodies in complex matrices. My work at BioScale taught me how to independently design, execute, and troubleshoot experiments, and present my results in a simple and effective way. I elected to pursue my graduate education at the University of Southern California under the supervision of Prof. Roberts, working to discover new ligands and new methods to characterize them. I generated peptide ligands against Streptavidin, HCV core protein, Gαi1, and Bcl-xL among others, developed three novel high-throughput methods to find the relative and absolute affinity of protein-protein interactions, and set up multiple collaborative projects both inside and outside USC. During my graduate work, I integrated my existing procedural knowledge with new skills such as protein expression and purification, estimation of protein secondary structure by CD spectroscopy, fluorescent spectroscopy, and selection of ligands through molecular evolution. I was also introduced to the field of structural biology. To enter this field, I selected and joined Dr. Gouaux's lab at OHSU due to his extensive record in using x-ray crystallography and cryo-EM to elucidate the molecular mechanisms for the function of receptors and transporters at chemical synapses. During my postdoctoral training, I have learned about membrane protein expression, purification, and imaging, as well as electrophysiological and functional assays to assess and characterize these proteins. I recently had my first manuscript in the Gouaux lab, *Mechanisms for zinc and proton inhibition of the GluN1/GluN2A NMDA receptor*, accepted in the journal Cell.

B. Positions and Honors

Positions and Employment

Year	Position, Place
09/2016 – Now	Postdoctoral fellow in Dr. Gouaux's lab at OHSU, Portland, OR
10/2015 – 07/2016	Research scientist at EvoRx Technologies Inc., Pasadena, CA
08/2015 – 12/2015	Lecturer for the chemical engineering graduate level thermodynamics course at USC, Los Angeles, CA
01/2015 – 05/2015	Teaching assistant for the introduction to chemical engineering course at USC, Los Angeles, CA
08/2014 – 05/2015	STEM educator at Synergy Academy Elementary School, Los Angeles, CA
08/2010 – 08/2015	Ph.D. candidate in Prof. Roberts' lab in the Chemical Engineering department at USC, Los Angeles, CA
06/2007 – 08/2010	Scientist/Engineer at BioScale Inc., Cambridge, MA
09/2006 – 05/2008	Undergraduate research assistant in Prof. Langer's and Prof. Cima's laboratories at MIT, Cambridge, MA
06/2006 – 08/2006	Biochemistry teaching assistant and resident advisor for the Minorities Introduction to Engineering and Science (MITES) at MIT, Cambridge, MA
06/2005 – 06/2006	Undergraduate research assistant in Prof. Cooney's laboratory at MIT, Cambridge, MA
02/2004 – 08/2004	Assay development and chemistry intern at Adamson Analytical Laboratory, Corona, CA

Honors

Year	Honor
2016	Viterbi Best Dissertation Award in Chemical Engineering
2014-2015	Body Engineering Los Angeles (BELA) Fellowship
2014	Viterbi Undergraduate Research Mentorship Award
2010-2014	Viterbi School of Engineering Doctoral Fellowship

C. Contributions to Science

1. **High-throughput characterization of ligand properties:** During my graduate career at USC, by combining mRNA Display and high-throughput sequencing I developed techniques capable of characterizing ligand affinities, protease resistance, and state selectivity in a high-throughput manner. Some of these projects are on-going, and the preliminary data that I generated are still being worked on by my colleagues and collaborators. Developing these methods of rapid high-throughput characterization of ligands has made mRNA display and other *in vitro* ligand generation techniques extremely powerful by reducing the time and efforts required to select the ligand with the desired properties from a pool of similar ligands.
    a. **Jalali-Yazdi F**, Huong Lai L, Takahashi TT, Roberts RW. High-Throughput Measurement of Binding Kinetics by mRNA Display and Next-Generation Sequencing. Angewandte Chemie. 2016;55(12):4007-10. doi: 10.1002/anie.201600077. PubMed PMID: 26914638; PMCID: 4834215.
    b. Roberts RW, **Jalali-Yazdi F**. "Methods for analyzing the interaction between a target protein and a ligand" United States Patent App. 15/738,366
    c. Takahashi TT, Roberts RW, **Jalali-Yazdi F**, Huong Lai L, Kamalinia G, Mac J. "High Throughput Method for Determining Multiple Biophysical Properties of Ligands." USC patent internal disclosure code: 2017-130
2. **Affinity Measurements of Protein-Protein Interactions:** I developed a method to assess the relative affinities of protein-protein interactions using mRNA display. This method allows for the affinity ranking of mRNA display generated ligands, without the need to synthesize and purify each one individually. I also developed a method to measure both the concentration and the affinity of a ligand for its target simultaneously, and showed under what conditions these values are accurate. To develop these methods, I set up a collaboration with BioScale, Inc., to be able to use their device in my experiments.

