

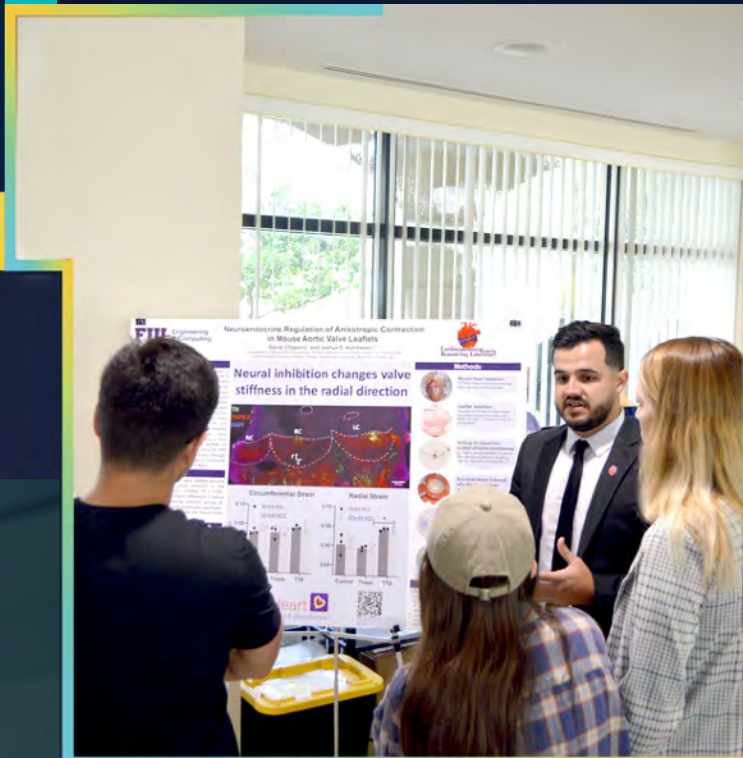
GRADUATE RESEARCH DAY

Wednesday, March 9, 2022

9:00 AM–4:00 PM ET | EC 2300 | EC Panther Pit



Presented through the generous support
of the Wallace H. Coulter Foundation.



DISCOVER | DESIGN | DEVELOP | DELIVER

Celebrate our graduate students in a day-long event intended to gain professional development experience, network, present research, and learn about advances in Biomedical Engineering.

Congratulations

Graduate Students!



Jorge Riera Diaz, Ph.D.

Associate Professor,
Interim Chair of Biomedical Engineering

CHAIRPERSON MESSAGE

Today we celebrate your achievements. You serve as the backbone of our Department, and you continue to push us to new heights. We are proud of your hard work and dedication in advancing human knowledge and developing technologies that will transform the future of medicine. Research involves pushing the limits of our collective understanding, which requires inquisitiveness, resiliency, creativity, innovation, and intelligence.

The work that you present today demonstrates that you have the necessary attributes to conduct research at the highest level. The Graduate Research Day provides an opportunity to reflect on your accomplishments and showcase your work with pride.

As you move forward in your graduate education, continue motivating yourself and others around you to enhance your knowledge, remain inquisitive, and continue to grow in all aspects of learning.

Thank you to all who have worked to make this Graduate Research Day a success!

Best wishes for continued success,

Jorge Riera

ABOUT OUR

Biomedical Engineering Program



The Department of Biomedical Engineering at Florida International University (FIU) located in Miami is committed to preparing ambitious students who want to combine their love of problem-solving with their desire to help others, through this fascinating growing field that applies cutting-edge technologies and modern engineering techniques to improve healthcare.

Our Biomedical Engineering department is ranked #1 for bachelor's degrees awarded to Hispanics and #6 for bachelor's degrees awarded to African Americans. Nationally, we are among the Top 20 to offer BS degrees, Top 65 for research expenditures, and considered in the Top 30 of the most popular in the country.* Florida International University is designated a Carnegie Highest Research (R1) and Carnegie Community Engaged Institution.

*ASEE 2019, NSF HERD 2018, and College Factual 2020



AGENDA

Room EC 2300

7:30 AM

Breakfast

8:45-9:00 AM

Welcome Remarks

9:00-10:00 AM

Seminar with **Dr. John X.J. Zhang**,
Professor of Engineering, Dartmouth College

10:00-10:30 AM

Short Break

Panther Pit

10:30 AM-12:00 PM

Poster Presentations

12:00-1:00 PM

Lunch and Networking with Students

Room EC 2300

1:00-3:30 PM

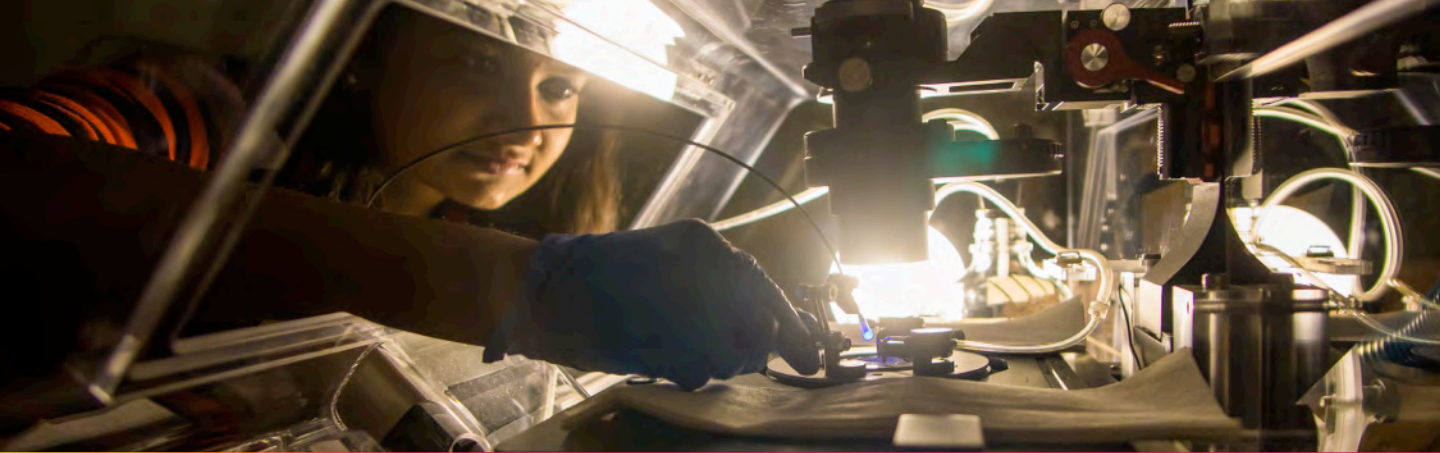
Student Oral Presentations

3:30-4:30 PM

Career and Talent Development Presents
CV Writing Workshop For Engineering
Graduate Students with **Nelly Leon**

4:30-5:00 PM

Award Ceremony



SPEAKERS

Room EC 2300



9:00 AM

Dr. John X.J. Zhang

Professor of Engineering,
Dartmouth College

Seminar Title
MICROCHIPS IN TRANSLATIONAL MEDICINE:
FROM CANCER DIAGNOSIS, BIOENERGY
HARVESTING TO WEARABLE APPLICATIONS



3:30 PM

Nelly Leon

Assistant Director,
Career and Talent Development

Seminar Title
CV WRITING WORKSHOP
FOR ENGINEERING GRADUATE STUDENTS

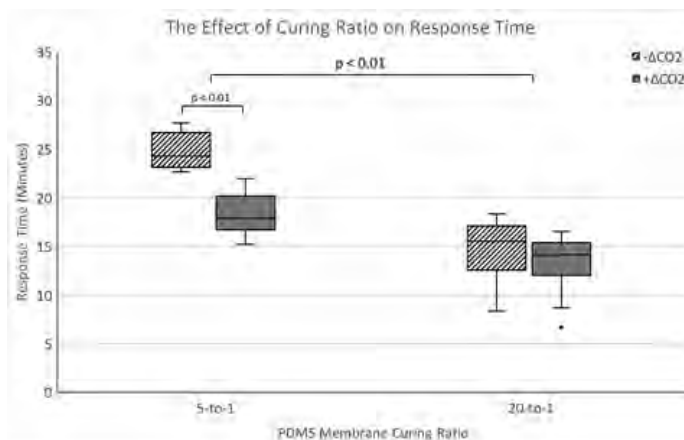
Response Time in Optochemical CO₂ Sensors Is Controlled Via Crosslink Density of Membrane

Faculty Advisor: Wei-Chiang Lin, Ph.D. | **Co-authors:** Wei-Chiang Lin

Funding Source: NSF Bridge to Doctorate; FEF McKnight Doctoral Fund



The response time of optochemical carbon dioxide (CO₂) sensors is thought to be limited by the diffusion of CO₂ across the selective membrane, which is usually a hydrophobic polymer such as polydimethylsiloxane (PDMS). Efforts to improve diffusion often begins with minimizing membrane thickness or sensor volume. However, this strategy is limited by the fabrication techniques available to a laboratory and the structural integrity of polymers at low thicknesses. Response time can be improved by increasing the membrane's diffusivity to CO₂ via surface modifications, but this effect is temporary. Alternatively, membrane diffusivity to CO₂ can be improved by reducing its crosslink density; a strategy shown to improve oxygen diffusivity across PDMS membranes. Therefore, this study explored the feasibility of improving response time of optochemical CO₂ sensors by modifying the composition of the PDMS membrane during fabrication. Optochemical Severinghaus sensors were built using HPTS-based sensing media encapsulated by PDMS membranes. The curing ratios of the prepolymer mixtures for the PDMS sheets were varied: 5-to-1 for the low and 20-to-1 for the high curing ratio groups. In this study, the increase in curing ratio led to a 26% improvement in response time of the CO₂ sensors ($p < 0.01$). The results of this study demonstrate a useful technique for improving response time in carbon dioxide sensors with minimal alterations to the fabrication process.

