

Biomedical Engineering

UNDERGRADUATE RESEARCH DAY FALL 2020

DISCOVER DESIGN DEVELOP DELIVER



AGENDA

11th Annual

Undergraduate Research Day Friday September 25th, 2020

8:45 AM-9:00 AM

Set-Up for Seminar, Meeting with Dr. Godavarty

9:00 AM-10:00 AM

Seminar: Dr. Martine LaBerge

10:30 AM-12:00 PM

2 Min. Undergraduate Student Research Presentation

12:00 PM-1:00 PM

Meeting with the Graduate/Undergraduate Research

Students

2:00 PM-3:00 PM

Panel Discussion with the BME Alumni

3:00 PM-3:30 PM

Award Ceremony / Closing Remarks

MEETING ID: 615 193 8236 PASSCODE: BME@305

MESSAGE FROM THE CHAIR

Congratulations Biomedical Engineering Undergraduate Researchers!

Today marks a milestone in your undergraduate education, where you showcase your self-motivated contributions to research. You set a great example to all, that learning does not end in the classroom and research is a vital component of your undergraduate experience.

I am delighted that there has been a steady increase in the number of undergraduate students participating in research. Each of you has a vital role in your research projects, no matter how big or small your contributions are. The Undergraduate Research Day presentations reflect your ability to work both individually and in teams, to converge information and ideas to discover the unknown, and to find innovative solutions.

As you move forward in your undergraduate 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 our BME Alumni for their active participation in our Undergraduate Research Day and for sharing their real-life experience as medical students, graduate students, academicians, or industry/corporate members. This truly reflects your enthusiasm to give back to the next generation of biomedical engineers!

Best wishes for continued success,

- W

Ranu Jung, PhD Chair, Biomedical Engineering

KEYNOTE SPEAKER

W H Coulter Foundation Biomedical Engineering Distinguished Lecture Series

"BUILDING A SKILLSET FOR SUCCESSFUL BME RESEARCH CAREER: FOCUS ON EMOTIONAL INTELLIGENCE "



MARTINE LABERGE, Ph.D.

Professor and Chair of Bioengineering at Clemson University

Director of the Biomedical Engineering innovation Campus (CUBEInC) in Greenville, SC.

DR. MARTINE LABERGE serves as Professor and Chair of Bioengineering at Clemson University and Director of the Biomedical Engineering innovation Campus (CUBEInC) in Greenville, SC. She received MS and PhD in Biomedical Engineering degrees from University of Montreal, and completed post-doctorate work in Mechanical Engineering at University of Waterloo, before joining the bioengineering faculty at Clemson University. She has numerous publications on the tribological performance of orthopaedic and vascular implants and is an inventor on several licensed patents. Since the beginning of her career, she served as the major advisor of 85 PhD and MS bioengineering students managing a research program exceeding \$12M. She served as President of the Society For Biomaterials (SFB) and received its Inaugural Service Award. She is a Fellow of the American Institute for Medical and Biological Engineering (AIMBE) and the Biomedical Engineering Society (BMES). She was inducted Fellow, Biomaterials Science and Engineering by the International Union of Societies for Biomaterials Science and Engineering, Dr. LaBerge received the South Carolina Governor's Award for Scientific Awareness for major program development. She received the Inaugural Herbert Voigt Distinguished Service Award from BMES and the SEMDA Spotlight Award recognizing her contributions to the development of the Southeastern medical device community.

Cardiac Electrophysiological Abnormalities in Chronic Kidney Disease

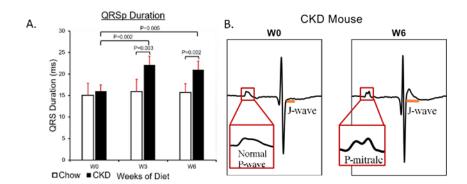
Authors: Anet Sanchez, Valentina Dargam, Hooi Hooi Ng, Joshua Hutcheson

Faculty Advisor: Joshua Hutcheson, Ph.D.

Chronic kidney disease (CKD) increases the risk of cardiovascular disease, but abnormal cardiac function is often undetected in CKD patients. While electrocardiogram (ECG) remains a noninvasive and inexpensive way to detect rhythm and conduction defects, literature has not reached a consensus on which electrophysiological markers are reliable for predicting cardiovascular events in CKD patients.

The purpose of this study was to identify temporal changes in cardiac electrophysiology in a CKD mouse model. ECG signals of eight-week old C57BL/6J male mice were recorded for the following groups for 12 weeks: 1) control group (n=6), and 2) CKD group (n=4), fed a CKD inducing diet. CKD mice showed a significant increase in QRSp duration (ms) (Fig. 1A). A P wave split, known as P-mitrale, was observed at week 6 in 50% of the CKD mice (Fig. 1B). Additionally, CKD mice exhibited a widened and longer J wave. An increase in QRSp duration and J wave alterations suggest left ventricular hypertrophy, whereas a P wave mitrale usually occurs due to left atrial enlargement, both of which are highly prevalent in CKD patients. The outcomes of this study will provide insight into the longitudinal electrophysiological changes that occur due to CKD.





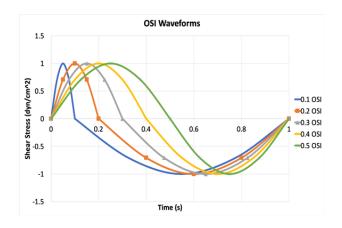
Time dependent ECG differences in CKD and control mice. A) CKD increases QRSp duration. B) P wave abnormalities, such as a P wave mitrale, are observed in 50% of the CKD mice at week 6.

Valve-relevant Gene Expression Responses by Human Mesenchymal Stem Cells after Exposure to Oscillatory Flow Conditions

Authors: Elizabeth Cheng, Brittany Gonzalez, Denise Hsu, Sharan Ramaswamy **Faculty Advisor:** Sharan Ramaswamy, Ph.D.

Heart valve disease is often treated by the replacement of the affected heart valve with a prosthetic heart valve. However, pediatric patients have no viable options since sizing and growth requirements are not met. Tissue engineered heart valves (TEHVs) may meet these added requirements with the addition of seeded cells that must be able to express certain genes to promote the valve phenotype. Mesenchymal stem cells (MSCs) have the ability to differentiate, gaining characteristics and functions of a different cell. Oscillatory shear stress has proved to be a factor in aiding the differentiation of human MSCs towards cardiovascular lineages. The project looks predominately to the gene expression of factors that can promote valve tissue regeneration so as to enhance integration and function of the implanted valve construct. Data will be collected in the form of gene expression of human MSCs exposed to various levels of fluid-induced shear stress oscillations (oscillatory shear index (OSI) 0.1, 0.2, 0.3, 0.4, 0.5 and a no flow static control). This study will serve to understand how specific oscillatory flow patterns can promote MSC-based gene expression that will ultimately lead to TEHVs with potentially enhanced regenerative capacities.





