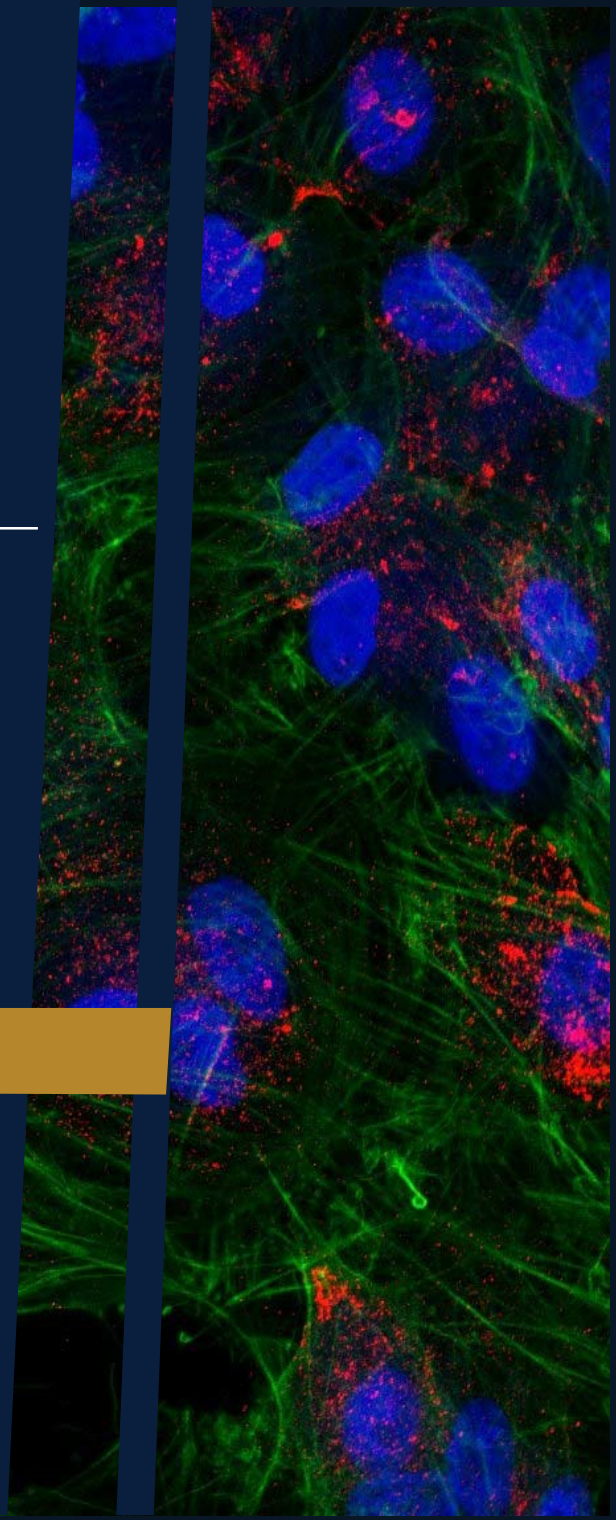
