



National Institute of
General Medical Sciences



Houston Area Molecular Biophysics Program (HAMBP)

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

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

Meet the Trainees

Currently appointed: Fall 2017 – Fall 2018



Sarah Alvarado

BioSciences, Rice University

Primary Mentor: George Phillips, BioSciences (Rice Univ)

Structural Determination of Hydroxylases and Methyltransferases for Anti-Cancer Drug

Design Collagen accounts for thirty percent of the human proteome and represents ninety percent of the extracellular matrix (ECM), reflecting its biomechanical significance as a scaffolding protein. Lysyl hydroxylase 2 (LH2) is responsible for the hydroxylation of telopeptide lysine residues and this modification modulates the biomechanical nature of fibrillar cross-links

that are formed in the ECM. Upregulation of LH2 has been implicated in cancer and a rare genetic disorder reflecting the importance of collagen hydroxylation regulation. Structural elucidation of LH2 using X-ray crystallography with collagen peptides will provide mechanistic insight into regulation of collagen biosynthesis.



J. Michael Bell

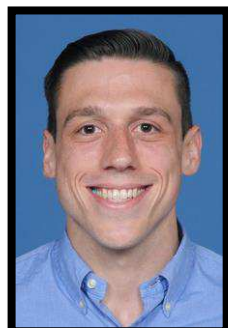
Quantitative and Computational Biosciences (previously SCBMB), Baylor College of Medicine

Primary Mentor: Steven Ludtke, Biochemistry (BCM)

Examining the structural variability and formation of nanodiscs via electron cryomicroscopy

My research combines biophysical studies of protein-lipid interactions with computational image processing of electron cryomicroscopy (cryoEM) data. In the wet lab, I am exploring the formation and structural variability of reconstituted nanodiscs, which are modeled after high-density lipoprotein (HDL) and used to study membrane proteins in their native environment.

In the dry lab, I am developing new approaches to correct for specimen motion by aligning sequential images acquired at high speed by direct detection devices (DDD). Additionally, I am exploring the influence of thickness-related electron absorption on three-dimensional electron cryotomography (cryoET) data and designing strategies to correct it.



David Boragine

Biochemistry and Molecular Biology, Baylor College of Medicine

Primary Mentor: Timothy Palzkill, Pharmacology (BCM)

Optimization of the BLIP-II Interaction with PBP2a as a Protein Based Therapeutic Option for MRSA

Methicillin-resistant Staphylococcus aureus (MRSA) confers resistance to the commonly prescribed β -lactam antibiotics through acquiring the novel penicillin-binding-protein (PBP2a), thus causing a rapidly growing global health crisis. Previously, our lab has discovered that β -lactamase inhibitory protein II (BLIP-II) can bind and inhibit PBP2a, albeit weakly. However, the binding affinity between BLIP-II/PBP2a can be enhanced through a directed evolution approach

to find a tighter binding BLIP-II variant in efforts to solve the first BLIP-II/PBP2a co-crystal structure. My project will focus on optimizing the BLIP-II/PBP2a binding interaction in order to further elucidate the binding mechanism via X-ray crystallography and to determine the effect of BLIP-II on β -lactam efficacy versus MRSA bacteria. Overall, this work has the potential to aid drug discovery by serving as a promising foundation for developing a potential protein based therapeutic option, or a diagnostic tool, for clinical use.



Jacob Ezerski

Physics, [University of Houston](#)

Primary Mentor: Maragret Cheung, Physics (Univ of Houston)

Charged residue mutation in CaMKII peptide alters CaM binding mechanism through alternate encounter complex contacts

My project seeks to model the calcium ion signaling cascade that occurs between the calcium sensitive protein calmodulin (CaM) and one of its biologically significant targets, calmodulin-dependent protein kinase II (CaMKII). Our model seeks to explain the drastic change in kinetic

binding rates between CaM and CaMKII illustrated the CaM trapping mechanism due to charged residue mutations.



Andrei Gasic

Physics, [University of Houston](#)

Primary Mentor: Maragret Cheung, Physics (Univ of Houston)

Critical Phenomena in the Temperature-pressure-crowding Phase Diagram of a Large Protein

My research aims to answer an important question at the interface of physics and biology: how does the crowded cellular environment influence the dynamics of a protein? Proteins are susceptible to small environmental agitations, yet stable enough to maintain structural integrity.