Oscillatory shear index sinusoidal waveforms at proposed tested intervals.

Data Analysis of Images Obtained with Two Near-Infrared Devices for Static Imaging and Dynamic Imaging with a Breath-Hold Paradigm in Patients with Diabetic Foot Ulcers

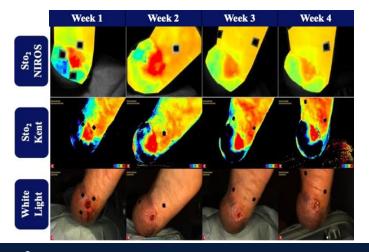
Authors: Valentina Roldan, Kevin Leiva, Kacie Kaile, Maximillian Weigelt, Aliette Espinoza,

Robert Kirsner, Anuradha Godavarty

Faculty Advisor: Anuradha Godavarty, Ph.D.

Diabetic foot ulcers (DFU) are a common ailment in diabetic patients, posing a risk to hospitalizations and/or amputations of extremities. Assessing DFUs over the course of treatment can be helpful in predicting wound healing status. The Optical Imaging Laboratory (OIL) at Florida International University began clinical studies at the University of Miami Wound Care Center using their NearInfrared Optical Scanner (NIROS) device to assess the tissue oxygenation (TO) of wounds. The objective of this study was to assess the TO changes across weeks of treatment in lower extremity ulcerated subjects, obtained with two NIRS-based devices, as well as those obtained from a dynamic setting during a breath-hold paradigm. Subject above showed a decrease in visual contrast between oxygenation levels in the wound (demarcated in red in both devices) and the rest of foot across the weeks, which is an indicator of healing. It was also possible to observe that for each of the four subjects, the outline of increased oxygenation around wound region is very similar across both devices. Dynamically acquired data was processed and Pearson's-based correlation assessment is being used to obtain Pearson maps that will allow for future assessments on how oxygenation flow patterns vary near wound sites.





Oxygen saturation maps from NIROS device, oxygen saturation maps from commercial device, and white-light images from commercial device (as labeled) for subject one's wound across all four weeks of imaging.

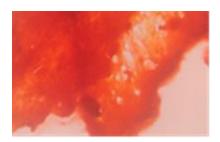
Response of Adhesion Forces During Calcified Tissue Indentation

Authors: Amanda Barreto, Asad M. Mirza, Nicole Bacca, Brittany A. Gonzalez, Pranjal Nautiyal, Joshua Hutcheson, Arvind Agarwal, Sharan Ramaswamy

Faculty Advisor: Sharan Ramaswamy, Ph.D.

Transcatheter aortic valve replacement (TAVR) is thought to be a safer treatment option for patients who suffer from aortic valve disease and are at high risk of undergoing openheart surgery. The primary objective of this study was to characterize the calcified plaque distribution in diseased aortic valve leaflets in terms of their adhesive properties, in order to further our subsequent efforts to develop a homogenized constitutive model of calcified leaflet deformation after TAVR deployment. Porcine aortic valve tissue samples were cultured and prepared for histological staining and indentation testing. Our indentation results showed that the adhesive forces characteristic of soft biomaterials dominated the response of the load during the displacement of the tip into the tissue and were greater in the calcified group. This implies that for constitutive modeling purposes, non-uniform regions of the calcified deposits on the leaflets would have to be carefully homogenized, only after having accounted for indentation-tissue adhesive effects. These findings will be incorporated in our next round of tests in order to build a highlyaccurate, homogenized constitutive model of calcified aortic valve leaflets in the deployed TAVR environment, which may help to predict the onset of sub-clinical thrombus in current, commercially available TAVR systems.





Alizarin red staining for group 4 (calcium presence in red orange).

Group # (N=2)	Mean (g)	SEM (g)
G1	-0.105	0.0106
G4	-0.275	0.0884

Tissue indentation results for group 1 and 4.

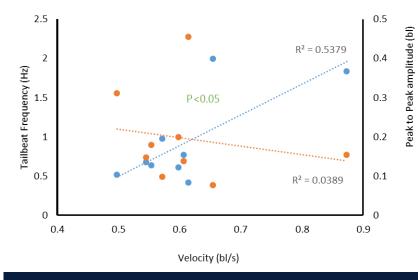
Head Shaking Kinematics of Lemon Sharks (Negaprion Brevirostris)

Authors: Maria Victoria Guzman, Braden Ruddy, Marianne Porter

Faculty Advisor: Marianne Porter, Ph.D.

Previous research on shark swimming has focused on straight movements and work on feeding has focused on feeding while stationary. In the wild, sharks will swim to capture food, and continue swimming during prey processing. The purpose of the research project is to quantify the swimming kinematics before, during, and after feeding of the lemon shark. We hypothesized that we would observe increases in velocity, anterior flexion frequency, anterior flexion amplitude, tail beat frequency, and tail beat amplitude. We used a total of 9 recordings of lemon sharks demonstrating feeding behavior that were previously acquired in a controlled environment. We tracked 11 anatomical landmarks using Vernier Logger Pro. From the motion-tracked data, we quantified kinematic values such as Tailbeat frequency, tail beat amplitude, velocity, anterior body curvature, posterior body curvature, Strouhal number. Preliminary data suggests increases in anterior flexion frequency and posterior flexion frequency after feeding, synonymous with head shaking. Knowing these patterns will allow us to create an automated point tracking template for the future in lab swimming analysis, using the program deep lab cut. The amplitude of the tail flick and the midpoint speed of the shark's body show a behavior opposite to that of the frequency, the head and cabbage width angles change when catching food. It was found that the frequency is inversely proportional to the width of the tail and the velocity of the midpoint of the shark's body.





Tailbeat Frequency and Peak to Peak Amplitude compared to Velocity.

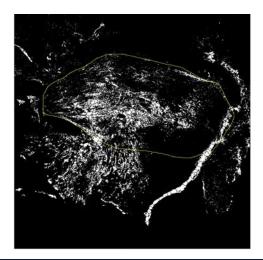
Quantification of Cells and Proteins in Aortic Valve Leaflets

Authors: Ana Valentin, Sana Nasim, Joshua Hutcheson

Faculty Advisor: Joshua Hutcheson, Ph.D.

