2nd Annual IBNR Graduate Student/Postdoctoral Research Showcase

Monday, April 29, 2019
Campus Center Atrium

NJIT
New Jersey Institute of Technology

MESSAGE FROM THE PROVOST

I congratulate the NJIT Institute for Brain and Neuroscience Research (IBNR) for their continued commitment to research and student training. I also express my personal appreciation to the co-directors, Professor Namas Chandra and Professor Farzan Nadim, for their leadership and efforts in organizing this important student/postdoctoral research showcase for graduate students and postdoctoral fellows. This is a showcase of NJIT's growing research talent, and we are proud of your efforts and accomplishments.

NJIT has been awarding doctoral degrees for more than 50 years. Since 2014, the Ph.D. student population has increased by 30 percent, while the number of degrees awarded last year was 73, the highest ever. NJIT graduate students in neuroscience and neural engineering have the opportunity to collaborate with faculty who are conducting exciting, cutting-edge research. This research is built around multidisciplinary efforts that encourage partnerships among disciplines and with other educational institutions, private enterprises and government agencies. We have already more than doubled research funding from external sources since 2014, the baseline for the university's strategic plan, *2020 Vision*. As evidence of our remarkable transformation, NJIT recently joined the top tier of research universities with a designation of R1 by the Carnegie Classification®. We are one of just three universities in New Jersey to occupy the category indicating "very high research activity."

This IBNR event features and promotes faculty research while simultaneously providing a platform for students at all levels of experience to practice the crucial art of communication. For each student, whatever your career plans are beyond graduation, you will surely find yourself describing your work, advocating for your ideas and explaining your results in a world where collaboration and communication grow ever more important. This event provides you the perfect environment to practice and improve your skills with an encouraging and receptive audience in a friendly setting. So seize the opportunity, enjoy it and learn from it.

Sincerely,

Fadi P. Deek

Provost and Senior Executive Vice President

MESSAGE FROM THE SENIOR VICE PROVOST

The World Health Organization calls neurological disorders — from strokes, to dementia, to traumatic brain injuries, to Parkinson's disease — among "the greatest threats to public health." With aging populations throughout much of the developed world, their incidence is rising. Accordingly, transdisciplinary research and its translational convergence aimed at improving the characterization and treatment of neurological disorders and brain injuries is now a major focus of the principal federal research funding agencies, including the National Science Foundation (NSF), the National Institutes of Health (NIH) and the U.S. Department of Defense (DoD).

Combining breakthroughs in imaging technology and biomolecular research that shed new light on the brain's fundamental operations, neuroscientists can now observe, for example, the activation of cells in the cerebral cortex that equip animals to navigate within territorial grids, and trace the formation of a sea slug's memory of a predator's attack. These same technological advances are revealing the routes by which genetic mutations unravel executive functioning, including the accretion of protein fragments that clog neural pathways and erase memories in people with Alzheimer's disease.

Researchers at NJIT take a multi-pronged approach to understanding neural circuits and their disruption. Neurobiologists Farzan Nadim, Dirk Bucher and Gal Haspel examine the simple nervous systems of animals such as crustaceans and worms, while mathematicians Casey Diekman and Horacio Rotstein develop models of neuronal patterns. Biochemist Yong-Ick Kim, who conducts laboratory analyses of the biochemical building blocks of the circadian clock, works with them to examine hypotheses about entrainment mechanisms — the means by which brainwave oscillations synchronize with external stimuli.

NJIT is equally committed to mitigating the effects of disabling neurological disorders and injuries by designing devices and therapies that help people function to their full potential. In these efforts, our neurorehabilitation and biomechanics engineers work closely with imaging experts such as Bharat Biswal, whose early work gave rise to important research in clinical neuroscience, including the mapping of brains affected by diseases such as Alzheimer's and developmental conditions such as ADHD and dyslexia. Biomedical engineers Tara Alvarez, Xiaobo Li and Antje Ihlefeld study the rerouting of brain patterns in response to visual, cognitive and hearing disorder therapies through interdisciplinary translational research with neural signal analysis, neuroimaging and neurobiological modeling and simulation to clinical applications. Partnering with the Kessler Institute and hospital-based rehabilitation centers, Sergei Adamovich and Saikat Pal continue to further develop exoskeletons and other devices that will help people with neurological disorders participate in classrooms and in workplaces. Namas Chandra and Bryan Pfister, who study traumatic brain injury, collaborate with New Jersey-based physicians and medical researchers on their work for the DoD.

It is very exciting to see the breadth of expertise represented by these groundbreaking new projects at the Institute for Brain and Neuroscience Research (IBNR), which include basic and applied research that has significantly contributed to the recent designation of NJIT as an R1 (top-tier) research institution under the Carnegie Classification®. With continuously evolving transdisciplinary synergy at the IBNR, we look forward to further enhancing our collaborative basic, applied and translational research with increased external funding, and earning recognition as a major research resource in New Jersey and the nation.

Congratulations to all of today's presenters!

Sincerely,

Atam P. Dhawan

Senior Vice Provost for Research

FROM THE DIRECTORS

We wish the graduate students, postdoctoral fellows and research associates will use this research showcase forum to understand the scope of research activities in the areas of neuroscience and neural engineering at NJIT. We hope you take advantage of the expertise of the IBNR faculty across departments and laboratories within NJIT, and help the IBNR promote interdisciplinary research in the neurosciences. The importance of this day is to focus on our current research activities in the areas of neuroscience and neural engineering in order to understand the potential for growth and collaboration. Today's research showcase is a testament to the outstanding research in our laboratories that we can further build upon in the future.

A major addition in the past year was three consortium groups that we have created within IBNR to include multidisciplinary and synergistic efforts through research. These groups include external collaborations with Princeton University, Mt. Sinai School of Medicine, Columbia University and its Medical Center, the University of Pennsylvania, the Veterans Administration of East Orange and various international institutions. The three consortiums are led by Bryan Pfister, a professor of biomedical engineering, Horacio Rotstein, a professor of mathematical biology and computational neuroscience and Casey Diekman, an associate professor of mathematical sciences. Each of these groups is interdisciplinary across three or four departments within NJIT and external institutions. We look for great things to come out of them this year and for years to come.

Namas Chandra and Farzan Nadim, IBNR Directors

Namas Chandra *is a distinguished professor of biomedical engineering and the founding director of the Center for Injury Biomechanics, Materials, and Medicine and the Institute for Brain and Neuroscience Research. Chandra is a fellow of ASME and AIMBE, and has 33 years of academic experience at NJIT, Florida State University (FSU) and the University of Nebraska-Lincoln (UNL) and 10 years of industrial experience. He was a university distinguished research professor at FSU and an associate dean for research at UNL. Chandra's research on the micromechanics of materials and biomechanics of blast-induced brain injury has been continuously funded by the U.S. Department of Defense since 1987. The blast facility directed by Chandra was recognized as a top 10 laboratory in the country by Popular Science, and pioneered shock tube design. He has published over 227 articles, including 116 in archival journals, has been cited 4160 times, edited four books and two book chapters, and delivered 75 colloquiums and six workshops. He has also supervised more than 50 master's, Ph.D. and post-doctoral students.*

Farzan Nadim *is a professor of neurobiology in the Federated Department of Biological Sciences and a founding director of the Institute for Brain and Neuroscience Research. Nadim's research focuses on understanding the neuronal and circuit mechanisms underlying dynamic activity in the central nervous system, with a focus on oscillatory networks. Nadim's research has been continuously funded by the National Institutes of Health since 2001.*

ABOUT INBR

IBNR Mission Statement

The Institute for Brain and Neuroscience Research (IBNR) aims to be the primary home for all neuroscience research initiatives at NJIT. Its goals are to promote high quality research in neuroscience and neural engineering, to train graduate students and postdoctoral fellows in an interdisciplinary environment so that they can compete in the academic and industry markets, and to identify and develop synergies among research groups across different departments and colleges. IBNR will holistically represent neuroscience and neural engineering research and training at NJIT in order to provide visibility at the national and international levels. IBNR will collaborate with similar institutes at Rutgers University, Princeton University and other local academic institutions and local industry to stimulate the formation of neuroscience research and education at the state level.