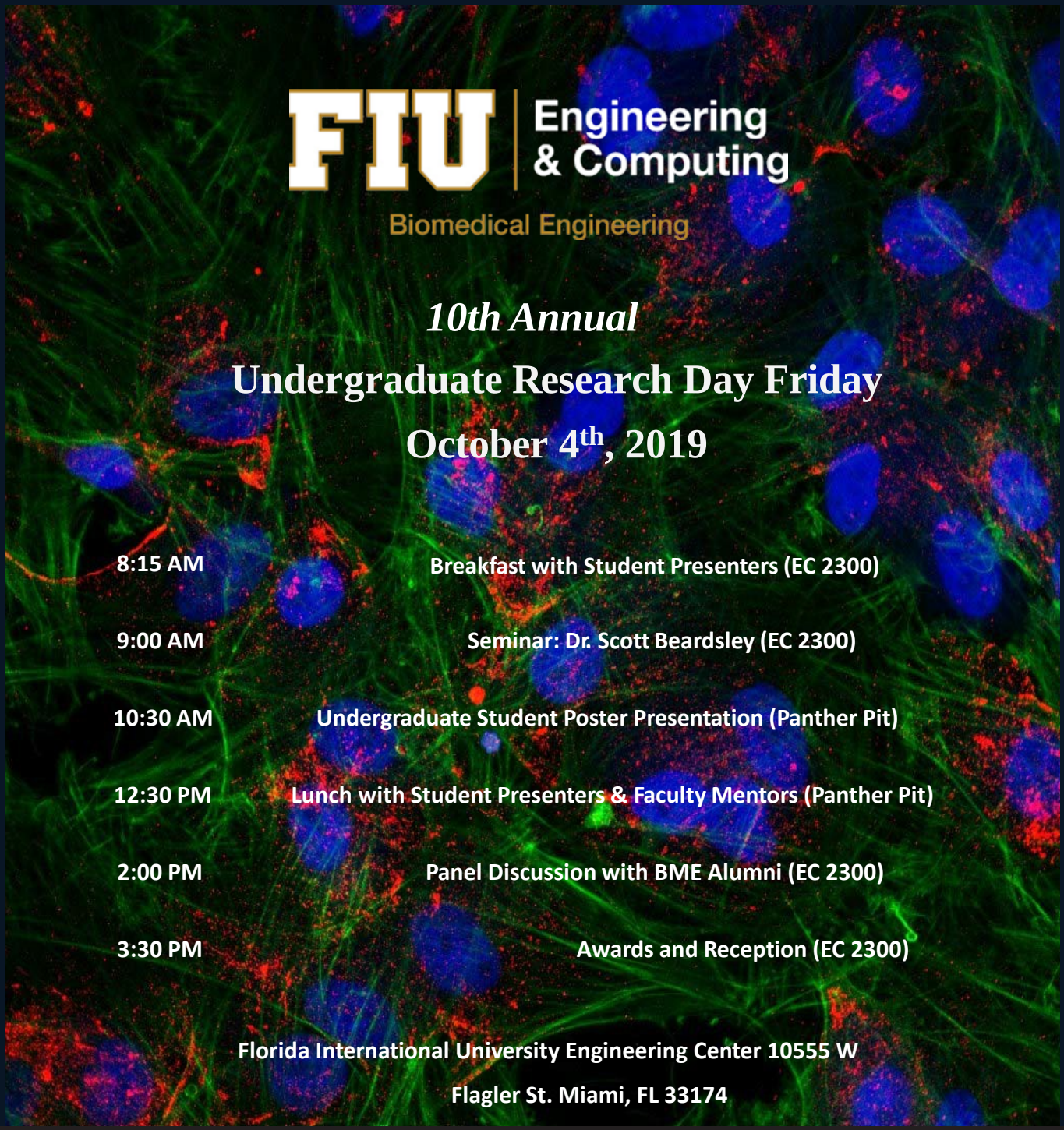
FIU | Engineering & Computing

