FIU BIOMEDICAL ENGINEERING

GRADUATE RESEARCH DAY

PRESENTED BY WALLACE H. COULTER FOUNDATION LECTURE SERIES

FRIDAY, MARCH 1, 2019

9:00 AM	Seminar: Jaffus Hardrick	EC 2300
10:30 AM	Graduate Students Poster Session	Panther Pit
1:00 PM	Graduate Students Oral Presentations	EC 2300
3:00 PM	Seminar: Hyungbae Kwon	EC 2300
4:00 PM	Awards Ceremony	EC 2300

Jaffus Hardrick
Interim President
Florida Memorial University

Hyungbae Kwon
Research Group Leader
Max Planck

FIU Engineering & Computing
Biomedical Engineering

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About the Keynote Speakers:

Jaffus Hardrick

Jaffus Hardrick, Ed.D is an award-winning senior academic executive with a proven track record for promoting student success, enhancing student outcomes, optimizing faculty and staff development, and cultivating a culture of excellence. Dr. Hardrick fully understands the promise of education. Through education, Dr. Hardrick was fortunate to earn significant roles as a higher education administrator. He served as the vice provost for Access and Success at Florida International University, the nation's fourth-largest public urban research university; assistant vice provost for Academic Affairs at Baylor University; and now the interim president of Florida Memorial University. As an education executive, he is committed to developing future leaders and closing achievement gaps among underrepresented students, and creating a culture of academic excellence in higher education. He is also the co-author of Making Global Learning Universal: Promoting Inclusion and Success for All Students (Stylus).

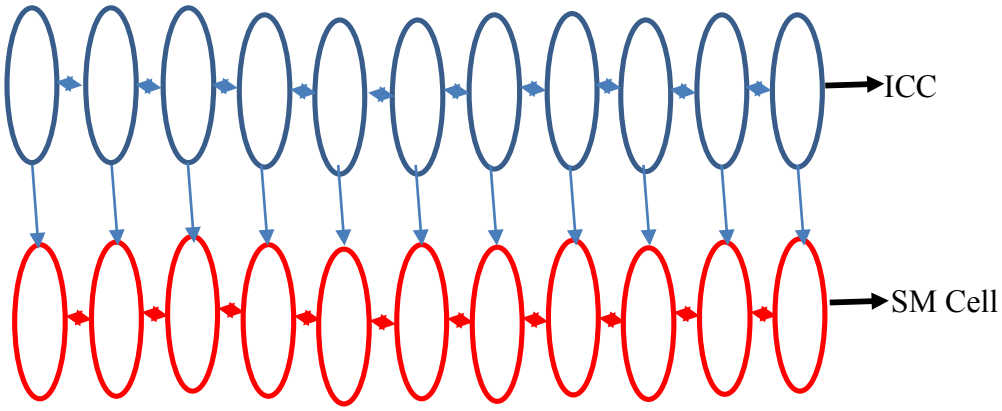
Hyungbae Kwon

Hyungbae Kwon received his Ph.D. in Dr. Pablo Castillo's lab at the Albert Einstein College of Medicine, and postdoctoral training with Dr. Bernardo Sabatini at Harvard Medical School. During his postdoctoral period, he used cutting-edge laser-based optics to understand mechanisms of excitatory synapse formation at single synapse resolution. In 2012, he began his independent laboratory at the Max Planck Florida Institute for Neuroscience, where he continued to study mechanisms of synapse formation during early brain development and created novel optogenetic approaches that enable to dissect animal sensation, cognition, behaviors at high spatiotemporal resolution. Using these newly developed techniques together with other approaches, current research in the Kwon laboratory focuses on understanding principles underlying various forms of cognitive brain actions. In 2019, Dr. Kwon's laboratory is moving to the Solomon H. Snyder Department of Neuroscience at Johns Hopkins University of School of Medicine.

Modeling of slow wave in the stomach and sensitivity analysis of excitatory neurotransmitter release

Authors: Ashfaq Ahmed and Ranu Jung

Faculty advisor: Dr. Ranu Jung



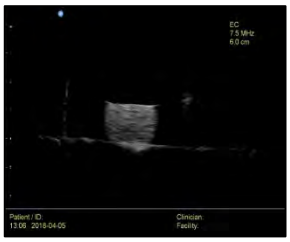
The stomach exhibits a characteristic slow wave of contraction. Slow waves originate from dominant pacemaker cells within the stomach wall along the greater curvature in the mid-corpus and spread aborally through the antrum to the pyloric sphincter. Disruption of the slow wave is supposed to play an active role in slowing down gastric motility. To better understand the mechanisms underlying slow wave anomalies, we have computationally modeled the slow waves as being generated by a chain of interconnected biophysical circuits of networks of cells. This biophysical circuit consists of interstitial cells of Cajal (ICC) and smooth muscle cells (SMC). The ICC have been modeled with a frequency gradient with the rostral most cell having the highest frequency and caudal most cell having the lowest frequency. The first and last ICC of the network have a constant phase delay of ~4 sec in steady state indicating entrainment in the network and ICC and SMC cells are in phase. Excitatory neurotransmitter release in ICC likely controls the frequency of slow wave in the stomach. Sensitivity analysis has been performed on the neurotransmitter release parameter. Previous studies have done this sensitivity analysis on a lumped model of slow wave in the stomach. This is probably the first study where sensitivity analysis of neurotransmitter release has been done in a biophysical model of slow wave.

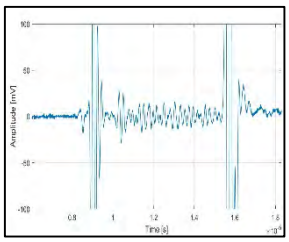
Toward Intraoperative Quantitative Ultrasound for Tissue Differentiation: A Phantom Study

Authors: Mohamed Almadi

Faculty advisor: Wei-Chiang Lin, PhD

Figures





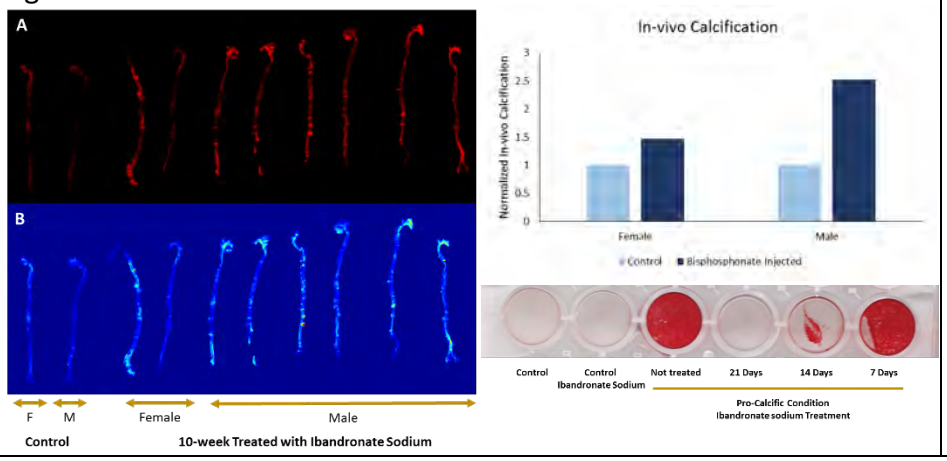
Ultrasound imaging uses relative echogenicity to differentiate different tissue types, and it is a valuable tool for the intraoperative detection of tumors. However, this modality is highly susceptible to various artifacts, which limit the neurosurgeon's ability to differentiate healthy and tumorous tissue intraoperatively. Quantitative ultrasound (QUS) provides improved tumor detection capability because it extracts valuable intrinsic acoustic and mechanical characteristics based on radio frequency echo signals. The major goal of this project is to build a probe-based, combined QUS/optical spectroscopy system that can measure intrinsic acoustic and optical properties from in vivo tissue and hence guide surgery in real time. The optical probe was developed and tested previously; therefore, the recent development focused on the QUS modality. In this pilot study, we developed a QUS methodology to estimate the acoustic properties of tissue-mimicking phantoms. To accomplish this goal, six ballistic gel-based phantoms, acquired from Humimic Medical, were used. The acoustic properties of the phantoms were measured using a portable ultrasound system. The results showed that our QUS system can differentiate the acoustic properties between the phantoms. Future work will include testing the tissue differentiation capability of the QUS methodology *in vitro* and *in vivo* using a rat brain tumor model.

In vitro and *In vivo* Assessments of Time-dependent Bisphosphonates Treatment in Development of Cardiovascular Calcification

Authors: Amirala Bakhshian Nik, Valentina Dargam, Joshua D. Hutcheson

Faculty advisor: Joshua D. Hutcheson

Figures

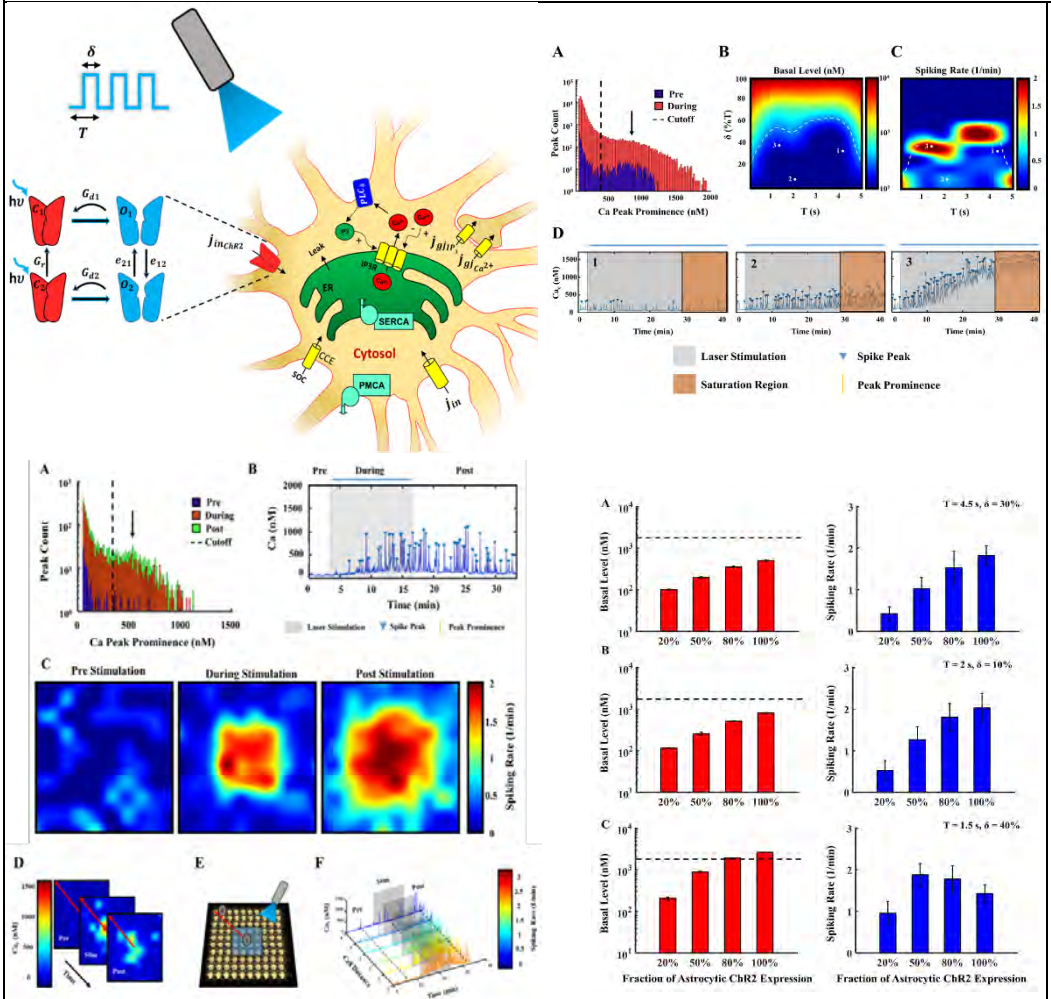


Calcium mineralization occurs either physiologically through bone formation or pathologically in cardiovascular calcification. Release of cell-derived particles, called extracellular vesicles (EVs) plays an important role in mineral formation. Calcifying EVs contain mineral promoting factors such tissue non-specific alkaline phosphatase (TNAP), an enzyme that hydrolyzes calcification inhibitors and produces free phosphate that is used in mineral formation. Bisphosphonates are common osteoporosis therapeutics, which stabilize calcium phosphate minerals. They also prevent mineral growth and maturation in cardiovascular tissue by chelating phosphate ions that are required for calcification. However, administration of these therapeutics demonstrated cardiovascular side effects, more prominent in patients with cardiovascular event history. In this study, we hypothesized that bisphosphonates prevent initial mineralization when given prior to the onset of vascular calcification, but exacerbate mineral formation if once calcification has begun. Our results show that in vitro treatment of human coronary artery smooth muscle cells with bisphosphonate for 21 days prevented calcification, whereas 7-day treatment did not hinder the formation of calcium-phosphate deposits. *In vitro* treatment with bisphosphonate ibandronate sodium (10 µM) reduced calcifying EV TNAP activity by 85% and 55% for 21- and 7-day treatments, respectively. Furthermore, we analyzed calcification growth over the course of 25 weeks in Apolipoprotein E-deficient ($Apoe^{-/-}$) mice on a western atherogenic diet (42% fat). Following 10 weeks of the diet, the mice received biweekly subcutaneous injections of bisphosphonate ibandronate sodium (2 mg/kg). A tail-vein injection of near-infrared calcium tracer OsteoSense was given after 25 weeks of the atherogenic diet. The results from near-infrared tissue scanning indicate that the bisphosphonate increased calcification in the aorta, in both male and female mice, compared to the control group (biweekly saline injection) by 2 fold. Both the *in vitro* and *in vivo* data support our hypothesis that bisphosphonate promotes cardiovascular calcification if given after initial mineral nucleation. These studies could inform clinical decisions regarding potential cardiovascular effects of bisphosphonate treatment.