The purpose of this project was to develop a method to quantify cells populations in the aortic valve. The role of different cell populations in patterning aortic valve tissue during development remains unclear. New methods are needed to identify and quantify cell phenotypes during valve development. Cells were identified using DNA-specific fluorescent stain 4',6-diamidino-2-phenylindole, otherwise known as DAPI. Proteins associated with different cell phenotypes, including neuron-specific class iii beta-tubulin (Tuj1), alpha- smooth muscle actin (aSMA), tyrosinase melanocytic protein 1 (TRP1), and glial fibrillary acidic protein (GFAP) were also stained by immunofluorescence. Optical image sections of the mouse aortic valve tissues were obtained by confocal microscopy and analyzed using the ImageJ image processing package from the National Institute of Health and Laboratory for Optical and Computational Instrumentation. Once selected, a stack of confocal images was split into three color channels based on their respective fluorescent staining. The area of interest, aortic valve leaflet tissue, could then be identified and the image threshold adjusted to reduce noise while converting the stack to binary images. Outlines of each individual cell were then approximated and quantified to determine the number of cells in the region. Differences in the abundance of valve cell populations across mice of different genotypes were observed. Future studies will seek to understand how the variations in cellular populations may alter valve function.





Segmented binary image of alpha smooth muscle actin within an isolated aortic valve leaflet.

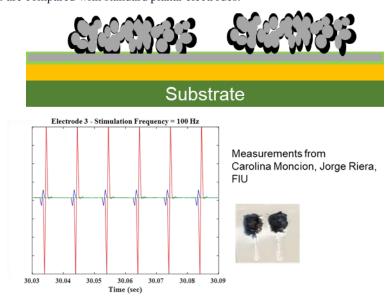
Low-Impedance Graphene - PEDOT-PSS Electrode Arrays

Authors: Kelly Nair Rojas and Huy Nguyen, Markondeyaraj Pulugurtha

Faculty Advisor: Markondeyaraj Pulugurtha, Ph.D.

Design and fabrication of low-impedance, biocompatible and miniaturized electrode arrays has been a key challenge to detect and control neural activity. With the concomitant incorporation of electrical and optical approaches, fine-pitch microelectrodes arrays (MEA) can be a novel solution to extend our understanding of microand neural activity dynamics. However, the high impedance constitutes a big challenge toward the widespread use of this technology. Nanoscale electrodes arrays coated with graphene are expected to enhance the neural recording and electrical stimulation by reducing the impedance and attaining better sensitivity. We are exploring the processing of graphene and pedot-pss-modified microelectrodes arrays for emerging neural-recording and neurostimulation technology. Printed graphene foams are dip-coated with pedot-pss to form patterned electrode arrays. Sensitivity of these electrodes to induced potentials at different frequencies are measured. The stability with high surface area graphene electrodes are compared with standard planar electrodes.





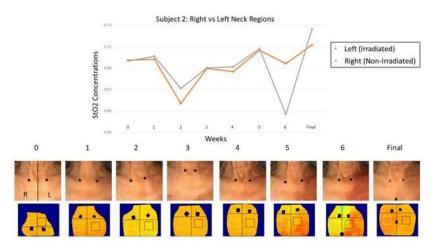
Graphene foam electrodes with PEDOT-PSS coating on metal traces.

Assessment of Radiation Dermatitis in Irradiated vs Contra-Lateral Chest Tissue of Breast Cancer Subjects using Near-Infrared Optical Scanner

Authors: Bridgette Meyer, Kevin Leiva, Edwin A. Robledo, Corina E. Beiner, Juan Murillo, Maria-Amelia Rodrigues, Joseph Panoff, Marcio Fagundes, Michael Chuong, Anuradha Godavarty **Faculty Advisor:** Anuradha Godavarty, Ph.D.

This year alone nearly 280,000 American's will be diagnosed with breast cancer and undergo radiation therapy (RT) treatment. While RT is a reputable method of killing malignant cells, a potential consequence is that healthy tissues may be damaged in the process. When the healthy surrounding tissue is afflicted it may present as several skin toxicities defined as a condition called radiation dermatitis (RD). Presently RD is diagnosed visually, but this method does not assist in the comprehension of how radiation affects both the irradiated and contra-lateral tissues alike. The Optical Imaging Laboratory (OIL) at FIU has employed the in-house Near-Infrared Optical Scanner (NIROS) to capture changes in the tissue oxygenation of the breast and chest regions. Both spatial and temporal hemoglobin maps were derived from the NIR images in terms of oxy-, deoxy, total hemoglobin, and saturated oxygen (that were calculated using Modified Beer-Lambert's Law). Utilizing both types of maps, comparisons between the radiation treated and non-treated breast tissues allowed for observing changes in tissue oxygenation across weeks. From our preliminary assessment, it was observed that the irradiated chest wall side showed greater changes in tissue oxygenation than that observed in the non-irradiated contralateral region.





Oxygen saturation maps of chest wall region in RT-treated breast cancer subject across weeks, differentiating the irradiated (left) and non-irradiated (right) regions.

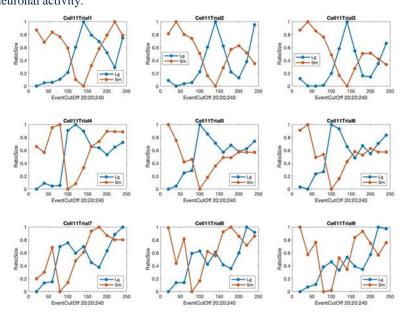
Black boxes are ROIs quantified to show differences in the line plot.

Understanding the Relationship between Visual Stimuli and Localized Calcium Events in Astrocytes

Authors: Gerson Romero, Tomas Suarez, Carlos Otero, James Schummers **Faculty Advisor:** James Schummers, Ph.D.

The brain consists of two main types of cells: neurons and glial cells. The focus of this work is on the glial cells known as astrocytes which for years were thought to have no role in higher processing other than neuronal support. Astrocyte activity is measured by the signals that are derived from an increase in intracellular calcium, which is evoked in the visual cortex of ferrets using a visual stimulus. Quantifying and analyzing astrocyte activity have proven to be a challenge as cell activity varies widely in the spatial and temporal domain. Through the implementation of a MATLAB-based software (AQuA) we have been able to begin the quantitative analysis of these events with respect to the spatial and temporal domain. Although AQuA provides more insight into cell activity, the tunning of the parameters to classify events in the cell as large and small events required further exploration with the event size threshold. By classifying of cell activity as large and small events a relationship between the visual stimulus and cell activity can be determined. We propose that as that the visual stimulus would evoke larger events in the cell and the smaller events could be classified as spontaneous events not related to neuronal activity.





Exploring the Event Cutoff Threshold of the cell events from 20 to 240 μ m2, and afterwards normalizing of event size ratios for comparison.

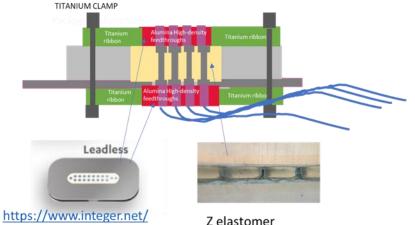
Fine-Pitch Area-Array Remateable Connectors for Active Implantable Medical Devices

Authors: Huy Nguyen, Anil Thota, Markondeyaraj Pulugurtha

Faculty Advisor: Markondeyaraj Pulugurtha, Ph.D.

