National Institute of General Medical Sciences

Houston Area Molecular Biophysics Program (HAMBP) Training Program

Grant No. T32 GM150582

Program Director: **Theodore Wensel**, PhD
Professor, Department of Biochemistry and Molecular Pharmacology
Baylor College of Medicine

http://www.gulfcoastconsortia.org/home/training/molecular-biophysics-hambp/

Meet the Trainees

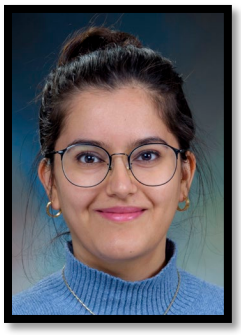
2025-2026

Mussie Araya
Appointed November 1, 2025 – October 31, 2026
Department of Integrative Biology and Pharmacology at University of Texas Health Science Center at Houston
Primary Mentor: Dr. Alemayehu A. Gorfe, Integrative Biology and Pharmacology (UTH)
Role of Membrane Lipid Composition in Arf1 Dynamics, Effector Engagement, and Ligand Binding

Small GTPase ADP-ribosylation factor 1 (Arf1) is a membrane-bound molecular switch of vesicle-mediated intracellular trafficking that maintains homeostasis of protein turnover in eukaryotic cells and initiates immune responses. Arf1 orchestrates the recruitment of cargo proteins and effector adapter protein type 1 (AP-1) to membranes to mediate vesicular trafficking between the Golgi and endosomes. During viral infection, viral proteins directly target the Arf1:AP-1 complex, and vesicular trafficking of defense proteins are subverted, resulting in down-regulation of the immune response. During the invasion and proliferation of many cancers, Arf1-mediated vesicle trafficking is upregulated. While membrane dynamics of many lipidated small GTPases are believed to facilitate effector engagement and cellular function as well as ligand binding, much less is known about the structural dynamics of Arf1 in its host membranes. This goal of my research is to understand and characterize the membrane dynamics of Arf1 monomer and in complex with its AP-1 in bilayers of different lipid composition, and the application of membrane dynamics to assess ligand binding properties of Arf1 monomer and in complex with effector. My approach involves development of bilayer-bound computational models of Arf1 and Arf1-AP1 complexes and conducting atomistic and coarse-grained molecular dynamics simulations to study their membrane binding, dynamics, effector interactions, and ligand binding in bilayers of complex lipid mixtures. The outcome of this proposed work will provide a basic understanding of how Arf1 functions in different membrane environments and identify small-molecule ligands that may modulate its function in specific endomembrane organelles.

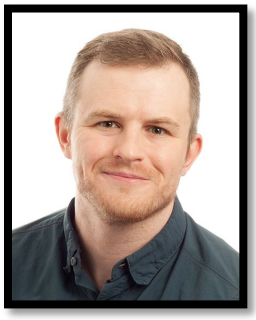
Erik Bergstrom
Appointed November 1, 2025 – October 31, 2026
Chemical, Physical & Structural Biology Graduate Program, Baylor College of Medicine
Primary Mentor: Dr. Joshua Riback, Molecular and Cellular Biology (BCM)
Nucleolar Nanoscale Remodeling Tunes Ribosome Biogenesis According to Environmental Signals
Biomolecular condensates are membranelles organelles formed by phase transitions driven by multivalent interactions among biomolecules. At the nanoscale, transient interactions within condensates create a dynamic meshwork, whose properties are dynamic and have the potential to influence biochemical processes. However, it is poorly understood if and how changes in the nanoscale organization of condensates relate to functional changes. My project aims to characterize how the nanoscale organization of the nucleolus, a condensate that is the site of ribosome biogenesis, is linked to nucleolar function by examining how nucleolar nanoscale organization and function are altered during stress.