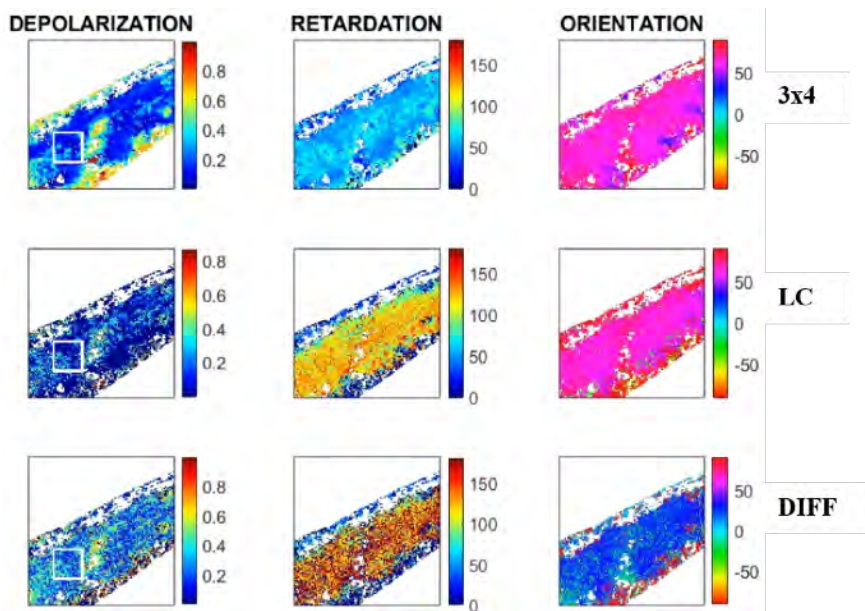


Polarimetric Imaging of the Uterine Cervix

Faculty Advisor: Jessica Ramella-Roman, Ph.D.



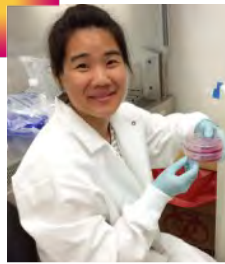
Cervical cancer is the fourth most common cancer in women, with more than half a million women diagnosed each year and a mortality of 311,000 women. According to the World Cancer Research Fund, developing countries have 84% of the global burden of the disease and 80% of the mortality due to a lack of effective screening programs. Several screening techniques have been developed and implemented to aid in low resource setting cervical screening, however, most require physician interpretation of color images. Mueller matrix polarimetry (MMP) is a quantitative technique used to probe a medium and extract information using polarized light. The introduction of polarized cameras have led to simplified and reduced MMP methods. A 3×4 Mueller matrix decomposition method is introduced and compared to established methods. Moreover, this new decomposition method is tested with ex vivo and in vivo biological tissue for future clinical deployment in low resource settings.



Valve Endothelial Cells Exposure to High Oscillatory Flow Leads to Valve Interstitial Cell Calcification

Faculty Advisor: Joshua D. Hutcheson, Ph.D., Sharan Ramaswamy, Ph.D. | **Co-authors:** Joshua D. Hutcheson, Sharan Ramaswamy

Funding Source: Dissertation Year Fellowship (DYF), UGS, FIU



Valve remodeling involves paracrine signaling between VECs and VICs under hemodynamics. In this study, we used oscillatory shear index (OSI) to quantify temporal changes in fluid-induced shear stress direction. OSI ranges from 0 (no oscillation) to 0.5 (full oscillation) [1]. We examined VIC calcification response to conditioned media from VECs under different OSIs.

Methods: Human VECs (LonzaBioscience) and VICs (Innoprot) were expanded in culture. VECs were seeded for 24hrs at 20000 cells per microfluidic channel in Bioflux plates (FluxionBiosciences) and conditioned for 48hrs in a shear assay system at 1 dyne/cm² under the following OSIs: static, steady flow, 0.25OSI, and 0.500SI. Conditioned media from VEC groups were collected, and a portion was ultracentrifuged at 50,000RPM. The non-exosomal supernatants were removed and the exosome pellets were resuspended in fresh media. Original VEC-conditioned media and the ultracentrifuged non-exosomal and exosome groups were then used to culture VICs (n=3/group) with equal concentrations of pro-calcifying (PC) ingredients: 1.8mM CaCl₂, 3.8mM NaH₂PO₄, and 0.4units/mL of inorganic pyrophosphate [2,3] at 5% FBS and 1% P/S. Fresh PC was used as control. VIC culture lasted 7 days, followed by alizarin red staining and quantification. Data was normalized to protein level and ANOVA statistical analyses was performed. Results: (Fig.1)

Conclusions: Significant VIC calcification was observed in high OSI non-exosomal group (0.50 CY-PC). This suggests that non-exosomal cytokines released by the VECs are primarily responsible for inducing VIC calcification under biomechanically-induced high OSIs in combination with pro-calcific environments.

References: [1] He&Ku.(1996). [2] Rathen et al.(2014). [3] Goto et al.(2019).

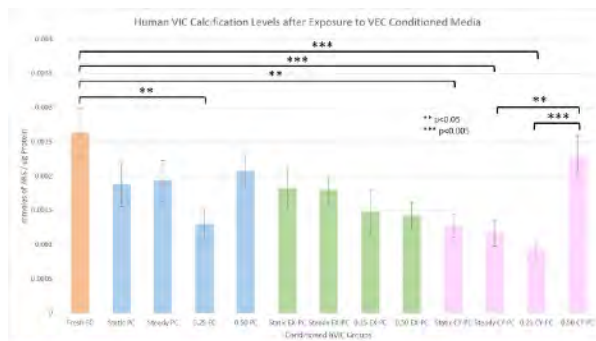


Figure 1: Alizarin red quantification per amount of protein in each group. PC group contains pro-calcifying ingredients. CY group corresponds to the conditioned media after ultracentrifugation while CY group corresponds to the non-exosomal cytokine supernatant after ultracentrifugation.

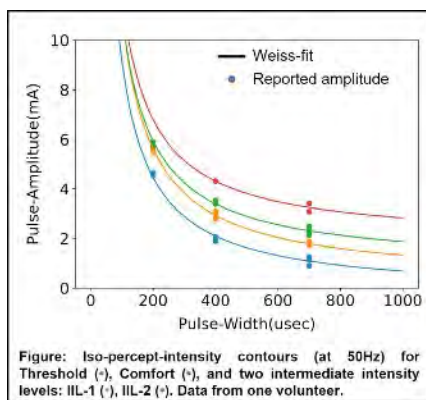
Multi-Dimensional Mapping of the Stimulation Parameter-Elicited Percept Intensity Space for the Development of an Automated Fitting System

Faculty Advisor: Ranu Jung, Ph.D. | **Co-author:** James J Abbas

Funding Source: USAMRAA-(W81WXH1910839), FIU Coulter Eminent Scholars Endowment



Lack of meaningful sensory feedback limits the utility of upper-limb prostheses and increases abandonment. Lab-based studies have demonstrated that electrical neurostimulation devices, programmed with parameters mapped to sensor signals from the prosthesis can provide task-relevant feedback to prosthesis users. Current methods to fit the device to the user require multiple parameter adjustments, are time-consuming, and require an expert clinician. An automated fitting system that can determine stimulation parameters with the user in the loop will aid with the successful translation of such devices. Mapping the stimulation parameter space is a first step in developing the automated fitting system. Seven able-bodied volunteers participated in a study to map the stimulation parameter space for a Transcutaneous Electrical Nerve Stimulation System with wrist-mounted electrodes. Stimulation at varying pulse widths and pulse frequencies were delivered and volunteers self-adjusted pulse amplitude to determine the value at which the elicited percept-intensity level matched one of four pre-specified reference percept-intensity levels (threshold, comfort, two-intermediate levels) (Figure). Iso-percept-intensity data was fit using the Weiss-equation to plot the iso-percept-intensity contours for all reference intensity levels. Weiss coefficients were extrapolated to develop a two-dimensional stimulation parameter space map. Each reference percept intensity level resulted in distinct contours on the strength-duration plot. For the intermediate intensity levels, higher pulse amplitude levels were required to elicit the same percept-intensity at lower pulse-frequency. These preliminary results provide further evidence to support a previously reported hypothesis that the percept-intensity is a function of the population firing rate.



Comparison of Oxygenated Flow Patterns in Diabetic Foot Ulcers Subjects and Controls in Response to Breath-Holding

Faculty Advisor: Anuradha Godavarty, Ph.D. | **Co-authors:** Kevin Leiva, Alexander Trinidad, Isabella Gonzalez, Aliette Espinosa, Thomas Zwick, Jason Edward Levine, Magaly Adelaida Rodriguez, Hadar Lev-Tov, Robert Kirsner, Anuradha Godavarty

Funding Source: National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health DiaComp Aware



Approximately 34% of people with diabetes will experience a diabetic foot ulcer (DFU) at some point throughout their lifetime. The perfusion of oxygen to the DFU is critical for promoting wound healing and closure. However, complications from diabetes can compromise the oxygenated flow to the wound site. Techniques such as transcutaneous oximetry and laser Doppler imaging have been used to assess perfusion to DFUs at discrete point-locations in the peri-wound. Wide-area measurements of temporal oxygenation changes, as an indirect measure of perfusion, can provide additional insight of the oxygenated flow in the (peri-)wound and background tissue. Herein, our objective is to assess the differences in oxygenation flow patterns in and around the DFU regions and in the feet of control subjects as a potential biomarker for monitoring wound healing. Breath-holding (BH), as a stimulus, holds the potential to induce oxygenated flow pattern changes in the presence of wounds. In this study, 10 DFU and 3 control subjects were imaged using a hand-held near-infrared optical scanner (NIROS). Spatial-temporal oxygenation maps of hemoglobin-based parameters were acquired across an 120-second paradigm with 20 seconds of breath-hold. The oxygenation flow patterns obtained from Pearson's-based correlation maps across controls, healing DFU, and non-healing DFU indicated that flow patterns varied distinctly between groups.