Relationship to the Departments, Colleges and University

Neuroscience and neural engineering are among the primary areas identified in the NJIT *2020 Vision* strategic research plan. IBNR provides a central hub for realizing NJIT's research initiatives in these areas. IBNR is an intercollegiate institute and its goals are aligned with both those of Newark College of Engineering and the College of Science and Liberal Arts. IBNR coordinates and provides collaboration incentives for faculty in biomedical engineering, biological sciences, mathematical sciences, physics and other departments.

About IBNR

The goal of the Institute for Brain and Neuroscience Research (IBNR) is to promote research and training in neuroscience and neural engineering and to provide an overall contact point for neuroscience initiatives at NJIT. IBNR encompasses basic, applied and translational neuroscience research of faculty members from a number of NJIT departments in Newark College of Engineering and the College of Science and Liberal Arts.

IBNR has two primary aims: to promote high-quality interdisciplinary research by developing synergies among research groups and to train graduate students and postdoctoral fellows in an interdisciplinary environment so that they can compete in the academic and industry markets.

The research goals of IBNR focus on fostering collaborations through seed grants and sponsoring graduate students involved in interdisciplinary research. The IBNR runs a neuroscience-themed seminar series and sponsors a program to support visiting research scholars at NJIT, both for short durations and for sabbatical leaves.

The training program of IBNR is currently under development and involves three components: IBNR is in the process of establishing an interdisciplinary doctoral program in neuroscience and neural engineering; IBNR promotes multidisciplinary undergraduate research across different labs, centers and research groups; IBNR will sponsor a training workshop series for postdoctoral scholars.

In our vision, the research and training components of IBNR work jointly to promote excellence in research and training in basic and applied neuroscience by supporting the interests of faculty and students at NJIT.

Namas Chandra
Distinguished Professor of Biomedical Engineering and Director

Farzan Nadim
Professor of Neurobiology and Director

KEYNOTE SPEAKER MESSAGE

Dr. Przekwas is the co-founder of CFD Research Corp. and is currently heading the Computational Medicine and Biology Division with the goal to develop multiscale computational tools for modeling human body biomechanics, physiology, organ/tissue/cell biology, injury, and pharmacology. He has been the principal investigator (PI) and co-PI on R&D projects with DARPA and the U.S. Department of Defense focused on biotechnology, military medicine and soldier protection, particularly on Traumatic Brain Injury. His latest projects involve modeling and design of in vitro "human on the chip" for drug discovery and development. He has published more than 250 papers and two book chapters.

"I am honored to be the keynote speaker at this wonderful research showcase event and am extremely humbled to meet all of you today. I see tremendous growth and potential within the Institute for Brain and Neuroscience; it is led by two great leaders in their respective fields. Additionally, it is a good foundation for future collaboration in R&D for military and civilian applications. After today, I am looking forward to working with the IBNR team and with other scientists at the Institute. Congratulations again on this extraordinary research event."

IBNR KEY NOTE PRESENTATION

Dr. Andrzej Przekwas

Chief Technology Officer
CFD Research Corporation

IBNR, NJIT, Newark, N.J. April 29 2019

A Computational Framework for Personalized Monitoring of Blast Exposure in Military Training and Operations

During training and operations, military personnel may be repetitively exposed to low-level blast waves while using explosives to gain entry, firing the heavy weapon systems or high-caliber sniper rifles. This repeated exposure, even within allowable limits, has been associated with cognitive deficits similar to that of accidental and sports concussions. There is a great need to understand and mitigate any potentially harmful effects from blast exposure. An integrated experimental and computational framework can help in better understanding the physics of blast exposure and neurological responses and to establish safety measures for training and combat.

Dr. Przekwas will present a novel framework for automated reconstruction of the weapon blast "signature" and overpressure loading on humans using wearable pressure sensor data. This framework utilizes data collected by pressure sensors on human subjects or equipment as inputs to an inverse problem solver to calculate the location and charge mass of an explosive device and detailed pressure loads on human bodies exposed to the blast wave. The results could be used for calculation of blast wave loads on the whole human body and on specific organs vulnerable to blast loads, such as the head and torso. The system will be demonstrated as a live, real-time, web/cloud-based CoBi simulation.

IBNR CONSORTIUM GROUPS AN OVERVIEW

Neuronal Oscillations Consortium: Experiments, Modeling and Computations

Horacio Rotstein
Group Leader

This group of researchers (faculty, postdoctoral researchers and students) is leading the efforts towards building successful scientific interactions and collaborations among the members of the NJIT and Rutgers University campuses, with other groups in the NYC/N.J. area, and visitors from other research institutions around the world.

An important activity of the collective is the weekly journal club where the participants discuss their research and ideas, present papers from the literature, and host visitors from other institutions who discuss their work. From its creation in 2016, these meetings have been highly interdisciplinary, involving theoretical, computational and experimental scientists, and have created bridges among the different communities and perspectives.

We are currently organizing a workshop to discuss ideas and approaches to the modeling and computations of neuronal oscillations based on experimental data across levels of organization. Some of the perspective groups we plan to invite are from NYU, Columbia University Medical Center, Mt. Sinai School of Medicine, the University of Pennsylvania, Princeton University, Rutgers and a few more.

Circadian Clock Consortium

Casey Diekman
Group Leader

Circadian (~24-hour) clocks can be found in almost all organisms including bacteria, plants and humans. Many health problems, including neurodegenerative diseases and depression, are associated with disruptions of the circadian clock. An important aspect of circadian rhythm generation that remains poorly understood is the link between intracellular molecular clocks based on transcriptional and translational feedback loops, and the neuronal mechanisms with which they interface.

During the first year of its existence, this collaborative group is exploring the most salient problems in the circadian field by hosting visits from prominent researchers, including Alessio Franci (National Autonomous University of Mexico), Ravi Allada (Northwestern University), Kristin Tessmar-Raible (University of Vienna) and Birendra Mallick (Jawaharial Nehru University). These two-day events consist of the visitor giving a formal seminar, leading an informal group discussion, and meeting with individual faculty members and students.

To gain insight into clock mechanisms, our consortium is going beyond the dominant model organisms used in the circadian field (mice, Drosophila, Neurospora and cyanobacteria) to study circadian clocks in C. elegans, zebrafish, crayfish and cave dwellers.

IBNR CONSORTIUM GROUPS
AN OVERVIEW

The Axonal Dynamics Consortium

Bryan Pfister
Group Leader

Axonal function is fundamental to most forms of neural signaling. Pathological changes in axonal function are central to the progression of nervous system injury and disease and contribute to acquired cognitive deficits. Neuronal degeneration involves a dynamic change in the structure and function of axons that can persist for long periods of time. With the advent of new technical approaches like sophisticated optical imaging techniques, and connectomics (in which axons naturally play an important role), we have a renewed interest in how the axon structure and function changes due to the perturbations from injury and disease. It is now clear that axons have substantially more interesting dynamical properties and therefore play a much more important role in shaping neural signal processing than historically known. It remains a challenge to synthesize novel findings on axons from molecular, anatomical, and physiological approaches, both in the context of normal function and in pathology and injury.

Our consortium research objectives are to bridge molecular, biophysical, physiological and biomechanical levels, where no single investigator nor the existing collaborations have conceptual and methodological expertise that spans all these levels. In the Center for Biomechanics, Materials and Medicine, we have collective strength in the area of axonal function through biochemical, structural and electrophysiological analysis. The overall goal of the consortium is to create a larger group that regularly meets for scientific discussion and cross-fertilization of ideas, with an emphasis on interactions among postdoctoral researchers and students. The consortium strives to use the strengthening of interactions to identify additional groups within IBNR, our existing collaborators at the University of Pennsylvania, Rutgers University, U.S. Department of Defense, the Veterans Administration and develop new collaborations with other research groups.