Remateability plays a critical role in the development of bioelectronic connectors to connect a high-value computing and communication system to a sensing or a signal delivery neural interface. It also has wide range application in medical fields, especially in neural recording and prosthetics. The objective of this research is to provide a theoretical ground for area-array remateable and deformable fine-pitch connector design concepts to achieve reliable mechanical and electrical performance for implantable neural applications. Area-array Z-interconnect or vertical-interconnect is proposed as a promising innovative approach to enhance the remateability requirements. Fine-pitch area array with vertical-interconnect design is achieved by employing a thermoplastic interposer with conductive elastomer composite through-vias. The via-fill interposer is used to clamp and make electrical contacts between hermetic feedthroughs. Clamping is achieved with titanium flanges. This novel approach will have a prevalent influence on the manufacturing of biomedical electronics, as remateable fine-pitch interconnects. The approach willalso prevent implementation constraints between heterogeneous module functions in low-cost, wearable, textile and flexible electronics.





interconnect

Schematic of a remateable z-interconnect layer structure between hermetic feedthroughs encased in titanium.

Hermetic feedthroughs with

titanium flange

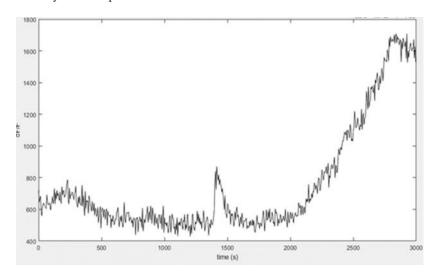
Synchronized Calcium Oscillations among Astrocytes

Authors: Nelson Abarca, Antonio Rosales, Karla Montejo, Jorge Riera

Faculty Advisor: Jorge Riera, Ph.D.

Deep brain stimulation (DBS) is a therapy where regions of the brain are hit with highfrequency electrical stimulation (HFS). This therapy can treat various diseases ranging from epilepsy to Parkinson's disease. How DBS works is still unclear. In the past, it has been studied that neurons are stimulated under HFS. Astrocytes, support cells in the brain, are not electrically stimulated like neurons but might be excited by voltage-gated calcium channels (VGCC) which could be activated during HFS. In this study, a protocol will be improved where astrocytic calcium oscillations will be measured from ex vivo acute cortical mice brain slices. HFS was delivered at 125 Hz, with asymmetric biphasic waveform using the Rhodes Tip Concentric Bipolar Electrode for acute applications SNE 100. Calcium imaging would come from a confocal microscope while astrocytes are injected with electrical stimulation and calcium elevations are measured as fluorescence via calcium indicator Fluo-4 AM and counterstain sulforhodamine 101 which differentiates between neurons and astrocytes. Fluorescent traces of calcium oscillations can be analyzed in MATLAB to look for synchronized elevations during the stimulation. We hypothesize that if there are synchronized calcium elevations in astrocytes when HFS is injected then astrocytes are important to the mechanism of DBS.





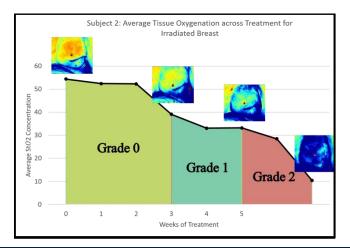
Average of calcium elevations from high-frequency stimulation ex vivo brain slice.

Analyzing the Extent of Tissue Oxygen Saturation on Irradiated and Non-irradiated Breast Tissue in Response to Radiation Therapy using a Commercial NIRS Device

Authors: Juan R. Murillo, Edwin A. Robledo, Kevin Leiva, Corina E. Beiner, Maria Amelia Rodrigues, Joseph Panoff, Marcio Fagundes, Michael Chuong, Anuradha Godavarty **Faculty Advisor:** Anuradha Godavarty, Ph.D.

Calcific aortic valve disease (CAVD) is a health condition which requires prosthetic valve replacement. The disease is expected to increase from 2.5 million cases in 2000 to 4.5 million in 2030 worldwide. The expression of the MMP-12 gene activates inflammation in the valves leading to the fragmentation of elastin in the valve extracellular matrix (ECM), which in turn, may contribute to an increase in calcium deposits, hence leading to CAVD. We hypothesized that tracking of aortic valve leaflet shape could be readily achieved via its time-dependent curvature during the cardiac cycle. The objective was to identify the mean anatomical spatial curvature distribution in an aortic valve without calcified deposits. A 3-dimensional model of a calcific aortic valve was acquired commercially (Materialise Inc, Plymouth, MI). The valve possessed calcific nodules, which were computationally removed to model a healthy valve. Mean curvature was computed along the three cusps of the aortic valve geometry. Our results showed that the mean curvature was relatively high along the free edges of the leaflet on the fibrosa-side. With future experiments the leaflet curvature changes could be used as a biomarker to assess abnormal valve extracellular matrix (ECM) remodeling activity, a potential precursor to CAVD.





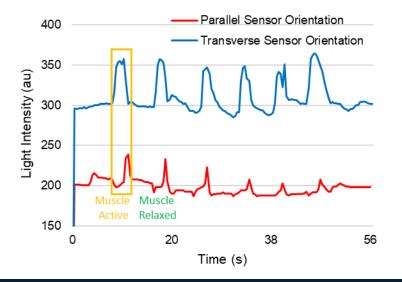
Average Tissue Oxygenation across Treatment for Irradiated Breast tissue correlated to the progression of radiation dermatitis. StO2 maps obtained from extracted images of NIRS device provided to visually represent the extent of oxygenation at various stages of RT treatment.

NIRS Monitoring of Muscle Activities: Towards Optical-Based Control of Prosthetic Devices

Authors: Shaylyn Grier, Wei-Chiang Lin **Faculty Advisor:** Wei-Chiang Lin, Ph.D.

Near-infrared spectroscopy (NIRS) is currently being investigated as a potential prosthesis control mechanism. It presents benefits such as portability, low cost, noninvasiveness, and electromagnetic interference-free. NIRS may also have the capability to detect partial activation of muscle and hence provide more independent signals for prosthesis control purposes. In this exploratory study, the effects of muscle activation on muscle optical properties and hence NIRS signals were investigated. Furthermore, the impact of NIRS sensor orientation with respect to the muscle fibers was explored. The results of this study show that the NIRS sensor is capable of detecting muscle activation. The cyclical activation of the brachioradialis muscle yields cyclical increases/decreases in the NIRS signal, as shown in Figure 1. It is also evident that the muscle activation-induced NIRS signals are sensor orientation-dependent. In comparison to the parallel sensor orientation, the transverse sensor orientation produces NIRS signals with a clear delineation of the muscle contraction and relaxation. These positive findings enable further investigation of the role of variables, including arm dominance, motion artifacts, and contraction intensity. Moreover, the feasibility of detecting partial activation of a muscle group using a NIRS sensor will be investigated.