Biomedical Engineering

UNDERGRADUATE RESEARCH DAY FALL 2019

DISCOVER DESIGN DEVELOP DELIVER




FIU
Engineering
& Computing
Biomedical Engineering
10th Annual
Undergraduate Research Day Friday
October 4th, 2019
8:15 AM
Breakfast with Student Presenters (EC 2300)
9:00 AM
Seminar: Dr. Scott Beardsley (EC 2300)
10:30 AM
Undergraduate Student Poster Presentation (Panther Pit)
12:30 PM
Lunch with Student Presenters & Faculty Mentors (Panther Pit)
2:00 PM
Panel Discussion with BME Alumni (EC 2300)
3:30 PM
Awards and Reception (EC 2300)
Florida International University Engineering Center 10555 W
Flagler St. Miami, FL 33174

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,

Ranu Jung, PhD
Chair, Biomedical Engineering

KEYNOTE SPEAKER

WH Coulter Biomedical Engineering Distinguished Lecture Series

"Timing matters: Sensorimotor dysfunction and individually targeted strategies to improve goal-directed movement "

Scott Beardsley, Ph.D.

Associate *Professor* at the Marquette University and Medical College of Wisconsin Biomedical Engineering Department

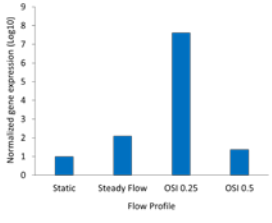
Scott Beardsley is an Associate Professor in Biomedical Engineering at Marquette Univer- sity and Medical College of Wisconsin. He is Director of the Integrative Neural Systems Laboratory and Director of Undergraduate Studies for Biomedical Engineering at Mar- quette. He earned bachelor's degrees in Physics and Mathematics from UW-Whitewater in 1995 and his Ph.D. in Biomedical Engineering from Boston University in 2001. His re- search employs a multi-disciplinary (multi-scale) approach that combines human behav- ioral studies with multi-model functional brain imaging and computational modeling to determine how brain areas interact to process and control visually-guided movement. His lab focuses on developing within-subject analyses and targeted neuro-rehabilitation strategies to mitigate the effects of sensorimotor dysfunction and on identifying novel strategies for seamlessly interfacing human visuo-motor control with external devices. He received a National Academies KFI Fellowship in 2006 and the Way Klingler Young Scholar Award in 2012. He is an advocate for undergraduate involvement in research and design, co-founding and directing the annual College of Engineering Design Day at Mar- quette and individually mentoring over 30 undergraduate research projects since 2009.

Vascular endothelial cell phenotypic-dependence on specific surface oscillatory shear stress patterns

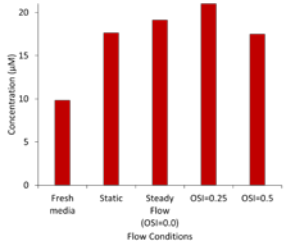
Authors: Alexandra Tchir, Denise Hsu, Sharan Ramaswamy
Faculty Advisor: Sharan Ramaswamy, Ph.D.

The vascular system is highly regulated by hemodynamic forces in blood flow. Oscillatory shear index (OSI) is used to quantify oscillatory flow (equation 1). We hypothesize that a specific range of OSI will have a key role in pathology and a different range will be implicated in homeostasis. The preliminary results showed substantial up-regulation of the CD31 gene under an OSI of 0.25. The 0.25 OSI group expressed CD31 at a 7.62 fold higher than the static group, showing substantial upregulation. CD31 is a widely used endothelial cell marker, specific to endothelial cell differentiation. Its upregulation may indicate that specific ranges of OSI, specifically 0.25, favorably regulate the vascular phenotype. At other ranges of OSI, the expression was lost. The nitric oxide assay showed increased activity in the steady flow and 0.25 OSI group. Nitric oxide production is atheroprotective; increased levels in steady flow and 0.25 OSI groups may show maintenance of vascular tone. Decreased levels at the 0.5 OSI group may correspond to an inhibition of NO production and a decrease of vascular integrity, possibly leading to disease.

The preliminary findings here point towards a non-linear, parabolic-type, rather than linear relationship between CD31 gene up-regulation and OSI, with a peak gene expression occurring at OSI = 0.25. In conclusion, these results may help towards delineating distinct ranges of oscillatory blood fluid-induced biomechanical stimuli that may play a critical role in normal versus abnormal vascular tissue remodeling. There may be regions in the arteries that never get disease, and the range of OSI at these regions may correlate to those that we have found in this study. Likely, the ideal conditions for vascular endothelial cells are not strictly either steady or oscillatory conditions, but rather how much oscillatory flow is present.



Gene expression from porcine valvular endothelial cells of the vascular endothelial phenotypic marker, CD31

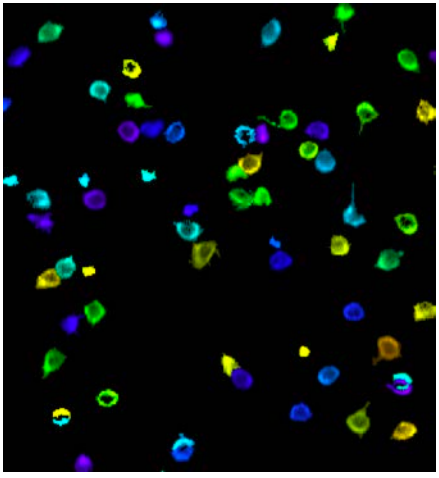


Nitric oxide activity from porcine valvular endothelial cells

Three-Dimensional Two-Photon Calcium Imaging for Visualization and Neuron and Astrocyte Activity in the Visual Cortex

Authors: Santiago Fossi, Sally Duarte, James Schummers
Faculty Advisor: James Schummers, Ph.D.

