BIOGRAPHICAL SKETCH

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NAME: Navid Bavi

eRA COMMONS USERNAME (credential, e.g., agency login): navidbavi

POSITION TITLE: Assistant Professor of Department of Physiology

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
Isfahan University of Technology, Iran.	BS	Sep/2009	Mechanical Engineering
Shahid Chamran University of Ahvaz, Iran.	MS	Sep/2011	Mechanical Engineering
The University of New South Wales, Australia.	PHD	July/2017	Molecular Biophysics
University of Chicago, USA.	Post Doc	Sep/2023	Structural Biology

A. Personal Statement

Dr. Navid Bavi is a tenure-track Assistant Professor (Step 3) in the Department of Physiology at UCLA and an affiliated member of the UCLA Jonsson Comprehensive Cancer Center. With a multidisciplinary background in mechanical engineering, molecular biophysics, and structural biology, Dr. Bavi brings a distinctive, integrative perspective to the study of sensory biology and disease.

As head of the Sensory Membrane Protein Lab, Dr. Bavi employs a suite of advanced biophysical tools including time-resolved cryo-electron microscopy, force spectroscopy, electrophysiology, and computational modelling to examine force transduction across biological scales. His main contribution to the auditory field includes solving the structure of prestin, the cochlear motor protein essential for sound amplification, an elusive goal that remained unresolved for more than two decades.

Dr. Bavi's research trajectory is supported by competitive fellowships, including the Chicago Fellowship and ARC DECRA, and bolstered by a genrous startup funding to launch his UCLA laboratory in late 2023. His work has been recognized with honors such as the Paul Korner and Gibson/Cox awards, and he has delivered over a dozen invited talks at premier scientific institutions and international symposia, reflecting his growing influence in mechanobiology and sensory science.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2024-(April) Visiting Scientist, Victor Chang Cardiac Research Institute, Sydney, Australia.
2023(Oct)- Assistant Professor, Department of Physiology, UCLA, Los Angeles, USA.
2018-2023 Chicago Fellow Program, The University of Chicago, Chicago, USA.
2017-2018 Postdoctoral Fellow, University of New South Wales, Sydney, Australia.
2017-(Jun) Research Assistant, Victor Chang Cardiac Research Institute, Sydney, Australia.

Other Experience and Professional Memberships

2024- Mentor Professor Search Committee, DGSOM, UCLA
2024 – Executive Committee Member, Department of Physiology, UCLA
2024 Co-Chair, Lipid-Protein Interactions Session at the 68th BPS Meeting, USA
2022–2023 Postdoctoral Advisory Board, University of Chicago
2022 Co-Chair, Mechanosensation Session at the 66th BPS Meeting, USA

2022 Thesis Examiner (1x), University of Sydney, Australia
2022 Australian Research Council Discovery Grant Assessor (1x), Australia
2021– Association for Research in Otolaryngology (ARO)
2021– eLife Early-Career Reviewer
2020 Scientific Judge, Undergraduate Poster Award at the 64th BPS Meeting
2018 Scientific Judge, Student Research Achievement Award at the 62nd BPS Meeting
2016–2017 Australian Physiological Society (APS)
2015– The US Biophysical Society (BPS)
2014–2015 Australian Bioinformatics and Computational Biology Society (ABCBS)
2013–2020 The Australian Society for Biophysics (ASB)
2013–2017 The Australian Nanotechnology Network (ANN)

Honors

2021 Discovery Early Career Researcher Award (DECRA) from the Australian Research Council.
2018 Chicago Fellow Award, School of Biological Sciences, The University of Chicago, Chicago.
2017 Gibson\ Cox Prize for Best Poster Award at Gage Conference on Ion Channels and Transporters.
2014 Paul Korner Best Ph.D. Student Award of the year, VCCRI, Australia.
2013 The University of New South Wales International Postgraduate Award (UIPA), Australia.
2013 Victor Chang Cardiac Research Institute (VCCRI) Top-up Scholarship, Australia.
2012 Ph.D. Merit-based Scholarship, Australian National University, Canberra, Australia.
2012 Best Presentation Award, The Iranian Conference on Manufacturing Engineering, Isfahan.

C. Contribution to Science

My work has led to advancements in instrumentation, methodology and functional insight in the field of mechanobiology. As a newly appointed junior faculty member, I have over 33 research articles, 13 of which are as first or co-first author, spanning research articles, reviews, book chapters, and proceedings. I have always adopted an interwoven array of state-of-the-art computational and experimental techniques to address the aims of my research, as exemplified below.

Molecular and structural basis of prestin's electromotility

The motor protein prestin (SLC26A5) is crucial for the electromotive behavior of outer hair cells and cochlear amplification. Genetic deletion or impairment of prestin results in severe hearing loss, underscoring its vital role in auditory function. In 2018, I joined the Perozo Lab as a Chicago Fellow, where I spearheaded a project focused on the structural and functional characterization of mammalian prestin. Utilizing cryo-electron microscopy, I successfully determined the structure of prestin in six distinct states and in complex with the inhibitor salicylate. This high-resolution visualization of the electromotility cycle not only differentiates prestin from closely related SLC26 anion transporters but also highlights the evolutionary specialization of the mammalian cochlear amplifier. Our work is further detailed in a manuscript currently in preparation, where I am leading a study on prestin's response to membrane tension using both patch clamp and single-particle cryo-EM techniques. This combination of advanced methodologies and my expertise in structural analysis is fundamental to the proposed project, which aims to deepen our understanding of the mechanisms underlying electromotility and sound amplification.

a. Lin, Xiaoxuan, Patrick R. Haller, **Navid Bavi**, Nabil Faruk, Eduardo Perozo, and Tobin R. Sosnick. "Folding of prestin's anion-binding site and the mechanism of outer hair cell electromotility." *Elife* 12 (2023): RP89635.
b. **Bavi, Navid**, Michael D. Clark, Gustavo F. Contreras, Rong Shen, Bharat Reddy, Wieslawa Milewski, and Eduardo Perozo. "The conformational cycle of prestin underlies outer-hair cell electromotility." *Nature* (2021) 600, no. 7889: 553-558.