FACULTY


Sergei Adamovich


Amitabha Bose


Dirk Bucher


Namas Chandra


Casey Diekman


Brooke Flammang


Eric Fortune


Simon Garnier


Jorge Golowasch


James Haorah


Gal Haspel


Antje Ihlefeld


Victor Matveev


Farzan Nadim


James McLaurin


Camelia Prodan


Bryan Pfister


Horacio Rotstein


Mesut Sahin


Daphne Soares


Kristen Severi


Yong-Ick Kim


Monuel Aulov
Business Manager

PROGRAM

Campus Center Atrium

Welcome

10 a.m. – 10:20 a.m.: Introduction of Provost Fadi Deek
Provost and Senior Executive Vice President

Atam Dhawan, *Senior Vice Provost for Research*

Namas Chandra, *Distinguished Professor of Biomedical Engineering and Director of IBNR*

Farzan Nadim, *Professor of Neurobiology and Director of IBNR*

10:20 a.m. – 10:25 a.m.: Speaker Introduction
Monuel Aulov, *Business Manager, IBNR & CIBM3*

10:25 a.m. – 10:50 a.m.: **IBNR Forum: Keynote Lecture:**
"Integrated Framework for Computing, Recording and Monitoring Blast Exposure during Military Training and in Operations"

Dr. Andrzej J. Przekwas, *Program Director, Chief Technology Office*
CFD Research Corporation

11 a.m. – 12 p.m.: **Consortium Group Leaders' Presentations**
(Overview)

12 p.m. – 1:30 p.m.: **Lunch and Networking**

1:30 p.m. – 2:30 p.m.: **Graduate Student/Postdoctoral Presentations**
(Data Blitz)

2:30 p.m. – 4 p.m.: **Poster Presentations and Networking Session**

This IBNR Research forum is a featured event for the Institute and is made possible in part by the generous support of the NJIT Research Enterprise.

ABSTRACTS

Agnieszka Agas

Graduate Student, Department of Biomedical Engineering, Center for Injury Bio Mechanics, Materials and Medicine – CIBM3
Advisor: James Haorah, Associate Professor of Biomedical Engineering

Title: Profiling the Effects of TAT on Neurotoxicity During Active HIV-1 Infection

TAT is the trans-activating protein involved in viral replication of human immunodeficiency virus associated acquired immunodeficiency syndrome or HIV/AIDS. TAT is actively shedded by infected cells and can be found circulating in blood and cerebrospinal fluid. A strong association exists between neuronal death and elevating levels of TAT concentration. To investigate the gradation of TAT-induced neurotoxicity we measured neuronal viability and cell appearance in the range of concentrations found in HIV-1 infected persons. Effects of ethanol exposure on toxicity were also considered as ethanol is recommended to work in tandem with HIV-I infection to exacerbate disease progression. We observed toxicity at the lowest physiological level of TAT concentration and progressive decline in neuronal viability paralleling increasing concentration thereafter. Toxicity featured neurite degradation and loss of functionality, fragmentation of axons (long filaments) and shrinkage of dendrites (short filaments), followed by necrosis of the soma. We also found that neuronal aggregates were less affected than single cell neurons. Paradoxically, the toxic effects of low concentration TAT were attenuated with low dose ethanol exposure. The data supports the toxicity of TAT and maps its effect on neurons. Future research will involve testing the neurotoxicity of TAT in the setting of interactive neuroimmune cell culture (brain endothelial cells, astrocytes, microglia, and neurons) with or without the presence of alcohol.

Nima Alamatsaz

G*raduate Student, Department of Biomedical Engineering, Neural Engineering of Speech and Hearing (NESH Lab)*
Advisor: Antje Ihlefeld, Assistant Professor of Biomedical Engineering

Title: Interaural time Differences: Lateralization Adapts to Stimulus Space

A wide range of species relies on sound localization for both navigation and auditory scene analysis. For low-frequency sound, interaural time differences (ITDs) are the dominant cue for determining the direction of a source in the horizontal plane, a phenomenon called sound lateralization. The mechanisms by which the nervous system maps ITD into perceived sound direction are incompletely understood. In anechoic spaces, a given source angle in the horizontal plane typically gives rise to the same ITD, across a wide range of source distances. However, in everyday environments where background sound and reverberant energy are often present, ITDs are much less reliable indicators of source direction. This raises the possibility that when estimating source direction, a listener's interpretation of ITD changes depending on the context of the listening environment. Indeed, previous work shows plasticity in perceived sound direction across a wide range of conditions, including ear plugging, modifications to shape of the pinnae, prolonged exposure to constant interaural delays, in presence of preceding distractors, long-term procedural learning and short-term stimulus history. However, we have an incomplete understanding of short-term adaptation of sound lateralization based on the overall range of ITDs.

Here, we randomly assigned 34 naïve normally-hearing listeners to 4 groups. Using a target-pointer matching task without visual feedback, listeners of three groups were trained on ITD lateralization for 3 sessions. A fourth naïve control group was tested without training. All 4 groups of listeners then performed a lateralization task which asked them to identify and plot the internal image of low-frequency noise tokens. For both training and testing, one trained group (RIGHT HEMI) was only presented with positive ITDs (right hemisphere), the second trained group (LEFT HEMI) only with negative ITDs (left hemisphere), and the third trained group (BOTH HEMIS) with the full range of bilateral ITDs (both hemispheres). The naïve group was tested with positive ITDs only (NAÏVE RIGHT HEMI). Listener responses across different groups and stimulus conditions were analyzed with a Nonlinear Mixed-Effects Model (NLME). Results show robust response expansion in all unilaterally tested listeners towards the contralateral side, with a larger effect for the trained groups versus the naïve. In contrast, bilaterally trained listeners did not display any response bias. Together, these results show that perceived direction adapts rapidly to stimulus space. Results will be discussed in the context of assessing spatial perception in patient groups with impaired binaural cues, including bilateral cochlear implant users and cochlear implant users with single-sided deafness.

Abdus Ali

Graduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Bryan Pfister, Professor and Chair of Biomedical Engineering
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: itle: Spatial and Temporal Changes to the Brain's Strains During Blunt Trauma Using Softer Surrogate Brains

The objective of our research is to determine the biomechanical link between the traumatic brain injury event and damage to the brain. Human surrogates, or dummies are used extensively to study injury scenarios. Dummies are instrumented and undergo experiments with a combination of load cells, strain gauges, pressure gauges, angular rate sensors, and accelerometers recording the event. For the head, the motion of the skull and intracranial pressures are typically captured. This approach does not capture any of the complex motions of the brain inside the skull. We developed head surrogates, which allow for visualization of the deformations occurring in the brain through a 'window' in the skull. These visual markers on the surface of the brain are recorded during blunt injury scenarios in a laboratory setting and motion tracked. We have shown that the span and degree of tissue deformation varies across different regions of the brain and is determined by the biomechanical parameters of the injury event (velocity, momentum, direction) and the anatomical boundary conditions of the human head, brain and neck. The focus of this report is the differences in strain distribution for blunt trauma with three surrogate brain formulations; 5%, 10%, and 20% synthetic ballistics gelatin (Clear Ballistics). Dummies were impacted with a ~10lb magnesium alloy headform at 3mph at either the crown or forehead. Maximum principal shear strains (~21-25%) in the brain during crown and forehead impacts were near the point of impact, but during forehead impacts the contrecoup region of the brain also experienced similarly large strains. Regions of the brain surrogate with increased strains remained elevated regardless of the ballistics gelatin percentage (at 20%, 10%, or 5%). However, the distribution of strain values shifted toward larger values as the gel became less stiff and the regions of increased strain had larger peak values.