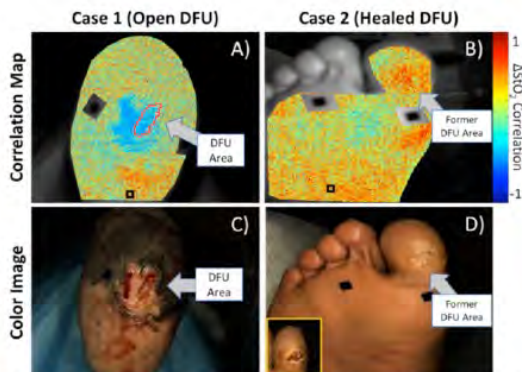


Figure 1: (A,B) Oxygen saturation-based correlation maps and (C,D) digital color images for case 1 (non-healing DFU) and case 2 (DFU that had healed) of DFU subjects, respectively. The red boundary in (A) is the segmented DFU region based on digital color image. The wound boundary was automatically calculated using a graph cut-based technique and co-registered onto the correlation map.^[6] The digital color image in the bottom left corner of (D) is the same DFU when the wound was open during the first session.

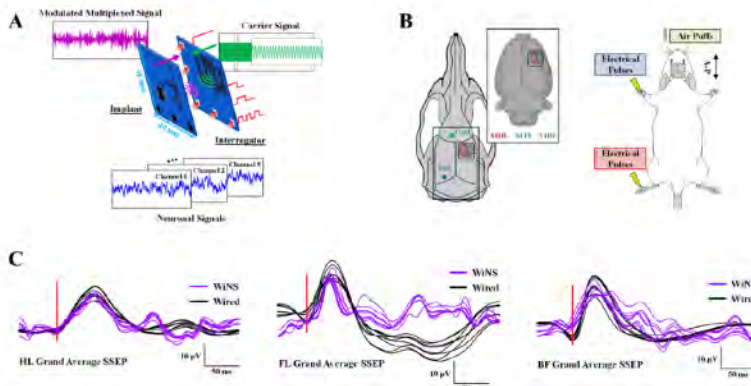
Monitoring Evoked Somatosensory Activity Using a Multichannel Passive Wireless Neurosensing System

Faculty Advisor: Jorge Riera, Ph.D. | **Co-authors:** Lakshmini Balachandar, Satheesh Bojja-Venkatakrishnan, John L. Volakis, Jorge Riera Diaz

Funding Source: US National Science Foundation (NSF), Dissertation Year Fellowship (DYF)



Electrophysiological recordings are essential in assessing neuronal activity. Wireless recorders have been proposed to evaluate brain function. However, current wireless systems are generally bulky and require integrated power sources (batteries), leading to undesirable heat generation. A next-generation wireless neurosensing system (WiNS), depicted in Fig. 1A, was proposed to address the need for battery-less systems. Using WiNS, an initial in vivo validation for evoked activation of ECoG signals was performed (Fig. 1B). More recently, WiNS was incorporated with an impedance matching network to address mismatches between neural probes and the recording circuits of the implanted wireless device. This adaptation, along with the capability of multichannel recordings via an optically-switched multiplexer, establishes WiNS as a complete system for implanted passive monitoring of neuronal activity. For multichannel recordings, the implant was redesigned to include photodiodes and photovoltaic cells to communicate with LEDs in the external interrogator. The photovoltaic cell output is then used to operate the multiplexer in the implant. Simultaneously, the LEDs with the photodiodes are used to select the recording channels. By switching these LEDs at a high frequency, we have demonstrated, using benchtop experiments, a recording sampling rate of up to 10 kHz per channel. Using 8-channel in vivo recordings of evoked neuron activity from different regions of the somatosensory cortex, we demonstrate the recording capability of a multichannel WiNS for collecting ECoG signals (Fig. 1C). These results indicate that WiNS can be used for multichannel recordings across a full range of brain-generated neuronal signals.



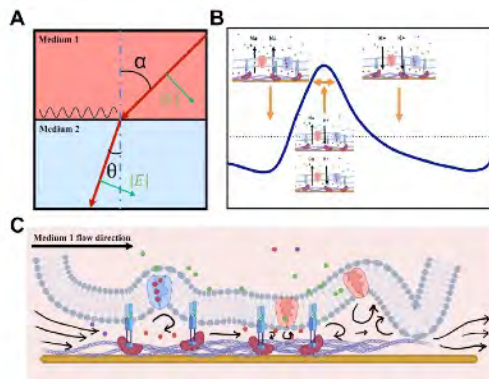
Development of a Plasmonic On-Chip System To Characterize Changes From External Perturbations in Cardiomyocytes

Faculty Advisor: Anthony J. McGoron, Ph.D. | **Co-authors:** Anthony J. McGoron.

Funding Source: University Graduate School, FIU



A comprehensive heart-on-a-chip device as a cell characterizing tool must encompass the capability to quantify cellular contractility, conductivity, excitability, and rhythmicity. Current state-of-the-art sensors for recording cardiomyocytes' (CM) electromechanical activities use a combination of fluorescent probes and microelectrode arrays (MEAs) or complex three-dimensional microfabricated devices. To subside the complexities of current methodologies for real-time monitoring of cardiac cells' electromechanical behavior, we explored the potential of plasmonic sensors in providing a simpler, faster, and cheaper platform for label-free, non-invasive, and high throughput cellular characterization. The surface plasmon resonance technique can quantify (1) molecular binding onto a metal film and (2) bulk refractive index changes of the medium near (<200 nm) the metal film. We used thin gold metal films (also called chips) as our plasmonic sensor and obtained a periodic signal from spontaneously contracting CMs on the chip. Furthermore, we took advantage of a microfluidic module for controlled drug delivery to CMs on-chip, inhibiting and promoting their signaling pathways under dynamic flow. We identified that ionic channel activity of each contraction period of a live CM syncytium on a gold metal sensor would account for the non-specific ion adsorption onto the metal surface in a periodic manner. Moreover, the contraction of cardiomyocytes following their ion channel activity displaces the medium, changing its bulk refractive index near the metal surface. Hence, we concluded that the real-time electromechanical activity of CMs using SPR sensors might be extracted as a time series we call the Plasmonic Cardio-Eukaryography Signal (P-CeG).



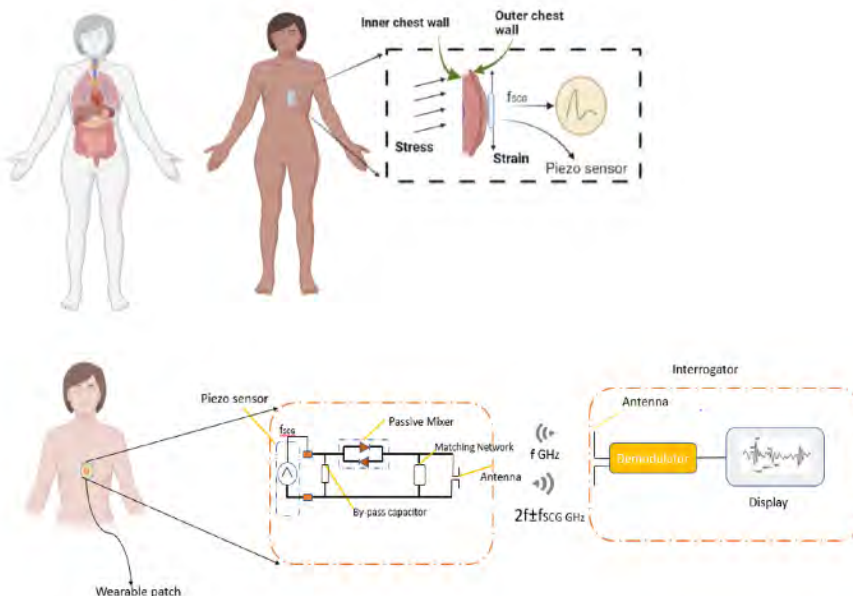
Fully Passive Non-Invasive Wireless Stretchable Seismocardiogram (SCG) Recording Patch for Cardiovascular Disease Monitoring

Faculty Advisor: Raj Pulugurt, Ph.D. | **Co-authors:** John Volakis, Raj Pulugurtha

Funding Source: Dissertation Year Fellowship (DYF)



Cardiovascular disease is the major cause of death and disability in united states. Though soft electronics are extensively reported for wearable ECG, wearable Seismocardiogram (SCG) are still on rigid, bulky accelerometer or non-stretchable electronics and there is no fully passive sensor has not been reported yet. In this work, we report battery less, no energy harvesting, flexible, stretchable non-invasive wireless SCG recording unit. An ultrathin (28 micron in thickness) passive uniquely patterned, highly compliant unidirectional Polyvinylidene fluoride (PVDF) converting chest wall vibration into electrical energy is integrated with another innovative passive harmonic transponder based on RF backscattering technique. The harmonic transponder is comprised of a simple RF telemetry, non-linear mixer and a bypass capacitor. The overall size of the Fully passive wireless patch is 38 mm X 18mmX1mm.



Two Dimensional Photonic Crystal Hydrogel Sensor: Computational Simulation and Biomedical Application

Faculty Advisor: Wei-Chiang Lin



Photonic crystals (PhCs) represent a unique class of materials with periodic changes in the dielectric element. This generates emergent properties such as the ability to control propagation of particular wavelengths ("photonic band-gap") and the potential for monitoring microstructure through assessment of the geometry of the diffraction pattern ("debye ring") generated by coherent illumination. PhCs encompass a variety of materials, including a photonic crystal fiber, an inverse opal and a photonic crystal hydrogel. Scientists have leveraged the unique properties of PhCs to develop sensors for physical force, pH, and chemical reagents.

This research utilizes a 2D PhC hydrogel, which is composed of a self-assembled monolayer of microspheres embedded within a hydrogel structure. First, a computational model was developed which provides the ability to predict the diffraction pattern generated by illumination of a collection of particles with defined positions in a PhC structure. This model was valuable due to its improvement over existing theoretical frameworks which cannot provide solutions beyond a perfect crystal structure. Second, a novel fabrication strategy was developed for PhC hydrogels and used to generate experimental diffraction patterns associated with particle positional data (extracted using confocal fluorescence microscopy) to validate the computational model. Finally, the fabricated PhC hydrogels were demonstrated to be capable of ultrasound detection between 2.25 and 10 MHz and sensitive to pressures ranging from 9 to 65 kPa, resulting from the elastomeric nature of the PhC hydrogel structure.