Biophysical gating mechanism of mechanosensitive ion channels

Throughout my research career, I have focused on understanding the gating cycle of mechanosensitive (MS) channels in different organisms. Using bacterial channels as a model system, my aim has been to reveal molecular insights into the structural mechanisms of bilayer-mediated mechanosensitivity in channels such as K2P and Piezo. By combining molecular dynamics simulations with patch-clamp electrophysiology, we identified an amphipathic anchor domain within the membrane that transmits force to the pore-forming helices—a feature likely common to most mechanosensitive channels. We also explored how surface-active agents, including

amphipathic drugs, differentially activate mechanosensitive channels.

Our research extended to mechanosensitive channels, particularly Piezo, at the cell-substrate interface, examining how these channels integrate mechanical inputs from both the plasma membrane and the cytoskeletal network underneath. We investigated how substrate properties, like stiffness and roughness, affect force sensitivity across different channels via cytoskeletal elements such as actin. Our findings reveal diverse responses of mechanosensitive channels to substrate changes, highlighting the varied force-sensing mechanisms crucial for our proposed research.

a. **Bavi, Navid***, Jessica Richardson*, Celine Heu, Boris Martinac, and Kate Poole. "PIEZO1 Mediated Currents are Modulated by Substrate Mechanics." *ACS nano* (2019); *Co-1st author.
b. **Bavi, Navid,** Omid Bavi, Manouchehr Vossoughi, Reza Naghdabadi, Adam P. Hill, Boris Martinac, and Yousef Jamali. "Nanomechanical properties of MscL α helices: A steered molecular dynamics study." *Channels* 11, no. 3 (2017): 209-223.
c. **Bavi, Navid**, Adam D. Martinac, D. Marien Cortes, Omid Bavi, Pietro Ridone, Takeshi Nomura, Adam P. Hill, Boris Martinac, and Eduardo Perozo. "Structural Dynamics of the MscL C-terminal Domain." *Scientific reports* 7, no. 1 (2017): 17229.
d. **Bavi, Navid**, D. Marien Cortes, Charles D. Cox, Paul R. Rohde, Weihong Liu, Joachim W. Deitmer, Omid Bavi et al. "The role of MscL amphipathic N terminus indicates a blueprint for bilayer-mediated gating of mechanosensitive channels." *Nature Communications* 7 (2016).

Cryo-EM structures of mechanosensitive ion channels in detergent and lipid nanodiscs

Cryo-EM structure determination of mechanosensitive ion channels in detergent and lipid nanodiscs presents significant challenges. Membrane protein structures can vary greatly depending on their detergent environment, potentially leading to artifactual conformational changes. Solving these structures in lipid nanodiscs and liposomes is difficult due to typically low sample yields. During my postdoctoral training, I have optimized methods for studying the cryo-EM structures of mechanosensitive ion channels in nanodiscs and native lipid membranes. My experience includes successfully resolving multiple mechanosensitive ion channel structures and prestin in nanodiscs with various lipid compositions and sizes (with a manuscript related to prestin currently in preparation). I plan to apply these approaches to determine the structures of prestin, PresTen, and other mechanosensitive membrane proteins under conditions that closely mimic their native states.

a. Zhou, Zijing, Xiaonuo Ma, Yiechang Lin, Delfine Cheng, **Navid Bavi**, Genevieve A. Secker, Jinyuan Vero Li et al. "MyoD-family inhibitor proteins act as auxiliary subunits of Piezo channels." *Science* 381, no. 6659 (2023): 799-804.
b. Park, Yein Christina, Bharat Reddy, **Navid Bavi**, Eduardo Perozo, and José D. Faraldo-Gómez. "State-specific morphological deformations of the lipid bilayer explain mechanosensitive gating of MscS ion channels." *eLlife* (2022).
c. Reddy, Bharat, **Navid Bavi**, Allen Lu, Yeonwoo Park, and Eduardo Perozo. "Molecular basis of force-from-lipids gating in the mechanosensitive channel MscS." *eLife* 8 (2019): e50486.

Biophysical implications of rheometric properties of plasma membrane for ion channel mechanosensitivity

Understanding the mechanical traits of lipid bilayers within cellular membranes is pivotal, particularly in their influence on membrane proteins, notably mechanosensitive channels. Hence, characterizing these properties becomes crucial. During my doctoral and postdoctoral research, I pioneered a distinctive conceptual framework employing excised patch fluorometry, a superior method compared to conventional approaches. This innovative approach allows a comprehensive examination of lipid bilayer behavior, providing insights discernible through computational analysis. The distinctions observed among various electrophysiological patch configurations are instrumental. They hold significance for the field, especially in leveraging patch-clamp electrophysiology as a model for studying diverse ion channels. This framework's versatility extends beyond mechanosensitive channels. Employing excised patch fluorometry, similar methodologies can probe other membrane proteins, unveiling their passive influence on surrounding lipid bilayers. Furthermore, this exploration unveils how the mechanical attributes of lipid membranes fine-tune the functionality of these proteins. These frameworks are fundamental in addressing the aims of the current proposal.

a. Bavi, Omid*, Zijing Zhou*, **Navid Bavi***, S. Mehdi Vaez Allaei, Charles D. Cox, and B. Martinac. "Asymmetric effects of amphipathic molecules on mechanosensitive channels." Scientific Reports 12, no. 1 (2022): 9976. (*co-first author).
b. Xue, Feng, Charles D. Cox, **Navid Bavi**, Paul R. Rohde, Yoshitaka Nakayama, and Boris Martinac. "Membrane stiffness is one of the key determinants of E. coli MscS channel mechanosensitivity." *Biochimica et Biophysica Acta (BBA)-Biomembranes* 1862, no. 5 (2020): 183203.
c. Nakayama, Yoshitaka, Radomir Slavchov, **Navid Bavi**, Martinac, Boris, "The energy of liposome patch adhesion to the pipette glass determined by confocal fluorescence microscopy" *Journal of Physical Chemistry Letters* 7, no. 22 (2016): 4530-4534.
d. **Bavi, Navid**, Yoshitaka Nakayama, Omid Bavi, Charles D. Cox, Qing-Hua Qin, and Boris Martinac. "Biophysical implications of lipid bilayer rheometry for mechanosensitive channels." *Proceedings of the National Academy of Sciences* 111, no. 38 (2014): 13864-13869.