Aswati Aravind

G*raduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3*
Advisors: Bryan Pfister, Professor and Chair of Biomedical Engineering
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: Behavioral Deficits in a Combined Model of Blast and Blunt Traumatic Brain Injury

Traumatic Brain injury (TBI) is the major cause of death and decreased quality of life in soldiers. Military personnel are often exposed to both blast overpressure waves and blunt impacts due to falls or motor vehicle accidents. While the cumulative effects of repeated exposure to a blast or blunt TBI has been under investigation, a combination of blast and blunt impact is yet to be examined. Here, we present a model of combined blast and blunt impact and a comparison of the neuronal loss and behavioral deficits caused by the single and combined impacts. Ten-week-old Sprague Dawley rats were exposed to primary blast (180 KPa) followed by a craniectomy (-3mm from bregma, 3.5mm lateral to the sagittal suture) to expose the site of blunt impact. The fluid percussion injury (FPI – 1.6-1.9 atm) was carried out 24 hrs post blast exposure using the pendulum FPI device. Single impact groups of blast or blunt animals as well as control groups of sham FPI, sham blast and blast + sham FPI were also generated. Immediate physiological measures such as apnea, righting reflex and weight loss 24 hrs post impact were measured across groups. Cognitive and motor functions were investigated using the Morris Water Maze test and Rota-Rod task tests respectively. Coronal hippocampal sections of the rat brains were stained for neurodegeneration with Fluoro-jade at 4hr and for long term neuronal survival using cresyl violet at 34 days post impact. Neurodegeneration and neuronal loss in the ipsilateral hilus of the combined impact was found to be significantly higher than the single impact groups ($p<0.008$). Both the FPI and combined impact animals manifested cognitive and motor deficits that improved over time. Combined impact animals showed significantly decreased cognitive performance than blunt animals at post injury day 2 ($p<0.008$). These results suggest that the blast impact conditions the brain to increased injury on a subsequent blunt impact. Ongoing investigations attempt to identify the biochemical sequelae leading to the increased susceptibility observed.

Yinbo Chen

Graduate Student, Department of Mathematical Sciences
Advisors: Victor Mateev, Professor of Mathematical Sciences, Cyrill Muratov, Professor of Mathematical Sciences

Title: Stationary Approximations to Single-Channel Ca2+ Nanodomains

Many fundamental cell processes such as neurotransmitter and hormone release are activated by Ca2+ influx through transmembrane Ca2+ channels. Since optical Ca2+ imaging has very limited spatial and temporal resolution, computational modeling played an important role in the study of vesicle release and other cell processes activated by local Ca2+ signals. Computational studies revealed that localized Ca2+ elevations, termed nanodomains, form and collapse very rapidly in response to Ca2+ channel gating. This suggests that quasi-stationary solutions of reaction-diffusion equations describing Ca2+ ion movement and binding to intracellular Ca2+ molecules (termed Ca2+ buffers) capture the properties of Ca2+ nanodomains with sufficient accuracy. Previously developed approximations of stationary Ca2+ nanodomains such as the rapid buffering approximation (RBA), and the linear approximation proved very useful for understanding the properties of local Ca2+ signals. However, the accuracy of these approximants is restricted to specific regions in parameter space, and apart from RBA, they cannot be extended to more realistic biological buffers with multiple Ca2+ binding sites. Here we present several new approaches to approximate stationary single-channel Ca2+ nanodomains with more accuracy in a wider range of model parameters. One of the new methods is based on matching the coefficients of short-range Taylor series and long-range asymptotic series of the Ca2+ concentration distance dependence using simple interpolants. A second method is based on the variational approach, and involves a global minimization of a relevant functional with respect to parameters of a chosen approximation. Finally, we present a global error reduction method that provides an even better approximation accuracy over a wide range of distances and parameter values. Importantly, some of the presented approximants can be extended to more realistic buffers with two binding sites characterized by cooperative Ca2+ binding, such as calmodulin.

Yiming Cheng

Graduate Student, Department of Biomedical Engineering, Center for Injury Bio Mechanics, Materials and Medicine – CIBM3
Advisor: James Haorah, Associate Professor of Biomedical Engineering

Title: Mechanisms of a New Waste Metabolites Clearance Pathway in the Brain

The lack of lymphatic clearance in the brain promotes the progression of neurological disease such as Alzheimer's disease (AD) and Parkinson's disease (PD). This is in part due to inability of cerebrospinal fluid (CSF) system for effective clearance of large waste metabolites like beta-amyloid protein. The present studies uncovered the dynamic exchange mechanisms of large size waste metabolites clearance from interstitial space and from CSF movement into the circulation via the perivascular space. We addressed this clearance mechanisms by tracing the dynamic bio-distribution of 2000 kDa and 3 kDa contrast fluorescent dye mixture movement that were injected through intracisterna magna or intracranial. The former injection route showed the movement of the large molecular weight tracer through the subarachnoid and subsequent penetration along the para- and peri-vascular space, while the later injection route moved into the perivascular space via the interstitial space and subarachnoid path. We found that the dilative/relaxation reactivity of endothelial cells and smooth muscle cells regulated the inter-convective osmotic gradient movement of the waste metabolites towards the perivascular space as well as purging of metabolites into the circulation. Intriguingly, low-dose ethanol expedited the dynamic clearance of waste metabolites by increasing the arterial endothelium-smooth muscle cell reactivity via the activation of endothelial specific nitric oxide synthase (eNOS). Whereas, chronic ethanol intake impaired this expedite clearance by activating the inducible nitric oxide synthase (iNOS) in arterial endothelium and smooth muscle cell. The finding has significant impact in preventing the commonly observed cerebral amyloid angiopathy in AD.

Kathryn Gallman

Graduate Student, Federated Department of Biological Sciences
Advisor: Daphne Soares, Professor of Biological Sciences

Title: Evolutionary Changes in Catecholaminergic Neuromodulation Underlie Behavioral Shifts in the Cavefish, Astyanax Mexicanus

Neuromodulation can cause alternate behavior responses to a stimulus in two animals with similar underlying circuitry. This makes neuromodulatory systems powerful tools evolutionary tools that shape how an animal interacts with its environment. Here we used the surface and cave forms of the teleost fish Astyanax mexicanus, that have opposing emotionally motivated response behaviors to the same water disturbance stimuli to reveal evolutionary changes in catecholaminergic neuromodulation. Catecholamines, such as dopamine and norepinephrine, play vital roles in a diversity of nervous system functions including, motor control, emotional response, arousal promotion, conditioned learning, and memory consolidation. Therefore, deficits or overproduction in catecholamine levels can have severe behavioral repercussions. Tyrosine hydroxylase is the rate-limiting enzyme in the biosynthesis of catecholamines and its expression throughout the brain is indicative of catecholaminergic neurotransmission. We examined the differential expression of Tyrosine hydroxylase immunoreactive (TH-ir) cells and fibers in the ancestral Astyanax surface fish and the derived cavefish from the Pachón cave. The localization of TH-ir cells and fibers is consistent with previous reports in teleost fish. Cell body and fiber diameters were measured and differential expression in surface and cavefish were observed, most notably those related to olfaction. A greater density of TH-ir cells and projections associated with the olfactory bulb and its projections were found in the cavefish. Since the cavefish rely on nonvisual sensory systems to locate food in constant darkness, it is therefore likely that the catecholaminergic modulation of olfactory signals modified the resulting response from one of fear to one of reward.

Michael Hanna

Graduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Bryan Pfister, Professor and Chair of Biomedical Engineering,
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: Effects of Brain Vasculature, Skull Size on the Spatial and Temporal Deformation of Brain under Blunt and Blast Trauma

The objective of our research is to determine the biomechanical link between the traumatic brain injury (TBI) event and damage to the brain. Damage to the brain has been directly correlated to the degree of brain deformation. Anatomical variabilities contribute to different injuries and responses. To elucidate these differences, we developed custom-made head surrogate models to visualize deformations occurring in the brain during different injury scenarios with high speed photography. Physical head models consisting of a midsagittal skull, brain, and neck were constructed. Brain materials tested include 5%, 10%, and 20% ballistics gelatin (Clear Ballistics). One surrogate iteration attempted to model the anterior cerebral artery and the other model compared strain values in 95th percentile head size with 5th percentile head size. Forehead Blunt injury scenarios were replicated with a uniaxial impact machine. Visual markers within brain surrogates were used to motion track deformations and extract principal strains: tension ($\varepsilon 1$), compression ($\varepsilon 1$), max shear (τmax). Larger head size appeared to have lower strains than smaller head size. Regions of the brain surrogate with increased strains remained elevated regardless of the skull size. Brain material around vasculature experienced significantly higher strains than control indicating that vasculature have impact on injury. Anatomical variables contribute to different injuries response and severity. This data can also be used to develop more precise tissue models of TBI, design better PPE and for validating finite element modelling to further the research.