In recent years, two-photon calcium imaging has been widely used to study the activity of neurons, astrocytes, and other types of cells, enabling researchers to obtain high resolution images in vivo. Using this technique, the Visual Cortical Circuits Laboratory views the spiking activities of different cells and analyze how they work in conjunction to form neural circuits that ultimately process visual sensations. Traditionally, two-photon calcium imaging allows for one to image at different depths of the brain at different times, which limits the time series data to a two-dimensional plane. These neural circuits have complex three-dimensional structure, through which activity can propagate in all directions. The goal of this project is to construct and install a microscope attachment with an ETL (electrically tunable lens) onto the two-photon calcium imaging microscope. The tunable lens changes its focal point depending on the pressure of the optical fluid inside the lens, which can be controlled by changing the current going through a voice coil that exerts a force onto the fluid. This mechanism makes it possible to image various depths at nearly simultaneous times with excellent accuracy. In this way, we will obtain images that represent volumetric slices, giving us a window into the third dimension of the neural circuit mechanisms underlying visual information processing.

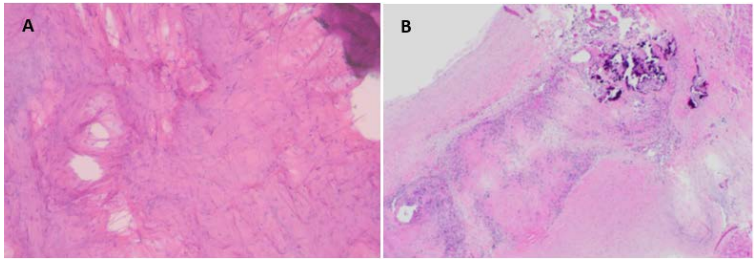


Neurons imaged using two-photon calcium imaging

Decellularization with the Enhanced Retention of Bioscaffold Matrix Components for Heart Valve Regenerative Applications

Authors: Ariadna Herrera, Sergio Rodriguez, Brittany Gonzalez, Carl Granath, Cecilia Österholm Corbascio, Sharan Ramaswamy
Faculty Advisor: Sharan Ramaswamy, Ph.D.

Congenital heart problems are the most common type of birth abnormality, affecting 8 out of 1000 live births in the U.S. (www.aha.org). Clinical solutions for critical valve defects in pediatrics are severely limited by the unavailability of small prosthetic valves; moreover, artificial valves cannot adapt to somatic growth. Therefore, tissue engineered heart valves are of interest as they can provide for growth, self-repair, infection resistance, and can be a permanent approach for replacing defective heart valves. We investigated porcine small intestinal submucosa (PSIS; Fig. 1A) (CorMatrix, Roswell, GA) longitudinally as a viable bioscaffold in an animal model. An explant of the PSIS mitral valve (11 months' post-implantation) exhibited a chronic immune response (Fig. 1B), which we speculate is due to the reminiscence of porcine cells (Fig. 1A). Thus, we hypothesize that the application of a more cautious, yet thorough decellularization technique will further remove porcine cells (acellular) while maintaining the integrity of the extracellular matrix (ECM), due to the added care involved in minimizing hostile detergent exposure to the ECM. Specifically, the decellularized PSIS scaffolds will be treated with a non-ionizing detergent for different periods of time to find the optimal processing time. After detergent removal the extent of cell removal and matrix integrity retention will be analyzed through histological staining specifically for collagen, GAGs and elastin, the main ECM components of the valve. The re-decellularized scaffolds will be compared to the original scaffolds to see how effective our gentle decellularization technique was at removing the cells while minimizing damage to the ECM. This acellular PSIS scaffold with intact ECM components is ideal for implantation because it will mitigate or completely remove the immune response that occurs, allowing for proper de novo growth. Moreover, the retention of additional ECM components in the bioscaffold will help to further promote de novo valvular tissue formation via chemotaxis.

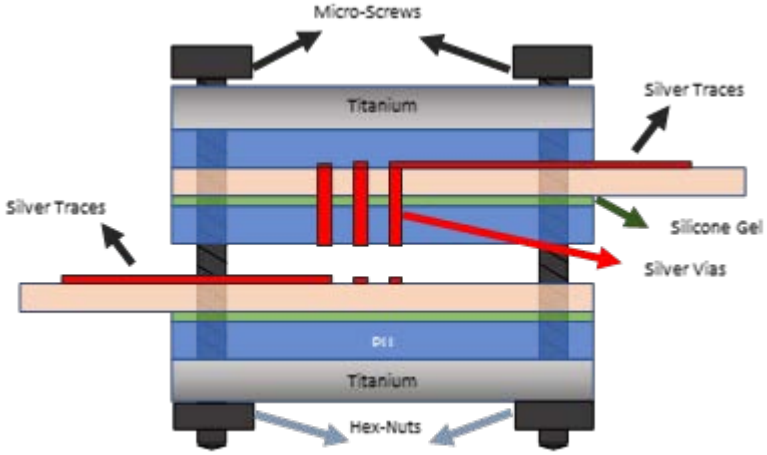


Porcine small intestinal submucosa (A) raw decellularized and (B) explant of baboon 11 months' post-implantation. H&E histological stains show (A) cells remaining of the raw scaffold and (B) a chronic immune