Contribution to Engineering and Nanotechnology Science:
In addition to my research in mechanobiology, I have formal training in mechanical engineering, with a specialization in optimizing adhesive joints for lightweight and composite structures. My studies focused on the mechanics of composite and smart materials, particularly within aerospace and other applications where weight reduction is critical. During my undergraduate and master's programs, I employed computational methods, including finite element modeling, alongside experimental techniques such as vibration analysis and wave propagation, to explore the behavior of composite materials under stress, particularly in the presence of defects or cracks. These studies have provided critical insights into the design of optimal adhesive joints for high-stakes applications, such as airplane fuselages, where preventing catastrophic failure due to material voids, cracks, or bond separations is paramount. These engineering principles are directly applicable to my current research, particularly as we investigate the force-generating properties of proteins involved in mechanosensation.

Additionally, my expertise extends to modeling both macro-scale structures and micro- to nanoscale applications, including the study of biomaterials and cellular biomechanics. This work has contributed to the development of novel nanomaterials and technologies aimed at combating cancer progression, bridging my engineering background with innovative approaches in nanotechnology.

a. Bavi, Omid, Mona Khafaji, and **Navid Bavi**. "Nanomaterial and Nanostructures for Cancer and Pathogenic Infection Diagnosis and Therapy." Editorial. Frontiers in Nanotechnology 7 (2025): 1552196.
b. Setoodeh, Alireza, Morteza Derahaki, And **Navid Bavi**. "DQ Thermal Buckling Analysis of Embedded Curved Carbon Nanotubes Based on Nonlocal Elasticity Theory." *Latin American Journal of Solids and Structures, an ABCM Journal* 12.2 (2015).
c. Bavi, Omid, **Bavi, Navid*** and Shishesaz, Mohammad. "Geometrical Optimization of the Overlap in Mixed Adhesive Lap Joints", *The Journal of Adhesion*, 89:12, (2013) 948-972. (*corresponding author).
d. Shishesaz, Mohammad, & **Bavi, Navid**. "Shear stress distribution in adhesive layers of a double-lap joint with void or bond separation**."** *Journal of Adhesion Science and Technology* 27.11 (2013): 1197-1225.

Complete List of Published Work in My Bibliography:
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BIOGRAPHICAL SKETCH

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NAME: **Gabriel Carmona-Rosas**

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

POSITION TITLE: **Assistant Project Scientist II**

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
National Autonomous University of Mexico (UNAM), Mexico City, Mexico	B.S.	08/2009	06/2014	Psychology, Neuroscience
National Autonomous University of Mexico (UNAM), Mexico City, Mexico	Ph.D.	08/2015	02/2019	Biochemistry, Cell Biology
The University of Chicago, Chicago IL, USA	Postdoctoral	04/2019	10/2024	Structural Biology

A. Personal Statement

I am an assistant project scientist II at the University of California, Los Angeles (UCLA), working on the structural biology of membrane proteins. My main goal is to become an independent and successful investigator dedicated to understanding the structure and function of macromolecular complexes in the context of neurodevelopmental and cardiovascular diseases. I started my scientific career while I was completing an undergraduate degree in Psychology at the National Autonomous University of Mexico (UNAM), where I became interested in the biological functions of GPCRs. Working under the mentorship of Dr. Adolfo Garcia-Sainz, I described the pharmacological properties of LPA receptors expressed in human lung cell lines. This project allowed me to complete an undergraduate thesis and acquire a deep knowledge in biochemistry. During the next years, I continued working on the regulation of the three human α1-Adrenergic receptors (α1-ARs). This group of GPCRs plays a key role in a plethora of cardiovascular functions, however, their deregulation also contributes to the onset of cardiovascular diseases. During my graduate training, I targeted different phosphorylation residues on the three α1-ARS, and I described how these phosphorylation events regulate the functions and trafficking of these GPCRs. This experience equipped me with a strong background in protein biochemistry, signal transduction and high-resolution microscopy.

After obtaining a Ph.D. degree, I took a different pathway to study protein-protein interactions using structural biology techniques. Under the mentorship of Dr. Demet Araç and Dr. Engin Özkan, I solved the structure of a previously unobserved interaction between the Latrophilin GPCR and the single Toll-like receptor in *C. elegans*. This interaction is key for embryo development in nematodes, and its absence leads to sterility, lethality, and malformed embryos. During this time, I acquired a strong background in protein purification, molecular cloning, X-ray crystallography, and cryo-EM. While I was working on membrane proteins, I became fascinated by how macromolecular complexes interact with RNA molecules to dictate protein synthesis and function. The survival motor neuron (SMN) is a protein that forms the oligomeric core of a multiprotein complex required for the assembly of spliceosomal snRNPs. Disruptions in the SMN complex are associated with spinal muscular atrophy, a neurodegenerative disease that is the leading heritable cause of infant mortality. In Dr. Hayne's lab, I worked on elucidating the structural basis of the SMN complex and RNA-ligase enzymes through cryo-EM and X-ray crystallography.

As an assistant project scientist II, I have taken full advantage of the exceptional resources available at UCLA, where I plan to keep learning cutting-edge experimental techniques to become an independent and successful researcher focus on understanding the biological basis of macromolecular complexes with unprecedented details.