Precious Castillo
Appointed January 1, 2026 – December 31, 2026
Department of Biosciences, Rice University
Primary Mentor: Dr. Cameron Glasscock, BioSciences (Rice)
Developing a High-throughput Binding Assay for Improving AI-Driven Design of DNA-Binding Proteins
DNA-binding proteins (DBPs) regulate essential cellular processes by controlling when and how genes are expressed. Recent advancements in artificial intelligence (AI) have enabled the design of DBPs, but these design tools are limited because they have only been trained on a small and biased set of known protein-DNA complexes. My project aims to develop a high-throughput platform capable of characterizing the binding interactions of tens of thousands of proteins against tens of thousands of DNA sequences. By combining high-throughput sequencing with automated protein purification and biophysical characterization, I will generate quantitative, reproducible maps of binding affinity and specificity. The resulting large-scale dataset will offer greater structural and sequence diversity than currently available. Training AI design models on this richer dataset will improve their accuracy in predicting protein-DNA interactions and designing candidate DBPs. The long-term goal is to enable the successful design of reliable, engineerable DBPs that selectively regulate disease-related genes. This capability would provide a foundation for new strategies in gene regulation for addressing diseases such as cancer, genetic disorders, and immune dysfunction.



Akanksha Gurtu
Appointed November 1, 2025 – October 31, 2026
Department of Pharmacology and Toxicology, University of Texas Medical Branch Galveston
Primary Mentor: Dr. Fernanda Laezza, Pharmacology and Toxicology (UTMB)
Uncovering the Non-Catalytic Signaling Role of GSK3β in Ion Channel Regulation: A Paradigm Shift in Kinase Biology and Neuropharmacology
Protein kinases are versatile regulators of signaling and highly conserved enzymes, best known for catalyzing ATP hydrolysis and phosphorylating substrates. Beyond this canonical role, kinases also perform non-canonical functions, such as mediating protein–protein interactions (PPIs). This project characterizes the non-canonical function of glycogen synthase kinase 3

beta (GSK3β), a kinase which drives early Alzheimer's disease-related neuronal network hyperexcitability (NH), through its interaction with the neuronal voltage-gated Na+ channel Nav1.6. Using surface plasmon resonance (SPR), high-throughput automated patch-clamp electrophysiology, and cheminformatics, I will define the PPI interface of the GSK3β/Nav1.6 complex and reveal the mechanisms underlying NH.



Tom Hennigan
Appointed November 1, 2025 – October 31, 2026
Chemical, Physical & Structural Biology Graduate Program, Baylor College of Medicine
Primary Mentor: Dr. Joshua Riback, Molecular and Cellular Biology (BCM)
Mapping the Nanoscale Mesh of Condensates to Understand Biomolecular Transport and Selectivity
Cells rely on tightly regulated biochemical reactions to survive. Many of these occur in membrane-less organelles called condensates, which compartmentalize essential processes such as ribosome assembly and mRNA storage during stress. Initially thought to be simple liquids, condensates display solid-like behaviors and are increasingly linked to diseases such as cancer and neurodegeneration. Yet their complexity and the field's infancy mean we still lack reliable ways to probe how they organize and function without membranes. My work focuses on developing molecular tools that measure condensate architecture at nanometer precision in living cells, to reveal how these dynamic assemblies form, function, and go awry in disease.

Haley Johnson
Appointed November 1, 2025 – October 31, 2026
Quantitative and Computational Biosciences Graduate Program, Baylor College of Medicine
Primary Mentor: Dr. Lynn Zechiedrich, Molecular Virology and Microbiology (BCM)
BaseHunter; A New Approach to Determining DNA Sequence in CryoEM Density Maps
Existing tools cannot model DNA sequence for cryoEM maps with resolution worse than ~3 Å. The industry standard is to replace the DNA density with a generic adenine-thymine repeat, which prevents any understanding of how DNA sequence impacts protein-DNA complexes. To fill this gap, we developed a shape-based approach that we call "BaseHunter" to distinguish shape differences between purines and pyrimidines, which is sufficient to determine DNA sequence. I aim to make BaseHunter an automated and quantitative method for analyzing cryoEM densities of protein-DNA complexes and plan to build it into widely used cryoEM modeling software, Chimera.