Accelerating Medical Device Development Through the Integration of Agile Process

Faculty Advisor: Ranu Jung, Ph.D. | **Co-authors:** James Abbas, Ranu Jung

Funding Source: NIH-R01EB025784



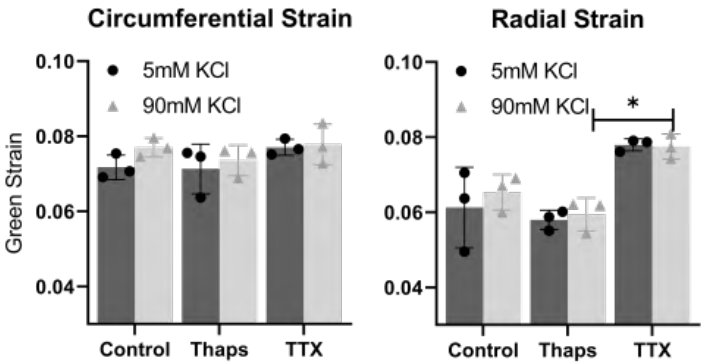
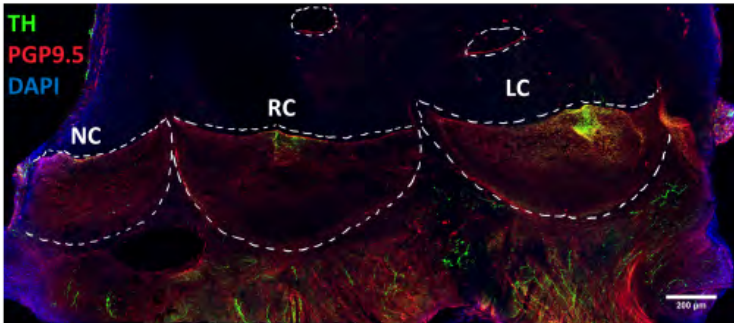
Bioelectronic medicine, an emerging research field, promises to improve and restore health without the debilitating side effects of the drugs. The field's primary focus is developing therapies and diagnostic tools by modulating neural communications between the brain and the end organs affected by disease or injury such as in diabetes, inflammatory diseases, and spinal cord injury. Neuromodulation using peripheral nerve electrodes is utilized. Amongst the various intraneural electrode interfaces utilized, the longitudinal intrafascicular electrodes are considered to be less invasive because each electrode is fabricated with a highly flexible, approximately 25 μm in diameter platinum-iridium wire. A tungsten needle is attached at one end to insert the wire longitudinally into the fascicle and discarded after the implantation. The primary challenge to implanting the electrodes is buckling of the nerve due to its compliance. To overcome this challenge, we proposed developing a mechanical device for supporting the nerve during the implantation of multiple intrafascicular electrodes. To develop the device, we evaluated an FDA-suggested, traditional waterfall method used to develop medical devices in most organizations. The first two prototypes and their revised versions fabricated using additive manufacturing following waterfall's stricter and sequential (define, build, test and release) process steps resulted in bulky devices that are not scalable to human nerve sizes. To further develop the device, we have explored the agile method, which is adaptive, flexible, and allows evolving the requirements during the development process. In this agile method, the device development cycle is iterated multiple times in short sprints with progressive use of the primary requirements. This approach has helped develop a revised device capable of being scaled for human use faster. We are in the process of validating the device in preclinical animal studies.

Neuroendocrine Regulation of Anisotropic Contraction in Mouse Aortic Valve Leaflets

Faculty Advisor: Joshua D. Hutcheson, Ph.D. | Co-author: Joshua D. Hutcheson



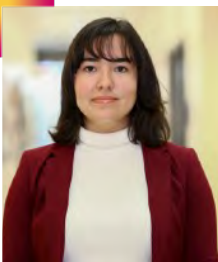
The aortic valve is largely regarded as a passive tissue, opening and closing due to changes in transvalvular pressures throughout the cardiac cycle. Recently, however, there has been increased interest in understanding how contractile cells within the tissue influence valve mechanics and function. We are particularly interested in the possible interplay between neuroendocrine and contractile valve interstitial cells (VICs) in tissue mechanics. In this study we mapped strains on the surface of mouse aortic valve leaflets (MAVLs) during 90 mM KCl stimulation after neural VIC inhibition through anhydro-tetrodotoxin (TTX) treatments or contractile VIC inhibition through thapsigargin. The data suggests that aortic valve leaflets become more compliant in the radial direction in the presence of neural specific inhibition ($P < 0.05$). However, there is no significant difference in tissue stiffness in the circumferential direction across all groups. Of note, although not statistically significant, the 90 mM KCl treatments made the tissue more compliant in both directions.



Retention of Core Bioscaffold Properties After Extensive Culture Periods

Faculty Advisor: Sharan Ramaswamy, Ph.D. | Co-authors: Brittany Rizo, Sharan Ramaswamy

Funding Source: Florida Heart Research Foundation



Infants born with critical congenital heart valve defects have limited treatment options, mainly due to inability to support somatic growth. Our current work has focused on creating a regenerable valve with dynamic culture. Our dynamic culture did produce robust engineered valvular tissues [1], however, this prolonged wet culture environment (22 days total) simultaneously caused the construct material to become distensible. Our aim here was therefore correct the valve mechanical properties and restore them to that of its core bioscaffold material, porcine small intestinal submucosa (PSIS; Cormatrix, Roswell, GA), which we have previously shown to function for months in a juvenile non-human primate model [2].

A preliminary analysis was performed by placing unseeded PSIS scaffolds in static culture for 22 days to simulate the total valve culture duration. The scaffolds then underwent a dehydration protocol which involved submerging PSIS in a 57% glycerol-DI solution and then air-drying them. The dehydrated scaffolds were subsequently subjected to uniaxial tensile testing in two orientations. Their mechanical properties were compared to a control group of "uncorrected" specimens and to raw PSIS (Table 1). A statistically significant difference ($p < 0.05$) was found between the Raw PSIS and control (Axial), as well as the 12 Hour Dehydrated group and all other groups (Axial). The preliminary results show that the dehydration protocol can restore the linear stiffness of cultured PSIS to that of Raw PSIS. Further work must nonetheless be done to further optimize the dehydration protocol before hydrodynamic functionality assessment can be performed on the valve constructs.

1. Gonzalez BA, et al: Physiologically-Relevant Fluid-Induced Oscillatory Shear Stress Stimulation of Mesenchymal Stem Cells Enhances the Engineered Valve Matrix Phenotype. Front. Cardiovasc. Med., 2020, May 19;7:69.
2. Gonzalez BA, et al: De Novo Valve Tissue Morphology Following Bioscaffold Mitral Valve Replacement in a Juvenile Non-Human Primate Model, Bioengineering (Basel) 2021, 8(7)-100.

Group	Orientation	Avg. Stiffness (MPa) ± SEM
Raw PSIS	Axial	336.37 ± 29.65
	Circumferential	51.76 ± 4.02
Control	Axial	73.74 ± 16.14
	Circumferential	37.96 ± 12.93
2 Hour Dehydration	Axial	218.37 ± 105.12
	Circumferential	35.98 ± 0.81
12 Hour Dehydration	Axial	644.14 ± 52.67
	Circumferential	22.34 ± 1.04

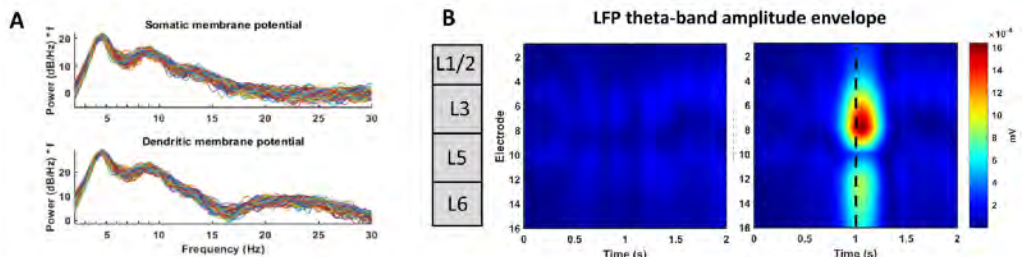
Table 1: Overview of the average linear stiffness values obtained for each group in each orientation.

Theta Spike-Field Synchronization for Error Monitoring in Medial Frontal Cortex: Empirical Findings and Biophysical Modeling

Faculty Advisor: Jorge J Riera, Ph.D. | **Co-authors:** Sajad, A., Errington, S. P., Schall, J. D., Jorge J Riera



The medial-frontal theta rhythm has been linked to error monitoring (Cohen, Trends Neurosci, 2014). However, the cortical mechanisms originating this rhythm remain uncertain. Here, we bring new insights combining computational simulations with neurophysiological data. We simulated the response of L3 and L5 PCs to excitatory synaptic inputs randomly activated. We found that theta oscillations in the membrane potentials can inherently arise from such stimulation in L5-PC, but not L3-PC. Furthermore, differences in phase of 100 (unconnected) simulated L5 PCs make this oscillation unobservable within local field potentials (LFPs). Yet, short interruption of these inputs resulted in a phase-reset, creating broad frequency band spectral changes of the LFPs and a transient elevated spike rate across all simulated neurons. Our previous work has reported similar spectral changes in the theta-band and increases in putative PCs spiking in neurophysiological data recorded from two monkeys performing a saccade stop-signal task (Sajad et al., Nat Neurosci, 2019). Motivated by the theoretical results, we quantified the strength of spike-field synchronization (SFS) of 293 neurons recorded across 16 penetrations sampling neural activity across all layers of the Supplementary Eye Field around the period in which a saccade was generated. Overall, the SFS of putative PCs was highest for the theta-band compared to other frequency bands. A significant increase in theta-band SFS on error compared to correct trials was observed on L3 and L5 putative PCs. With this, ongoing work aims to investigate whether individual pyramidal cells (PCs) can act as pacemakers of neocortical theta oscillations.