Fine-Pitch Area-Array Remateable and Deformable Interconnects in Smart Sensor Packages

Authors: Jose F. Solis-Camara, Juan Bermudez, Daniel Wilding, P. M Raj
Faculty Advisor: P. M Raj, Ph.D.

The need for miniaturized implanted or wearable electronics has created the need for 3D interconnections that can undergo severe bending, deformation and mechanical strain, and yet remain reliable. For several emerging applications in implantable, wearable and textile electronics, the interconnections should be reworkable or remateable. This is to replace and repair the device or remove the sub-system during certain sensitive operations and re-insert later, without affecting the rest of the system. In this paper, innovative and scalable approaches are designed, developed and demonstrated to achieve deformable and remateable interconnects between flexible packages. Fine-pitch interconnects are formed on flexible metal-core laminates through semi-additive patterning approaches that are scaled down to sub-micron lines and spacing. High-conductivity contacts are achieved through the compression of the polyurethane film inserts with conductive metal-elastomer through-vias. The compressible forces are created with microscrews with precision alignment. The 3D flex-to-flex and device-to-flex interconnects attained reliable and stable high conductivity throughout multiple bending cycles to a curvature of less than 1 cm. Testing of the microwave losses of the interconnection materials will be characterized through RF transmission line structures.

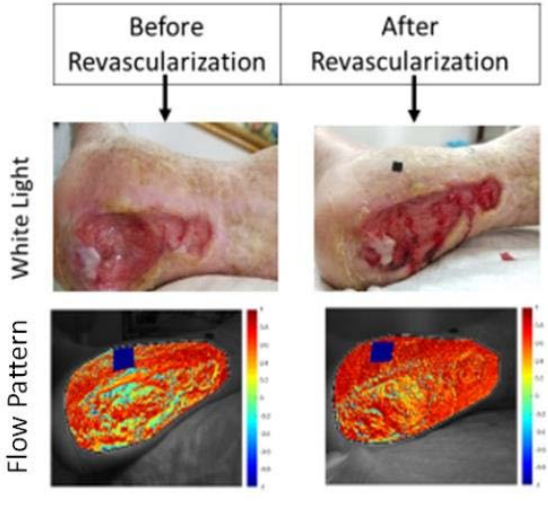


Cross-sectional area of deformable and remateable 3x3 via array design concept, with screws and nuts as fastening mechanism

Effect of Re-vascularization on Oxygenation Flow in a Chronic Diabetic Foot Ulcer

Authors: Bridgette Meyer, Kevin Leiva, Maria Saavedra, Francisco Perez-Clavijo, Anuradha Godavarty
Faculty Advisor: Anuradha Godavarty, Ph.D.

It is estimated that of the world's population, 415 million people are diagnosed with diabetes, with the United States alone contributing 30.3 million. Of this population, approximately 25% are afflicted with diabetic foot ulcers (DFUs), which in the most chronic cases require specialized wound care and possibly limb amputation. Past studies using a non-contact, hand-held Near Infrared Optical Scanner (NIROS), developed in the Optical Imaging Lab (OIL) at FIU have detected a decrease in wound-to-background contrast in terms of tissue oxygenation. More recently, studies using NIROS have expanded into dynamic imaging, capturing changes in oxygenation with respect to time that can provide more physiological information that can attribute to wound healing. In this study, data was acquired from a mixed arterial/DFU subject across 50 weeks of treatment via dynamic imaging with NIROS using a breath-hold stimulus. Hemoglobin parameters in terms of oxy-, deoxy, total hemoglobin, and saturated oxygen were calculated from dynamic imaging data using modified Beer-Lambert's Law. Changes in tissue oxygenation were assessed from these parameters to identify changes in oxygenated flow within the wound site. Pearson's correlation maps for oxy- and total hemoglobin showed that post-re-vascularization the region of interest had a positive correlation in compared the weeks previous. These results indicate that NIROS was able to detect an improvement in oxygenated flow, in terms of oxy- and total hemoglobin, to the wound site.