Omar Itani

Graduate Student, Federated Department of Biological Sciences
Advisors: Horacio G. Rotstein, Professor of Math Bio & Computational Neuroscience, Biological Sciences,
Jorge Golowasch, Professor of Biological Sciences

Title: Mechanisms of the Emergence of Conductance Correlations from an Activity-Dependent Homeostatic Rule

Neurons are routinely classified on the basis of their electrical activity. However, the mechanisms by which neurons acquire and maintain the proper balance of ion channels needed for their activity is not yet known. Experimental results demonstrates balanced expression of mRNA for different channels, resulting in cell-type specific ion channel correlations. These cell-type specific correlations are also observed electrophysiologically as correlations between certain currents. In this work, we address the relation between neuron activity and conductance correlations that emerge from activity-dependent homeostatic regulation of the ion channel conductances. We describe the mechanisms by which correlation lines form and their implications for neuron activity. Further, we discuss the implications of an activity-dependent homeostatic regulation rule on the observed biological variability of conductance correlations.

Sudeepto Kahali

P*hD Student, Department of Mechanical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3*
Advisors: Molly Townsend, Post-Doctoral Research Associate of Biomedical Engineering
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: The Evolution of Secondary Flow Phenomena and their Effects on Primary Shock Conditions in Shock Tubes: Experimentation and Numerical Model

Compressed gas-driven shock tubes are widely used for laboratory simulation of primary blasts by accurately replicating pressure profiles observed in areas surrounding explosions. However, investigations into primary blasts using shock tubes lack sound understanding of shock wave propagation. The goal of the research is to characterize shock wave propagation in and around a shock tube through an understanding of shock wave propagation, shock front decay, and secondary flow phenomena. To this end, a nine-inch shock tube and a cylindrical sensing apparatus were used to determine incident and total pressures outside of the shock tube, highlighting the presence of additional flow phenomena. Blast overpressure, impulse, shock wave arrival times, positive phase duration and shock wave planarity were examined using a finite element model of the system, to understand the decay of the shock front and to elucidate the temporal and spatial effects of secondary flow phenomena. The shock wave remained planar along the length of the shock tube and lost its planarity upon exiting. The peak overpressure and pressure impulse decayed rapidly upon exit from the shock tube, reducing by over 95% pressure. Two distinct flow phenomena were observed to result from the shock wave exiting the confines of the shock tube. A vortex ring was formed as the shock wave exited the shock tube into still, ambient air, causing a large increase in the total pressure impulse. Additionally, a rarefaction wave was following shock front expansion, which travelled upstream into the shock tube, reducing the total and incident pressure impulses for approximately half of the simulated region. Ideal primary blast conditions were observed deep within the shock tube along the longitudinal axis.

Manpreet Kaur

Graduate Student, Department of Chemistry and Environmental Science
Advisors: Yong-Ick Kim, Assistant Professor of Chemistry and Environmental Science
Casey Diekman, Associate Professor of Mathematical Sciences

Title: CikA Modulates the Effect of KaiA on the Period of the Circadian Oscillation in KaiC Phosphorylation

Cyanobacteria contain a circadian oscillator that can be reconstituted in vitro. In the reconstituted circadian oscillator, the phosphorylation state of KaiC oscillates with a circadian period, spending about 12 h in the phosphorylation phase and another 12 h in the dephosphorylation phase. Although some entrainment studies have been performed using the reconstituted oscillator, they were insufficient to fully explain entrainment mechanisms of the cyanobacterial circadian clock due to the lack of input pathway components in the in vitro oscillator reaction mixture. Here, we investigate how an input pathway component, CikA, affects the phosphorylation state of KaiC in vitro. In general, CikA affects the amplitude and period of the circadian oscillation of KaiC phosphorylation by competing with KaiA for the same binding site on KaiB. In the presence of CikA, KaiC switches from its dephosphorylation phase to its phosphorylation phase prematurely, due to an early release of KaiA from KaiB as a result of competitive binding between CikA and KaiA. This causes hyperphosphorylation of KaiC and lowers the amplitude of the circadian oscillation. The period of the KaiC phosphorylation oscillation is shortened by adding increased amounts of CikA. A constant period can be maintained as CikA is increased by proportionally decreasing the amount of KaiA. Our findings give insight into how to reconstitute the cyanobacterial circadian clock in vitro by the addition of an input pathway component, and explain how this affects circadian oscillations by directly interacting with the oscillator components.

Emel Khan

Graduate Student, Department of Mathematical Sciences
Advisor: Casey Diekman, Associate Professor of Mathematical Sciences

Title: Circadian Oscillations in Cyanobacteria

Circadian rhythms are daily oscillations of activity which occur in living organisms including animals, plants, fungi, and cyanobacteria. These rhythms have the defining properties of being persistent in constant conditions, entrainable to external time cues, and sustainable over different temperatures. Our focus is on circadian rhythms in cyanobacteria, whose core clock is comprised of just three proteins, KaiA, KaiB and KaiC. When these proteins are mixed with ATP in a test tube, KaiC phosphorylates and dephosphorylates in an oscillatory manner. Here we analyze the mathematical model developed by Rust et al. to understand the circadian oscillations in cyanobacteria. Furthermore, we also address issues in the model and propose possible solutions. We are using simulations and dynamical systems theory to gain insight into the mechanisms of the core oscillator, as well as how the system entrains to light-dark cycles. Our long-term goal is to fully understand the time-keeping mechanism in cyanobacteria and how the properties of this clock may relate to circadian rhythms in mammals.

Ying Li

Post-Doctoral Research Associate, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Bryan Pfister, Professor and Chair of Biomedical Engineering
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: Mild Strech Injury Induces Inflammatory Pyroptosis In-Vitro

Mild traumatic brain injury has shown to lead to progressive cell death leading to long-term functional impairments including cognitive and motor deficits. The mechanism(s) underlying these physiological changes that ensue after injury remain eluded. We have shown in a previous published study of neuronal injury using an in vitro stretch model and an in vivo model of fluid percussion injury (FPI) that injury induces the activation of Caspase-1 enzyme which triggers neuroinflammatory cascades ultimately leading to neurodegeneration. Due to Caspase-1 showing to lead to programmed inflammatory cell death, pyroptosis, we investigated whether neuronal cell death observed after injury was a consequence of the activation of Caspase-1 induced inflammatory pathway. Neuronal injury was simulated using a custom stretch injury model. Stretch injury (40% at rate 20s-1) and LPS (1 ug/ml) induced increase of ASC, AIM2, caspase-1, NLRP3 and Gasdermin D protein in cells by western analysis, immunohistology and IL-1b, IL18 in supernatant by ELISA. NLRP3 inhibitor CY-09 (5 uM) and caspase-1 inhabitor VX-765 (10uM) significantly suppressed the increase of ASC, AIM2, caspase-1, NLRP3 and Gasdermin D, as well as IL-18 and IL-1b after injury and LPS application, respectively. A live/dead cell assay indicated that CY-09 and VX-765 rescued neuronal cell death induced by stretch injury. Our results suggest that pyroptosis-inflammatory neuronal cell death is a possible mechanism of progressive cell death after mild traumatic brain injury.