Unraveling ChR2-driven stochastic Ca^{2+} dynamics in astrocytes

Lakshmini Balachandar*, Arash Moshkforoush*, Carolina Moncion*, Josue Santana, Jorge Riera
* equal author contribution

Faculty advisor: Dr. Jorge Riera

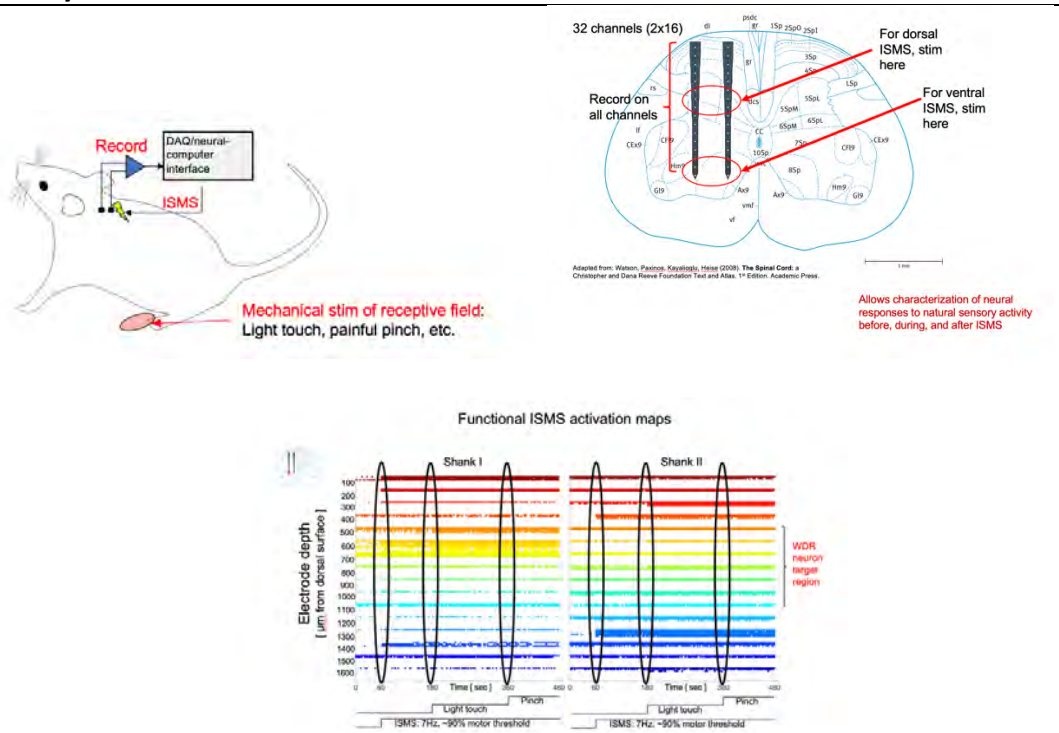


Control of astrocytes via modulation of Ca^{2+} oscillations using techniques like optogenetics can prove to be crucial in therapeutic intervention of a variety of neurological disorders. However, a systematic study quantifying the effect of optogenetic stimulation in astrocytes is yet to be performed. Here, we propose a novel stochastic Ca^{2+} dynamics model that incorporates the light sensitive component – Channelrhodopsin2 (ChR2). Utilizing this model, we studied the effect of various light stimulation paradigms on astrocytes for select variants of ChR2 (wild type, ChETA and ChRET/TC) in both an individual and a network of cells. Our results exhibited a consistent pattern of Ca^{2+} activity among individual cells in response to optogenetic stimulation, i.e., showing a steady rise in the Ca^{2+} basal level with increase in pulse width, and distinct regions with maximal spiking probability. Additionally, our global sensitivity analysis indicated that directing variants towards the first open state of the photo-cycle of ChR2 (O_1) enhances spiking activity in astrocytes during optical stimulation. Evaluation of the effect of ChR2 transduction efficiency (heterogeneity) on Ca^{2+} signaling revealed that the optimal stimulation paradigm of a network does not necessarily coincide with that of an individual cell. Collectively, the framework presented in this study provides valuable information in the selection of paradigms that elicit optimal astrocytic activity using existing ChR2 constructs, as well as aid in the engineering of future optogenetic constructs.

Intraspinal microstimulation in motor regions modulates neural transmission in spinal pain pathways

Authors: Maria F. Bandres; Valentina Melero; Jacob McPherson

Faculty advisor: Jacob McPherson



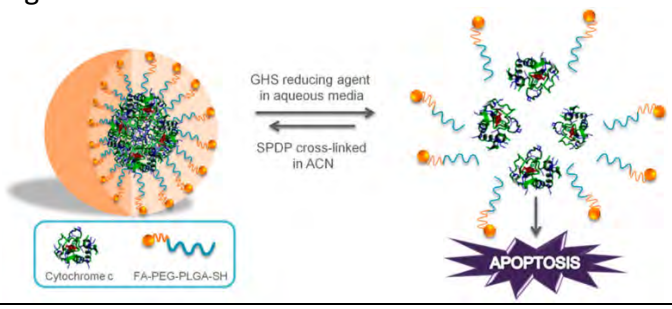
Spinal cord injury (SCI) results in dramatic changes in neural excitability below the lesion, leading to debilitating motor impairments, dysregulation of reflexes, and neuropathic pain. Therapies seeking to restore sensorimotor function after SCI face the challenge of increasing spinal motor output while decreasing the spinal responses to sensory feedback that contribute to hyperreflexia and pain. We have previously shown that focal electrical stimulation of motor regions of the spinal cord (i.e., intraspinal microstimulation; ISMS) can increase spinal motor output after SCI. Here, we characterized the ability of ISMS to simultaneously modulate neural transmission in spinal pain pathways. All experiments were approved by the FIU IACUC and conducted in adult Sprague-Dawley rats under urethane anesthesia. We recorded intraspinal neural activity in the territory of the L5 spinal nerve before, during, and after ISMS. We found that even short periods of ISMS could modulate transmission in pain pathways, indicated by changes in the number of neurons recruited and/or their firing rate during mechanical stimulation of the L5 dermatome. Our results demonstrate that neuroprosthetic therapies using ISMS to increase motor output have the potential to concomitantly reduce transmission in spinal pain pathways. Future work is required to optimize these effects.

Comparison of nanoparticle and nanoparticle-free formulations for the active delivery of cytochrome c by targeting folate receptors

Authors: Vanessa Barcelo-Bovea, Irivette Dominguez-Martinez, Freisa Joaquin-Ovalle, Anthony McGoron, Kai Griebenow and Yancy Ferrer-Acosta.

Faculty advisor: Anthony J McGoron

Figures



Cytochrome c (Cyt-c) is a protein that induces apoptosis by activating the caspase cascade. We previously developed a drug delivery system consisting of Cyt-c nanoparticles decorated with folate-poly(ethylene glycol)-poly(lactic-co-glycolic acid)-thiol (FA-PEG-PLGA-SH). In this study we lowered the diameter of the reported FA-PEG-PLGA-Cyt-c nanoparticles and synthesized a nanoparticle free formulation (cyt c-PEG-FA). Cyt-c nanoparticles were obtained via nanoprecipitation and characterized using Dynamic Light Scattering and SEM. FA-PEG ligand was conjugated to Cyt-c using an amine-to-sulfhydryl crosslinker and the product characterized using UV-Vis spectroscopy. The integrity of the protein was accessed using circular dichroism (CD) and caspase activity assay. Cell viability was determined using the MTS assay. Internalization was studied using confocal microscopy. We were able to conjugate FA-PEG to Cyt-c and according to CD spectra and caspase activity assay results the protein integrity was maintained after the conjugation. Nanoparticles diameter were 338 and 287 nm. MTS experiments showed that nanoparticle formulation lower viability more efficiently than the nanoparticle free formulation. The confocal microscopy results showed that the formulations tested were internalized by the cancer cells tested. Our results show that FA-PEG-PLGA-Cyt-c nanoparticles may be the best formulation for Cyt-c probably due to a higher drug payload.

Embedded Devices with Remateable Interconnections for Wireless Neural Recording and Stimulation

Author: Sk Yeahia Been Sayeed

Faculty advisor: P. Markondeya Raj, John Volakis

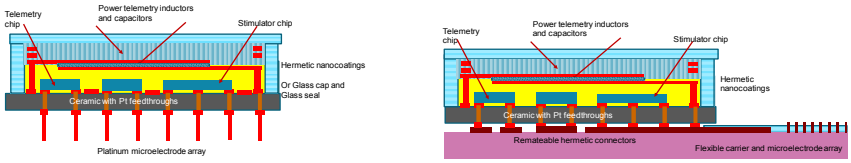


Figure 1. 3D bioelectronic package (left); Processing hub integrated with a flexible electrode array (right).

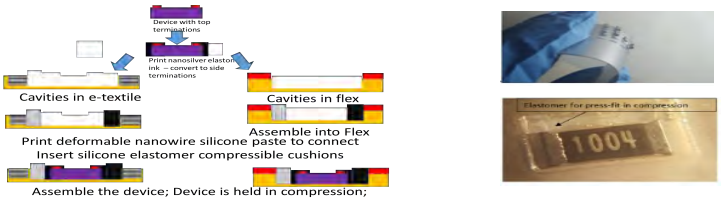


Figure 2. Process flow for deformable and remateable interconnects (left); Demonstration of remateable connections devices embedded in substrate cavities (right).

Figure 3. Package-integrated antennas for wireless sensing (Courtesy: Jordan Lewis, ECE).

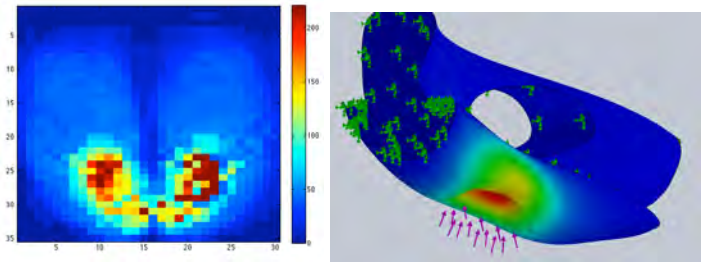
Next-generation embedded electronics are being developed for wearable and implantable electronics. The primary motivation for embedded packaging in biomedical electronics is to reduce the size and thickness. In addition, embedding eventually allows complete integration of modules in a single package with heterogeneous components such as actives and passives (Figure 1). Such systems should meet key requirements such as high-density integration of sensing, analog, digital and RF functions; remateable device assembly for easy replacement in surgical environment; high reliability for long-term operation. The key building blocks that will be developed in this project are: a) remateable and flexible high-frequency low-loss contacts or connectors between devices and interconnects, or between sub-systems in the wearable packages, b) flexible substrate with high-density interconnects, c) embedded thinfilm wireless passive sensors. Deformable and remateable interconnects are demonstrated to simultaneously attain high conductivity for easy deformation. Remateability is achieved with nanowire-elastomer composites for the interconnects between the device termination and substrate pads (Figure 2). Strong contact is achieved with gap-fillers that enable compression-based press-fit interconnections. The assembled substrate was bent to a radius curvature of 1 cm without any effect of the device. Planar high-density biocompatible electrode arrays are developed on thin metal carriers with embedded devices. Miniaturized RF thinfilm antenna components are integrated (Figure 3) with embedded ICs for seamless integration of digital and RF functions.

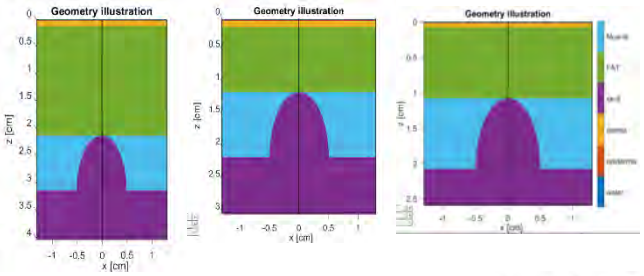
Voxilization-based Monte Carlo simulations of the ischial tuberosity

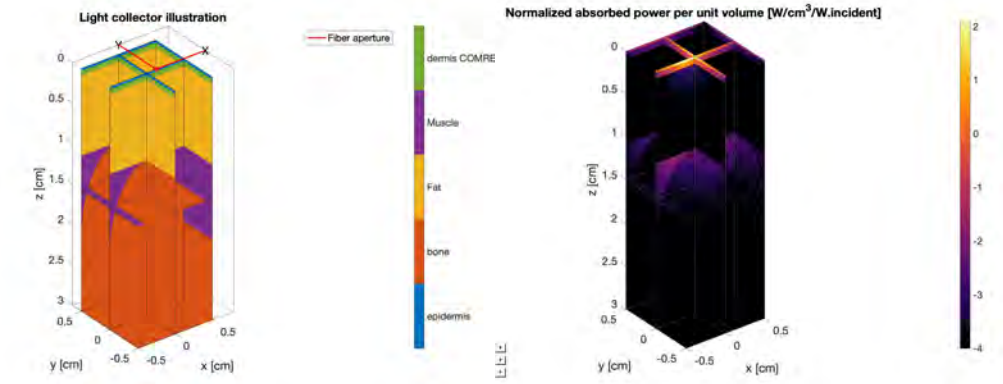
Authors: Tananant Boonya-ananta, Jessica Ramella-Roman

Faculty advisor: Jessica Ramella-Roman

Figures







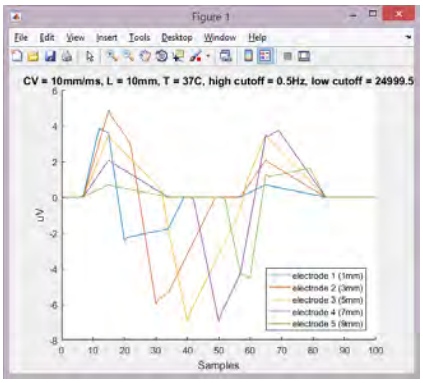
Patients with spinal cord injuries (SCI) are often subject to continues stationary pressure on prominent bony areas which, over and extended period of time, become high risk regions for pressure ulcers. Pressure ulcers are as prevalent as 30% in those with SCI and are one of the leading causes of re-hospitalization. In order to develop a better understanding of the methods of treating and preventing these pressure ulcers, we have developed a voxilization based model of the ischial tuberosity based on a Monte Carlo framework. The 3D model of the underside of the pelvis, the ischial tuberosity, allows for variation of the layers of the skin, fat, and muscle created in Solidworks. From the three-dimensional structure, a Matlab based Monte Carlo system is used to model the system. Tissue layer changes due to movement of the muscle and compression when sitting which results in a significant reduction of the muscle thickness have been accounted for in the model. Skin and muscle profusion of SCI patients is not well known and limited experimental work has been conducted in this environment. This model can aid in the study of methods of improving and maintaining skin health and help with rehabilitation and prevention of pressure ulcers.