These apparently competing behaviors are commonly exhibited by physical systems near a critical point, where distinct phases merge.

By varying temperature, pressure, and the amount of crowding from surrounding macromolecules, we are able to characterize the structural phases of a large protein, phosphoglycerate kinase (PGK), in a cellular environment. Using a combination of theory and computer simulation, I demonstrate a critical transition where several phases of PGK coexist. At the critical regime, we observe fluctuations that produce large conformational changes without a costly barrier, which would be necessary for enzymatic function.



Douglas Litwin

Biochemistry and Molecular Biology, [University of Texas Health Science Center - Houston](#)

Primary Mentor: Vasanthi Jayaraman, Biochemistry and Molecular Biology (UT Health)

Modulation of glutamate receptors by auxiliary proteins and ions: a structural investigation

The glutamate receptor family is responsible for the majority of excitatory neurotransmission in the central nervous system and comprises the AMPA, kainate and NMDA receptor subtypes.

The kainate receptor subtype is of particular interest due to its function in both postsynaptic neurotransmitter reception and the presynaptic regulation of neurotransmitter release.

Additionally, kainate receptors have been shown to be functionally modulated by sodium ions (Na⁺) and auxiliary proteins (NETOs). These modulators contribute to the functional specificity of individual glutamatergic synaptic events; however, no data is available regarding the structural dynamics and conformational states involved in their modulation. The aim of this project is, therefore, to characterize the structural dynamics and conformational states involved in the modulation of kainate receptors by Na⁺ and NETO proteins.



Jonathan Mercado

Molecular and Cellular Biology, [Baylor College of Medicine](#)

Primary Mentor: Francis T.F. Tsai, Biochemistry and Molecular Biology (BCM)

Targeting Leishmania Hsp100 to abolish infective parasite stage differentiation

Leishmania is the causative parasite of the vector-borne neglected tropical disease,

Leishmaniasis. The activity of the *Leishmania* Hsp100 chaperone protein allows for the parasite to differentiate into its infective stage in humans. My project will provide insight into the potential use of small molecules for manipulating chaperone function. Identifying small

molecules that interact with *L.mexicana* Hsp100 could then be used as chemical probes for future studies to understand Hsp100 activity (or lack thereof) during mammalian infections. The results of my work will be used to combat Leishmaniasis and other human infections caused by pathogenic microbes.



Dan Nguyen

Biochemistry and Molecular Biology- MBET, Univ of Texas Medical Branch at Galveston

Primary Mentor: Junji Iwahara, Biochemistry and Molecular Biology (UTMB-Galveston)

Biophysical Analyses of Intermolecular-Ion Pairs in Protein-DNA Complexes

Ion pairs, which are formed by electrostatic interactions between the cationic and anionic moieties of proteins and nucleic acids, play a significant role in protein-DNA interactions. Ion pairs have been observed in numerous three-dimensional structures of protein-protein and protein-DNA/RNA complexes, and are even found in protein-drug complexes. However, despite the importance of ion pairs for macromolecular interactions, many properties remain unknown and need to be elucidated. It is crucial to deepen the understanding of the roles of ion pairs in order to improve drug design and macromolecular engineering. This is why my project focuses on understanding how dynamic transitions of ion-pairs affect protein-DNA interactions on a macromolecular level.



Matthew Ykema

BioSciences, Rice University

Primary Mentor: Yizhi (Jane) Tao, BioSciences (Rice Univ)

Characterizing Astrovirus Particles To Investigate The Mechanism Of Proteolytically-Mediated Viral Maturation

Understanding the structure of viral capsid proteins allows for the determination of key infectious domains and targets for vaccines and anti-viral compounds. One target for structural studies is the human Astrovirus, a single-stranded RNA virus that causes gastroenteritis in children and immunocompromised individuals. The virus has a unique maturation process, in which the capsid must be proteolytically cleaved in order to induced host cell entry and exit. I aim to identify the structural changes of the capsid that occur during the proteolytically-mediated maturation using X-ray crystallography and cryo-electron microscopy.

The TIPS program is Administered by the:



www.gulfcoastconsortia.org

Questions: Contact Vanessa Herrera

herrera@rice.edu , (713)348-4752

The GCC is a collaboration of:

Rice University

Baylor College of Medicine

University of Houston

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