Theta oscillations can inherently arise from random stimulation of L5-PCs. A Power spectrum density of membrane potentials. B. LFP theta-band amplitude envelope evoked by the activity of 100 unconnected L5-PC under random stimulation (left) and random stimulation plus a time-locked input to all synapses at 1s (right).

A Smartphone Based Optical Device With Integrated App Measures Tissue Oxygenation in Diabetic Foot Ulcers

Faculty Advisor: Anuradha Godavarty, Ph.D. | **Co-author:** Alex Trinidad, Kevin Leiva, Aliette Espinoza, Thomas G Zwick, Jason Edward Levine, Magaly Adelaida Rodriguez, Hadar Lev-Tov, Robert Kirsner, Anuradha Godavarty



United States is the third diabetic capital of the world with 34.2 million Americans diagnosed with diabetes. Complications from diabetes are debilitating including Diabetic Foot Ulcers (DFUs) occurring in 33% of diabetics. Technologies utilizing non-contact imaging approaches are attractive for 2D analysis of infectious wounds such as DFUs. In our past work, a non-contact near infrared smartphone-based optical imaging device (SPOT) was developed to obtain 2D maps of tissue oxygenation (TO), shown in Figure 1. The objective of this work was to develop SPOT as a standalone, integrated device for estimating TO maps along with preliminary efforts to validate these oxygenation measurements with a commercial imaging device. In study one, SPOT app was developed to automate TO maps directly on the smartphone platform in ~1 minute. In study two, SPOT was used to image DFUs in an IRB approved study. In an effort to validate TO measurements obtained using the SPOT device, DFU images were sequentially obtained using a commercial imaging device. Images obtained from both devices were cropped and co-registered using fiducial markers placed on each subject. Linear intensity profiles of TO were extracted (along the x-axis and y-axis) from the wound bed. A Savitzky-Golay filter was applied to these linear measurements prior to performing a correlation coefficient analysis which was found to be between $54.8 \pm 0.23\%$ – $98.4 \pm 0.02\%$ across 5 subjects, demonstrating a strong positive correlation between the two devices. On-going studies using an optical phantom has been initiated to systematically validate our SPOT device.

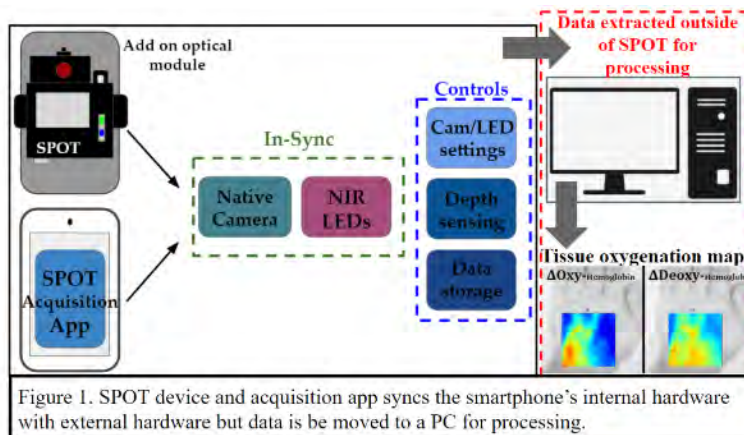


Figure 1. SPOT device and acquisition app syncs the smartphone's internal hardware with external hardware but data is moved to a PC for processing.

Dimensionality Reduction Methods for Brain Machine Interface Control of High Degree of Freedom Robotic Manipulators

Faculty Advisor: Zachary Danziger, Ph.D. | **Co-author:** Zachary Danziger



Invasive brain machine interfaces (iBMIs) translate the electrical activity of cortical neurons into commands for an assistive device, such as a robotic arm. Although iBMIs have the potential to restore substantial independence to the hundreds of thousands of paralyzed individuals in the United States their adoption has been hampered, in part, by their difficulty of use. Improving the performance of iBMIs has been challenging because their invasiveness (brain penetrating electrodes) severely limits the number of subjects that can be incorporated into an iBMI study, which in turn limits the scope of what they can investigate. In our lab, we employ the use of a non-invasive BMI model which uses hand kinematics as a stand in for cortical neuron activity. Using our model, we will investigate the impact of the choice of dimensionality reduction algorithm on the performance of human participants operating a 5 degree of freedom robotic manipulator. Dimensionality reduction methods are typically characterized by their reconstruction error or variance explained, however, we hypothesize that when using these algorithms to control a robotic arm the distribution of the variance captured amongst the latent dimensions is more important. To investigate this, three groups of human participants will pilot the robotic manipulator to pick up and move objects. Each group will use a different dimensionality reduction algorithm for control: Principal Components Analysis, Egalitarian Principal Components Analysis (a novel dimensionality reduction method that solves for latent dimensions which each capture the same amount of variance), or a Non-linear auto encoder network.

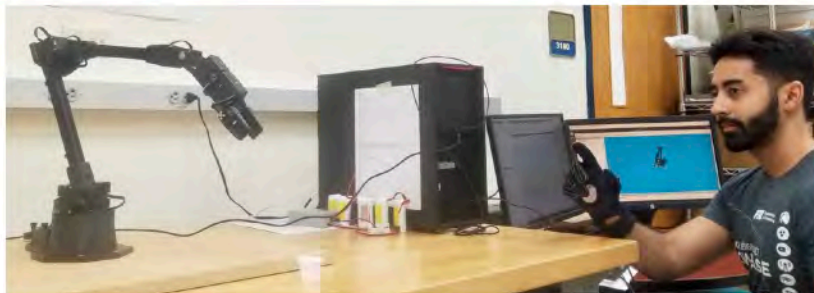


Image of the experiment setup. The user wears a sensor glove which records the 19 joint angles of their hand. The hand joint angles are then translated into a command for the 5 robot joints via one of the dimensionality reduction algorithms.

Investigation of Minimal Detectable Activity of I131 for SPECT and its Clinical Relevance

Faculty Advisor: Anthony McGoron, Ph.D. | **Co-author:** Seza Gulec, Mike Georgiou, Xiaodong Wu, Malek Adjouadi, Wei-Chiang Lin



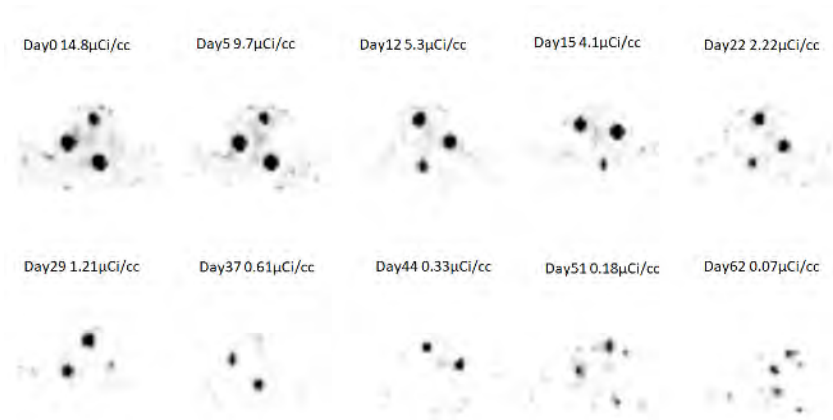
Purpose: To investigate the minimal detectable activity (MDA) of I-131 SPECT under simulated clinical conditions.

Methods: Two 13cm diameter plexiglass cylindrical containers filled with water were used to mimic neck. Different volumes of liquid I-131 (from 0.2cc to 1cc) were drawn into three different size syringes (1cc Φ 4.76mm; 3cc Φ 8.73mm and 5cc Φ 12.7mm). For each container three syringes were taped to the outside wall. 11 scans were acquired for a Siemens Symbia Intevo SPECT/CT and 10 scans were acquired for a GE Infinia SPECT.

I-131 regions of interest (ROI) were drawn on the SPECT images. The contrast to noise (CNR) ratio was evaluated. The RadiAnt DICOM viewer with assessment tools was used to measure signal strength, background noise and calculate CNR. The Curie equation was utilized to evaluate lesion detectability. A CNR of 5 is accepted as the cutoff threshold.

Results: The CNR trend lines for different I-131 volumes were plotted against activity. The trend-lines show little to none size dependence when approaching the threshold. The I-131 MDA under optimal conditions for Siemens Symbia is 0.18uCi. For Siemens Non-AC SPECT, MDA is 0.25uCi. For GE Infinia, MDA is 0.40uCi.

Conclusion: For clinical detectability of thyroid remnant and metastatic lymph nodes, based on 20% uptake of 1mCi injection of a 20gram thyroid, for thyroid remnant, the corresponding volume is 0.018cc, 4mm in diameter. RAS-like nodes (40% uptake) require a 5mm in size. BRAF-like nodes (3% uptake) require a 1.2cm in size.



Macrophage Effects on Engineered ECM Valves

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-authors:** Claudia Ponce Aportela, Oriana Marrone Mantovani, Sharan Ramaswamy

Funding Source: Florida Heart Research Foundation and National Science Foundation



While heart valve replacement is a mature technology, it has distinct limitations, especially in specific sub-populations, such as in children with critical valve anomalies. Tissue engineered heart valves (TEHVs) are being developed to overcome limitations that prosthetic valve replacements have and to be able to support the somatic growth needed in pediatric patients. As we made progress in the making of a new engineered extracellular matrix (ECM) valve (Fig. 1; [1]), that we have recently identified possesses high elastin content for promoting cell chemotaxis, the question of initial immune responses to this valve construct will be important to assess. Therefore, M1 and M2 macrophages response assessments to this tissue engineered heart valve will be carried out. The experimental plan is as follows: separate 3-dimensional cultures of human M1 and M2 cells will be performed on two different types of valve construct materials: (i) the engineered elastin-rich valves and (ii) the raw bio-scaffold valves, known as porcine small intestinal submucosa (PSIS; Cormatrix, Roswell, GA) which was used as a scaffold to develop (i). Once the cultures have been carried out, histology and immunostaining will be conducted in order to identify whether there is any evidence of inflammation in the case of M1 culture and if cytokines that can accelerate tissue regeneration will be produced during the culture of M2 macrophages. Signal intensity maps will be performed to provide quantification and subsequent statistical assessment for significance ($p < 0.05$) between the two groups.