Band-pass filtering impacts ideal electrode placement in microchannels for neural recording

Author: iian Black

Faculty advisor: Ranu Jung

Raw (unfiltered)



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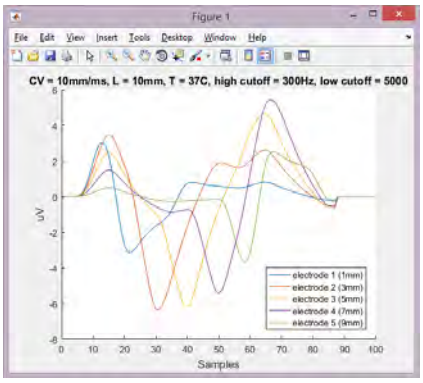


Microchannel electrodes are promising devices for recording neural signals. Theoretical models predict that the amplitude and shape of the recorded signal changes as the action potential travels through the channel. These predictions can be used to optimize electrode placement inside the channel. Band-pass filters are often used in practice to remove unwanted low and high frequency noise from recorded neural signals. However, filtering also alters the shape and amplitude of the recorded signals and, therefore, impacts ideal electrode placement. This analysis compares signals recorded using different band-pass filters to explore their potential impact on ideal electrode placement inside microchannels.

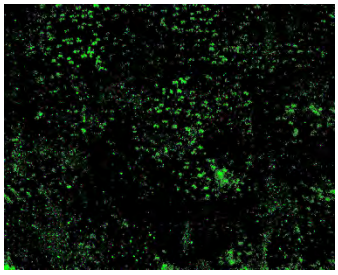
Fast Scanning OCT-guided Integrated Multimodal Photoacoustic Microscopy for Understanding Complex Diseases Progression: *"Brain and Retina Imaging"*

Author: Arash Dadkhah

Faculty advisor: Shuliang Jiao

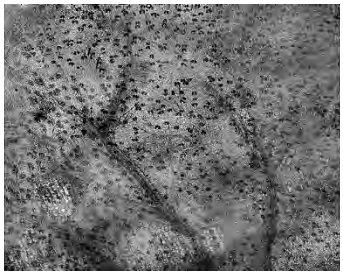
Figures

Mouse ear multimodal imaging



Fluorescence image

Photoacoustic image



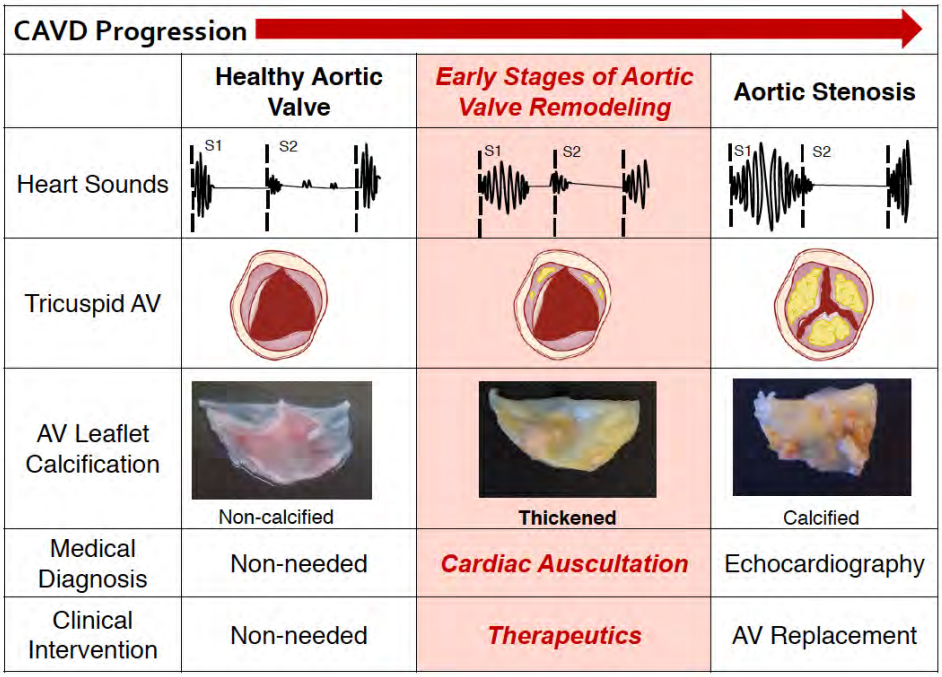
OCT image

Complex diseases, such as Alzheimer's disease, are associated with sequences of changes in multiple disease-specific biomarkers. However, disease progression from the preclinical to advanced stage can take decades, and different biomarkers, reflecting different pathologies may show dynamic changes at specific disease stages. Thus, testing each biomarker independently in diseases studies provides insights into one specific disease-related process in a limited time window. To acquire more comprehensive information of biological tissues requires imaging multiple optical contrasts, which is not typically offered by a single imaging modality. Different optical imaging modalities providing absorption, scattering and molecular information of biological tissues, have been developed and used in many biomedical investigations in the past decades. Large field-of-view (FOV) and high imaging speed are desired for all these imaging techniques. Uneven surface of a sample can lead to uneven depth focus, resulting in images with non-uniform resolution and signal intensity especially in large FOV imaging. We have developed a novel OCT-guided surface contour scanning methodology along with combining optical and mechanical scanners for simultaneous multimodal optical imaging of large area with fast scanning speed. This imaging system integrates photoacoustic microscopy (PAM), optical coherence tomography (OCT), optical Doppler tomography (ODT) and fluorescence microscopy in one platform providing comprehensive structural, functional and molecular information of living biological tissues.

Diagnosing Early Aortic Valve Disease: Correlation Between Heart Sounds and Remodeling

Authors: Valentina Dargam, Amirala Bakhshian Nik, Joshua D. Hutcheson

Faculty advisor: Joshua D. Hutcheson



Calcific aortic valve disease (CAVD) occurs when extracellular matrix (ECM) remodeling and calcium minerals hinder biomechanical function of aortic valve leaflets. Around 2.5 million people are affected with CAVD[1] and current diagnostic methods can only identify the disease after its irreversible stage. The second heart sound predominantly occurs from the closure of the aortic valve where ECM components have been hypothesized to control vibrations within aortic leaflets[2]. In this study, we hypothesize that microstructural differences in early CAVD remodeling can be identified by changes in the valvular acoustic frequency (S2 sound) response prior to traditional symptom manifestation. Starting at 10 weeks of age, 40 (20F; 20M) ApoE KO mice were fed a high-fat/high-cholesterol diet and their heart sounds were recorded weekly. The mice were given a tail vein injection of calcein dyes every 5 weeks to track the progression of calcification. At 35 weeks of age, the mice were given an intravenous injection of near-infrared calcium tracer and sacrificed for analysis of mineral growth. Data are still being collected. Preliminary results show that frequencies of the heart sounds can be identified and classified. The target of this study would be to map the changes of frequencies over time per mouse and correlate them to calcification growth of the aortic as detected by the different fluorescent dyes. The development of a non-invasive diagnostic technique could allow for the clinical advancement of a wide range of CAVD therapeutics currently blocked in preclinical development due to difficulty of identifying the disease prior to its irreversible calcification at the targeted stages.

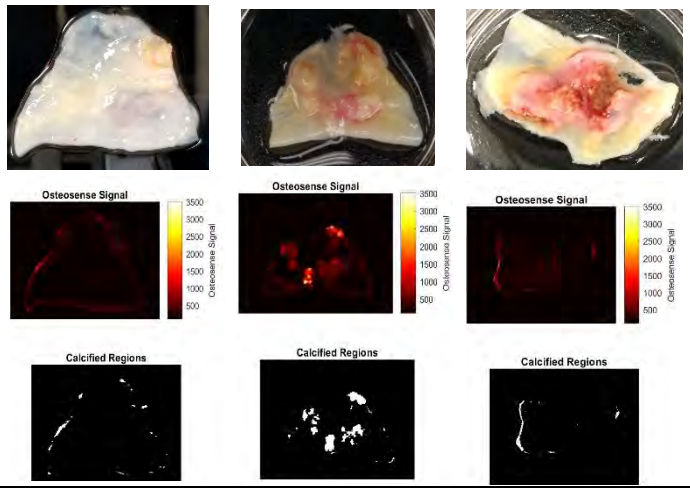
1. Yutzey, Katherine et al. Arteriosclerosis, thrombosis, and vascular biology. 2014;10.1161/ATVBAHA.114.302523.
2. Tseng H, et al. Acta Biomater. 2011;7:2101-8.PMC4497587

Correlating 3-Dimensional Aortic Valve Mechanics to the Onset of Valvular Disease in Post-Surgically Explanted Valve Leaflets

Authors: Daniel Chaparro[1], and Joshua D. Hutcheson[1].
[1] *Department of Biomedical Engineering, Florida International University, Miami, FL.*

Faculty advisor: Dr. Joshua D. Hutcheson

Figures

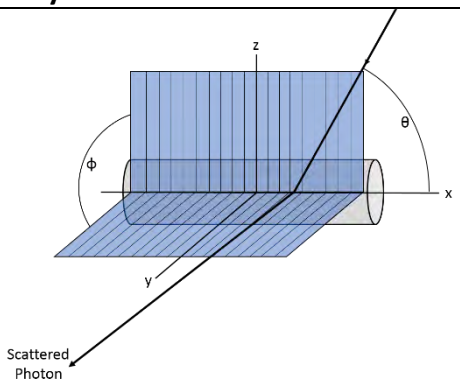


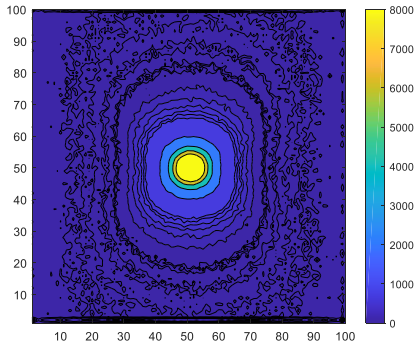
Calcific aortic valve disease (CAVD) is a major contributor to cardiovascular mortality and morbidity. The onset and progression of CAVD is characterized by asymptomatic unfavorable extracellular matrix (ECM) remodeling, which alters the biomechanics and function of the aortic valve. Aortic stenosis and regurgitation are clinical signs of irreversible ECM remodeling, usually calcification or fibrosis, only treatable by invasive surgical intervention. Thus, there is a clinical need to better understand valve mechanics during early stages of remodeling to aid in the development of noninvasive diagnostic modalities that can detect initial ECM changes prior to irreversible stages of CAVD that necessitate surgical intervention. Valve mechanics have traditionally been quantified in non-physiologically relevant 1-dimensional or 2-dimensional systems which have contributed greatly to the field's understanding of the valve's material properties. However, 3-dimensional analysis of native intact valve tissue has yet to be conducted and could shed light on complex interactions of cellular and ECM components and their role in the progression of CAVD. The purpose of this ongoing study is to develop a system to quantify intact aortic valve tissue biomechanics in 3-dimensions during end diastolic loading as seen throughout the cardiac cycle. This will help us determine how regional AV mechanics correlate to the presence of pathological remodeling in post surgically explanted valves from the Miami Cardiac & Vascular Institute (MCVI).