B. Positions and Honors

2012-2015	Undergraduate Research Assistant, Cellular Physiology Institute (IFC-UNAM).
2013-2014	Undergraduate Teaching Assistant: Neurocognition and Cognitive Neurosciences (UNAM).
2014	Undergraduate *Magna Cum Laude*: Bachelor Degree in Psychology and Neuroscience (UNAM).
2015-2019	Graduate Student, Cellular Physiology Institute (IFC-UNAM).
2019	Doctoral *Magna Cum Laude:* Ph.D. Degree in Biomedical Sciences – Biochemistry (UNAM).
2019	Postdoctoral Research Scholar, University of Chicago, Chicago IL, USA.
2024	Assistant Project Scientist II, University of California, Los Angeles (UCLA).

C. Contributions to Science

1. Structure and Function of a Novel Interaction at the Cell Surface: LAT-1 and TOL-1: My most recent contribution to science was the structural and functional characterization of a novel form of interaction between the Latrophilin GPCR (LAT-1) and the single Toll-Like receptor (TOL-1) in the nematode *C. elegans*. Existing literature demonstrates that LAT-1 plays critical roles during the early stages of development in nematodes, however, its mechanistic roles in embryogenesis and interaction with other cell-surface receptors remained unknown. Using a high-throughput interactome assay, I identified TOL-1 as a novel binding partner for LAT-1. To determine if TOL-1 regulates LAT-1 functions in embryogenesis, I employed a multidisciplinary approach: I determined the high-resolution crystal structure of the extracellular lectin domain of LAT-1 binding to the second leucine-rich repeat domain of TOL-1, and I obtained a 6.3 Å resolution cryo-EM structure of the full extracellular domains of the LAT-1/TOL-1 complex. This protein structure reveals an unexpected molecular architecture that had not been observed before. Using this structural information, I engineered point-mutations to break the binding interface *in vitro*. Finally, I used CRISPR/Cas9 to generate worms carrying the homozygous alleles of LAT-1 and TOL-1 with the mutations that specifically disrupt the LAT-1/TOL-1 complex. I found that these genetic manipulations resulted in severe developmental defects in *C. elegans*, strongly suggesting that this interaction represents a receptor-ligand axis that is essential for animal morphogenesis.

a) **Carmona-Rosas, G.**, Li, J., Smith, J., Nawrocka, V., Cheng, C., Baltrusaitis, E., Zhao, M., Araç, D., Kratsios, P. & Özkan, E. (2023). Structural basis and functional roles for TOL-1/Toll-like receptor binding to LAT-1/Latrophilin adhesion-GPCR in *C. elegans* development. *BioRxiv 2*023.05.04.539414. https://doi.org/10.1101/2023.05.04.539414. *Nat Struct Mol Biol. Accepted, 2024.*

2. Role of Differential Phosphorylated Residues on the Signaling and Trafficking of the Human α1D-AR: My most impactful contribution to the GPCR field has been the characterization of the phosphorylation pattern of the α1D-AR and its role in the function and trafficking of the receptor. This GPCR is considered one of the most difficult receptors to study, due to its constitutive activity and localization in intracellular compartments. Using mass spectrometry, I was able to identify fifteen phosphorylated residues distributed along the intracellular domains of the receptor. The activation and phosphorylation of this receptor by NA and PMA, relays on the initial phosphorylation of T442, which acts as a master regulator of the entire phosphorylation pattern. Additionally, differential phosphorylation events allow for the α1D-AR to behave as a biased receptor, triggering the mobilization of intracellular calcium and / or the activation of MAPK kinases. One of the most interesting findings of this project, was the association of scaffold proteins, like β-arrestin 1/2, to the α1D-AR under different structural and cellular conditions. Regardless of the phosphorylation pattern, the lack of intracellular domains or the subcellular localization of the α1D-AR, the β-arrestin 1/2 proteins are recruited by such receptor and are used as scaffold proteins to activate multiple downstream signaling pathways. Finally, the hallmark of this research was the discovery of a new form of feedback between the phosphorylation of the receptor, and its insertion in the plasma membrane; contrary to all the GPCRs studied so far, the phosphorylation of a cluster of residues in the C-terminal tail of the α1D-AR, dictates its localization in the plasma membrane and its trafficking through multiple intracellular compartments.

a) *#**Gabriel Carmona-Rosas**, Rocío Alcántara-Hernández and David A. Hernández-Espinosa. The role of β-arrestins in G protein-coupled receptor heterologous desensitization: A brief story. *Methods in Cell Biology, 149, 195-204, 2019.*

b) ***#Gabriel Carmona-Rosas,** Rocío Alcántara-Hernández and David A. Hernández-Espinosa. Dissecting the signaling features of the multi-protein complex GPCR/β-arrestin/ERK1/2. *European Journal of Cell Biology, 97, 349-358, 2018*.

c) ***Gabriel Carmona-Rosas**, David A. Hernández-Espinosa, Rocío Alcántara-Hernández, Marco A. Alfonzo-Méndez and J. Adolfo García-Sainz. Distinct phosphorylation sites/clusters in the carboxyl terminus regulate α_{1D}-adrenergic receptor subcellular localization and signaling. *Cellular Signaling, 9;53:374-389, 2018.*

d) Marco A. Alfonzo-Méndez, **Gabriel Carmona-Rosas,** David A. Hernández-Espinosa, M. Teresa Romero-Ávila and J. Adolfo García-Sainz. Distinct phosphorylation patterns regulate α_{1D}-adrenoceptor signaling and desensitization. *BBA – Molecular Cell Research, 1865, 845-854, 2018.*