Kevin Juarez
Appointed January 1, 2026 – December 31, 2026
Biochemistry and Cell Biology Graduate Program, Rice University
Primary Mentor: Dr. Yimo Han, Materials Science and NanoEngineering (Rice)
Structural Investigation of the Foreign Body Reaction at Neural Interfaces
Neural prosthetics represent next-generation technologies for treating debilitating CNS disorders, but their long-term stability is critically limited by the Foreign Body Reaction (FBR). While the FBR has been investigated using optical microscopy, advances in microfabrication have shifted this paradigm, now requiring higher-resolution

techniques to identify ultrastructural hallmarks. This project aims to establish a standardized methodology using both room-temperature and cryogenic electron microscopy to characterize the probe-tissue interface. We hypothesize that novel ultrastructural FBR hallmarks, yet to be characterized, contribute to the instability at the prosthetic-tissue interface. These results will provide an updated structural understanding of the FBR, supporting the development of next-generation neuroprosthetics for rehabilitation and diagnostics.

Steven Nguyen
Appointed November 1, 2025 – October 31, 2026
Department of Biochemistry and Molecular Pharmacology, Baylor College of Medicine
Primary Mentor: Dr. Furqan Fazal, Biochemistry and Molecular Pharmacology (BCM)
Identifying RNA Structural Elements Dictating Subcellular RNA Localization Using RNA Proximity Labeling
RNA plays many roles in regulating gene expression, and while high RNA abundance often implies high expression, where an RNA is delivered is just as critical—like ordering a package that never arrives if it's sent to the wrong address. Cells use precise delivery mechanisms and RNA "zipcodes" to ensure transcripts reach the right place, and when this system fails, diseases like cancer and neurodegeneration can emerge. Recent evidence shows that many RNAs carry molecular delivery addresses that target them to mitochondria, where they serve as blueprints for key proteins, and high-throughput tools now allow us to discover these elements on a massive scale rather than one gene at a time. My goal is to leverage these advances to identify such zipcode elements, uncover their protein partners, and determine how they contribute to mitochondrial function.

Leah Peralta
Appointed January 1, 2026 – December 31, 2026
Department of BioSciences, Rice University
Primary Mentor: Dr. Yang Gao, BioSciences (Rice)
Structural Insights into DNA Polymerase θ in DNA Repair and Integration
DNA polymerase θ (Pol θ) is a multifunctional eukaryotic enzyme that repairs lethal DNA double-strand breaks through the Theta/microhomology-mediated end-joining (TMEJ) pathway. Pol θ is an emergent synthetic lethal partner in homologous repair-defective tumors and is essential for Agrobacterium-mediated transformation (AMT). Pol θ consists of an N-terminal helicase and a C-terminal polymerase linked by a long, disordered central region; although studies have resolved individual helicase and polymerase structures, the ATPase-driven dynamics of the helicase, the architecture of full-length Pol θ, as well as the higher-order assemblies that promote foreign DNA integration during AMT, are not defined. This project uses cryo-EM, fluorescence spectroscopy, and biochemical methods to investigate the structure, dynamics, and mechanisms of full-length Pol θ in DNA repair and integration.

Anya Porter

Appointed January 1, 2026 – December 31, 2026

Quantitative and Computational Biosciences Program, Baylor College of Medicine

Primary Mentor: Dr. Steven Ludtke, Biochemistry and Molecular Pharmacology (BCM)

Incorporating Microscope Effects into a Gaussian Reconstruction Method for Cryo-EM Data

Studying the structure of proteins and other biomolecules is key to understanding how the molecules function or misfunction in disease which can then be used for structure based drug design. Electron cryo-microscopy (cryoEM) is a technique used to image individual biomolecules and assemblies and study their structures and motions at an atomic level. The current methods used to convert 2D cryoEM images into high resolution structures use the weak phase approximation, which reduces the physical accuracy of how the imaging process is modeled and leads to representing atoms in the structure as a set of converging lines rather than the distinct objects they are. While these methods have been surprisingly effective, we are developing a new reconstruction method based on representing discrete objects as spherical Gaussian blobs. Preliminary results have already developed improved structures. I aim to further improve structures by extending this method to refine orientations, as well as better account for the physics of the microscope such as Ewald sphere curvature and beam tilt.