Representative results from the cyclical forearm activation tests. The signals recorded with two different sensor orientations are significantly different in waveform and peak amplitude.

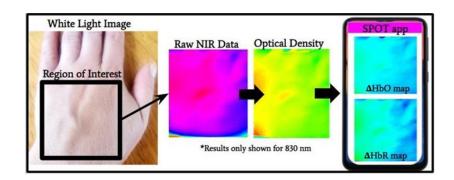
Smartphone App Designed for Automated Tissue Oxygenation Measurements

Authors: Alex Trinidad, Kacie Kaile, Anuradha Godavarty

Faculty Advisor: Anuradha Godavarty, Ph.D.

Medical imaging apps have been developed to analyze 2D white light (RGB) images of wounds for area estimates and 3D reconstructed depth measurements. These white light images can also be used to assess spatial differences in tissue oxygenation. However, these visible estimates are limited to only oxygenation in the superficial (dermal or exposed) tissue regions. Recently, an add-on SmartPhone-based Oxygenation Tool (SPOT) was developed to measure effective concentrations of Oxy and Deoxy-Hemoglobin (ΔHbO/ΔHbR) using Near Infrared (NIR) light. Since NIR light is minimally absorbed and preferentially scattered in biological tissues, imaging depths can be achieved up to ~2cm. Currently, the SPOT device is controlled using a custom app to sync the camera and NIR source, measure the imaging depth (between source and surface), and store acquired data. The stored files are then manually named, extracted onto a PC, and processed using Matlab. This entire process is a large rate-limiting step in the production of $\Delta HbO/\Delta HbR$ maps. The objective of this research is to develop a custom app for native data retrieval, data processing, and storage in a clinical-friendly framework. Further development of SPOT as a near-real time, bedside imaging device is dependent on eliminating the current off-board processing approach.





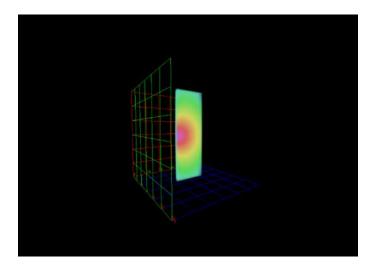
NIR images are processed using custom SPOT app for visualizing 2D oxygenation maps (Δ HbO and Δ HbR).

Flexible Near-Infrared Spectroscopy Sensors for In Vivo Tissue Condition Assessment: A Monte Carlo Simulation Validation

Authors: Condell Eastmond, Wei-Chiang Lin, Markondeyaraj Pulugurtha **Faculty Advisor:** Wei-Chiang Lin, Ph.D.; Markondeyaraj Pulugurtha, Ph.D.

At our Optical Imaging Laboratory, a hand-held near-infrared optical scanner (NIROS) has been developed for real-time oxygenation imaging of wounds. NIROS has been operated by a laptop for data acquisition and analysis, which adds substantial bulk and difficulty of use in clinical settings. Thus, an integrated NIROS (I-NIROS) was developed (as shown in Figure 1) that performs image acquisition and analysis from a single device, without requiring a laptop. In order for data acquisition and analysis to be accurate and stable, the source light (LEDs) need to be optimized for its output wavelengths, and illumination light intensities. The output wavelengths are optimized to values such that they obtain oxy- and deoxy-hemoglobin concentrations effectively. The output intensities are optimized for a stable performance as well as to avoid over saturation of the detected signal from non-uniform illumination intensities at different near-infrared (NIR) wavelengths. Following optimization studies, validation studies will be carried out using I-NIROS to detect physiological changes in tissue oxygenation, via phantom and in-vivo studies.





A 3D plot of fluence from a Monte Carlo simulation of the spinal cord.

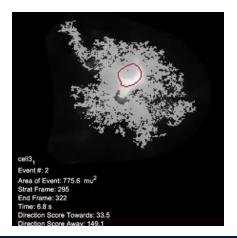
Visual and Analytical Characterization of Localized Calcium Events in Astrocytes within Cortical Circuits in vivo

Authors: Carlos Otero, Thomas Suarez, Gerson Romero, James Schummers

Faculty Advisor: James Schummers, Ph.D.

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 increases 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. Analysis with AQuA has proven challenging due to the extensive parameters needed for the image processing and event extraction. Input parameters can determine whether separate events are merged, change the propagation direction and speed, reshape events and exclude some events completely. The Visual Cortical Circuits lab is working on comparing the data extracted across the vast range of parameters in order to detect not only which parameter is closely correlated with current literature, but also if there are any differences or commonality across the varying parameters that can shed some light on the characteristics of calcium events of astrocytes during visual processing. In this work, we quantitatively assess the effect of input parameters on event size, number, and propagation parameters. Optimization of these parameters will enable more accurate biological interpretation of calcium events for future functional studies.





Movie and Event Details extracted from data processed through spatial-temporal calcium detection software (soma of astrocyte circled red).

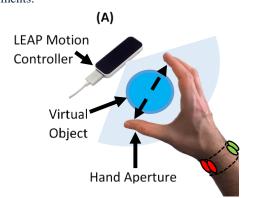
Non-Invasive Neuromodulation to Provide Haptic Feedback During Virtual Object Classification

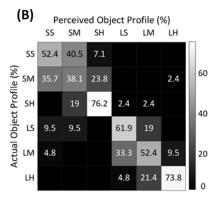
Authors: Heriberto Nieves, Komel Patel, Sierra Stocker, Andres Pena, Ranu Jung

Faculty Advisor: Ranu Jung, Ph.D.

Haptic feedback can provide useful sensory information while interacting with virtual objects. Current mechanical haptic approaches (vibration/pressure) can limit the mobility of the user. Electrical neurostimulation can be used as an alternative, evoking distally referred sensations of force when manipulating virtual objects. We explored the extent to which the haptic feedback from electrical neurostimulation enables the user to perform virtual object classifications. Seven subjects received transcutaneous electrical stimulation using a novel approach designed to evoke comfortable sensations in the hand while performing a virtual object squeeze task. Six virtual objects were created based on combinations of size (small/large) and hardness (soft/medium/hard). The subject's range of percept intensities was mapped to the unique compressive range of each object to simulate grip force. Percept intensity change was indexed to the hand aperture detected by a markerless tracking system (Fig. 1A). Blindfolded subjects completed 6 blocks of 6 non-repeating random grasp trials by "squeezing" the virtual object and identifying it based on the percept intensity. Subjects classified the virtual objects (Fig. 1B) at a higher rate than chance by size (p<0.0001), hardness (p<0.005), or both (p<0.005), indicating the potential of electrical neurostimulation to provide haptic feedback in virtual environments.