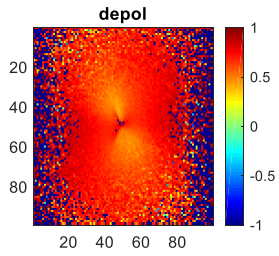
Polarized light Monte Carlo simulation of cervical collagen ultrastructure

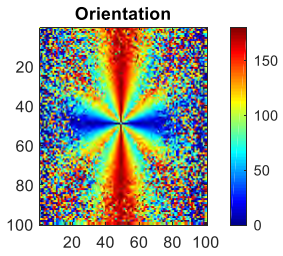
Authors: Joseph Chue-Sang, Jessica C. Ramella-Roman

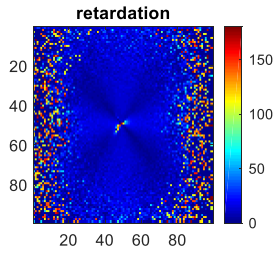
Faculty Advisor: Jessica C. Ramella-Roman

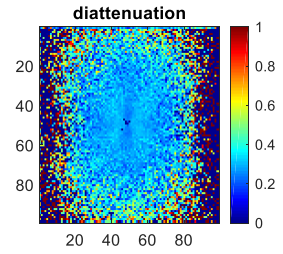












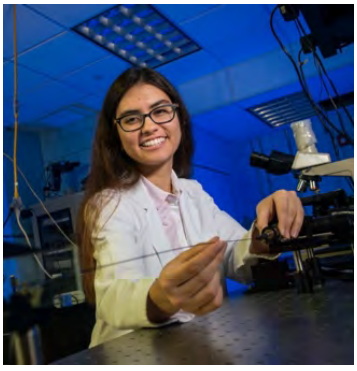
Polarized light microscopy and polarimetry has been used to assess changes in cervical structure by targeting its collagen. 75% of the human cervix is in fact composed of highly arranged collagen which is birefringent. Recently we have used Mueller Matrix polarimetry to image the human cervix *in-vivo* to determine loss of collagen arrangement associated with later stages of pregnancy. In an effort to improve our system capability and better determine the provenance of the polarized signal we have developed a Polarized Light Monte Carlo model capable of characterizing polarized light interaction with a birefringent, scattering, and absorbing medium such as the cervix. We have utilized this model to investigate the effect of cervical collagen arrangement on polarized light. In this talk we will illustrate the model framework, its validations, and provide several test cases in model cervices.

Assessment of commercialization pathways for a low-cost hand-held near-infrared optical scanner

Authors: Christopher Estrella, Nicole Sevilla, Dr. Anuradha Godavarty

Faculty advisor: Dr. Anuradha Godavarty

Integrated near-infrared optical scanner (I-NIROS) for oxygenation measurements

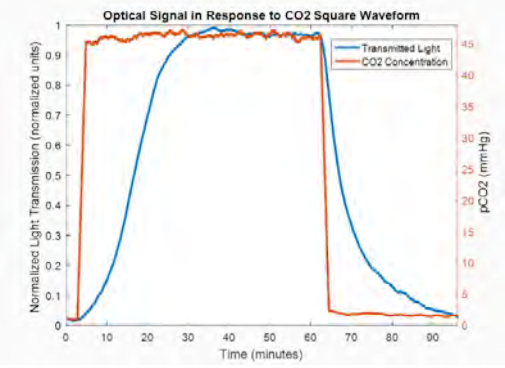


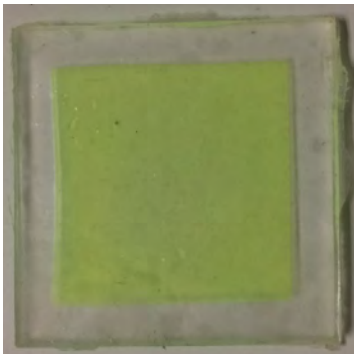
Gold-standard clinical assessment of wound healing is mostly done by visual inspection. Since tissue oxygenation plays a vital role in the healing process, the Optical Imaging Laboratory developed a Near-Infrared Optical Scanner (NIROS). This non-contact handheld device functions to complement the gold standard clinical assessment. The NIROS differentiates a healing from non-healing wound in real-time by tracking its oxygenation and perfusion changes. Consequently, the device aids clinicians in predicting the healing potential of a wound using a quantifiable method of assessing oxygen saturation. The existing NIROS analyzes near-infrared light returned from target tissue to calculate HbR and HbO levels. As NIROS transitions into the medical device market, the device was modified into a more user-friendly, integrated version for clinical use. Thus, research on FDA requirements and the medical device market determined suitable predicate devices, such as the Kent camera, and compared them to the NIROS. Based on this, the development of relevant documentation for classification and premarket approval was conducted. The results of this research are presented to outline the pathway that is required for a device to transition from its research and development stage to a market approved device.

Implantable Carbon Dioxide Sensor

Francis, Teshaun. Lin, Wei-Chiang

Lin, Wei-Chiang





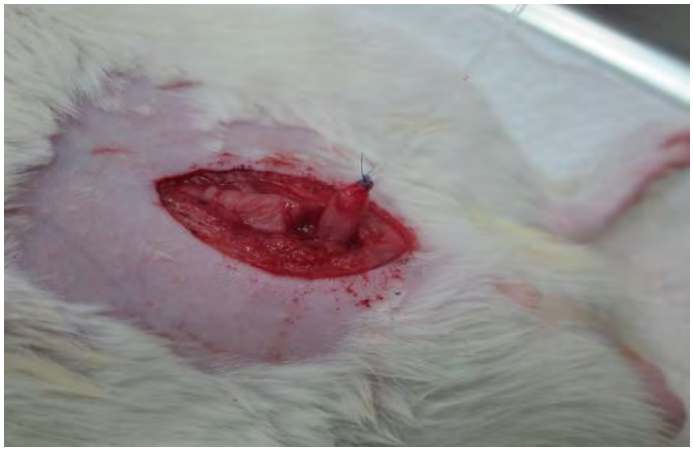
In the field of biomedicine, arterial carbon dioxide (aCO_2) is a diagnostic tool for respiratory and metabolic health. The aCO_2 waveform provides diagnostic power to physicians treating patients who suffer from diseases such as chronic sleep apnea, traumatic brain injury, and acute respiratory dysfunction. Existing modalities such as blood draws, end-tidal capnography, and transcutaneous capnography work well to estimate aCO_2 in healthy patients or in controlled research environments. In the clinic however, large changes in aCO_2 can occur rapidly, and if undetected can induce coma, cerebral ischemia, or respiratory acidosis. Current technologies fail in these situations because of unreliable measurement techniques that limit accuracy and sampling speed. We propose a novel CO_2 sensing strategy, which implants an optochemical sensor in the subcutaneous fat layer to passively measure interstitial CO_2 as an estimate for arterial CO_2. The response of our sensor is measured noninvasively using absorption spectroscopy. In this presentation we describe the optochemical carbon dioxide sensing mechanism and demonstrate the impact of several design factors, including size and chemical composition, on response time and sensitivity *in vitro*.

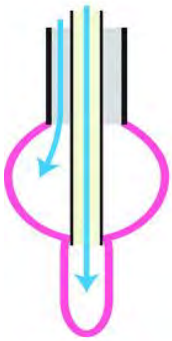
Age-related degradation of urinary tract reflexes

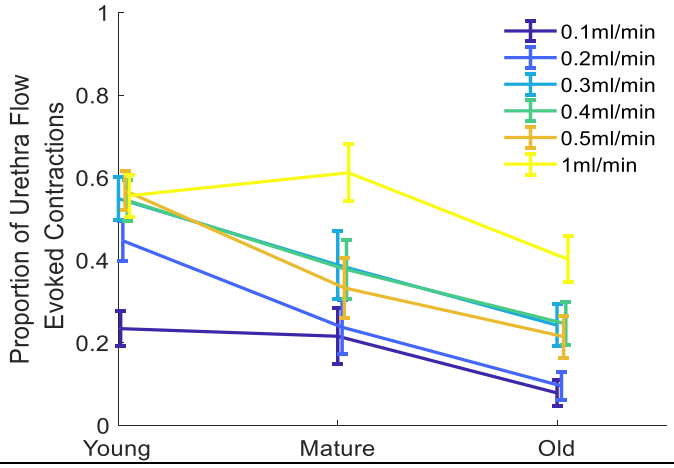
Authors
Arezoo Geramipour, Zachary Danziger

Faculty advisor: Zachary Danziger

Figures







Student's picture

The prevalence of lower urinary tract (LUT) dysfunction is correlated with age, and the median age of the US population is projected to increase substantially; therefore, understanding the etiology of age-related underactive bladder (UAB) is an important public health concern. In this work, the weakness of urinary tract reflexes was investigated. We used a suprapubic bladder catheter for intravesical saline infusion and a urethra catheter to infuse saline into the proximal urethra in urethane-anesthetized female rats. This preparation prevented bladder contractions from expelling urine through the urethra and enabled us to control the bladder infusion rate, bladder volume, and urethral flow rate independently. In three groups of animals, young, mature, and old, we systematically investigated LUT reflex responses to bladder filling and urethral infusion as a function of age.
The results showed that the augmenting reflex in older animals is functionally weaker than young animals. Furthermore, the volume at which the bladder switches from continent mode to micturition mode increased in older animals, meaning that the augmenting reflex for aged animals was engaged far later in the micturition mode than for young animals. Therefore, the degradation and dysregulation of the LUT reflexes in older subjects might result in UAB symptoms.

Longitudinal Echocardiographic Functional Assessment of a Bioscaffold Mitral Valve in a Non-Human Primate Model

Authors: Brittany A. Gonzalez[1], Lazaro Hernandez[2], Krishna Rivas[3], Frank Scholl[2], Steven Bibevski[1, 2], Jennifer Bibevski[4], Vincent Brehier[2], Mike Casares[2], Pablo Morales[3], Jesus Lopez[3], Joseph Wagner[3], Sharan Ramaswamy[1]

[1] Department of Biomedical Engineering, Florida International University, Miami, FL, [2] Joe DiMaggio Children's Hospital, Memorial Regional Hospital, Hollywood, Florida, United States, [3] Mannheimer Foundation Inc, Homestead, Florida, United States, [4] Cor Veterinary Specialists, Hollywood, Florida, United States

Faculty advisor: Dr. Sharan Ramaswamy

Figures:

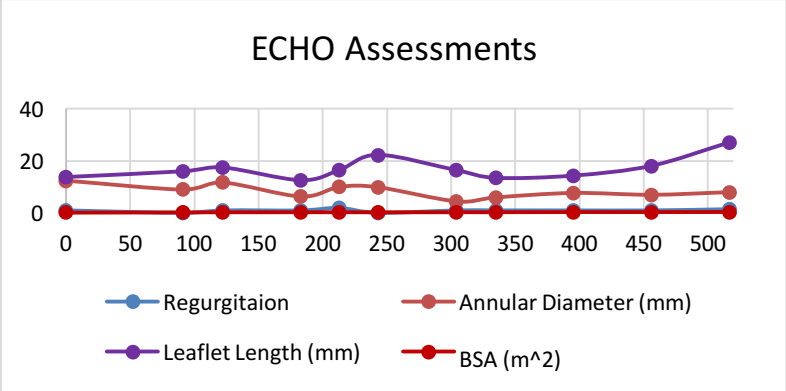


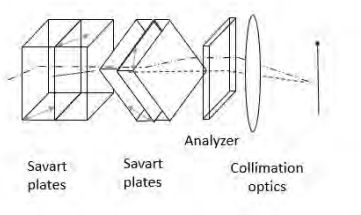
Figure 1: Parameters assessed from ECHO to determine the valve's growth potential post-implantation.

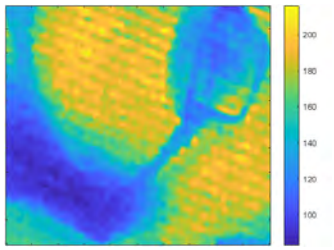
Congenital heart defects (CHDs) are the most common type of birth anomaly, affecting 8 out of 1,000 newborns; each year about 35,000 infants in the United States are born with these defects [1]. Critical congenital heart valve defects (CCHVDs) are a subset of CHDs, which account for ~25% of all CHD cases [2]. Timely treatment plays a key role in CCHVDs. However, CCHVDs in newborns have very limited treatment options due to challenges associated with the unavailability of small-sized commercial valves and the inability of prosthetic valves to support somatic growth. In the current study, a non-human primate model (juvenile Hamadryas baboon) was selected for porcine small intestinal submucosa (PSIS) mitral valve replacement *in vivo* to assess valve function over time using echocardiography (ECHO). A juvenile baboon (12 months) was implanted with a bicuspid PSIS valve in the mitral position. ECHO (LOGIQ e VET, GE Healthcare, Chicago, IL) was performed prior to valve replacement surgery, post-operatively immediately following PSIS replacement, two weeks post-operation and one (or two) month(s) thereafter as needed up to 17 months. From ECHOs, regurgitation (R), annular diameter (AD), leaflet length (LL) and body surface area (BSA) were assessed. Overtime, the BSA was found to be consistent for 517 days (17 months). Overall, there was a 35% decrease in AD and 97% increase in LL post-implantation. The R was generally trivial or mild, with an exception at 213 days (7 months) and at the final time point (517 days), where R was moderate. 17 months of ECHO evaluation of an implanted PSIS mitral valve in a baboon model preliminarily exhibited promising growth potential. We conclude that the functional abilities of PSIS mitral valves may contribute satisfactorily towards a regenerative treatment for CCHVDs.

Cellphone based attachment for low-cost cervical health diagnosis

Authors: Mariacarla Gonzalez, Jessica Ramella-Roman

Faculty advisor: Jessica Ramella-Roman





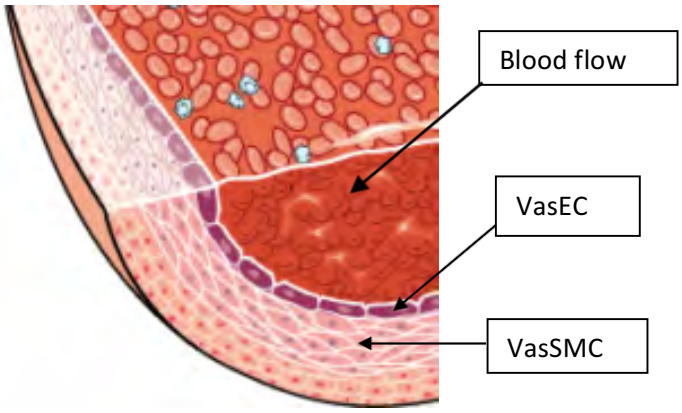
Cervical cancer is the fourth most common cancer for women worldwide. The highest mortality comes from less developed countries, where 90% of cases result in death. The absence of regular screenings and preventive care (such as vaccines) are largely at fault for the high incidence of cervical cancer. There is a need for diagnostic devices that are low cost and can be used by a non-expert in order to increase access to cervical cancer screenings. A cellphone attachment based on snapshot Mueller Matrix (MM) imaging is proposed for the diagnosis of cervical cancer. The attachment is capable of capturing a wide field of view using low power and cost-effective parts. We present the device.