a. **Jalali-Yazdi F,** Corbin JM, Takahashi TT, Roberts RW. Robust, quantitative analysis of proteins using peptide immunoreagents, in vitro translation, and an ultrasensitive acoustic resonant sensor. Analytical chemistry. 2014;86(10):4715-22. Epub 2014/04/23. doi: 10.1021/ac500084d. PubMed PMID: 24749546; PMCID: 4030805.
b. **Jalali-Yazdi F,** Takahashi TT, Roberts RW. General, Label-Free Method for Determining Kd and Ligand Concentration Simultaneously. Analytical chemistry. 2015;87(23):11755-62. doi: 10.1021/acs.analchem.5b03069. PubMed PMID: 26485531.
c. Roberts RW, **Jalali-Yazdi F**. "A General, Label-Free Method for Determining Dissociation Constant and Ligand Concentration Simultaneously." United States Provisional Patent Application No. 62/183,111

3. **Designing and Characterizing Therapeutic Peptides and Proteins.** Using mRNA display, I have been able to generate therapeutic peptide ligads against the hepatitis C virus core protein (manuscript submitted to eLife), HDM2, and Bcl-xL (manuscript submitted to Nature Communications). I also collaborated on other projects in the lab by helping identify and characterize and polypeptide ligands against Gαi1, RAS, Nicotinic acetylcholine receptor (nAChR), and Calcineurin.
   a. Roberts RW, **Jalali-Yazdi F**, Huong Lai L, Mac J. "Captin - an mRNA selected peptide inhibitor of Calcineurin." USC patent internal disclosure code: 2017-155
   b. Garri C, Howell S, Tiemann K, Tiffany A, **Jalali-Yazdi F**, Alba MM, Katz JE; Takahashi TT, Landgraf R, Gross ME, Roberts RW, Kani K. Identification, characterization and application of a new peptide against anterior gradient homolog 2 (AGR2). Oncotarget 2018, 9 (44), 27363-27379.
   c. Nichols AL, Noridomi K, Hughes CR, **Jalali-Yazdi F**, Eaton JB, Lai LH, Advani G, Lukas RJ, Lester HA, Chen L, Roberts RW. α1-FANGs: Protein Ligands Selective for the α-Bungarotoxin Site of the α1-Nicotinic Acetylcholine Receptor. ACS chemical biology 2018, 13 (9), 2568-2576.
   d. Cetin M, Evenson WE, Gross GG, **Jalali-Yazdi F,** Krieger D, Arnold D, Takahashi TT, Roberts RW. RasIns: Genetically Encoded Intrabodies of Activated Ras Proteins. Journal of molecular biology. 2017;429(4):562-73. doi: 10.1016/j.jmb.2016.11.008. PubMed PMID: 27865780.
   e. Howell SM, Fiacco SV, Takahashi TT, **Jalali-Yazdi F,** Millward SW, Hu B, Wang P, Roberts RW. Serum stable natural peptides designed by mRNA display. Scientific reports. 2014;4:6008. Epub 2014/09/23. doi: 10.1038/srep06008. PubMed PMID: 25234472; PMCID: 4168267.