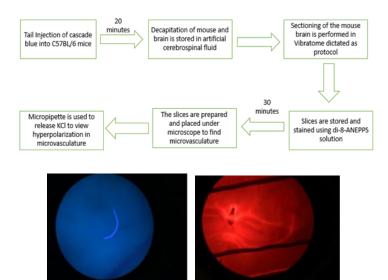
Virtual object classification. (A) Tracking device (Leap Motion Controller) monitors hand aperture while performing virtual object grasp trial. Hand aperture was average of the linear distance between the thumb pad and the index, middle or ring finger pads (dashed line). (B) Confusion matrix quantifying the perceived size and hardness combined (left-right), in relation to the actual object profile (up-down). Each block indicates the percentage of responses that were given when all subjects were presented a profile (actual) and classified it (perceived). SS=Small-Soft, SM=Small-Medium, SH=Small-Hard, LS=Large-Soft, LM=Large-Medium, LH=Large-Hard.

The Effect of Vasodilation in Penetrating Arteries when Deep Capillaries are Exposed to Potassium

Authors: Antonio Rosales, Ricardo Blanco, Arash Moskoroush, Jorge Riera **Faculty Advisor:** Jorge Riera, Ph.D.

Neurovascular coupling (NVC) is the name of the relationship between local neuronal activity and subsequent changes in cerebral blood flow (CBF). Through the theoretical model developed by Dr. Arash Moskoroush, a novel mechanism of vasodilation of penetrating arteries can be tested when deep capillaries are exposed to 10 mM of potassium. Based on the model, a backpropagation of hyperpolarization will occur in the endothelial cell (EC) when deep capillaries are exposed to potassium. The goal of the project would be to focus on the measurement of the backpropagating hyperpolarization through the EC's with a voltage sensitive dye imaging technique. The experiment would require the use of Cascade blue dextran which would be injected into the tails of mice to visualize the vascular system in the brain. Following, through a protocol developed in the Neural Mass Dynamics lab, the brain of the mouse will be sliced and stained with voltage sensitive dye. Afterwards, a fluorescent microscope would be used to observe changes in the EC's of the slice once 10 mM of potassium is exposed to the capillaries. Final results would be compared to theoretical results developed in the theoretical model of Dr. Moskoroush. We expect that the results will present a clear hyperpolarization backpropagation that leads to vasodilation.





The flow chart above represents the proposed outline of the experiment. The slice image to the bottom left represents the microvascular dyed in cascade blue. The image to the bottom right is a brain slice stained using di-8-ANEPPS at 50x Magnification. Slice images are provided by Ricardo Blanco.

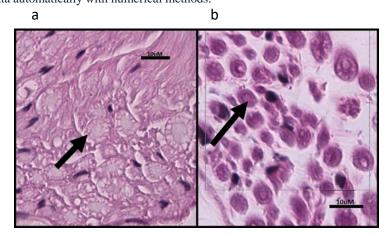
Age-related Degradation of Urethral Afferents

Authors: Nicolas Valencia-Diaz, Arezou Geramipour, Zachary Danziger

Faculty Advisor: Zachary Danziger, Ph.D.

Statistics indicate that around 10% of U.S. elderly people have an underactive bladder (UAB), which is characterized by incomplete bladder emptying and high residual volume. The lack of completely successful care is due to the unresolved etiology of UAB. One of the conditions that may cause age-related UAB symptoms is nerve degeneration of the lower urinary tract (LUT) system. The pudendal nerve is important in efficient voiding, and the lack of that leads to incomplete bladder emptying. Agerelated nerve degradation may cause difficulties in the signaling process from the bladder and the urethra, resulting in problems with contraction and micturition. We analyzed histological cross-section samples of the pudendal nerve of young (4-7 months) and old (18-24 months) rats, which were stained in H&E and examined in a microscope at 400x and 1000x magnification. These images were evaluated with the software Image J to calculate the area and the number of axons of each sample and assess how nerve structure changes with age. This will enable us to understand how aging affects the functionality of LUT. The counting and calculation are part of a semi-automatic process; however, with the information collected, we can start the structure of a program that will calculate the data automatically with numerical methods.





a) Image of the cross-section of a young rat (3 months) with 1000x magnification. b) Cross-section of an old rat (18 months) a 1000x of magnification. Black Arrows show myelinated axons in both images. Scalebar= 10μ M.

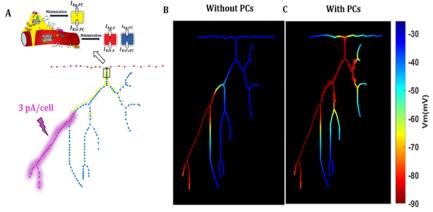
The Effect of Pericytes on the Conduction of the Vasodilatory Signal in the Cerebral Microcirculation

Authors: Allison Martinez Mejia, Arash Moshkforoush, Nikolaos Tsoukias

Faculty Advisor: Nikolaos Tsoukias, Ph.D.

Pericytes (PCs) are contractile cell types that can modulate the vasoactive responses in microvascular networks. Their contribution to electrical conduction along capillary network is not fully elucidated. They express functional inwardly rectifying potassium (Kir) channels. We have recently proposed that Kir channels can enable a regenerative conduction of vasodilatory signals along the brain microvasculature (Moshkforoush et al. PNAS, 2020). Here, using a mathematical model, we investigate under what conditions PCs can affect electrical signaling in capillary networks. A multicellular network of an arteriole and branching capillaries was reconstructed by electrically coupling endothelial cells (ECs) and PCs, with higher PC density near the arteriole (proximal). Each cell comprises of a Kir current, and a non-specific background current(Ibg), representing the rest of the transmembrane currents. The network response was analyzed upon an injection of a hyperpolarizing current in presence or absence of pericytes. Simulations predict that the level of upstream arteriole hyperpolarization depends on the ratio of PC's Kir to be conductances (i.e., GKir/Gbg). At high GKir/Gbg ratios, PCs amplify hyperpolarizing stimuli and enable robust arteriolar dilation. At low GKir /Gbg ratios, PCs inhibit conduction and limit arteriolar responses. Results suggest that depending on their relative Kir channel density, PCs can act as a sink or an amplifier of electrical signals. Experimental studies should further examine the model predictions and the potential role of PCs in modulating spreading vasodilatory response in capillary networks.