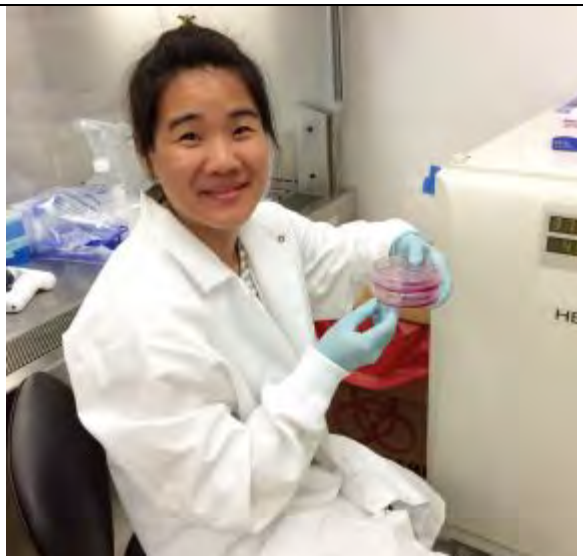
The Effects of Oscillatory Shear Regulation on Paracrine Signaling Between Vascular Endothelial Cells and Vascular Smooth Muscle Cells

Authors: Denise Hsu, Alexandra Tchir, Joshua Hutcheson*, Sharan Ramaswamy*
*Co-advised principal investigators

Faculty advisors: Joshua Hutcheson, Sharan Ramaswamy

Figures



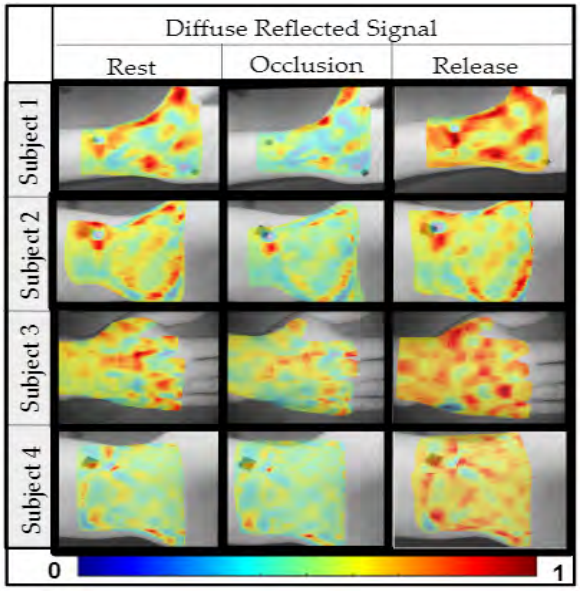


The vascular wall consists of a layer of vascular endothelial cells (VasEC) and a sublayer of vascular smooth muscle cells (VasSMC). Vascular remodeling often involves paracrine signaling between VasECs and VasSMCs and diseases such as calcification can result from improper communication between these cells. Various oscillatory flow profiles alter cell responses to its immediate environment via both cell-to-cell paracrine and autocrine communication. Different flow groups experienced by VasECs may lead to the secretin of factors that enable paracrine regulation of VasSMC's phenotype. There may be a range of oscillations that maintains vascular tissue integrity. In this study, we conditioned VasECs under various specific oscillatory flow profiles quantified by the oscillatory shear index (OSI) parameter. With this parameter, we are able to determine the most suitable physiological relevant pulsatile flow conditions for valve tissue maintenance and development by assessing the cell phenotype. Oscillation dependent changes in vascular cell communication and molecular regulation have not been thoroughly investigated, we therefore would like to examine the paracrine signaling of biochemical end-products between VasECs and its sublayer, VasSMCs through the biochemical environment resulting from physiologically relevant oscillations.

Development and validation of smartphone based oxygenation tool for in-vivo imaging

Authors: Kacie Kaile, Anuradha Godavarty

Faculty Adviser: Dr. Godavarty



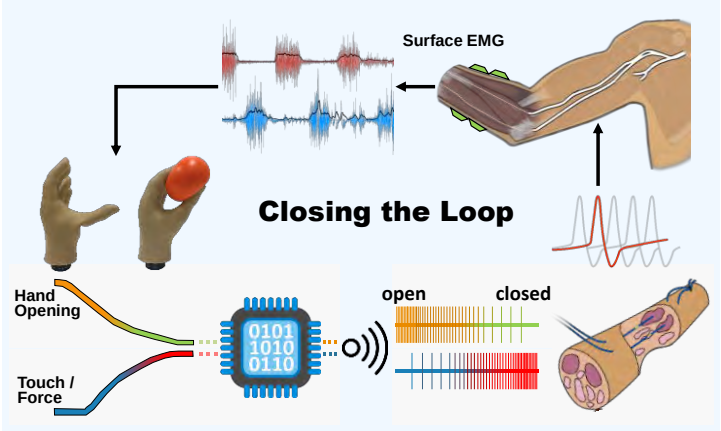
Venous occlusion studies were utilized to induce tissue oxygenation changes and images were acquired at three timestamps: (1) At rest (left), (2) during occlusion (center), and (3) immediately following release (right).

Recent advances in smartphone based technologies for medical imaging of wounds are limited, providing no physiological information of tissues. Physiological assessment is necessary for improved wound care, especially in chronic wound cases such as Diabetic Foot Ulcers. Oxygen supply is a key limiting factor for successful healing, thus differences in tissue oxygenation are a precursor to visual changes in the wound. Using multi-wavelength near-infrared light allows for subcutaneous mapping of tissue oxygenation in/around a wound. Smartphone based assessment of wounds will assist clinicians in any clinical or in-house setting, including low resource settings. Herein, a SmartPhone based Oxygenation Tool (SPOT) was developed to measure physiological changes in tissues across a wide area, without contact. Sensitivity of the device to measure physiological changes was validated via blood occlusion studies. Noise removal techniques using singular value decomposition algorithms effectively removed surface noise and differentiated physiological changes in response to occlusion. Future goals for this project include a custom designed smartphone app for automated data extraction using machine learning algorithms that will provide near, real-time wound assessment. In future, patients with chronic wounds can actively participate (and comply) in their treatment process, storing results for comparison across days/weeks with the aid of SPOT.

Neural-enabled prosthetic hand system to restore sensation in upper-limb amputees

Author: Sathyakumar Kuntaegowdanahalli, Andres Pena, Anil Thota, James Abbas, Ranu Jung

Faculty advisor: Dr. Ranu Jung

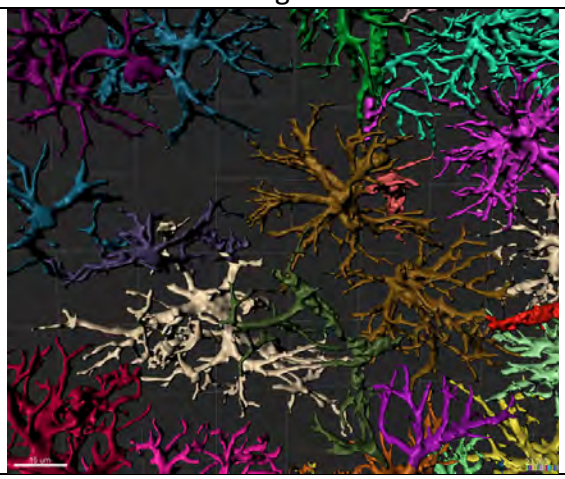


Today's upper limb amputees have needs that are not being met by current prosthetic technology because these systems do not provide effective sensory feedback from the prosthesis. This results in reduced quality of life and limitations in performing day-to-day activities. To address this problem, we have developed the Neural Enabled Prosthetic Hand (NEPH) system to provide amputees with sensations that are synchronized with sensor-derived signals from the prosthetic hand. The system includes an implanted electronic neurostimulator to deliver stimulation via fine-wire longitudinal intrafascicular electrodes (LIFEs) implanted in peripheral nerves of the residual limb and an external, prosthesis socket-mounted module that utilizes a wireless link to communicate stimulation commands to the implanted electronics. The NEPH system has been designed for use outside a controlled lab environment. To date, the NEPH System has been deployed in one subject who is using it outside laboratory settings for over 7 months. In order to characterize the performance of the NEPH system, a battery of tests have been developed to assess the nature and quality of elicited sensations, the impact of sensation on prosthesis control capabilities and functional tasks, and impact of sensation on phantom pain, body image, and quality of life.

Network Architecture & Connectivity Analysis of Cortical Brain Tissue through Simultaneous Immunofluorescent Staining of Neurons, Astrocytes, Vasculature and Nuclei

Authors: Jared Leichner, MBA; Dr. Wei-Chiang Lin, PhD.

Faculty advisor: Dr. Wei-Chiang Lin

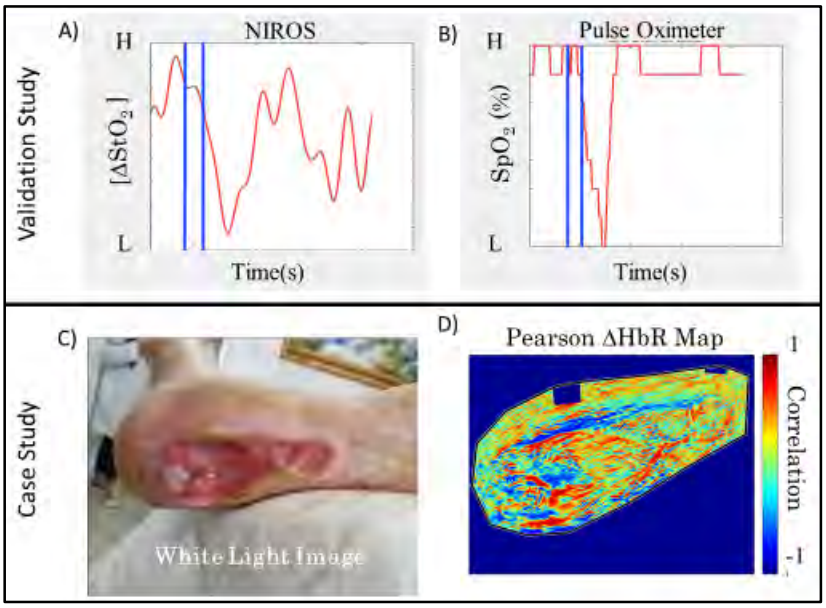


Comprehending the interwoven network architecture of neurons, astrocytes and vasculature within cortical brain tissue requires a resolution fine enough to identify detailed cell-level morphology and a stitched multi-panel dataset large enough to assess network connectivity through all layers of the cerebral cortex. This project presents a novel combination of immunofluorescent staining targets alongside an optimized staining and confocal imaging methodology for Adult Wistar rat cortical brain tissue that highlights four key components simultaneously – neurons, astrocytes, vasculature and nuclei – within 36 large cortical column datasets [800µm x 3mm x 70µm] at an extremely fine theoretical voxel resolution [0.2µm x 0.2µm x 1µm]. Due to spherical aberration, it is critical to deconvolve the datasets before conducting morphological analysis. Hence, this raw data next undergoes preprocessing and blind deconvolution utilizing a custom-designed depth-variant routine employing refractive index-matched PSFs which are sparsely distributed over the depth of investigation. Subsequent modeling of the deconvolved data from two functional regions, M1 and S1BF, is used to answer key questions regarding the unique network characteristics of each functional region and whether their properties are unique to the rat, unique to the functional region or unique only to the particular hemisphere.

Assessment of localized oxygenated flow changes induced by breath-holding using NIROS

Authors: Kevin Leiva, Priscilla Lozano, Maria Saavedra, Kacie Kaile, Francisco Perez-Clavij, Anuradha Godavarty

Faculty advisor: Anuradha Godavarty



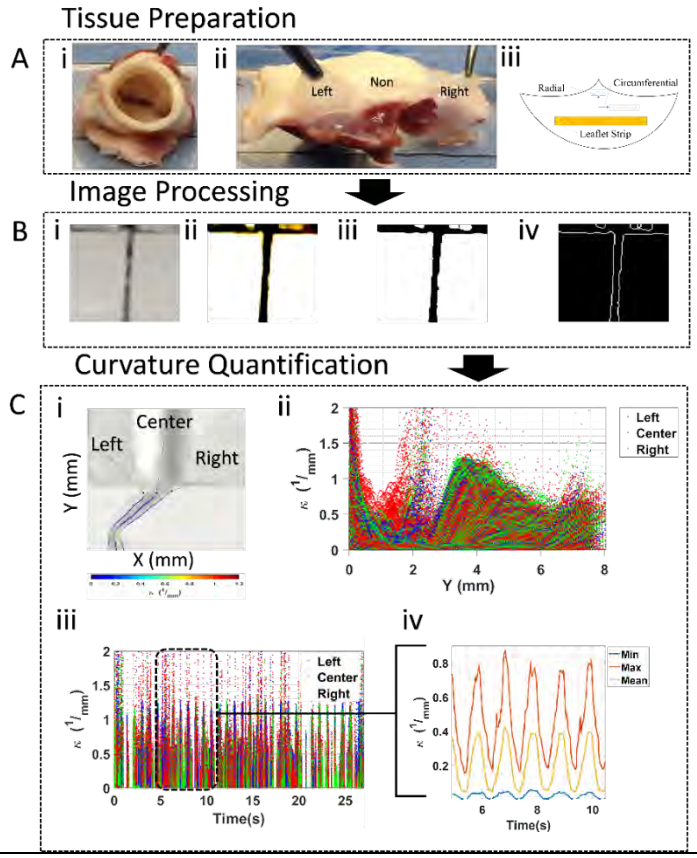
Preliminary data indicates that NIROS can detect changes in tissue oxygen saturation (A) similar to peripheral oxygen saturation (B) from breath holding. In a mixed arterial/DFU subject (C), we were able to detect regions of differing oxygenated flow (D).