Xiaotang Ma

Graduate Student, Department of Biomedical Engineering, Center for Injury Bio Mechanics, Materials and Medicine – CIBM3
Advisor: James Haorah, Associate Professor of Biomedical Engineering

Title: Cerebral Hemorrhage Initiated Neuroinflammation and Neurodegeneration in Fluid Percussion Animal Model

Traumatic brain injury (TBI) is a major health problem for over 3.17 million people in the USA. Meanwhile, hemorrhage and coagulation caused by TBI lead to severe issue for patients to recover. The objective of this project is to understand the mechanisms of brain injury and to facilitate regenerative medicines for the reversal of the brain injury and progression of neurological complications. We observed an increase hemorrhagic lesions and infarct volume in the injured brain with increment of pressure. To correlate this extent of injury, we examined the bio-distribution of fluorescent tracer (FITCI=d2000) after post-injury injection of the tracer through intracisterna magna. Surprisingly, the bio-distribution of the tracer was specifically diminished at the site of injury compared with non-injured side or the sham controls, suggesting that coagulation at the hemorrhagic site could have blocked the movement of the tracer. Immunohistochemical observation of coagulation factor XII expression and necrotic cell death in and around the impact site confirmed the blockade of the tracer bio-distribution at the injured side of the brain. Different biomarkers, including tight junction proteins, immune cells accumulation and neuronal death demonstrated blood brain barrier disruption, neuroinflammation and neurodegeneration surrounding impact site. Altogether, these results suggest that instant focal hemorrhagic injury resulting from rupturing the brain vessels causes onsite perivascular inflammation and neurodegeneration due to thrombosis. Understanding the multiple processes occuring after TBI is crucial to develop neuroprotective and regenerative therapeutics to ameliorate the short and long-term consequences of TBI.

Matthew Moye

Graduate Student, Department of Mathematical Sciences
Advisor: Casey Diekman, Associate Professor of Mathematical Sciences

Title: Data Assimilation Methods for Neuronal State and Parameter Estimation

This work explores the use of data assimilation algorithms to estimate unobserved variables and unknown parameters of conductance-based neuronal models. Data assimilation (DA) is the optimal integration of noisy observations from a system with the output of a model describing that system in order to improve estimates of the system's states and the model's parameters. Modern DA techniques, such as the Unscented Kalman Filter (UKF) and 4D-Variational methods (4D-Var), are widely used in climate science and weather prediction, but have only recently begun to be applied in neuroscience. Sequential data assimilation techniques, such as the UKF, iteratively take in observational recordings to produce system estimates, whereas variational techniques attempt to minimize a cost function over a fixed time window. We demonstrate how to use DA to infer several parameters of the Morris-Lecar model from a single voltage trace, and then extend our approach to more complex conductance-based models. The Morris-Lecar model can exhibit qualitatively different types of neuronal excitability with different parameter sets due to changes in the underlying bifurcation structure. Specifically, different bifurcations from quiescence to repetitive spiking occur as the applied current is increased. For a given applied current in the region where a stable limit cycle (corresponding to repetitive spiking) exists, each regime displays a distinct firing frequency and action potential shape. We show that when presented voltage traces from each of the various excitability regimes, the DA techniques can identify parameter sets that produce the correct bifurcation structure even with initial parameter guesses that correspond to a different excitability regime. The model can be extended to exhibit square-wave and elliptic bursting, and we show that these techniques can infer parameter sets that recover the correct bifurcation structure even with initial parameter guesses that produce the alternative bursting pattern. These DA techniques have advantages and disadvantages. Namely, there is typically a gain in precision in exchange for computational time with the variational approach, but it has limitations when working with large time series data. We explore the utility of a two-stage approach in which the fast timescale dynamics of a system are estimated via 4D-Var, and slow timescale dynamics through the UKF. We apply this approach to current-clamp recordings of Drosophila clock neurons.

Madhuvika Murugan

Post-Doctoral Research Associate, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisor: Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: Consequences of Microglia Activation and Monocyte Infiltration on Chronic Neuroinflammation and Behavioral Outcomes after Blast-induced Brain Injury

Moderate blast-induced traumatic brain injury (bTBI) is associated with microglia/macrophage accumulation, chronic neuroinflammation and neurobehavioral deficit. However, the origin of macrophages, whether it is sourced by local microgliosis alone, or supplemented by infiltration of peripheral monocytes remains to be investigated. In this study, we investigate the infiltration of circulating blood borne monocytes into the brain following bTBI. Using state of the art tools such as two-photon imaging and double transgenic mice- CCCR2RFP/+: CX3CR1GFP/+, in which CX3CR1-positive resident microglia are tagged with GFP and CCR2-positive infiltrating monocytes are tagged with RFP, we were able to identify a spatial and temporally distinct pattern of microglia activation and monocyte infiltration following moderate bTBI (180 kPa). The microglia activation and monocyte infiltration occurred as early as 4h and lasted up to 30 d after blast exposure, suggesting the presence of chronic inflammation. Additionally, bTBI-induced infiltration of monocytes and production of IL-1β was prevented in mice lacking CCR2 (CCR2KO). Finally, this study showed that interference of monocyte infiltration using CCR2 KO, ameliorated the chronic effects of bTBI such as anxiety and short-term memory decline. Taken together, these data suggest that bTBI leads to activation of both resident microglia and infiltrated monocytes. The infiltration of monocytes was partly mediated by CCL2-CCR2 signaling, which in turn contributes to increased production of IL-1β leading to behavioral deficits after bTBI. Furthermore, bTBI induced behavioral outcomes were reduced by targeting CCL2-CCR2 signaling, highlighting the significance of this signaling axis in bTBI pathology.

Rodrigo F. O. Pena

Post-Doctoral Research Associate, Federated Department of Biological Sciences
Advisor: Horacio G. Rotstein, Professor of Math Bio, Computational Neuroscience, Biological Sciences

Title: Theta-band Resonance in a Neocortical Microcircuit Model

The neocortex is a region of the brain responsible for many higher-order functions. Sensory signals arrive from different areas are integrated into the neocortex. Oscillations at certain frequency bands function for coordination of activity in many areas. Recent work showed the role of inhibition on the control of theta (4-11 Hz) oscillations through resonance. Optogenetic activation of interneurons (inhibitory) induced theta-band-limited spiking in pyramidal (excitatory) neurons. Although it is clear that this pattern is neuronal specific, the network architecture responsible for this resonance and how this is related to the correct gating of the signals in such a network is currently unknown. We address this problem with a computational model of the neocortex. We consider pyramidal cells (PYR), parvalbumin-positive (PV), and somatostatin-expressing (SOM) interneurons. These cells are interconnected with exponential decaying event-driven synapses where short-term depression/facilitation is present when appropriate. Every cell receives a noise input process to simulate in vivo synaptic barrage. By applying oscillatory stimulation in PVs, theta-band resonance was induced in PYRs whereas direct stimulation of PYRs did not present resonance, as it was experimentally reported. Our results show that SOMs regulate these resonance effects. We further studied scenarios where asynchronous stimulation arrives in different neurons. The neuronal output firing rate upon asynchronous stimulation was named its the natural frequency. Additionally, we checked scenarios where an oscillatory stimulation was applied in the PV cell at the same time as the asynchronous stimulation in another neuron. These scenarios show that PVs gate asynchronous stimulation. If asynchronous stimulation is applied to PYRs, their activity resonates towards the natural frequency. If asynchronous stimulation is applied to a PV while another receives oscillatory stimulation, the former resonates with activity lower than the natural frequency. Our results highlight the importance of the combined activity of different neocortical cells in flexibly selecting inputs.

Arunreddy Ravula

Graduate Student, Federated Department of Biological Sciences, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Namas Chandra, Distinguished Professor of Biomedical Engineering
Venkata Kakulavarapu, Research Assistant Professor of Biomedical Engineering

Title: Low-level Repeated Blast TBI Results in Neurobehavioral Deficits in Animal Model

Traumatic brain injury is a leading cause of mortality and morbidity in individuals resulting from automobile accidents, falls and injuries caused by a variety of sports events. Blast induced neurotrauma at very milder level (repeated low-level blast, rLLB) is usually experienced by Service Members (SMs) in heavy weaponry training. The injuries/symptoms of rLLB are very often undiagnosed but may this may exert long term consequences. A comprehensive survey on SMs exposed to rLLB previously in various training facilities reported a spectrum of symptoms ranging from headache, sleep disturbances, cognitive impairment and anxiety. Lack of well-established animal model to represent rLLB by far is major constrain to understand the pathology and behavioral alterations. So far, studies have confined to 3 repetition of low level blasts, which is by far less compared to SMs concurrently experience during training sessions. We have developed animal model of repeated low-level blast (rLLB) and asked rLLB induces neurobehavioral changes similar to occurring in SMs?. Accordingly, Sprague-dawley rats were exposed to 10 psi overpressure one-time or repeated 5 successive times within a duration of 1 min. using a helium-driven shock tube housed in CIBM3 at NJIT. Animals with rLLB at different time points post injury showed significant motor deficits as indicated by altered latency to fall in a rotarod; anxiety and depression-like symptoms as revealed by less exploratory behavior and animals confined to closed corners in elevated plus maze. Animals also exhibited loss of short term memory as they were unable to recognize and distinguish between. Interestingly, animals exposed to single low-level blast did not display these behavioral abnormalities, indicating that multiple blast cumulatively exert pathological changes which ultimately leads to neurobehavioral deficits. Currently, we are investigating the molecular/biochemical changes that contribute to the behavioral abnormalities in rLLB animals.