3. Regulation of the Three Human α1-ARs by Different Phosphorylation Patterns: My graduate research contribution to science was focused on analyzing the phosphorylation patterns, signaling features, and trafficking pathways of the three human α1-ARs (α1A-AR, α1B-AR, and α1D-AR) using different biochemical assays and advanced microscopy techniques. These receptors are key regulators of multiple cardiovascular functions, such as heart rate, blood pressure, and blood vessel contraction. The deregulation of these GPCRs leads to the development of severe heart diseases, including hypertension, arrhythmia, atrial fibrillation, and congestive heart failure. I identified the exact residues that are phosphorylated on these adrenergic receptors when they are stimulated with noradrenaline (NA) and phorbol 12-myristate, 13-acetate (PMA). In particular, the α1A-AR strongly interacts with the Glycogen Synthase Kinase-3 (GSK-3), which can phosphorylate such receptor in different intracellular domains. This interaction contributes to the mobilization of intracellular calcium and the distribution of the receptor in intracellular compartments. On the other hand, the phosphorylation of the α1B-AR by the G protein-coupled receptor kinase 2 (GRK) and the PKC, leads to the activation of different signaling pathways, and the intracellular trafficking of the receptor into early and late endosomes. The exact location of the α1B-AR was tracked by its interaction with small GTPases, such as Rab9 and Rab5. The outcomes of this set of projects strongly suggest that the three adrenergic receptors have a specific phosphorylation pattern, depending on the type of stimuli and the structural composition of the receptor.

a) Rocío Alcántara-Hernández, **Gabriel Carmona Rosas,** David A. Hernández-Espinosa and J. Adolfo García-Sainz. Glycogen Synthase Kinase-3 modulates α_{1A}-adrenergic receptor action and regulation. *European Journal of Cell Biology. 99(2-3):151072, 2020.*

b) David A. Hernández-Espinosa, **Gabriel Carmona Rosas**, Rocío Alcántara-Hernández and J. Adolfo García-Sainz. Sites phosphorylated in human α_{1B}-adrenoceptors in response to noradrenaline and phorbol myristate acetate. *BBA – Molecular Cell Research, 1866 (10), 1509-1519, 2019.*

c) Marco A. Alfonzo-Méndez, David A. Hernández-Espinosa, **Gabriel Carmona-Rosas,** M. Teresa Romero-Ávila, Guadalupe Reyes-Cruz and J. Adolfo García-Sainz. Protein kinase C activation promotes α_{1B}-adrenoceptor internalization and late endosome trafficking through Rab9 interaction. Role in heterologous desensitization. *Molecular Pharmacol, 91:296-306, 2017.*

4. Pharmacological Characterization of Endogenous LPA Receptors in Human Lung Cells: My early contribution to science was focused on the pharmacological characterization of endogenous GPCRs for Lysophosphatidic Acid (LPA), expressed in the human pulmonary cell line A549. LPA receptors are key players in the pathogenesis of asthma, chronic obstructive pulmonary disease, and lung fibrosis. In this project, I identified the LPA receptor subtypes expressed in the A549 cells, and their pharmacological features using natural and synthetic ligands. I found that upon activation, these receptors induce the mobilization of intracellular calcium, the activation of MAPK kinases, and the phosphorylation of LPA receptors by the activity of the $G\boldsymbol{\alpha}_{q/11}$ protein and the protein kinase C (PKC). Interestingly, I found a group of synthetic antagonists that revealed that the LPA_1 receptor subtype is constitutively active, resulting in the activation of different signaling pathways and the constitutive phosphorylation of the receptor. Finally, I identified a biased agonist for the LPA_3 receptor that

triggers significant changes in the phenotype of A549 cells through the activity of two different G proteins. The outcomes of this research are pivotal to identify and design better drugs that can potentially target the LPA receptors to treat a significant number of pulmonary diseases.

a) ***Gabriel Carmona-Rosas,** Marco A. Alfonzo-Méndez, David A. Hernández-Espinosa, M. Teresa Romero-Ávila and J. Adolfo García-Sainz. A549 cells as a model to study endogenous LPA1 receptor signaling and regulation. *European Journal of Pharmacology*, *815, 258-265, 2017.*

*First Author
#Corresponding Author

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1zIbfltpCYIIrv/bibliography/public/

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

Research Support:

2013 Support for Research Projects - National Council of Science and Technology (CONACyT).
2013 Support for Research Projects and Technological Innovations (PAPIIT).
2014 Degree Scholarship for High Performance Undergraduate Students (UNAM).
2015 Doctoral Degree Scholarship - National Council of Science and Technology (CONACyT).
2016–2018 Financial Support Program for Graduate Students (PAEP) – Scientific Meetings.
2019 Economic Stimulus for Timely Ph.D. Graduation (UNAM).
2019 Postdoctoral Training Grant, National Institute of Health (NIH-University of Chicago).
2024 Postdoctoral Training Grant from the Center for Motor Neuron Disease (CMND).

Professional Memberships:

2016 Mexican Society of Biochemistry.
2019 Society for Neuroscience.

Journal Reviewer:

2020 British Journal of Pharmacology.

Grant Reviewer:

2019 Frontier Science Projects 2019 - National Council of Science and Technology (CONACyT).

Scholastic Performance:

YEAR	COURSE TITLE	GRADE
2015	Molecular Pharmacology	90
2015	Microscopic Techniques Workshop	100
2015	Molecular Biology	90
2016	Signal Transduction and Vesicular Trafficking	100
2016	Cell Biology	100
2016	Bioinformatics	100
2017	Writing Workshop	100
2017	Signal Transduction and Cancer	100
2018	Biochemistry	90

Scale: 0 - 100

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Rastegarpouyani, Hosna

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

POSITION TITLE: Postdoctoral Scholar

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 Tehran, Tehran	BS	09/2013	Cellular & Molecular Biology
Shahid Beheshti University, Tehran	MS	09/2016	Microbiology
Florida State University, Tallahassee Florida	PHD	05/2024	Cellular & Molecular Biology

A. Personal Statement

In 2018, I was accepted into Florida State University's Biology Ph.D. program. After completing my first-year rotations, I joined Dr. Kenneth Taylor's lab, where I became immersed in electron microscopy—a field that was completely new to me but quickly became my passion. Transitioning from traditional biology to the highly interdisciplinary world of cryo-EM, which blends biochemistry, physics, and computational analysis, was initially a challenge, but one that I was eager to take on. Over the past several years, I've built a broad skill set in sample preparation, cryo-grid freezing, data collection, and 3D reconstruction.