A hand-held, non-contact, Near Infrared Optical Scanner (NIROS) was developed to measure tissue oxygenation in wounds. In this validation study, the capabilities of NIROS to assess tissue oxygenation changes due to breath-holding was investigated by comparing NIROS to a hospital-grade pulse oximeter. A breath hold paradigm was used to induce oxygenation changes, with data recorded from the right index finger of healthy subjects. Results indicate that observed changes in tissue oxygen saturation (using NIROS) and peripheral oxygen saturation (using the pulse oximeter) from simultaneous recordings yielded correlated changes. These preliminary validation results indicate that NIROS can capture physiological relevant changes in tissue oxygenations induced by breath-holding. In parallel, a technique was developed to identify regions of differing oxygenated flow from single-visit diabetic foot ulcer subjects using breath-holding. Currently, a mixed arterial/DFU subject has been monitored for more than 50 weeks of treatment, to help determine if regions with poor oxygenation flows improve with healing and various treatment interventions. This work is significant as it has potential to help better cater the wound treatment process via subclinical physiological assessments that precedes clinical visual assessments.

Axial curvature evaluation in aortic valve tissue-strips following elastin degradation

Authors: Asad M. Mirza, Melake D. Tesfamariam, Daniel Chaparro, Rachel Montlavan, Brittany Gonzalez, Ahmed Z. Ali, Amanda Barreto, Joshua D. Hutcheson, Sharan Ramaswamy

Faculty advisor: Dr: Sharan Ramaswamy



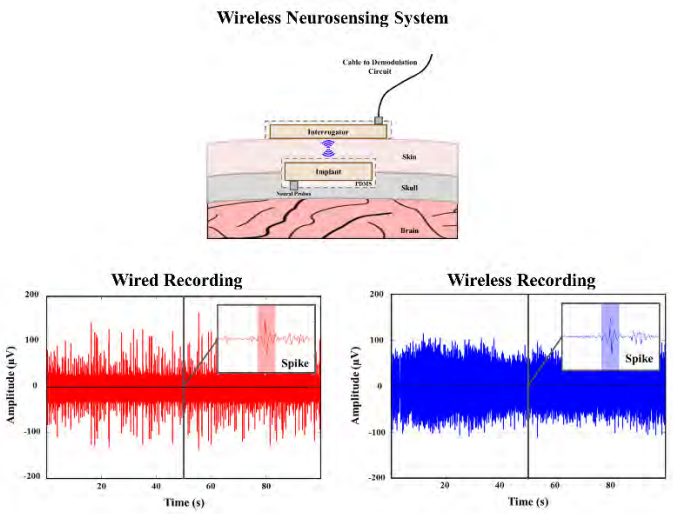
Calcific aortic valve disease (CAVD) is the most frequent condition that necessitates surgical valve replacement. In developed nations, an alarming rate of incidence of CAVD is projected, from 2.5 million cases in 2000 to ~4.5 million in 2030. Hence, the development of pharmaceutical interventions as well as early detection capabilities for CAVD is necessary. Components of the aortic valve extracellular matrix (ECM), specifically elastin, may play an important role in the onset and development of calcific processes. In the current study, we wanted to determine if changes to aortic valve structure due to elastin degradation could be detected and subsequently quantified by the leaflet curvature. Porcine valvular tissue was sourced from a local abettor and cut into rectangular strips (10 mm x .25 mm). Cyclic flexure experiments were done at various degradation times using a mechanical testing instrument. A camera system was mounted to take images along the axial edge of the sample. Curvature assessment was done using an in-house written script in MATLAB where the axial edge of the sample was fitted with a nth degree polynomial equation and then evaluated using a curvature formula. Results showed that curvature significantly increased with degradation time for both minimum and maximum curvature, when compared to its control. Thus, valve leaflet curvature, either minimum or maximum, could be used to track elastin changes which could lead to it being a potential biomarker for early detection of CAVD.

Fully-Passive Wireless Recording of Neural Activation in Wistar Rats

Authors: Carolina Moncion*, Jordana Borges, Lakshmini Balachandar, Satheesh Bojja-Venkatakrishnan, John L. Volakis, and Jorge Riera Diaz

Faculty advisor: Jorge Riera Diaz

Figures



High-resolution systems for monitoring neural activation is crucial for studying different neural disorders. This is especially true when diagnosing and treating epilepsy, as it has been reported that about 80% of surgeons use these systems to identify seizure origin site for surgical removal. These systems are typically highly-invasive as they require wires that are left protruding from the scalp. This exposes the subject to infections, is detrimental to the quality of life and often limits recordings to a clinical setting thereby hindering the physician's analysis. Many implantable devices have been designed, however, most require the use of a power source, which can generate tissue-damaging heat. To address these pitfalls, we proposed a novel fully-passive and fully-implantable neurosensing system. This device consists of an implant and interrogator antenna, neural probes along with a demodulation circuit. Experiments proved an RF sensitivity of ~-135 dBm along with an ability to detect emulated neural signals with amplitude in the microvolt scale, implying the system is capable of sensing the signals generated by the brain. The *in vivo* validation of this device entailed a series of electrophysiological recordings of spontaneous cardiac activity, evoked neural activity and most recently epileptiform activity resulting using the pilocarpine model to induce temporal lobe epilepsy (TLE). Each in vivo experiment was performed using the neurosensing system and with a wired commercially-available system (AD Instruments Animal Bio Amp) for reference. Results indicate the neurosensing system can record both cardiac and neural activation in a manner comparable with wired systems. A major contributor to achieving these recordings was the low-impedance neural probes designed especially for the neurosensing system. This process involved several design considerations that directly affect probe impedance, including material selection and probe geometry. Most neural probes are closely impedance-matched to available biopotential acquisition systems which can be in the order of MΩ. Probes used to record with our system are currently in the order of several hundred Ω to kΩ. The neurosensing system will greatly impact future neurological research, as it offers a novel and unobtrusive option.

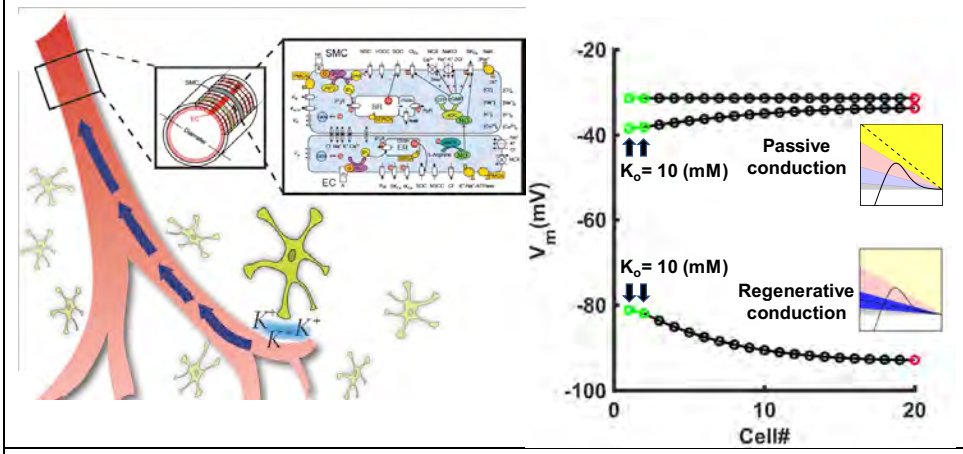
Kir mediates Regenerative and Directional Conduction of Hyperpolarization in Brain Capillaries: Importance for Neurovascular Coupling

Authors: Arash Moshkforoush[1], Thomas Longden[2], Fabrice Dabertrand[2], Osama F Harraz[2], Mark T Nelson[2], Nikolaos M Tsoukias[1]

[1]*Department of Biomedical Engineering, Florida International University, Miami, FL*

[2]*Department of Pharmacology, University of Vermont, Burlington, VT*

Faculty advisors: Dr. Nikolaos Tsoukias/Dr. Jorge Riera



Rapid increase in local blood perfusion in response to elevated neuronal activity, a process referred to as neurovascular coupling (NVC), is crucial to the functioning and survival of neurons. Impairment of NVC is associated to a variety of neurological disorders including Alzheimer's disease, stroke, and vascular dementia. Recent evidence suggests an active role of capillary endothelial cells (Cap-ECs) in NVC. Inwardly rectifying potassium channels (K_{ir}) enable capillaries to a) sense K^+ release by nearby active neurons and b) amplify and conduct the resulting hyperpolarization to upstream feeding arterioles to increase local cerebral blood flow (CBF). In this study, we use a mathematical model of a capillary network and its feeding parenchymal arteriole (PA), to examine the biophysical determinants that allow capillaries to sense modest elevations of K^+ and transmit vasodilatory signals. We hypothesize that capillary level NVC is feasible through mechanisms that promote regenerative signal propagation in a preferentially upstream direction in the microvascular network. Detailed mathematical models of Cap-ECs and PA ECs and smooth muscle cells (SMCs) are constructed. The models entail the dynamics of major ionic channels and intracellular components and predict membrane potential (V_m) and Ca^{2+} dynamics. Cap-ECs are coupled through gap junctions to form a branched capillary network that is connected to a feeding PA. Both local and distal hyperpolarizations are examined in response to K^+ stimuli at different locations along the capillary network. Model simulations suggest that Kir channels can mediate preferential and regenerative propagation of vasodilatory signals upstream the vascular network. Simulations predict a critical level of Kir density for generating local and conducted K^+-induced hyperpolarization in a network of Cap-ECs. When Kir current is small relative to the total transmembrane current, a passive spread of hyperpolarization is predicted. Conversely, when Kir is dominant, the local hyperpolarization is significantly larger, and the vasodilatory signal is conducted along the endothelial layer without signal attenuation.

Heart-on-a-Chip : Non-Invasive Plasmonic and Electrochemical Characterization of Cardiac Tissue

Authors: Maedeh Mozneb*, Asad Mirza, Elisa Bravo, Pablo Rodriguez, Chen-Zhong Li.

Faculty advisor: Dr. Chen-Zhong Li

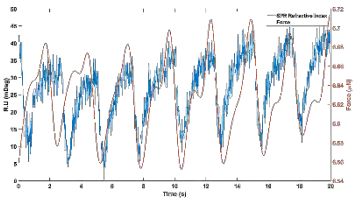


Figure 1. Contractile forces of cardiomyocytes monitored using Surface Plasmon Resonance (SPR) shown in blue, validated with simultaneous force measurements of image correlation analysis from contraction videos, shown in red.

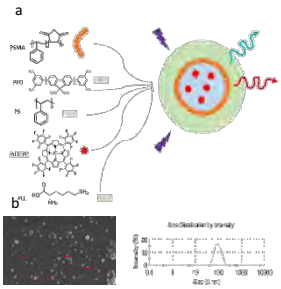
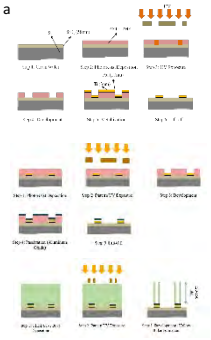


Figure 2. a. Design of a Oxygen sensitive and self-referencing nanosensor. b. Size and charge analysis of the sensors' distribution in solution (SEM on the left and Zeta-sizer on the right)



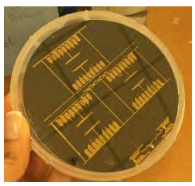


Figure 3. a. Microfabrication process of the standalone device. b. Device with first- and second-layer electrodes (Gold and Passivation) fabricated

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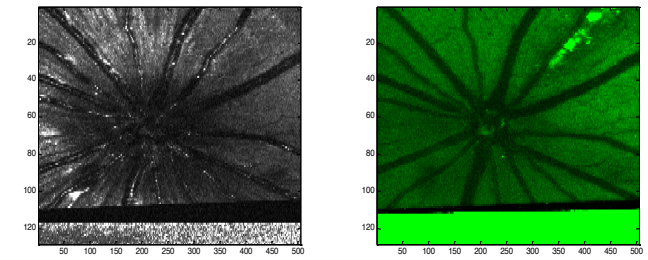
With heart-disease being the leading cause of death in United States, with 23.5% of all deaths, an essential need to develop and market innovative drug treatments, rises. However, with the long-term and cumbersome animal and human trials, as well as their ethical factor to consider and FDA bottlenecks, drug development takes decades without the guarantee of marketing. In this research, we are developing a heart-on-a-chip along with novel methodologies for non-invasive monitoring of cardiac tissue in vitro. We have successfully demonstrated the use of surface Plasmon Resonance technology for the first time to characterize the contractility of cardiac tissue as well as drug effect analysis in real-time. We have developed a Nanosensor for continuous monitoring of cellular respiration with different stimuli and environmental conditions. We have also developed a stand-alone device for analysis of cardiac tissue's metabolic activity, in terms of glucose, lactate and NADH, using electrochemical concepts. The device not only allows monitoring cardiac tissue in real-time, it also allows electrical stimulation analysis, fast drug screening and fundamental biology analysis of cardiac tissue.