Nicolette Valdez

Appointed December 1, 2025 – November 30, 2026

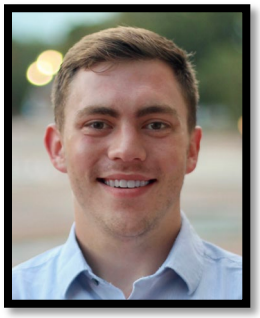
Department of Biochemistry and Molecular Biology, University of Texas Medical Branch Galveston

Primary Mentor: Dr. Matthieu Gagnon, Microbiology & Immunology (UTMB)

Structural Basis of Ribosome Rescue and Antibiotic Resistance

The ribosome is the molecular machinery responsible for translating mRNA into proteins through four crucial steps: initiation, elongation, termination, and recycling. During elongation, the growing polypeptide chain can interact with the ribosome and force the ribosome to stall prematurely. The ribosome is also forced to stall by ribosome-targeting antibiotics. Bacteria have evolved ways to detect and resolve ribosomal stalls by both the polypeptide chain and antibiotics. One such mechanism is the ATP-Binding Cassette subfamily F (ABC-F) proteins which can result in antibiotic resistance. This project will investigate the various ribosome rescue mechanisms employed by ABC-Fs by elucidating what ribosome features are altered, as well as what molecular interactions occur between the ribosome and ABC-F proteins. We will combine cryo-electron microscopy and biochemical methods such as protein purification and single-particle analysis to obtain high-resolution structures.

Affiliates



Andrew J. Ensenberger
Appointed November 1, 2025 – October 31, 2026
Department of Pharmacology & Toxicology, University of Texas Medical Branch at Galveston
Primary Mentor: Dr. B. Montgomery Pettitt, Sealy Center for Structural Biology and Molecular Biophysics (UTMB)
Investigating the Role of Polarizability in Biomolecular Condensate Structure
We use large-scale molecular dynamics simulations to help understand how atomic forces and, in particular, electronic polarizability shape the structure and electrostatic environment of biomolecular condensates. By comparing traditional fixed-charge force fields with more advanced polarizable and Drude models, we quantify how properties such as peptide solubility, internal water content, and the local dielectric constant differ between dilute solutions, condensates, and folded protein environments. This work is the link between atomistic dipole correlations and phase behavior, with implications for how cells organize electrostatic signaling inside membraneless organelles. Ultimately, these insights may help guide the design of therapeutics that selectively target proteins within condensates by exploiting their distinct dielectric environment.

Silvia Summers
Appointed November 1, 2025 – October 31, 2026
Department of Biochemistry and Molecular Pharmacology, Baylor College of Medicine
Primary Mentor: Dr. Lynn Zechiedrich, Biochemistry and Molecular Pharmacology (BCM)
Wielding DNA Looping and Supercoiling to Uncover Chromatin Structure and Dynamics
Nucleosomes, the building blocks of chromatin, regulate access to DNA. Most studies of nucleosomes are currently done with linear DNA, which lacks the structural changes associated with looping and torsional strain of DNA in cells. I utilize supercoiled minicircle DNA to model a more physiologically relevant environment. My project aims to uncover how DNA supercoiling and looping impact nucleosome structure, stability, and dynamics through single particle cryoEM and biophysical methods and to build the first polynucleosome model.

The HAMBP program is Administered by the:

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

www.gulfcoastconsortia.org
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The GCC is a collaboration of:
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University of Texas Health Science Center at Houston
University of Texas Medical Branch at Galveston
University of Texas MD Anderson Cancer Center
Institute of Biosciences & Technology at Texas A&M Health Science Center
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