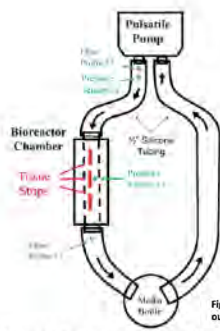


Figure 1: Pulsatile flow-based dynamic culture of stem cell-derived engineered ECM valves in our laboratory, with the tissue strips representing the valve constructs [1].

Non-Contact Near-Infrared Analysis of Perfusion of Mice Tail During the Progression of Chronic Kidney Disease

Faculty Advisor: Anuradha Godavarty, Ph.D. | **Co-author:** Valentina Dargam, Kevin Leiva, Haniyeh Alirezaei, Joshua Hutcheson, Anuradha Godavarty

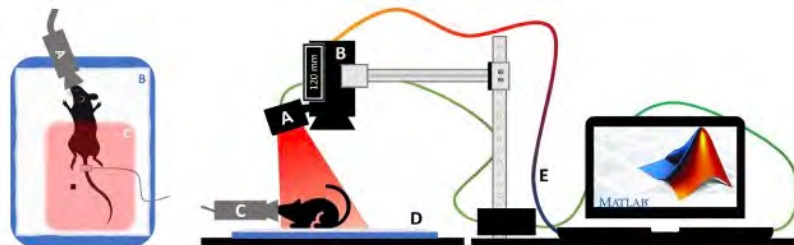


Chronic kidney disease (CKD) results in a decrease of renal function which causes buildup of uremic toxins and eventually the development of calcification on vessel walls. With a restriction in blood flow, cardiac work increases then leads to a decrease in capillary density and perfusion [1]. Non-invasive techniques to analyze vascular function and blood perfusion could help assess cardiovascular risk in CKD patients.

Since no study has correlated CKD and perfusion in the extremities, the objective of this study was to observe temporal-changes of peripheral vasculature oxygenation in a mouse model with CKD-induced cardiovascular disease and vascular calcification.

Six mice were placed on a high adenine+phosphate diet to induce advanced CKD of which led to arterial calcification. Each near-infrared optical imaging session (baseline and week 12) was performed with an occlusion stimulus for a 5-minute period with 60-second stimulus cycles. The extent of reperfusion of total hemoglobin was compared between baseline and week 12.

Results showed a reduction in the extent of reperfusion in the mice with advanced CKD and arterial calcification when compared to baseline. Future studies will extend the observational comparisons while the disease is developing.



Engineered Cardiac Tissues Derived From hiPSC-Cardiomyocytes Seeded Onto a Cardiac Patch Under Rotisserie Culture

Faculty Advisor: Sharan Ramaswamy, Ph.D. | Co-authors: Sharan Ramaswamy

Funding Source: National Science Foundation



The irreversible damage to cardiac muscle from a myocardial infarction causes cardiomyocytes to lose contractility and induces scar tissues eventually leading to heart failure. The use of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) to enhance cardiac function is currently being investigated. However, the maturity of hiPSC-CM and the generation of hiPSC-CM derived tissues still needs further improvement. Hence, the first and the only FDA approved cardiac patch (CorTMPATCH) for epicardial infarct repair was utilized for this study. It is noted that as an acellular extracellular matrix biomaterial with structural proteins incorporated, CorPATCH is thought to be a robust substrate for the cells to grow. After hiPSC has been differentiated into hiPSC-CM (Fig. 1i), hiPSC-CM is seeded onto the patch via a 22-Day rotisserie culture (static). The cell seeding density was about 10,000 cells/mm². At the end of rotisserie culture, it showed visible cell attachment to the patch (n=3) compared to the unseeded raw patch (n=3; Fig. 1ii). Both raw and cell seeded patches were then sectioned at 7 um in thickness for comparison. The cardiac markers used for staining were NKX2-5, cardiac troponin T (TNNT2), alpha actinin 2 (ACTN2), and myosin heavy chain (MHC). The results of immunofluorescence showed that hiPSC-CM in round shape and clumps grew on the gel-coated well-plates (Fig. 1i). The fact that hiPSC-CM seeded onto the patch stained positive for cardiac markers (ACTN2 and MHC) has demonstrated the possibility of hiPSC-CM to be successfully grown on the patch, with maintenance of their phenotype (Fig. 1ii).

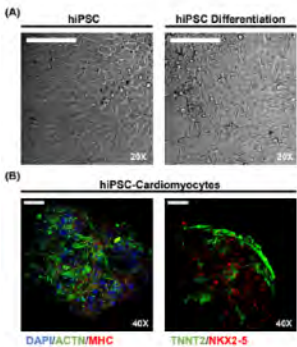


Figure1: (i) hiPSC-CM cultured on well-plates.

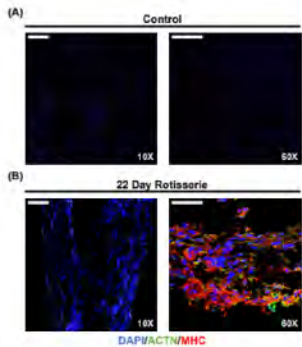


Figure1: (ii) Raw CorPATCH versus hiPSC-CM seeded onto CorPATCH.

Preliminary FSI Model of a Healthy Vs Severely Calcified Aortic Valve

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-author:** Sharan Ramaswamy

Funding Source: Koerner Family Foundation



Fluid-structure interaction (FSI), as the name implies, refers to dual physics coupling between fluid dynamics and structural mechanics. Modeling of the aortic valve is a challenging FSI problem whereby the hemodynamics and aortic structure undergo rapid, dynamic, changes across a cardiac cycle that greatly influence each other. Towards building an accurate FSI model of calcific heart valves for potential interventional benefits, a comparative FSI simulation between a healthy and a severely calcified aortic valve was initiated here. The geometry consists of the aortic sinus and three valve leaflets. The sinus's ventricle and aortic outflow tracts were fixed in displacement and rotation along with the leaflet edge's connecting to the sinus. Sinus and healthy leaflet properties were set to 2 MPa for the Young's Modulus, calcified leaflets were set to 20 MPa. The inlet had a physiologic transvalvular pressure waveform with the outlet being 0 mmHg. The fluid, blood's, viscosity was assumed Newtonian, 3.3 cP, with a density of 1060 kg/m³. Results indicated that the time averaged WSS (TAWSS) were overall lower in the severely calcified case, 2.1 dynes/cm², than in the healthy case, 4.3 dynes/cm². Peak pressure drops and inlet velocities for healthy, 8.91 mmHg and 1.05 m/s, and severely calcified, 99.52 mmHg and 3.7 m/s, correspond well with literature [Otto, C. M., & Prendergast, B. (2014)]. Concluding, FSI simulation for the purposes of aortic valve disease modeling is feasible and can be done to deduce biometric (TAWSS, ΔP , Q-Criterion, etc) differences between healthy and severely calcified aortic valves.

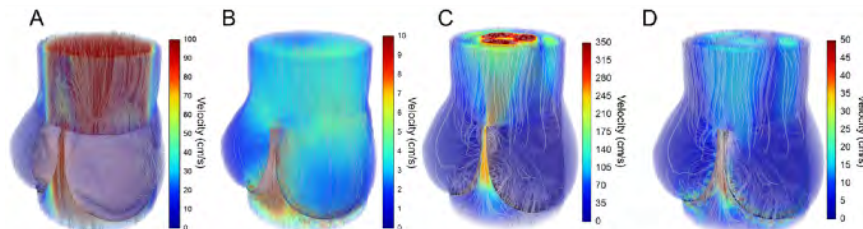


Figure 1: Velocity streamlines around aortic valve at two time points: Healthy A) Peak B) Minimum. Severely Calcified C) Peak D) Minimum.

Examine the Role of Astrocytes in Cortical Circuits With Spatiotemporal Event Detection Package

Faculty Advisor: James Schummers, Ph.D. | **Co-authors:** Tomas Suarez Omedas, Gerson Romero, Sally P. Duarte, Vered Kellner, Monica Lopez Hidalgo, James Schummers

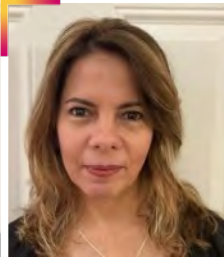


Astrocytes are the most common glial cells in the central nervous system, but their connection to higher brain functions is still unknown. The primary excitable signaling in astrocytes is via increases in intracellular calcium, which can be evoked by visual stimulation in ferret visual cortical astrocytes in-vivo. These calcium signals can vary widely in size, timing, location, and propagation, making analysis challenging. Tools for quantitative analysis of localized astrocyte calcium events are lacking. A recently developed analysis package, AQuA (Astrocyte Quantitative Analysis), is a MATLAB-based platform able to characterize both spatial and temporal aspects of astrocyte events. Input parameters to AQuA determine whether separate events are merged, change the propagation direction and speed, reshape events, and exclude some events completely. Accurate astrocyte analysis requires optimization of the parameters input to AQuA. The primary output of AQuA is a list of discrete events which are characterized by their spatial footprint at each point in time. Two event characteristics are of particular interest: their size and their movement towards or away from the soma. We are also interested in identifying “hot spots”, regions with a significant amount of overlapping calcium events in the same spatial area of the cell to further analyze the activity in the cell and where calcium activity is more prominent. These hot spots may provide insight into the dynamics of the calcium events of the cell in a spatial sense.