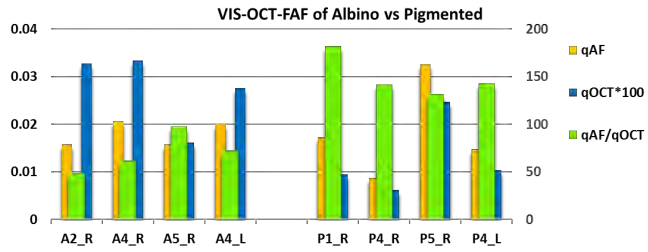
VIS-OCT based quantitative imaging of RPE Lipofuscin with customized A2E-PMMA reference target

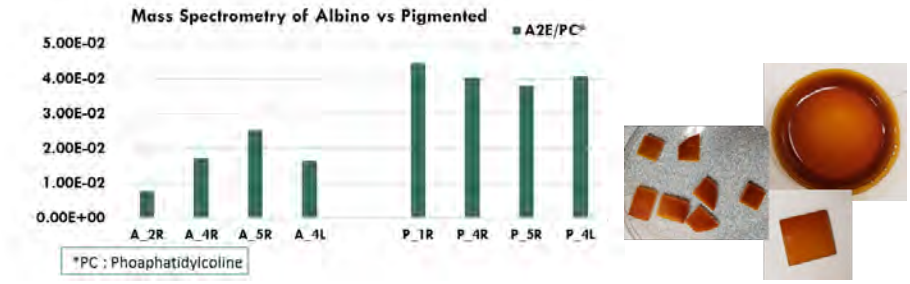
Authors: Zahra Nafar, Rong Wen, Shuliang Jiao

Faculty advisor: Shuliang Jiao

Figures







RPE lipofuscin, the major source of fundus auto fluorescence, accumulates with age and in some retinal degenerative diseases. Thus, quantification of this biomarker is important in diagnosis and monitoring the disease. N-retinylidene-N-retinylethanolamine (A2E) is the major lipofuscin fluorophore with maximum excitation peak at 488nm and has a significant role in shortwave FAF imaging. However, fluctuations of FAF imaging systems such as different illumination power and detection sensitivity, as well as the attenuation effects of the media prior to RPE, introduce unwanted factors to AF signal. Further, the attenuation pre RPE media may vary for different people and for individuals over time. We have previously introduced a simultaneous VIS-OCT and AF imaging with a single light source centered at 480nm with two reference targets. By normalizing AF and OCT signals to that of the targets, respectively, we eliminated the effects of varying laser power and detector sensitivity. Since AF and OCT signals are generated from the same group of photons and pass through the same medium, by finding the ratio of qAF/qVIS-OCT, pre-RPE attenuation effects were eliminated. In this study we introduce customized reference standard to serve as a common target for both AF and OCT. This reference target is composed of PMMA and synthesized A2E. Using synthesized A2E, the main fluorophore of lipofuscin, in reference fabrication, provides a similar excitation and emission spectrums to RPE lipofuscin and minimizes detection efficiency differences. We have successfully fabricated and tested the new A2E-PMMA reference target in vivo imaging of rat retina.

Aortic valve elastogenesis requires neural crest derived valvular interstitial cells

Authors: Sana Nasim[1], Beatriz Abdo Abujamra[2], Joshua Hutcheson[1], Lidia Kos[2]
Department of Biomedical Engineering[1], Department of Biological Sciences[2]

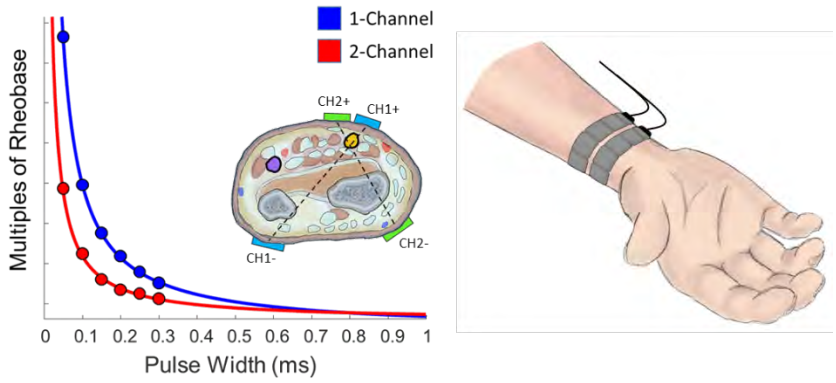
Faculty advisors: Dr. Lidia Kos and Dr. Joshua Hutcheson

The aortic valve (AoV) controls unidirectional blood distribution from the left ventricle of the heart to the aorta for systemic circulation. During the systolic and diastolic phases, AoV leaflets rely on a precise extracellular matrix (ECM) microarchitecture for appropriate biomechanical performance. The ECM structure is maintained by valvular interstitial cells (VICs), which reside within the leaflets. AoV biomechanical function relies on a precise ECM trilaminar microarchitecture of collagen, glycosaminoglycans and elastin. VICs are a heterogeneous population of cells that are derived from a mixture of developmental precursors. Mainly, VICs arise from endocardial and neural crest cells that migrate into the cardiac cushions during development. The contribution of these developmental populations to the formation of the ECM microarchitecture remains unknown. Relatively little is known about regulation of elastin fibers, though elastin abnormalities result in congenital AoV defects and elastin degradation initiates AoV disease. Preliminary evidence suggests that neural crest derived-VICs with a melanocyte phenotype are required for appropriate elastin fiber patterning. Mice lacking melanocytes have no visible AoV elastin fibers, whereas mice with increased numbers of melanocytes exhibit elevated and disoriented AoV elastin. The melanocyte VICs also have shown to exhibit phenotypic markers of neuronal and glial cells. For future work, we hypothesize that the neural crest derived-VICs direct elastogenesis in a non-cell autonomous manner and are required for appropriate biomechanical function. This will provide insights into the VIC subpopulations that govern AoV homeostasis.

Evoked Referred Sensations through Multichannel Interfering Transcutaneous Electrical Neurostimulation

Authors: Andres Pena, Luis Herran, Ranu Jung

Faculty Advisor: Dr. Ranu Jung

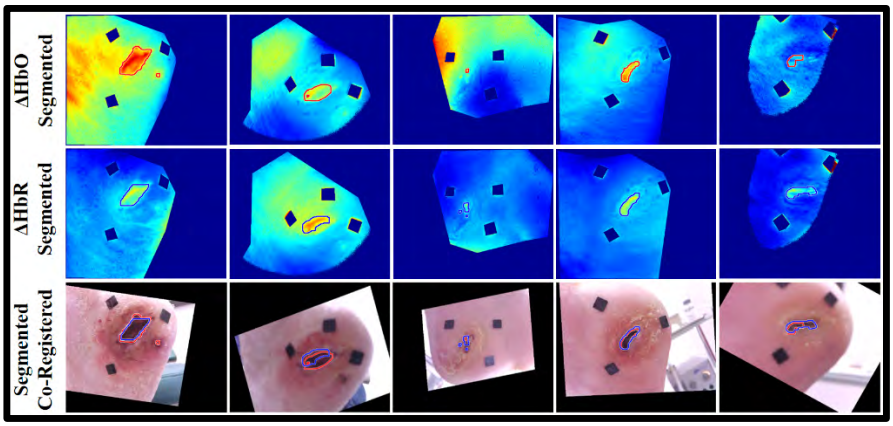


Loss of sensory function due to disease or limb amputation can be a devastating, life-changing event. Implantable neural stimulators have shown potential for providing naturalistic referred sensations, however they require invasive surgical procedures not acceptable to all. Transcutaneous electrical neurostimulation has been explored as a non-invasive alternative for delivering sensory feedback. However, traditional single-channel stimulation approaches are hampered by large charge requirements, low selectivity, distracting local sensations, and limited stability. This study investigates the potential benefits of using interfering multichannel stimulation through surface electrodes to evoke distally referred sensations more comfortably, efficiently and consistently than single-channel stimulation. In a pilot study, charge-balanced biphasic current pulses were delivered to the median nerve of able-bodied participants (n=6, 21.3±0.5 years) using single-channel (1CH) and interfering multichannel (2CH) stimulation at the wrist level. The strength-duration relationship was characterized for each approach under 6 different pulse durations, revealing lower threshold amplitudes at shorter durations during 2CH. Psychophysical questionnaires revealed comfortable and stable, distally referred tingle-like sensations with 2CH, while most participants (n=4) reported both distal and local sensations after 1CH stimulation, with one of them reporting them as uncomfortable. Future work will explore stimulation waveform patterning and frequency modulation to deliver wide-range sensation intensities.

Computational approach to wound assessment using image processing techniques

Authors: Edwin Robledo, Cristianne Fernandez, Rebecca Kwasinski, Francisco Perez-Clavijo, Anuradha Godavarty

Faculty advisor: Anuradha Godavarty



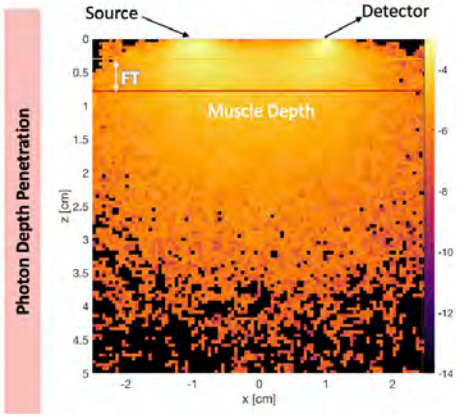
Hemoglobin concentration maps segmented and co-registered onto visual image of a diabetic foot ulcer across weeks of healing.

As of 2017, approximately 4 million people in the U.S suffer from diabetic foot ulcers (DFUs). Currently the gold-standard approach for DFU assessment is visual inspection by a clinician. This method of assessment is subjective and must be complemented by an objective method of wound assessment for improved wound care management. Hence, my objectives are to create a quantitative means to analyze wounds using computational algorithms. In the past we had developed a Near-Infrared scanner (NIRS) to provide the behavior of oxygenation inside tissue, within and around a region of interest (wound). Herein, I have developed and applied a semi-automatic image segmentation and co-registration approach using machine learning to objectively and quantitatively assess wounds based on their oxygenation maps. A graphs-cut algorithm combined with machine learning was applied for semi-automatic segmentation to isolate regions of increased or decreased oxygenation in the tissue. A co-registration technique was also developed which allows for the alignment of two images of the same object. Therefore, when we register an image that contains tissue oxygenation behavior and one that contains a digital white light image of the same region, physiological changes can be seen in relation to their location in color images.

Optical characterization of the skin in the obese

Authors: Andres Rodriguez, Tananant Boonya-Ananta, Jessica Ramella-Roman

Faculty advisor: Dr. Jessica Ramella-Roman



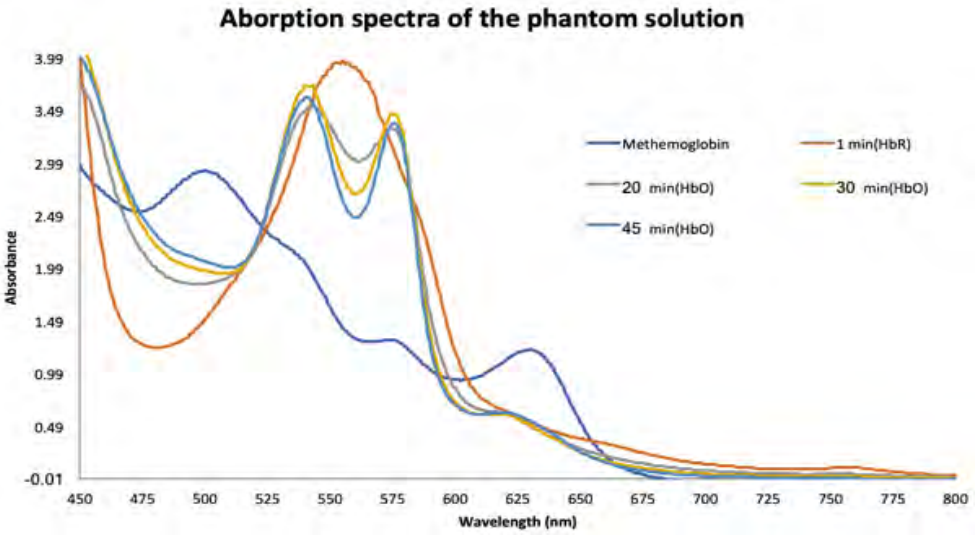
Normalized fluence rate of collected light from source in 0.5 cm of subcutaneous fat thickness obtained through Monte Carlo simulation , **λ** =638nm

Obesity, defined as individuals with a Body Mass Index (BMI) of 30 or more, affects more than 93 million adults in the U.S. Obesity increases the chances of developing cardiovascular disease and diabetes. In recent years, Near Infrared Spectroscopic (NIRS) devices have been used to diagnose, categorize, and monitor the disease state of CVD— specifically those with peripheral arterial disease. NIRS is a non-invasive, reproducible, and inexpensive methodology, yet fail to produce accurate results in the obese population due to excess adipose thickness (AT), and angiogenic vascularization that alter the optical signal. We have used Monte Carlo models of light transfer to study how the angiogenic effect of vasculature and water losses in the dermal layer will affect NIRS readings in the obese. We conclude that there is an overestimation of signal in the obese when compared with normal concentrations.