Effect of pericytes (PCs) on the propagation of the vasodilatory signal along capillary networks. 35 cells (purple) are stimulated with 3pA of hyperpolarizing current(A) and results are shown in the presence(C) or absence(B) of PCs. Arterioles are in red, PCs in yellow, and capillary endothelial cells (cECs) are in blue. The inset of panel A depicts the detailed and minimal electrical models of cECs, PCs, and Arterioles.

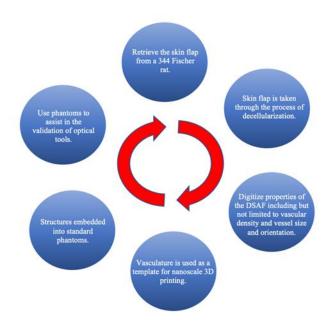
Optical Phantoms for the Skin Through the Process of Decellularization

Authors: Quianna Vaughan, Ajmal Ajmal, Jessica Ramella

Faculty Advisor: Jessica Ramella, Ph.D.

Standards or optical phantoms are used to mimic the complexity of tissue and provide validation to biomedical optical tools. Optical phantoms for the skin have been devised to mimic bulk optical properties like absorption and scattering of light by using materials such as carbon black and titanium dioxide. However, these phantoms fall short in comparison to the complexity of the skin structure. The aim of our project is to devise more realistic optical phantoms. To do so we propose the use of tissue decellularization and tissue clearing to expose the skin vascular plexus. This step will be followed by a 3D rendering of the viable vasculature. Nanoscale 3D printing approaches will then be used to reconstruct the capillaries of the skin in a permanent structure to be embedded into standard phantoms. The developing of this new type of phantom will give us the ability to optimize and validate novel optical tools for diagnosis of disease.





Schematic of the process for developing advanced optical skin phantoms.

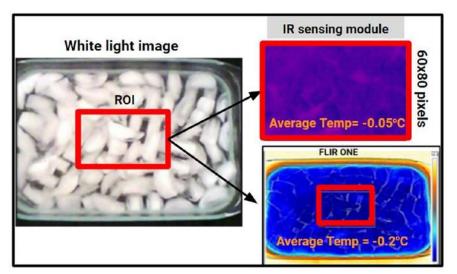
Development of a Thermal Imaging System to Obtain 2D Heat Maps without Contact

Authors: Pablo Rodriguez, Kacie Kaile, Anuradha Godavarty

Faculty Advisor: Anuradha Godavarty, Ph.D.

It is estimated that 1 to 2% of the population will experience a chronic wound during their lifetime and some may develop complications such as infection, possibly requiring amputation. Heat measurements obtained using Infrared (IR) imaging are a beneficial biomarker in assessing wound progression. Temperature changes greater than 2.2oC have been found to be clinically significant using FLIR based devices. Currently, a remote thermal sensing module is being developed to acquire, store, and process 2D maps without contact. The thermal device is composed of the IR thermal sensor, breakout board, and data is transferred to a computer. Preliminary testing of the IR sensing module against the commercially available FLIR ONE device was conducted by imaging a region of ice. The IR module measured an average temperature of -0.05°C, and the FLIR ONE measured an average temperature of -0.2°C. Further comparisons between the two sensors will be determined with respect to spatial and temporal changes in relation to the ground-truth. Additional measures will be implemented to attempt data extraction onto a fully remote system without the need for a computer.





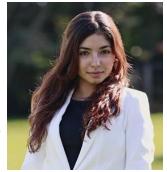
White light (RGB) image of ice tray (left) with red box indicated the region of interest (ROI) assessed using the newly developed IR module (top) and commercial FLIR ONE device (bottom).

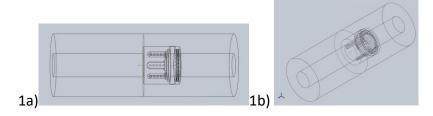
Computational Fluid Dynamic (CFD) Simulation of a Bioreactor System to Study the Effect of Oscillatory Shear Environments on Progression of Valvular Pathology

Authors: Paulina Alvarez Armel, Denise Hsu, Sharan Ramaswamy

Faculty Advisor: Sharan Ramaswamy, Ph.D.

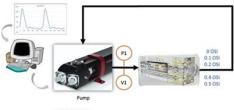
Oscillatory shear index (OSI) is a term used to quantify flow disturbance, and even though it has been previously shown to be a key regulator of cardiovascular tissue remodeling and valve disease by promoting calcification processes, the levels of flow disturbance associated with remodeling or pathology are still unknown. We will design a bioreactor to obtain full control of OSIs in an in vitro system to bridge the gap between hemodynamic shear stress and calcification in valvular tissues. SolidWorks assemblies will be translated into ANSYS where mesh processing and FEM (finite element method) analysis will be conducted. Computational simulations will be performed to determine waveforms for each desired oscillatory shear indexes, which will range from 0.0 to 0.5 in 0.1 intervals. Once the waveforms and bioreactor dimensions are determined, the device will be fabricated for use in mechanobiology related tissue engineering investigations. One of the goals is to produce de novo calcified human valve tissues that mimic the morphology of calcific aortic valves at early, intermediate, and late stages of pathology. This device could also serve as a platform for the development of future therapeutics.





1a & 1b: Valve ring holder SolidWorks assembly.

Bioreactor schematic

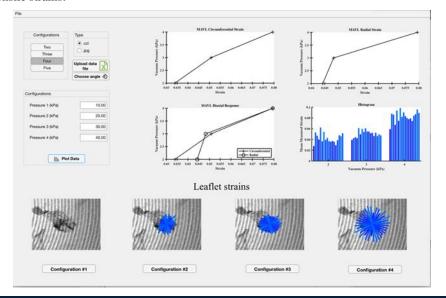


Graphical User Interface to Quantify Tensile Biaxial Properties on Mouse Aortic Valve Leaflets

Authors: Paulina Alvarez, Joshua Hutcheson **Faculty Advisor:** Joshua Hutcheson, Ph.D.

A lack of understanding of the mechanisms responsible for pathological remodeling occurring in Aortic Valve Disease (AVD) has resulted in limited and invasive clinical solutions. Mouse aortic valve leaflets (MAVL) offer great insight into this pathological progression, as they can be genetically modified to evaluate different aspects of AVD. However, due to their microscopic size, MAVL tissue mechanics are difficult to assess and thus its contribution to AVD progression almost impossible to determine. We recently developed a method in which the biaxial tensile properties of MAVL tissues can be assessed by adhering the tissues to a silicone rubber membrane utilizing dopamine as an adhesive. Then, the biaxial biomechanical properties of the tissue were characterized through a custom MATLAB code. A Graphical User Interface (GUI) was developed to streamline and optimize the analysis process for the custom code used in the method published by Chaparro, et al. (2020). The built-in App Designer in MATLAB was used to create the GUI making it editable for future researchers to come. Creating an easy to use interface facilitates the analysis of leaflet biomechanical properties as well as bridging the gap between MAVL, which are easy to modify, and the evaluation of biaxial tensile strains.