Jose J. Rodriguez

Graduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Namas Chandra, Distinguished Professor of Biomedical Engineering
Maciej Skotak, Research Assistant Professor of Biomedical Engineering

Title: Using 2D Planar Geometries to Investigate the Effect of ShockWave Duration on the Reflected Pressure Profiles.

Blast-induced traumatic brain injury (bTBI) is an active research area covering clinical studies and models aimed at identifying injury mechanisms. Compressed gas-driven shock tubes are able to replicate field blast conditions in a controlled and repeatable manner. By optimizing our 9-inch square cross-section shock tube's operating variables, tailored Friedlander waveform shock waves can be generated where the peak overpressure remains constant, and impulse varies, e.g., 1) 130 kPa: 220 and 440 Pa·s. and 2) 180 kPa: 330 and 720 Pa·s. This allows us to elucidate how incident loading conditions translate to corresponding injury metrics (reflected pressure). We used a 3 x 3-inch square plate fixed inside of the shock tube's test section located 3 meters from the breach. The front face of the plate was perpendicular to the direction of the oncoming shock wave. Pressurized driver gas (helium or nitrogen) was introduced into the driver section and separated from the driven section of the shock tube with a stack of Mylar membranes until failure. Test were performed at two discrete overpressures 130 and 180 kPa (18 and 26 psi). Incident overpressures were measured using a series of PCB Piezotronics (Depew, NY) model 134A24 pressure sensors distributed along the length of the shock tube. The plate was instrumented with PCB102B pressure sensors, placed flush with the target surface at the center and diagonally every .85 inches as permitted with size constraints. All data were recorded at 1.0 MHz sampling frequency with a total acquisition time of 50 milliseconds. When comparing between blasts of similar incident overpressures but varying impulse, we noted while peak reflected overpressures for both configurations remain constant, the reflected impulse values were significantly amplified: in the range of 480-520 Pa·s for short duration (approximately 1.6 amplification), and in 1300-1550 Pa·s for the long duration (approximately 2.1 amplification). This work sheds new light on understanding of how incident shock wave characteristics affect the reflected pressure measurements. Our findings aid experimental data interpretation and thus strongly related to the practical aspects of the pressure measurements pertinent to occupational low-level blast exposures.

Anna C. Schneider

Post-Doctoral Research Associate, Federated Department of Biological Sciences
Advisors: Dirk Bucher, Associate Professor of Biological Sciences
Farzan Nadim, Professor of Neurobiology

Title: Frequency-dependent Actions of Neuromodulation

Neuromodulators provide flexibility to the output of a nervous system by allowing neural circuits to produce distinct activity patterns, depending on the animal's behavioral need, by modifying both synaptic strength and dynamics, and neuronal excitability. Neuromodulator effects on circuit output can depend on the system's state, e.g. it's cycle period or excitability. Here, we focus on state-dependent effects of neuromodulation on a single ionic current: the voltage-gated modulator-activated inward current, IMI. In the crustacean stomatogastric pyloric circuit, this current is enough to drive rhythmic activity in otherwise quiescent pacemaker neurons. We used the identified lateral pyloric (LP) neuron of the crab, which produces slow-wave bursting activity. The transition of LP's membrane potential to burst scales with the pyloric cycle frequency and, in principle, the depolarization rate of the neuron could influence the amplitude of voltage-gated currents such as IMI. To address this question, we stimulated the voltage-clamped LP with two protocols. In one protocol, we used pre-recorded (realistic) waveforms of LP activity, applied at different cycle frequencies, and measured the levels of IMI activated by the neuropeptide proctolin (1μM). At steady state, the IMI levels did not appear to change with the frequency of the realistic waveform. In the second protocol, we noted that LP's depolarization can be approximated by a linear voltage ramp. We therefore matched the ramp slopes to the depolarization rates at different cycle frequencies, and stimulated LP with symmetrical triangular ramps. With increasing depolarizing ramp slopes, the maximum IMI increased and the voltage at peak current shifted to more depolarized potentials. However, IMI did not depend on the hyperpolarizing ramp slopes. This indicates an inactivating component with a slow time-constant. To study this inactivation, we stimulated LP with repetitive ramp-and-hold stimuli. In steady state, IMI was reduced during the depolarization. However, the voltage at peak current still shifted to depolarized voltages with faster ramp slopes. Overall, our results demonstrate that the activation of the modulatory current is influenced by the rate of membrane depolarization.

Ningning Shao

Graduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Madhuvika Murugan, Post-Doctoral Research Associate of Biomedical Engineering,
Venkata Kakulavarapu, Research Assistant Professor of Biomedical Engineering
Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: Innovative and Cost-Efficient Method for Diagnosis of Hearing Loss and Tinnitus in Rat Model of Repeated-low Level Blast Injury

Hearing loss and tinnitus are the most prevalent conditions among both soldiers and civilians. In the United States, according to National Institute on Deafness and Other Communication Disorders (NIDCD) approximately 37.5 million adult population report some trouble hearing, among which approximately 25 million people have tinnitus. In order to investigate the pathology of hearing problems in a laboratory setting, we need a reliable animal model and an effective method to diagnose hearing loss and tinnitus. In this study, we developed a cost efficient methodology to detect blast induced hearing loss and tinnitus in a rat model. To this end, 10 week old male Sprague-Dawley rats were subjected to either 1 or 5 shots of low level blast (shock wave overpressure level: 70 kPa, 10 ms duration each). In order to diagnose hearing loss/ tinnitus, we modified an existing piezoelectric transducer (Signal Solutions), originally designed for investigating sleep pattern for the detection of acoustic startle response (ASR) at 25d following blast exposure. We then utilized specific paradigms of acoustic stimuli, including gap sound (GAP) and prepulse inhibition sound (PPI), which allows us to identify tinnitus-like and hearing deficits, respectively, based on the changes in the acoustic startle response (ASR) that they evoke. We found that both single blast and multiple blasts caused tinnitus and hearing loss, but at different frequency bands. Data confirmed that hearing loss at 10-12kHz frequencies were prominent at 25d post blast exposure for both blast conditions, which can shed light on the pathology of region and neural tracks identifications based on the frequency mapping. Hence, with the diagnosis procedure, investigation into the peripheral and central mechanisms following blast injury is much warranted and is currently underway.

Molly Townsend

Post-Doctoral Research Associate, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisor: Namas Chandra, Distinguished Professor of Biomedical Engineering

Title: The Limitations of a Modeling Shockwave Development in a Shocktube using Commercially Available Finite Element Tools

The compressed-air driven shocktube is a powerful research tool that, when properly designed, operated, validated, and calibrated, is capable of reliably replicating free-field primary blast waves. However, variations in design and experimental procedures between experimental facilities make the validation process arduous and expensive. To this end, a computational model capable of simulating various shocktube configurations is being developed, to enable validation of shocktube experimental setups with other shocktubes and minimizing the need for free-field validation. A finite element model of the CIBM3 shocktube was created and the output of the model was compared to experimental data. The Eulerian model was developed that enables simulation of a shockwave, using only ambient atmospheric conditions, the driver gas, the shocktube shape, and the burst pressure. Methods of increasing the fidelity of the baseline model were investigated to improve validation by eliminating model assumptions. The baseline model matches (<10% error in pressure measurements) experimental conditions at 130 kPa overpressures. It proved to be limited in the prediction of lower and higher blast overpressures, unacceptably underpredicting pressures at lower blast overpressures (100 kPa) and overpredicting pressures at higher blast overpressures (240 kPa). Upon increasing model fidelity, results indicate that the assumptions investigated, including membrane inclusion, gas mixture ratio, and temperature variability, cause the model prediction to deviate from experimental results further. Initial conclusions indicate that the error may exist in the gas flow constitutive equations used by the commercial finite element solver. Work is ongoing to circumvent the native constitutive equations to implement a higher fidelity numerical approximation of the mechanics.