My early research involved purifying Ca^{2+}-insensitive gelsolin for actin filament stabilization and isolating thick filaments from rabbit psoas muscle for negative stain and cryo-EM. I optimized filament preparation for both rabbit skeletal and cardiac muscles, as well as human cardiac tissue, eventually producing the first near-atomic model of vertebrate thick filaments from frozen-hydrated samples. I also explored PEGylation as a strategy for improving sample preservation without the resolution limits of crosslinking.

I then shifted focus to *Drosophila* flight muscle, where I discovered two distinct forms of thick filaments—ordered-head and disordered-head filaments. My most significant Ph.D. achievement was reconstructing these filaments at 2.8 Å resolution—the highest resolution ever reported for thick filaments—vastly improving on the previous 4.7 Å model. This work, published in the *International Journal of Molecular Sciences*, revealed clear differences in filament organization and enabled atomic modeling of both states, providing new insights into thick filament architecture and muscle function. I also collaborated on studies of cardiomyocyte structure and function, including research with Dr. Jose R. Pinto's lab that led to published work on cardiomyopathies and nuclear mechanosensing.

Currently, I am a postdoctoral researcher in Dr. Navid Bavi's lab at UCLA, where I focus on cryo-EM studies of pendrin (SLC26A4), an anion exchanger critical for inner ear and kidney function. My work centers on capturing pendrin in nanodiscs with and without small-molecule modulators like sodium salicylate to investigate ligand-induced conformational changes. I am responsible for grid optimization, data collection on the Titan Krios, and image processing. Our aim is to understand how lipid environments and ligands influence pendrin's structure and function, which could provide molecular insight into drug-induced hearing loss.

B. Positions, Scientific Appointments and Honors

Positions and Employment

Spring 2017	Teaching Assistant, University of Tehran, Department of Biology, Tehran
2017 – 2018	Researcher at Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences, Tehran
2018 - 2020	Teaching Assistant, Florida State University, Tallahassee, Florida
2020 - 2024	Research Assistant, Florida State University, Tallahassee, Florida
2024 - 2025	Postdoctoral Scholar, Florida State University, Tallahassee, Florida
2025 -	Postdoctoral Scholar, UCLA, Los Angeles, California

Other Experience and Professional Memberships

2020 -	Member, Biophysical Society
2020 -	Member, Graduate Women in Science at FSU
2021 - 2022	Event Coordinator, Graduate Women in Science
2022 -	Member, Microscopy Society of America
2022 -	Member, American Heart Association

Honors

2017	Outstanding academic record, Shahid Beheshti University
2018	Dean's Doctoral Scholarship for international students, Florida State University
2020	Admitted for a paid 3-month summer intern at MyoKardia Inc. which unfortunately got canceled due to the covid-19 pandemic
2021	Donna Jung Scholarship Award in fields of cryogenic studies
2022	M&M 2022 Poster Award Winner
2022	ACA 2022 Student Travel Award
2022	Ben and Karen Thrower Award
2023	Donna Jung Scholarship Award in Fields of Cryogenic Studies
2024	Microscopy and Microanalysis (M&M) Meeting Student Scholar Award
2025	Caspar Award for Outstanding Research and Scientific Publication

C. Contributions to Science

1. **Structural Analysis of Thick Filaments in Insect Flight Muscle**
   Although insect and vertebrate muscles differ morphologically, both rely on stretch activation for contraction and share conserved molecular elements. Insect flight muscles, especially those in *Drosophila melanogaster*, exhibit the most refined stretch activation mechanisms. Using cryo-EM, I isolated and reconstructed thick filaments from *Drosophila* and *Bombus ignitus*, resolving their structures at 2.8 Å and 6 Å, respectively—the highest resolution achieved for thick filaments to date. These reconstructions revealed two structurally distinct filament classes in *Drosophila*—ordered- and disordered-head filaments—and uncovered non-myosin protein details. I performed all sample preparation, grid freezing, and supported 3D reconstructions.
   Selected peer-reviewed publications:

   - Rastegarpouyani, H., Hojjatian, A., & Taylor, K. A. (2024). Two Forms of Thick Filament in the Flight Muscle of *Drosophila melanogaster*. *Int J Mol Sci*, 25(20), 11313.

- Yeganeh, F. A., Rastegarpouyani, H., Li, J., & Taylor, K. A. (2023). Structure of the *Drosophila* Flight Muscle Myosin Filament at 4.7 Å Resolution. *Int J Mol Sci*, 24(19), 14936.

- Li, J., Rahmani, H., Abbasi Yeganeh, F., Rastegarpouyani, H., Taylor, D. W., Wood, N. B., ... & Taylor, K. A. (2023). Structure of the Flight Muscle Thick Filament from the Bumble Bee, *Bombus ignitus*, at 6 Å Resolution. *Int J Mol Sci*, 24(1), 377.

2. **Toward High-Resolution Structures of Vertebrate Cardiac Thick Filaments**
   I optimized isolation and freezing conditions for vertebrate thick filaments from rabbit psoas and human cardiac muscle. These methods enabled the first high-quality cryo-EM samples of vertebrate thick filaments, which are more fragile than their invertebrate counterparts. My work contributed to two studies on native cardiac thick filament structure and the effects of mutations linked to cardiomyopathies.
   Selected peer-reviewed publications:

   - Chen, L., Liu, J., Rastegarpouyani, H., Janssen, P. M., Pinto, J. R., & Taylor, K. A. (2024). Structure of mavacamten-free human cardiac thick filaments within the sarcomere by cryoelectron tomography. *Proc Natl Acad Sci USA*, 121(9), e2311883121.

   - Landim-Vieira, M., Ma, W., Song, T., Rastegarpouyani, H., Gong, H., Coscarella, I. L., ... & Pinto, J. R. (2023). Cardiac troponin T N-domain variant destabilizes the actin interface resulting in disturbed myofilament function. *Proc Natl Acad Sci USA*, 120(23), e2221244120.