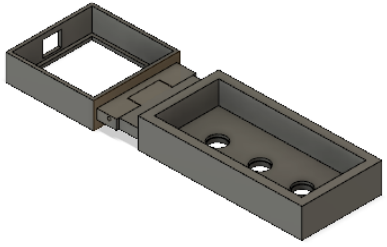


Flow oxygenation patterns before and after vascularization procedure in diabetic ulcer subject

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

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

Current approaches for controlling prosthesis include myoelectric control using electromyography (EMG) and EEG based brain-computer interfaces. In this project, we will explore the feasibility of prosthesis control using muscle hemodynamics. To measure muscle hemodynamics near infrared spectroscopy (NIRS) will be used to monitor local optical changes in muscle tissue in response to muscle activity. This method presents benefits such as its portability, noninvasiveness, and the lack of effect of electromagnetic noise. NIRS may also have the capability to detect partial activation of muscle and hence provide more independent signals for control purposes.
A prototype mini NIR spectroscopy system was designed and developed in house over the past three months. It contains a high power NIR light emitting diodes (LEDs) and a chip-based spectral sensor (AS7263, AMS, Austria). A special case, as shown in Figure 1, was designed to control the distance between the NIR LEDs and the detector, which has been shown to have an effect on the resulting signal measurements. An ideal distance between the NIRS LED and detector will ensure muscle tissue contributes significantly to the measured signal. A Monte Carlo simulation for photon migration will be performed theoretically evaluate the performance of the prototype mini NIR spectroscopy system.

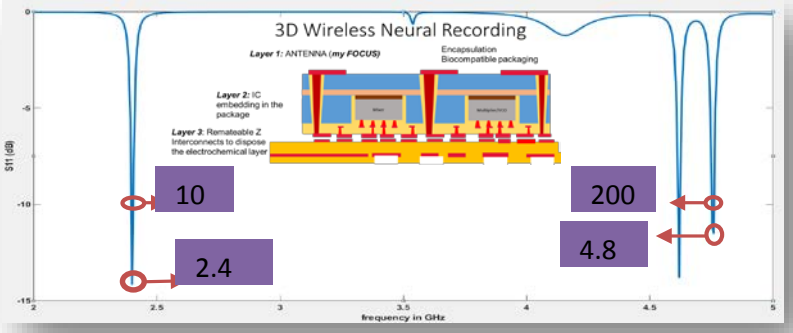


Three-dimensional modeled case intended for determination of proper distance between source and detector

Zero-Power Neural Recording with Microminiaturized Implanted Medical Devices

Authors: Jazzmin Harris, Sk Yeahia Been Sayeed, Carlos Riera Cercado, Satheesh Bojja Venkatakrishnan, P.M Raj
Faculty Advisor: P.M Raj, Ph.D.

Innovative data telemetry interfaces for passive neural recording systems are developed for diagnosing, monitoring and treating neurological disorders. These bioelectronic systems are recognized as passive or zero-power systems because they do not need any external or internal power sources for their basic operation. In passive neural recording, the incoming RF carrier or resonant inductive link is directly modulated with the neural signal and radiated back to the external reader. Such systems typically need a dual-band or dual antenna scheme to receive the incoming signal and simultaneously transmit the outgoing signal. The conversion from the incoming carrier frequency to the outgoing carrier frequency is performed with a frequency multiplier, antiparallel diode pair (APDP) or other frequency conversion circuits. The outgoing carrier is picked up an external antenna. Miniaturization of wireless data telemetry interfaces is a key barrier in realizing such passive recording systems. Miniaturization is the key as these systems are implanted inside the human body. We will analyze antenna miniaturization technologies, which requires advances in antenna designs, substrate materials, and their package integration technologies. High-permittivity ceramic and dielectric composites are studied as antenna substrates. Fabrication of miniaturized ceramic antennas will be described. Electromagnetic modeling software HFSS is utilized to design and simulate the antennas. A complete system analysis with the frequency multiplier and mixer chips and their performance comparison will be provided.