Graphical User Interface designed with MATLAB builtin App Designer.

Designing Biocompatible Packaging for a Novel Subcutaneous Biosensor

Authors: Brianna Valdes, Teshaun Francis, Wei-Chiang Lin

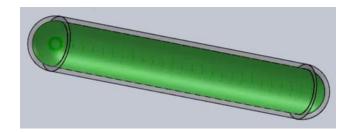
Faculty Advisor: Wei-Chiang Lin, Ph.D.

Eventually, all implantable biosensors will fail. The high stress concentrations present at the interfaces of an implanted biosensor, signal to the nearby cells that a foreign object is present in the subcutaneous tissue. Macrophages respond to the foreign object by forming a granuloma to encapsulate and isolate it, preventing the analyte from reaching the sensor to cause biofouling. This chain of events is the foreign body response (FBR) and mitigating its effects on our biosensors is the goal of this project.

The objective of this research is to design an implantable package for our upcoming CO2 biosensor. To ensure that the FBR is mitigated, we have identified target values for size, shape, and elasticity that are compatible with the mechanical properties of the subcutaneous tissue.

We are using Solidworks computer aided design (CAD) software to build virtual models of the sensor and simulate shear, tensile, and compression tests in order to capture the sensor's respective elastic moduli. This presentation will demonstrate our work-in-progress towards the design and characterization of a mechanically biocompatible package.





A 3D rendering of the proposed package, built using Solidworks CAD software. The proposed sensor package is composed of PDMS and hydrogel. The capsule geometry, modeled after similar implantable devices, minimize edges and corners, which are the source of large stress concentrations.

Analysis of IPSC-Derived Cardiomyocyte Contractility in a Cardiac Gel Substrate

Authors: Marcos Gonzalez Perez, Asad Mirza, Yih-Mei Lin, Manuel Perez, Alberto Sesena Ribfiaro,

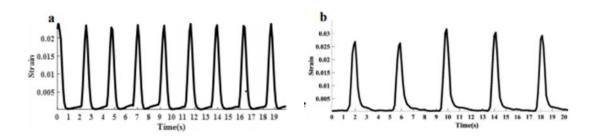
Jin He, Sharan Ramaswamy

Faculty Advisor: Sharan Ramaswamy, Ph.D.

Cardiomyocytes differentiated from human Induced Pluripotent Stem cells (iPSC) have the potential to be used for therapy. The objective of this investigation was to determine if a substrate that mimicked cardiac tissue mechanical stiffness would enhance iPSC cardiomyocyte contractility in in-vitro culture. iPSC-derived cardiomyocytes were seeded in Matrigel and Silicone Gel-coated 6- well plates. Strain maps were created using digital image correlation (DIC). Images were first recorded 24-days after initial cell seeding, during a ~20 second interval. For DIC processing, a region of interest (ROI) was first demarcated using a spline fitting. The full Green-Lagrangian strain fields were subsequently calculated. An open source MATLAB based software, Ncorr, was the used to calculate the displacement and strain fields of the cardiomyocytes.

There was an increase of 70% cycle frequency in Matrigel cultivated cardiomyocytes when compared to iPSCs in Silicone-based, cardiac-stiffness mimicking gels. Note that the frequency of the cells in Matrigel (0.425 Hz) was 36% of the typical human heart rate of 1.2 Hz or 72 bpm, in comparison to only 21% in the case of the cardiac tissue stiffness-mimicking gel (0.25 Hz). Moreover, less restrictions to deformations in iPSC-derived cardiomyocytes in Matrigel, in comparison to the cells seeded within a gel which mimicked cardiac stiffness (7,800 Pa), i.e., the Silicone Gel was confirmed, since the stiffness of Matrigel is 44 Pa, which is considerably lower than the stiffness of the Silicone Gel (8,000 Pa). Owing to a dominance of interactions at the microscale, we conclude that cell substrate linkages rather than bulk mechanical properties drive the physiological-relevance of the cell's contractile behavior.





a. Time series strain profile of IPSC-cardiomyocytes in Matrigel. b. Time series strain profile of IPSC-cardiomyocytes in Silicone Gel.

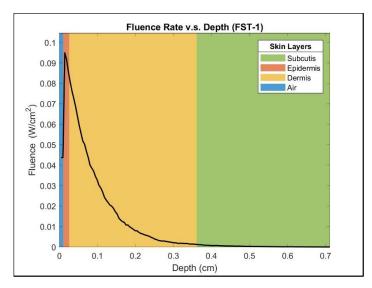
Monte-Carlo Based Near-Infrared Light Propagation Modeling for Different Skin Types and Melanin Concentrations

Authors: Daniela Leizaola, Edwin A. Robledo, Anuradha Godavarty

Faculty Advisor: Anuradha Godavarty, Ph.D.

Light propagation analysis is widely used in the optical field to understand the movement and effects of photon travel. A diagnostic imaging devices' analysis capabilities and limitations are categorized by the wavelength emission from the electromagnetic spectrum. The Optical Imaging Laboratory concentrates on the development of noncontact near-infrared imaging devices with the aim of correlating changes in oxygenation of skin tissues. Therefore, it is important to understand the efficacy of the devices' wavelength propagation depth on a subject. The objective is to emulate the movement of photons (at 600nm) on a three-layered skin model to understand the influence of skin pigmentation on effectiveness of light transmittance. Melanin concentration has been shown to have a positive correlation with skin pigmentation, in which pigments are categorized as Fitzpatrick Skin Type (FST) with grading scale I-VI. Simulated diffuse reflectance signals were created based on a three-layer skin model: epidermis, dermis, and subcutaneous layers. Simulations used the Monte Carlo method on MATLAB software to emulate largest layer depths from literature and melanin concentrations based on the FST of healthy human subjects. Maximum fluence rate showed a negative correlation with respect to skin pigmentation when simulated at 600 nm.





Fluence rate of 600 nm light propagation on a Fitzpatrick Skin Type 1, (FST-1). Simulation of photons on a 3 layered skin model Epidermis (orange), Dermis (yellow), and Subcutis (green) inclusive of an air layer to model noncontact imaging.

BME ALUMNI PANELISTS

Anderson Milforte (Spring 2019)
Regulatory Affairs Specialist, Johnson & Johnson Vision
Care

Deimitri Rodriguez (Fall 2019) Associate Research & Development Engineer, Terumo Aortic Inc

Daniel Chapparo (Summer 2018)
PhD Student, Florida International University, Biomedical Engineering

Salease Randolph (Spring 2016)
Safety Health and Environmental Coordinator, Nutranext,
A Clorox Company

Jessyka Desrosiers (Spring 2016)
Medical Student, Nova Southeastern University

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