In Vitro Effects of Bone Marrow Stem Cell-Secreted Exosomes on Cardiac Fibrosis

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-author:** Manuel Perez, Sharan Ramaswamy

Funding Source: National Science Foundation



Post-myocardial infarction remodeling is a tissue repair process in which adversely effected cardiac tissue is replaced by non-contractile fibrotic scar tissue. This progressive scar tissue growth combined with the poor regenerative capacity of the heart eventually can lead to heart failure. Cardiac patches with bioactive molecules have recently been investigated [1] as a promising treatment for promoting cardiac functional recovery (Fig. 1 [1]).

In our lab, bioactive factors from engineered stem cells-derived exosomes are currently being investigated for enhancing cardiac patch development. Specifically, we propose that exosome-enriched bio scaffold patches will modulate Human Cardiac Fibroblasts (HCF) towards reducing fibrotic response. For this purpose, samples consisting of HCF seeded within a Bioscaffold (CorPatch, Cormatrix, Rosewell GA))-microgel constructs with and without fibrotic stimulation will be used. Bioscaffolds enriched with exosomes derived from stem cells exposed to oscillatory shear stresses will be applied to these samples, representing the treatment group, while remaining untreated samples will serve as a control group. Analysis of specific pro and anti-fibrotic related markers and vasculogenic factors will be assessed through gene and protein expression, histology and biochemical and functional assays. Confirmation of substantial reduction in cardiac scar tissue growth in vitro with our exosome strategy, will enable us to objectively proceed towards in vivo studies next.

[1] Silveira-Filho LM, et al (2021): Can a Biohybrid Patch Salvage Ventricular Function at a Late Time Point in the Post-Infarction Remodeling Process? JACC Basic Transl Sci. 2021 Mar 24;6(5):447-463.

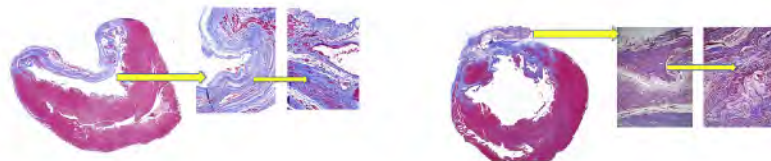


Figure 1: Example of study (Silveira-Filho LM, et al, 2021 [1]) showing a rat left ventricle treated with a bioactive patch on the right and untreated control on the left. Red and blue colors indicate healthy and infarcted cardiac tissues respectively [1].

Oscillatory Flow Conditioned Exosomes for the Treatment of Myocardial Infarcts

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-authors:** Brittany Gonzalez, Yih-Mei Lin, Asad Mirza, Sharan Ramaswamy

Funding Source: National Science Foundation



Heart disease is the leading cause of death in the United States [1]. A large sub-set of patients suffering from myocardial infarction (MI) will still deteriorate towards heart failure post infarct. Current clinical treatments for MI such as angioplasty and arterial grafting, focus on restoring blood flow to affected cardiac tissues, but are not able to prevent the subsequent remodeling of injured cardiac tissue and progression to eventual heart failure.

Recently, stem cell-injection therapy to the heart has also been investigated as an option to treat MI with the goal of restoring heart function. Scientists have used human, adult bone marrow mesenchymal stem cells (BMSCs) to induce regeneration of affected cardiac tissues. However, the use of undifferentiated BMSCs has produced only marginal results due to their poor retention and engraftment in the injured tissue. Recent findings suggest that the beneficial effect of stem cells is derived from the secretion of bioactive trophic factors. A subset of these secreted factors, exosomes, contain growth factors and cytokines that can potentially be used as therapeutic agents for the repair of diseased heart tissue.

To investigate the production of these therapeutic exosomes, we seeded human, adult BMSCs onto bio-scaffolds and subjected them to oscillatory flow [2], leading to exosomal secretion (Fig. 1) into the conditioned media, with these exosomes containing proteins that can promote cardiac wound healing. Under exposure to this oscillatory fluid-induced shear stress environment, the BMSCs will potentially secrete exosomes, rich in molecular factors that can be beneficial for cardiac repair, post-MI.

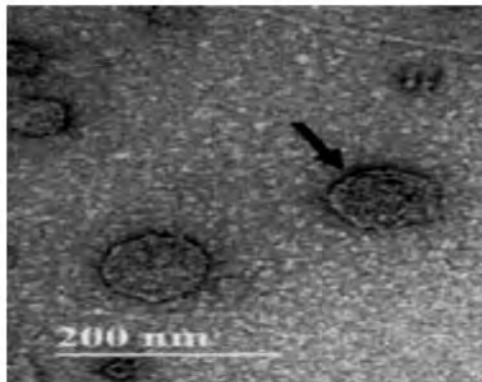
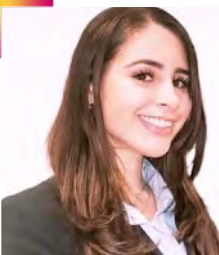


Figure 1: Microscopy image of exosomes isolated from stem cells [2].

Increased Engineered Collagen Production After Co-Culture of Valvular Cells and Macrophages on a 3D Engineered Tissue Substrate

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-authors:** Oriana Marrone Mantovani, Sharan Ramaswamy

Funding Source: Florida Heart Research Foundation



Critical congenital valve defects have a high mortality in young children. This is due to the unavailability of small prosthetic valves and their inability to support somatic growth. To promote accelerated de-novo tissue growth on the valve after valve implantation, in our lab, we had previously seeded porcine small intestinal submucosa (PSIS; Cormatrix, Roswell, GA) with mesenchymal stem cells [1] which results in the production of an elastin-rich layer. To test the extracellular matrix (ECM) elastin-rich engineered valves for accelerated de-novo tissue formation, in-vitro experiments were done by comparing ECM elastin-rich against the control group of raw PSIS substrates (n=4 samples/group). Valvular interstitial cells (VICs) were seeded on these substrates for 8 days and conditioned dynamically for 2 weeks with induced wall shear stress (3.1 dynes/cm²) and oscillatory flow (oscillatory shear index (OSI) of 0.20) per previous work in our lab [1]. In addition, VICs were co-cultured with macrophages on the ECM elastin-rich and raw PSIS substrates for 3 days and were then assessed histologically. Our results were quantified using heat intensity mappings performed on histological sections. We found statistically significant ($p < 0.05$) de-novo collagen formation in ECM elastin-rich engineered substrate when seeded in VICs-Macrophage co-culture (Fig. 1). Our preliminary in vitro findings suggest that the ECM elastin-rich substrate can facilitate accelerated tissue formation for the regenerative heart valve application.

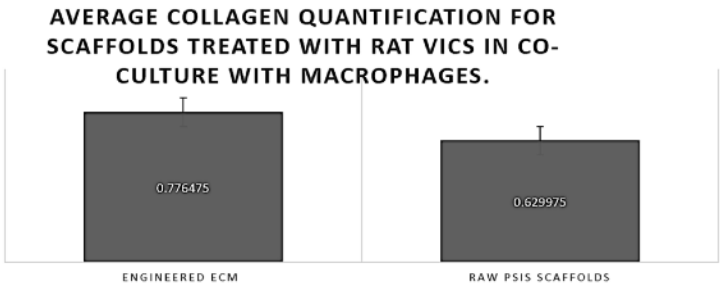
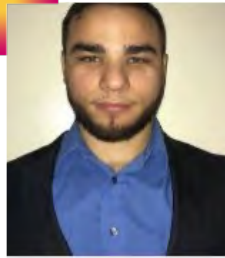


Figure 1: Statistically significant collagen formation via VIC+Macrophage co-culture on ECM elastin-rich substrates (Engineered ECM) compared to equivalent co-culture on raw PSIS bio-scaffolds.

Biochemical Induction of an Engineered Tissue Model System for Severely Calcified Heart Valves

Faculty Advisor: Sharan Ramaswamy, Ph.D. | **Co-authors:** Amanda D. Barreto, Sharan Ramaswamy



When calcified aortic heart valve disease progresses into its late stages, the valve becomes severely calcified and requires prosthetic valve replacement. Although current valve replacement options are mature technologies, there are no pharmaceutical options to manage aortic valve disease. A major limitation of finding new therapeutic options is that no current animal models can accurately predict these experimental pharmaceutical effects on human aortic valve calcification. The study being conducted here was to develop an in vitro engineered severely calcified valve tissue model system as a platform for testing emerging therapeutics Using Porcine Small Intestinal Submucosa (PSIS, Cormatrix, Roswell, GA) as a substrate, rat valve interstitial cells (VICs) were seeded onto the PSIS material and cultured in a rotisserie for 8 days. The specimens were then transferred into a well-plate and cultured in pro-calcific media for 7 days to chemically induce severe calcification. Next, the engineered tissues were prepared for alizarin red histological staining for evidence of calcification. Our results showed that the pro-calcific media did indeed cause calcification on the VIC-seeded PSIS substrates due to the red staining from the alizarin red (Fig. 1). Our immediate next step is to transition this work to Human VICs.

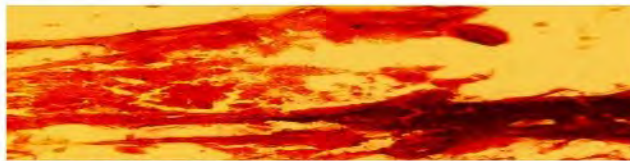


Figure 1: Positive histological staining for calcium in VIC-seeded PSIS bio-scaffolds.