Validation of a Near-Infrared Optical Scanner to Measure Changes in Oxygenation: Phantom Studies

Authors: Maierhaba Sailaijiang, Kacie Kalie, Anuradha Godavarty

Faculty Advisor: Dr. Anuradha Godavarty



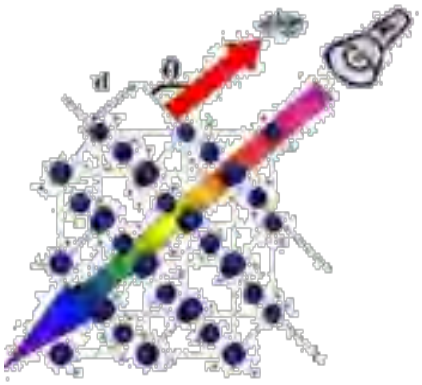
Spectrophotometer results show that methemoglobin is reduced to HbR in the reaction and in time equilibrates with air become HbO.

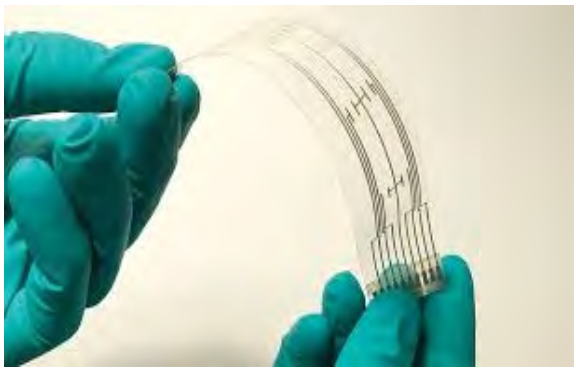
For wound healing processes, oxygen supply to the wound site is a key limiting factor. A non-contact near-infrared optical scanner (NIROS) was developed to differentiate healing and non-healing ulcers by detecting tissue oxygenation changes in terms of oxyhemoglobin (HbO) and deoxyhemoglobin (HbR). NIROS has shown promise in clinical settings, but there still remains a need to verify that measurements obtained from it truly reflects oxygenation changes at the wound site. Therefore, validation studies need be performed to quantify NIROS accuracy in assessing oxygenation measurements utilizing controlled phantom studies. Phantoms designed in this study will mimic tissues containing different oxygenation states in terms of HbO and HbR and will be imaged using NIROS. A spectrophotometer is used to measure actual changes of HbO and HbR in the phantom throughout the reaction. The resulting images are analyzed in terms of the diffuse reflected signal and compared with the spectra obtained for validation. Validation will help to quantify the tissue oxygenation measurements obtained from NIROS prior to clinical translation of the technology and play an important role in gaining FDA approval.

Determination of Glucose Level in Interstitial Fluid through Reusable Colorimetric Hydrogel Sensor

Authors: Mehenur Sarwar, Dr. Chenzhong Li

Faculty advisor: Dr. Chenzhong Li



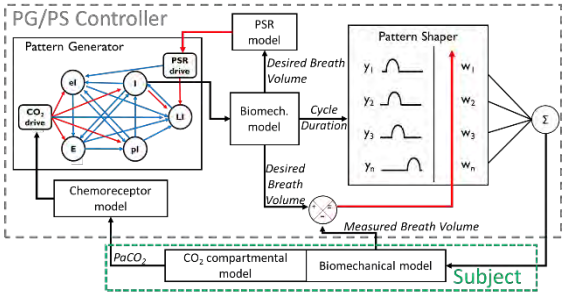


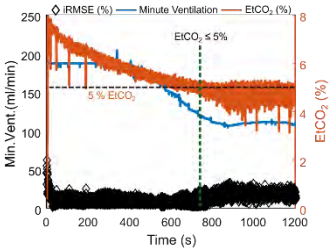
Due to the epidemic of obesity, type 2 diabetes patient populations are burgeoning. For this patient, the everyday challenge is to determine the level of glucose to manage the disease. This is often done by pricking the finger, which on a regular basis causes extreme discomfort and unnecessary fear to the patient. Interstitial fluid is proven to carry sufficient levels of glucose and hence can be used to deduce valuable physiological information. Thermally induced secretion of interstitial fluid on demand can be an exciting alternative approach to the blood test. We here report a flexible, wearable sensor to stimulate interstitial fluid secretion, a PDMS reservoir to collect the fluid and transport it to our colorimetric sensing platform. In this platform, an amorphous crystal colloidal array upon binding with glucose results in a red-shift of reflection wavelength, perceived as a blue to red color change. The advantage of this sensing platform is that it can be reused for a long time, minimizing the cost of the system. A photosensor is implemented to convert these changes into meaningful, user friendly data.

Bio-inspired adaptive controller for ventilatory pacing

Authors: Ricardo Siu, James J Abbas, Brian K Hillen, and Ranu Jung

Faculty advisor: Ranu Jung



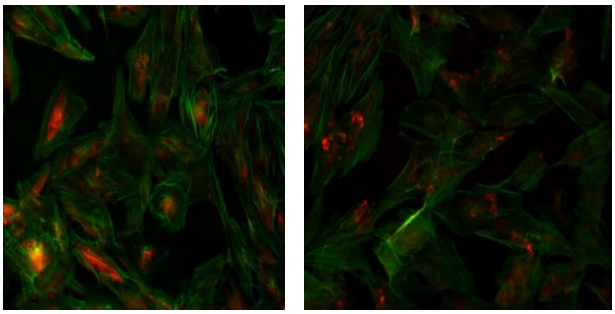


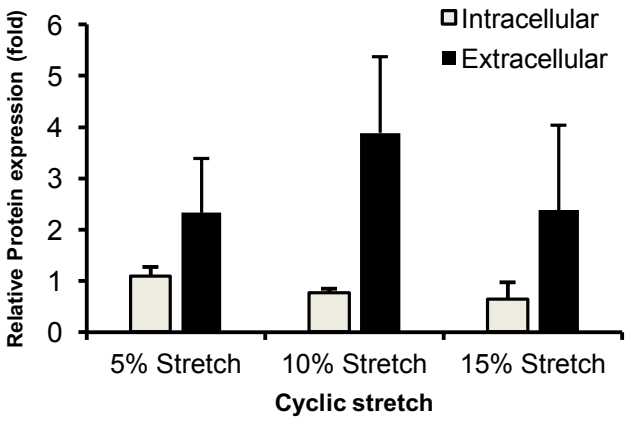
Trauma, disorder, or disease of any of the components that comprise the ventilatory control loop may lead to impairment of ventilatory function, and consequentially to respiratory insufficiency. While mechanical ventilators are the standard for ventilatory support, the risk of inducing alveolar damage and causing diaphragm atrophy is often present. Ventilatory pacing circumvents these risks by inducing a breath through electrical stimulation of the diaphragm muscle or phrenic nerve. However, commercially-available ventilatory pacing systems are all open-loop, leading to inability to adapt to changes in metabolic demands and other changes that may affect effectiveness of pre-set stimulation parameters. We have developed a biologically-inspired closed-loop adaptive controller for ventilatory pacing capable of autonomously modulating stimulation delivered to maintain proper ventilation. Experimental studies in anesthetized Sprague-Dawley rats showed that the controller was able to lower $etCO_2$ levels toward normocapnic values after anesthesia-induced respiratory depression. Furthermore, a human model of respiratory mechanics and a CO_2 compartmental model were paired with the neuromorphic controller to assess its behavior in humans. These computational trials showed that the closed-loop controller was able to maintain normocapnia within a wider range, 20% to 160% basal metabolic rate (BMR) vs 90% to 110% BMR, when compared to an open-loop controller.

Caveolin-1 Redistributes Into Extracellular Vesicles In Stretched Vascular Smooth Muscle Cells

Authors: Mohammad Shaver, Joshua D.Hutcheson

Faculty advisor: Dr.Hutcheson



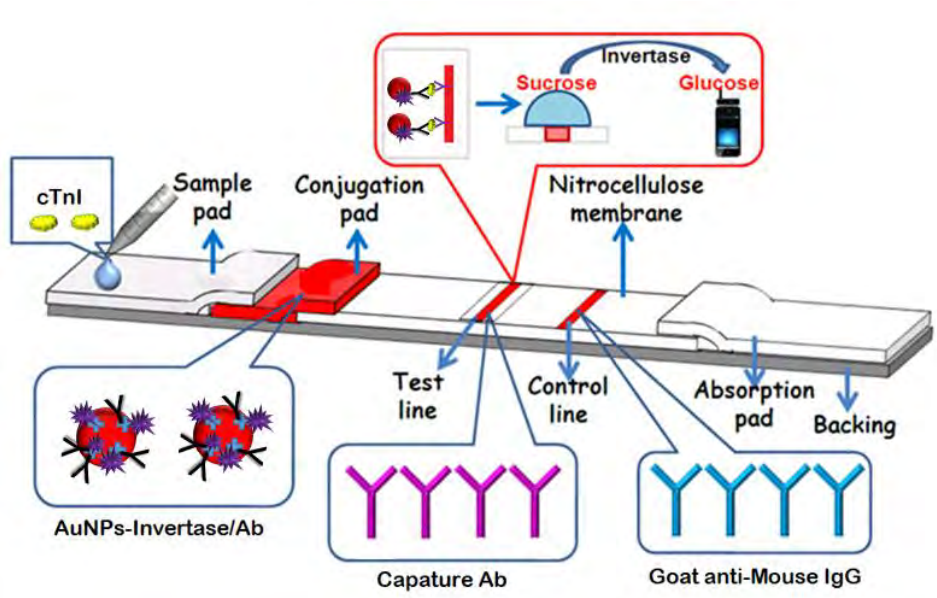


Caveolae are invaginations in the plasma membrane, and Caveolin-1 (Cav-1) is a scaffolding protein that forms caveolae. During cyclic stretch, tension increases on the plasma membrane of vascular smooth muscle cells (SMCs), and caveolae dynamics help buffer the membrane from rupture. Cav-1 can also direct the formation of extracellular vesicles (EVs) that mediate cardiovascular tissue remodeling and intercellular communication. The aim of this study is to investigate changes in Cav-1 trafficking and EV formation through application of mechanical stretch to SMCs *in vitro*. For this purpose, cyclic stretch (5, 10 and 15%, 0.5 Hz) was applied to porcine left coronary artery SMCs for 72h. Non-stretched SMCs were used as controls. Cav-1 level in SMCs and conditioned media was assessed via western blotting. Immunofluorescence imaging was performed to assess changes in Cav-1 distribution within SMCs. The application of cyclic stretch resulted in intracellular trafficking and formation of Cav-1-positive EVs. These EVs may play an important role in communication between SMCs and adjacent cells (e.g., endothelial cells) in response to biomechanical changes in the arterial wall.

Nanozyme integrated immunological microfluidic sensing platforms

Authors: Lin Tong

Faculty advisor: Chenzhong Li



Precise Advanced Technologies and Health Systems for Underserved Populations (PATHS-UP) is aiming to develop 1) cost-effective and 2) accurate tools to monitoring chronic diseases for 3) underserved people. The two major chronic diseases we are targeting on are cardiac diseases and diabetes. The most successfully marketed over-the-counter POCT device is the personal glucose meter (PGM), widely used by diabetes patients to monitor blood glucose levels at home. In Dr. Li's lab, low-cost, high sensitivity point of care testing (POCT) technology has been under research and explored for years. One of our goal is to convert chronic disease biomarkers signal to glucose concentration signal, which can be detect by glucose meter. Several attempts have been successfully made to transform non-glucose target into glucose in solution by using enzyme invertase to hydrolyze the undetectable target-labeled sucrose to glucose.

A universal nanozyme integrated paper based lateral fluidic sensing platform by using a glucose meter to quantitatively detect cardiac disease biomarkers has been developed as above figure. The patients' status can be sent to their doctors / hospitals by using a smart phone device, which could prospectively enhance patients cardiac disease monitoring and benefit for their prognostic rehabilitation.

Adaptive ventilatory pacing through synergistic activation of respiratory muscles

Authors: Rabeya Zinnat Adury, Ricardo Siu, Dr. James Abbas, Dr. Ranu Jung

Faculty advisor: Dr. Ranu Jung

Neuronal control of breathing may be affected following a cervical spinal cord injury or any kind of brain stem injury, stroke or trauma. Individuals with compromised respiratory system rely on mechanical ventilation or artificial ventilation support to maintain proper ventilation. Commercially available artificial ventilators are open loop system which stimulate muscles at constant amplitude and rate and thus provide constant breathing rate and volume which may lead to increased risk of alveolar collapse. To prevent alveolar collapse and enhance gas exchange, an augmented breath volume, or sigh, can be introduced. While pacing, additional stimulation of other supporting respiratory muscles can provide greater volume to accomplish sighing behavior. Previously, a neuromorphic closed-loop controller for stimulation of the diaphragm muscle for ventilatory pacing had been developed. This closed loop system responds to the changes in end-tidal CO2 and paces the diaphragm to attain a desired breathing pattern. However, it lacks the ability to provide stimulation to the supporting external intercostal muscles. To address this issue, the proposed system will also pace external intercostal muscles periodically which will have a synergistic effect on the breath volume. The addition of sighing behavior, could reduce the need for stimulation delivered to the diaphragm, therefore decreasing stimulation-induced muscle fatigue. Experiments have been conducted with Sprague Dawley rats (n=3) to get Strength-Duration curves to determine the proper stimulation parameters for use in external intercostal muscles pacing. Future work will focus on assessing the effect of synergistic intercostal stimulation with the previously existing diaphragm stimulation paradigm and its ability to evoke sighing behavior.