4. **List of Other Publication and Presentations.** In my graduate career, during a collaboration with another USC lab, I helped reconstitute a purified membrane protein in polymer vesicles, and measure its activity after reconstitution. In my undergraduate career, I worked on characterizing the membranes used in an implantable cancer monitoring device, and was also involved with a project designed to understand the mechanism of solid-solid blending of pharmaceutical excipients and active ingredients.
   a. Gutierrez MG, **Jalali-Yazdi F**, Peruzzi J, Riche CT, Roberts RW, Malmstadt N. G Protein-Coupled Receptors Incorporated into Rehydrated Diblock Copolymer Vesicles Retain Functionality. Small. 2016;12(38):5256-60. doi: 10.1002/smll.201601540. PubMed PMID: 27529518; PMCID: 5148614.
   b. Elman NM, Daniel K, **Jalali-Yazdi F**, Cima MJ. Super permeable nano-channel membranes defined with laser interferometric lithography. Microfluidics and Nanofluidics. 2010;8(4):557-63. doi: DOI 10.1007/s10404-009-0537-z. PubMed PMID: ISI:000276474200012.
   c. Daniel KD, Kim GY, Vassiliou CC, **Jalali-Yazdi F,** Langer R, Cima MJ. Multi-reservoir device for detecting a soluble cancer biomarker. Lab Chip. 2007;7(10):1288-93. Epub 2007/09/27. doi: 10.1039/b705143c. PubMed PMID: 17896012.
   d. Pernenkil L, **Jalali-Yazdi F**, Whittaker J, Cooney C. Continuous Dry Powder Blending: Effect of Process Variables and Material Properties. AIChE Annual Meeting; 2007; Salt Lake City, UT2007.

A Complete list of my published work in my Bibliography:
https://scholar.google.com/citations?hl=en&user=GS9M_XIAAAAJ

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

Research Support:

NIH 1 F32 MH 115595 Jalali-Yazdi, Farzad (PI) 12/01/2017-11/30/2020

Elucidating the molecular mechanism underpinning NMDA receptor gating

Mutations in the NMDA receptors, leading to an increase or decrease in activity, have been linked to neurological disorders such as epilepsy, Alzheimer's, schizophrenia, depression and chronic pain. Understanding the mechanism of receptor activity modulation is the first step in designing therapeutic reagents for such disorders. This grant aims to answer fundamental questions with regards to the structural underpinnings of NMDA receptor channel opening/activation and zinc inhibition. I am involved in all aspects of these studies, from experimental design to manuscript preparation.

Role: PI

Courses:

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
University of Southern California (cummulitive GPA 4.0/4.0)					
2010	Viscous Fluid Flows	A			
2010	Modeling and Analysis of Chemical Engineering Systems	A			
2011	Chemical Engineering Kinetics and Reactor Analysis	A			
2011	Mass Transfer	A			
2011	Thermodynamics for Chemical Engineers	A			
2011	Heat Transmission	A			
Massachussetts Institute of Technology (cummulitive GPA 4.3/5.0)					
2008	Integrated Chemical Engineering II	A	2008	Environmental Policy and Economics	B
2007	Integrated Chemical Engineering I	A	2007	American Authors	B
2007	Development and Evolution Biology	A	2007	Principles of Microeconomics	B
2007	Microbial Physiology	A	2006	Film Experience	B
2007	Cellular Neurobiology	B	2006	Islam, Middle East, and the West	B
2007	Cellular Biology	B	2005	Intro to Western Music	B
2006	Biological Engineering Lab	A			
2006	Transport Processes	B			
2006	Intro to Experimental Biology and Communications	B			
2006	Fluid Mechanics	B			
2006	Intro to Biology	B			
2006	Thermodynamics and Kinetics	A			
2005	Organic Chemistry	B			

BIOGRAPHICAL SKETCH

NAME: Gouaux, James Eric

eRA COMMONS USER NAME: GOUAUX

POSITION TITLE: Senior Scientist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	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

I have long standing experience in the structural biology of integral membrane proteins and am well recognized for having the insight and knowledge required to solve important problems in membrane protein structural biology. My research focuses on the molecular mechanisms underpinning signal transduction at chemical synapses. To do this, until 2013 I primarily employed x-ray crystallographic methods to elucidate atomic resolution structures of crucial neurotransmitter receptors and transporters, while also enthusiastically engaging in complementary biochemical and biophysical methods, with the ultimate aim of using all possible approaches to elaborate structure-based mechanisms. In 2013 I began training in single particle cryo electron microscopy (cryo EM) by working in the laboratory of Yifan Cheng at UCSF and by intensive interactions with Tom Walz (Harvard), Niko Grigorieff (Janelia) and Craig Yoshioka (OHSU). I have now established single particle cryo EM in my laboratory as an exciting and highly promising method by which to elucidate neurotransmitter receptor structures. As evidence of my progress in this area, I have published 8 major papers in which we have used single particle cryo-EM as the primary tool to elucidate molecular structure