3. **Mechanistic Insights into Cardiac Thin Filament Regulation**
   In collaboration with the Pinto lab, I contributed to a study investigating how mutations in cardiac troponin T disrupt actin-myosin interactions. This work uncovered how N-terminal variants can destabilize the actin interface and disturb myofilament function—mechanisms implicated in inherited cardiomyopathies.
   Selected peer-reviewed publications:

- Landim-Vieira, M., Ma, W., Song, T., Rastegarpouyani, H., Gong, H., Coscarella, I. L., ... & Pinto, J. R. (2023). Cardiac troponin T N-domain variant destabilizes the actin interface resulting in disturbed myofilament function. *Proc Natl Acad Sci USA*, 120(23), e2221244120.

4. **TEM-Based Studies of Cardiomyocyte Ultrastructure and Nuclear Mechanics**
   I performed embedding, ultramicrotomy, and imaging of mouse cardiac tissue to investigate nuclear pleomorphism and structural changes associated with hypertrophic cardiomyopathy. This contributed to understanding mechanosensing defects in cardiac muscle. I also collaborated on multiple studies examining mechanobiology and myofilament regulation.
   Selected peer-reviewed publications:

- Coscarella, I. L., Landim-Vieira, M., Rastegarpouyani, H., Chase, P. B., Irianto, J., & Pinto, J. R. (2023). Nucleus Mechanosensing in Cardiomyocytes. *Int J Mol Sci*, 24(17), 13341.

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	UNIVERSITY OF TEHRAN	
2011	Overall GPA	3.3 out of 4
	SHAHID BEHESHTI UNIVERSITY	
2015	Overall GPA	4 out of 4
	FLORIDA STATE UNIVERSITY	
2018	Advanced Molecular Biology	B+
2018	Academic Spoken English for TAs	S
2018	Responsible Conduct of Research	S
2019	Advanced Cell Biology	A
2019	Colloquium/Biological Sciences	S
2020	Programming for Chemists and Biochemists	A
2020	Prelim Doctoral Exam	P
2021	3D EM of macromolecules	A

BIBLIOGRAPHY

NAME: Hao, Liu

eRA COMMONS USER NAME (credential, e.g., agency login): hliu96

POSITION TITLE: Postdoctoral Researcher of the Department of Physiology

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
Fuzhou University	BS	06/2018	Medicinal Chemistry
Fuzhou University	PhD	03/2024	Biomedical Engineering
University of California, Los Angeles	Postdoc	To date	Physiology

A. Personal Statement

I am a postdoctoral researcher at UCLA with a strong background in cancer biology and drug discovery. My current research focuses on elucidating the molecular mechanisms of phosphate transporters, particularly SLC34A2 and its oncogenic fusion SLC34A2-ROS1, and their roles in cancer progression and drug resistance. To achieve this, I integrate advanced structural and functional techniques, including cryo-electron microscopy (Cryo-EM), hydrogen-deuterium exchange mass spectrometry (HDX-MS), molecular modeling, and electrophysiology, to characterize membrane protein structures and investigate their functional properties. During my Ph.D., I worked extensively on photodynamic therapy (PDT) and tumor-targeted drug delivery, pioneering the identification of organic anion transporting polypeptides (OATPs) as key mediators of tumor-selective sensitizer uptake. In addition, I developed supramolecular nanomedicines and investigated their tumor cytotoxicity based on redox behavior. Building on these nanomedicines, I further explored the combination of photodynamic therapy with immune checkpoint blockade to overcome tumor hypoxia and enhance antitumor immunity. These interdisciplinary projects provided me with valuable expertise in protein-ligand interactions, membrane transporter biology, and targeted cancer therapy. This proposal logically builds upon my current research by integrating cutting-edge structural biology and electrophysiology approaches to address critical questions related to drug resistance and transporter-targeted therapy. With my expertise, interdisciplinary background, and commitment to scientific discovery, I am confident in my ability to make meaningful contributions to this research project and advance our understanding of transporter biology in cancer.

In addition to my research accomplishments, I have mentored graduate and undergraduate students, collaborated across multidisciplinary teams, and presented my work at national conferences. My mentoring has led to collaborative publications and earned various research accolades. These experiences have honed my communication and leadership skills and deepened my appreciation for collaborative science. Furthermore, I am committed to promoting medical knowledge among women, minorities, and socioeconomically disadvantaged populations, with the aim of providing support to a broader community.

Looking ahead, my long-term goal is to establish a comprehensive research team that integrates membrane protein biology, the elucidation of drug resistance mechanisms, and the development of targeted therapies. I firmly believe that combining in-depth molecular understanding with translational research holds great promise for delivering innovative therapeutic strategies for cancer and other diseases characterized by transporter dysregulation.

Citations:

1. **H. Liu**, Z. Li, X. Zhang, Y. Xu, G. Tang, Z. Wang, Y.-Y. Zhao. M.-R Ke, B.-Y. Zheng, S. Huang, J.-D. Huang* and X. Li*. Phthalocyanine Aggregates as “Semiconductor-like” Photocatalysts for Hypoxic-Tumor Photodynamic Immunotherapy [J]. **Nat. Communi.** 2025, 16, 326. DOI: 10.1038/s41467-024-55575-2. (Research Article)

2. **H. Liu**, L.-L. Lv, H. Wen, D.-M. Zhao, J. Wu, M.-R. Ke, B.-Y. Zheng, J. Li, X. Li*, J.-D. Huang*. Molecular and supramolecular approach to highly photocytotoxic phthalocyanines with dual cell uptake pathways and albumin-enhanced tumor targeting. **ACS Appl. Mater. Interfaces**, 2022, 14, 28581-28590. DOI: 10.1021/acsami.2c05814. (Research Article)

3. **H. Liu**, X.-Y. Li, X. Li*, J. D. Huang*, Nanostructured self-assemblies of photosensitive dyes: green and efficient theranostic approaches, **Green Chem. Eng.**, 2022, 4, 399-416. DOI: 10.1016/j.gce.2022.06.006. (Review Article)