Daniel Younger

Graduate Student, Department of Biomedical Engineering, Center for Injury Biomechanics, Materials and Medicine – CIBM3
Advisors: Namas Chandra, Distinguished Professor of Biomedical Engineering
Venkata Kakulavarapu, Research Assistant Professor of Biomedical Engineering

Title: Sustained Microglial Activation and Associated Neuroinflammation in Moderate Blast TBI: Role of NLRP3 Inflammasome

Traumatic brain injury (TBI) is a leading cause of death and disability in individuals due to automobile accidents, falls, blast injuries and sports-related injuries. Among these, blast-induced neurotrauma (BINT) is becoming a leading cause of morbidity and mortality in soldiers in the battle field as well as training sites. While primary mechanical injury caused by direct shockwave loading may perturb brain physiological homeostasis, down-stream propagation of various biochemical events leading to brain injury are not fully understood. Of several factors that induce brain pathology in TBI, neuroinflammation is an important pathway triggered by upstream factors including microglial activation and associated consequences such the production of inflammatory cytokine IL-1 β ultimately leading to neurobehavioral deficits. A major pathway for the production of IL-1 β is the activation of Nod-Like Receptor Protein3 (NLRP3) inflammasome, a multimeric protein complex consisting of apoptosis-associated speck-like protein (ASC1) and caspase-1 (IL-1β converting enzyme). Here we examined the activation pattern of NLRP3 and associated proteins ELISA, immunostaining, and western blot analysis over a range of time points (4 hours, 24 hours, 3 days, 7 days, 15 days, and 30 days) after exposing rats to moderate blast (180 kPa). Results showed that microglia were activated as early as 4h post injury and such activation sustained for up 30 days. Microglial number also peaked at 24 hours following injury but remained elevated compared to control at all time points. Levels of NLRP3 proteins increased in a biphasic manner significantly upregulated for the first 24 hours, returning to control levels at 3 days and again increased at 7 days peaking at 30 days following injury. This data collectively suggests that mild/moderate bTBI induces both an acute and chronic neuroinflammatory response by triggering a cascade of events potentially resulting in perturbations in cellular homeostasis in bTBI

Min Zhang

Graduate Student, Department of Biomedical Engineering, Neural Engineering of Speech and Hearing (NESH Lab)
Advisor: Antje Ihlefeld, Assistant Professor of Biomedical Engineering

Title: Correlation between Performances in Informational Masking and Visual Crowding

In everyday environments, two types of masking, called Informational versus Energetic Masking, commonly occur. While Energetic Masking mechanisms are well characterized, we still do not understand the mechanisms causing Informational Masking. A potentially related phenomenon in vision, called Visual Crowding, occurs when observers excessively integrate perceptual features in the visual scene. Here, we compare performance in Informational Masking versus Visual Crowding in the same individuals to test the hypothesis that Informational Masking and Visual Crowding share a common processing limitation. Task 1 used a detection task of 8-tone melodies in IM to measure Melody-IM susceptibility. Task 2 tested Speech-IM-susceptibility with a previously established paradigm (Arbogast et al. JASA 2002). Task 3 assessed visual crowding using a paradigm developed by Pelli et al. (F1000 Research 2016) measured in Critical Spacing.
Linear regression fits reveal a correlation between Melody-Informational-Masking- versus Speech-Informational-Masking-susceptibility ($R2 = 0.38$, $p = 0.014$). In addition, Critical Spacing negatively correlates with both Melody-Informational-Masking-susceptibility ($R2 = 0.362$, $p = 0.018$) and Speech-Informational-Masking-susceptibility ($R2 = 0.4$, $p = 0.011$). Informational Masking and Visual Crowding were not simultaneously tested in our experiment design, however we observed anti-correlation between their task performances. Results hint at competition for a shared resource when separating similar audio or visual objects. This bias towards one sensory modality could be formed during development.

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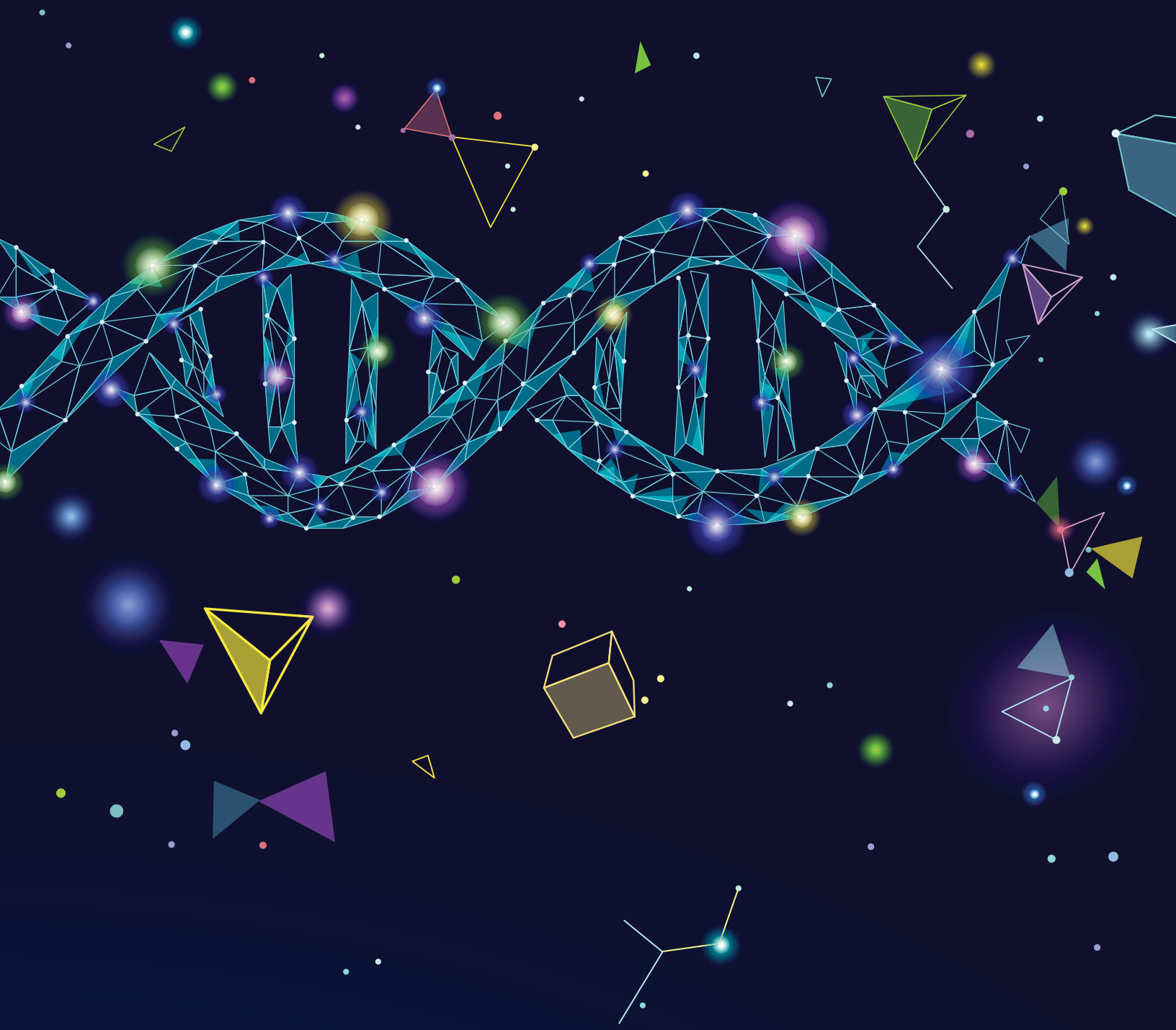

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