Mechanical Stretch Leads to the Caveolin-1-Dependent Release of Mineral Forming Extracellular Vesicles From Vascular Smooth Muscle Cells

Faculty Advisor: Joshua D. Hutcheson, Ph.D. | Co-author: Joshua D. Hutcheson



Extracellular vesicles (EV), small enclosed structures released from cell membranes, mediate intracellular communication and arterial wall remodeling. Caveolin-1 (Cav-1), an integral structural component of plasma membrane invaginations, is required for the formation of a specific class of EVs released by vascular smooth muscle cells (VSMCs) in pathological vascular remodeling. These EVs nucleate the formation of vascular calcification, which is the most significant predictor of cardiovascular morbidity. Caveolin-1 is a mechanosensitive protein, and VSMCs reside in dynamic cardiovascular tissues. However, the role of mechanics in Cav-1-induced EV formation from VSMCs has not been reported. We hypothesized that pathological levels of mechanical stretch would induce formation of mineral-promoting Cav-1-positive EVs from VSMCs. To test this hypothesis, porcine VSMCs were cultured under two different cyclic stretches (10 and 15%, 0.5Hz) for 72hrs. Compared to non-stretched VSMCs, the 10% and 15% stretch regimes led to $144 \pm 4\%$ and $253 \pm 14\%$ increases in Cav-1-positive EVs, respectively (Fig.1A). The EVs also appeared bigger than those from non-stretched samples with a 27% and 75% increase in size of EVs from the 10% and 15% stretched VSMCs, respectively. Mineralization potential of EVs can be measured by incubating EVs in phosphate solution and measuring light scattering by mineral at 340nm. The EVs from stretched VSMCs demonstrated higher mineralization potential than the EVs from non-stretched VSMCs (Fig.1B). These data provide new insights into the effect of mechanical stimulation on EV formation and calcifying potential.

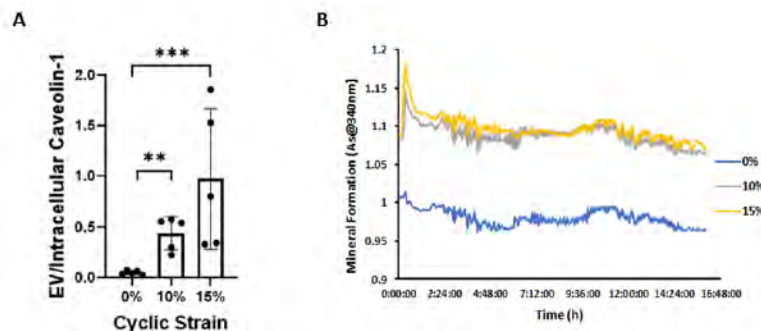


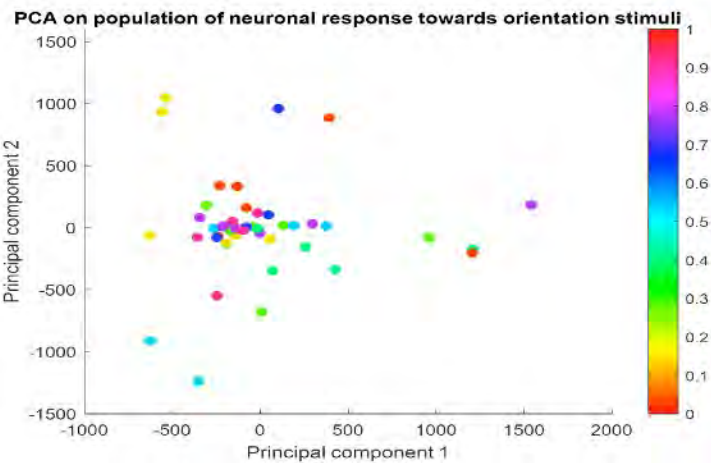
Fig. 1. A) Cyclic stretch causes caveolin-1 release in EVs. B) EVs from stretched VSMCs form more calcific mineral as assessed by absorbance of 340nm light.

Revealing the Geometry of Populations Response of Neuron in Visual Cortex of Ferret

Faculty Advisor: James Schummers, Ph.D. | Co-author: Sally P. Duarte, James Schummers



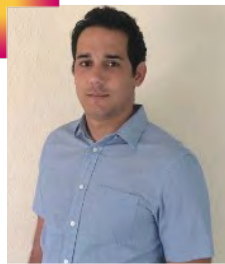
Traditionally, sensory processing in the brain has been studied using the responses of single neurons. However, new technology now allows us to record the activity of many hundreds of neurons at once. The core concept of analyzing large populations of neuronal responses is to determine whether there are network-level mechanisms at play that do not exist at the level of the single neuron. The aim of this project is to examine the responses of large populations of neurons that are actively processing visual stimuli. We will image the activity of populations of visual cortical neurons with two-photon calcium imaging microscope and analyze the response of the population of neurons whether and how the neural activity correlated at population level. We will then reduce the high dimensional data collected from the visual cortex in response to dynamic visual stimuli. We will apply novel analytical and statistical methods such as PCA on the response of a population of cortical neurons to generate a low dimensional projection of high dimensional data that will represent whether the response of a population of cortical neurons evoked by a particular shape or cluster in response to various visual stimulation. This will reveal whether there are certain components of the neuronal response that are responsible for determining most of the variance in the response for different orientation stimuli.



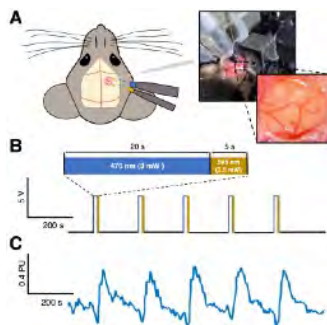
A Novel Non-Linear Approach to Characterizing Astrocytic Neurovascular Coupling With Optogenetics and Computational Modeling

Faculty Advisor: Jorge Riera, Ph.D. | **Co-author:** Lazaro Fernandez, Lakshmini Balachandar, Jorge Riera

Funding Source: Wallace H. Coulter Foundation



The role of astrocytes in neurovascular coupling remains hotly contested with various proposed mechanisms of hemodynamic response. Past findings have proven calcium activity to be the essential component in all astrocytic pathways of vascular control. However, these findings have proven contradictory over the last two decades, suggesting that an additive approach may not be appropriate for the quantification and characterization of astrocytic neurovascular coupling. We hypothesize that these astrocyte-governed biochemical pathways have an unequal contribution and that they enact hemodynamic change in a dynamic, non-linear fashion. Using a tetracycline-based transgenic mice model, expressing ChR2-EYFP solely in astrocytes, we optogenetically stimulated the production of a calcium wave in mice cortical astrocytes and evaluated hemodynamic change with a Laser Doppler Flowmetry (LDF) modality. Under these conditions, a sustained increase in localized perfusion of around 20% was found within stimulated areas. Subsequent pharmacological inhibition of phospholipase (PLA2) governed pathways facilitated the characterization of PLA2 isoforms within cortical astrocytes. Furthermore, we created a computational biophysical model of hemodynamic response aiming to reproduce the experimental data generated from this study and previous ones. This data better elucidates the role of astrocytes in regional resource delivery, suggesting a new perspective in the diagnosis, treatment, and prevention of neurodegenerative diseases with vascular presentations such as Alzheimer's Disease. We believe our findings provide a new approach by which future studies may revisit the use of pharmacology to characterize the neurovascular coupling phenomenon.



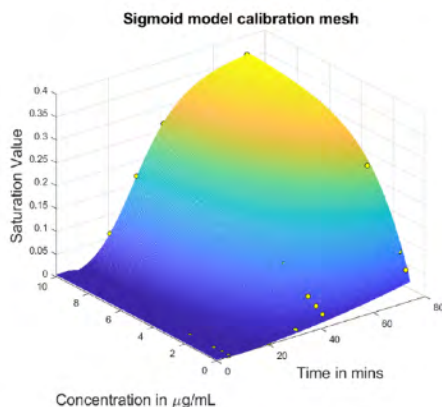
A Surface-Based Calibration Approach To Enable Dynamic and Accurate Quantification of Colorimetric Assay Systems

Faculty Advisor: Joshua D. Hutcheson, Ph.D.



Cardiac troponin (cTn) has become a gold standard biomarker for identifying and monitoring heart failure and predicting future cardiovascular morbidity. A recent HUNT study showed that high sensitive cTn I type (hs-cTnI) gives a better cardiac risk classification than Framingham, and is more suitable for CVD screening within the asymptomatic general population. However, developing a point-of-care assay system for both acute diagnoses and cardiovascular risk stratification using cTnI is difficult due to its wide clinical range. An ideal assay system would allow detection of low circulating concentrations for cardiac risk stratification and high concentrations associated with acute cardiac events. Colorimetry is widely used in assay systems for its low-cost, ease-of-use, rapidity, moderate storage requirements and intuitively visible effects. Traditional colorimetric assays often have limited dynamic ranges that cannot cover large concentrations in a single system.

We developed a novel “calibration mesh” method based on a sigmoid model of saturation color signal. In comparison to a conventional calibration curve obtained at a single assay time, the calibration mesh provided a faster output for high enzyme concentrations and reached a lower limit of detection by extending the reaction time. This method improves robustness, detection range and provides a dynamic and faster assay output. Utilization of this technique could yield a low-cost assay system to measure cTn for both risk stratification and acute diagnoses.





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This academic event is made possible by the generous support of the Wallace H. Coulter Foundation. To learn more about the Wallace H. Coulter Foundation please visit whcf.org.

Project Judges

On behalf of the entire Biomedical Engineering staff, we'd like to thank our judges for their dedication and skill when it came to the judging of our Graduate Research Day oral and poster presentations. Without your generosity, knowledge and patience, this celebration would not have gone as smoothly as it has. Thank you for volunteering your services, especially during such a busy academic term.

Guest Speakers

On behalf of the entire Biomedical Engineering staff, we wanted to express our paramount gratitude to **Dr. John X.J. Zhang**, and **Ms. Nelly Leon** for presenting your seminar during Graduate Research Day. Your outstanding participation was appreciated and we are highly grateful to you for your treasured contribution.

To Our Dedicated & Distinguished Faculty



Michael Brown, M.D., Ph.D.



Michael C. Christie, Ph.D.



Zachary Danziger, Ph.D.



Anuradha Godavarty, Ph.D.



Joshua Hutcheson, Ph.D.



Shuliang Jiao, Ph.D.



Wei-Chiang Lin, Ph.D.



Anthony McGoron, Ph.D.



Raj Pulugurtha, Ph.D.



Sharan Ramaswamy, Ph.D.



Jessica Ramella-Roman, Ph.D.



Jorge Riera, Ph.D.



James Schummers, Ph.D.



Nikolaos Tsoukias, Ph.D.

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