4. M. Chen, Y. Jiang, Y. Zhang, X. Chen, L. Xie, L. Xie, T. Zeng, Y. Liu, **H. Liu**, M. Wang, X. Chen, Z. Zhang, Y. He, X. Qin, C. Lu, Q. Chen, H. Yang. Visualization of Biomolecular Radiation Damage at the Single-Particle Level Using Lanthanide-Sensitized DNA Origami. **Nano Lett.**, 2024, 24, 11690-11696. DOI: 10.1021/acs.nanolett.4c03307. (Research Article)

5. Y.-Y. Zhao, Z. Chen, L. Zhang, X.-W. Qin, **H. Liu**, B.-Y. Zheng, M.-R. Ke, J.-D. Huang*, X. Li*. A self-degradable nanostructured phthalocyanine assembly with high photothermal efficacy to enhanced biosecurity in photothermal therapy [J]. **Chem. Eng. J.**, 2023, 474: 145921-145931. (Research Article)

6. M.-R. Ke, Z. Chen, J. Shi, Y. Wei, **H. Liu**, S. Huang, X. Li, B.-Y. Zheng and J.-D. Huang*. A smart and visible way to switch the aromaticity of silicon (IV) phthalocyanines [J]. **Chem. Commun.**, 2023, 59: 9783-9908. (Research Article)

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2024(Aug) – To date Postdoctoral Fellow, University of California, Los Angeles, USA.

Honors

2024 National Scholarship of China, Department of Chemistry, Fuzhou University, CN.
2024 Outstanding PhD Graduates of 2024, Fuzhou University, CN.
2024 Outstanding Graduation Thesis Graduate, Department of Chemistry, Fuzhou University, CN.

C. Contributions to Science

1. **Found evidence for the transport of nanomedicines into cells via organic anion transporters.**

The first part of my PhD work focused on the design and synthesis of novel anti-tumor photosensitizers. These phthalocyanines I designed can target cancer cells through two distinct uptake pathways: the organic anion-transporting polypeptide (OATP) pathway and the albumin-mediated uptake pathway, significantly enhancing cellular uptake and exhibiting remarkably high photodynamic anti-cancer activity. Investigating the structure-activity relationship between drugs and membrane proteins greatly fostered my interest in studying drug-protein interactions and laid the foundation for my research in structural biology.

a. **H. Liu**, L.-L. Lv, H. Wen, D.-M. Zhao, J. Wu, M.-R. Ke, B.-Y. Zheng, J. Li, X. Li*, J.-D. Huang*. Molecular and supramolecular approach to highly photocytotoxic phthalocyanines with dual cell uptake pathways and albumin-enhanced tumor targeting. **ACS Appl. Mater. Interfaces**, 2022, 14, 28581-28590. DOI: 10.1021/acsami.2c05814. (Research Article)

2. **Elucidate the mechanism of nano photosensitizers damage tumors under hypoxic conditions.**

The second part of my Ph.D. work focused on regulating the aggregation equilibrium of nanomedicines to enhance drug targeting and therapeutic efficacy, as well as elucidating the chemical mechanism by which photosensitizers kill cancer cells under hypoxic conditions. The core highlight of this work lies in the discovery that these photosensitizers generate reactive oxygen species (ROS) through an efficient “self-substrate” symmetry-breaking charge separation (SBCS) mechanism. Moreover, these aggregates exhibit pronounced photocurrent responses under light irradiation, demonstrating semiconductor-like photocatalytic properties. Based on these findings, a novel approach for designing “semiconductor-like” aggregated photosensitizers from molecular photosensitizers were proposed. The chemical insights gained from this work have deepened my

understanding of the role of various chemical bonds at the target sites and their interactions with small-molecule drugs, providing a foundation for the rational design of new nanodrugs and small molecule inhibitors.

a. **H. Liu**, Z. Li, X. Zhang, Y. Xu, G. Tang, Z. Wang, Y.-Y. Zhao. M.-R Ke, B.-Y. Zheng, S. Huang, J.-D. Huang* and X. Li*. Phthalocyanine Aggregates as “Semiconductor-like” Photocatalysts for Hypoxic-Tumor Photodynamic Immunotherapy [J]. **Nat. Communi.** 2025, 16, 326. DOI: 10.1038/s41467-024-55575-2. (Research Article)
b. **H. Liu**, X.-Y. Li, X. Li*, J. D. Huang*, Nanostructured self-assemblies of photosensitive dyes: green and efficient theranostic approaches, **Green Chem. Eng.**, 2022, 4, 399-416. DOI: 10.1016/j.gce.2022.06.006.

3. **Design of Novel Synergistic Therapeutic Strategies Based on Combination Immunotherapy**

The third part of my doctoral research focused on the development and optimization of combination therapy strategies, particularly addressing one of the major clinical limitations of PDT, tumor hypoxia. I designed and implemented an innovative therapeutic approach that combines PDT with immune checkpoint inhibitors (ICIs), aiming to enhance antitumor immune responses through synergistic mechanisms. This approach demonstrated significant synergistic therapeutic effects on both primary and metastatic tumors under hypoxic conditions and markedly enhanced the infiltration of cytotoxic T lymphocytes (CTLs) in tumor. These research experiences in immunotherapy and combination strategies have laid a solid theoretical foundation and provided strong technical support for my future efforts to develop novel therapeutic approaches that combine tyrosine kinase inhibitors (TKIs) with immune checkpoint inhibitors.

a. **H. Liu**, Z. Li, X. Zhang, Y. Xu, G. Tang, Z. Wang, Y.-Y. Zhao. M.-R Ke, B.-Y. Zheng, S. Huang, J.-D. Huang* and X. Li*. Phthalocyanine Aggregates as “Semiconductor-like” Photocatalysts for Hypoxic-Tumor Photodynamic Immunotherapy [J]. **Nat. Communi.** 2025, 16, 326. 2024. DOI: 10.1038/s41467-024-55575-2. (Research Article)