B. Positions and Honors

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

1994	Searle Scholar
1995	National Science Foundation Young Investigator
1997	Alfred P. Sloan Research Fellow
1998	Klingenstein Research Fellow
2000	P&S Doctor Harold & Golden Lamport Award for Excellence in Basic Science Research, Columbia University
2003	P&S Dean's Distinguished Award in the Basic Sciences, Columbia University
2007	American Association for the Advancement of Science Fellow

2008	NINDS Javits Investigator Award
2009	NIHMH MERIT Award
2009	Medical Research Foundation Discovery Award, Oregon Health & Science University
2010	National Academy of Sciences Member
2010	Distinguished Faculty Awards Winner for Outstanding Research
2013	Physiological Society Annual Review Prize Lecture
2014	Alexander M. Cruickshank Lecture, Gordon Research Conferences
2014	W. Alden Spencer Award, Columbia University
2014	Honorary Doctorate, University of Copenhagen
2016	Anatrace Membrane Protein Award, Biophysical Society

C. Contribution 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 publically 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. Lü W, Du J, Goehring A, Gouaux E. Cryo-EM structures of the triheteromeric NMDA receptor and its allosteric modulation. *Science* 355: eaal3729 (2017). NIHMSID: NIHMS856429
    b. Zhao Y, Chen S, Yoshioka C, Baconguis I, Gouaux E. Architecture of fully occupied GluA2 AMPA receptor-TARP complex elucidated by cryo-EM. *Nature* 536: 108-11 (2016). PMCID: PMC4998972
    c. 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

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, Green EM, Gouaux E. X-ray structures and mechanism of the human serotonin transporter. *Nature* 532: 334-39 (2016). PMCID: PMC4898786
    b. Wang KH, Penmatsa A, Gouaux E. Neurotransmitter and psychostimulant recognition by the dopamine transporter. *Nature* 521:322-27 (2015). PMCID: PMC4469479.
    c. Penmatsa A, Wang K, Gouaux E. X-ray structure of the dopamine transporter illuminates mechanism of antidepressant action. *Nature* 503:85-90 (2013). PMCID: PMC3904663

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. Hattori M, Gouaux E. Molecular mechanism of ATP binding and ion channel activation in P2X receptors. *Nature* 485:207-212. (2012). PMCID: PMC3391165
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

---

D. Research Support

NIH 2 R01 NS038631-20 Gouaux, James Eric (PI) 03/19/1999-02/28/2020
3D Structure and Function of Ligand-Gated Ion Channels

The focus of this work is on determining the atomic structure of ligand-gated ion channels activated glutamate (AMPA receptors) or protons (ASICs) using x-ray diffraction techniques, on developing mechanisms for the activity of these channels, and on testing the mechanisms by a variety of techniques that include electrophysiology and other biochemical and biophysical methods. I am involved in all aspects of these studies, from experimental design to manuscript preparation.
Role:
PI

NIH 4 R37 MH070039-15 Gouaux, James Eric (PI) 07/01/2004-02/28/2019
Structure and Function of Neurotransmitter Transporters

The research supported by this grant is concentrated on determining structures of bacterial homologs of human neurotransmitter transporters by x-ray crystallography and on studying the mechanism of these bacterial proteins using a combination of site-directed mutagenesis, flux assays and other biochemical and biophysical studies, with the aim being to understand the architecture of this important family of proteins and how that architecture relates the function of both prokaryotic and eukaryotic transporters. I am involved in all aspects of these studies, from experimental design to manuscript preparation.
Role: PI

NIH 5 R01 GM100400-05A1 Gouaux, James Eric (PI) 06/01/2012-03/31/2021
NIH/NIGMS
Structural biology of neurotransmitter ion channels

The aim of this work is to solve high resolution x-ray crystal structures of P2X and Cys-loop receptors bound to their cognate neurotransmitter and to competitive antagonists, to test the veracity of the mapped sites by site-directed mutagenesis and ligand-binding assays, and to develop molecular mechanisms for the action of agonists and antagonists in these receptors. I am involved in all aspects of these studies, from experimental design to manuscript preparation.
Role: PI

HHMI (no number) Gouaux, James Eric (PI) 09/01/2010-08/31/2020
Molecular Studies of Synapses

The research supported by these funds is focused on developing new methods for the purification of native membrane proteins from their endogenous context - on a nanogram scale - using novel fluorescently labeled affinity tags, in the development of new methods for EM grid preparation and in the isolation and structural study of complexes involved in mechanotransduction. I am involved in all aspects of these studies, from experimental design to manuscript preparation.
Role: PI