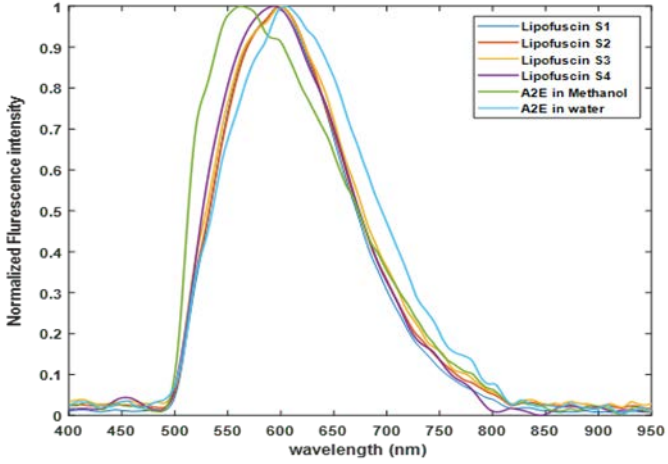


Dual band Antenna Simulation. Antenna works at two frequencies 2.4 GHz and 4.8 GHz with sufficient bandwidth. (Inset: 3D neural recording packaging illustrating the need for mm size antennas)

Customized Reference Target with Synthesized A2E for VIS-OCT-FAF Quantitative Imaging of the Retina

Authors: Khaleel Atkinson, Zahra Nafar, Shuliang Jiao
Faculty Advisor: Shuliang Jiao, Ph.D.

Lipofuscin is a heterogenous mixture of proteins and lipids. It is found in the retinal pigment epithelium (RPE), and excessive amounts present in the RPE is linked to several retinal diseases such as age-related macular degeneration and Stargardt disease. Lipofuscin is fluorescent and can be detected by Fundus autofluorescence (FAF), a non-invasive imaging technique that is widely used to monitor lipofuscin accumulation in RPE. Quantification of FAF signal is necessary to assess the amount of lipofuscin in the RPE for diagnosis and monitoring disease progression. However, FAF quantification is challenged by first differences in acquisition system parameters such as laser power and detector sensitivity, and further attenuation caused by the ocular media prior to the RPE. Thus, a fluorescence standard is needed for in vivo imaging, which can be imaged each time a FAF image is acquired. In this paper, we present the fabrication of a new reference target with synthesized A2E, a major fluorophore of lipofuscin. A2E has a similar quantum yield, excitation and emission spectrum to lipofuscin. The customized target was implemented into the visible-light OCT-based multimodal imaging system (VIS-OCT-FAF) as a common reference for both OCT and FAF and was successfully tested in vivo. With similar characteristics of the A2E target to retinal lipofuscin, quantification of absolute content of lipofuscin with an A2E-equivalent unit can be possible.

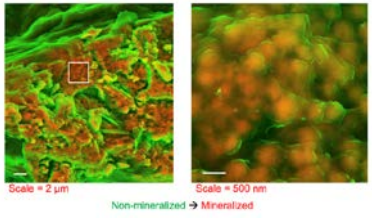


Human lipofuscin compared to synthesized A2E

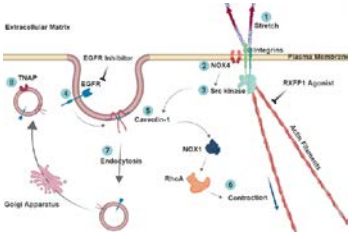
Mechanistic and Quantitative Analysis of Calcific Extracellular Vesicle Formation in Mineralization

Authors: Jessica Molina, Amirala Bakhshiannik, Joshua Hutcheson
Faculty Advisor: Joshua Hutcheson, Ph.D.

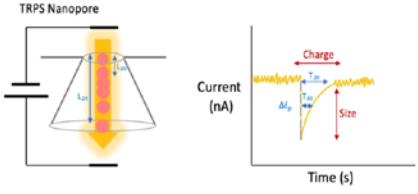
Calcification, a leading contributor to cardiovascular disease, begins with the release of ~100 nm-sized extracellular vesicles (EVs) by resident vascular smooth muscle cells (VSMCs). Under pathological conditions, VSMCs undergo an osteogenic phenotypic change to osteoblast-like cells and release calcifying EVs. These calcifying EVs exist within larger populations of EVs released during normal cellular processes. It has been shown that calcific EVs originate in caveolae, flask-shape invaginations in plasma membrane. Previous studies on mesenchymal stem cells indicate that calcification requires elevated cell contractility. In VSMCs, increased contractility can occur through a mechanistic pathway that includes Src tyrosine kinase-induced activation of epidermal growth factor receptor (EGFR) within caveolae. The caveolae alterations result in RhoA protein kinase activity and subsequent VSMC contraction. In this study, we investigate the relevance of this pathway in calcifying EV formation from two cell types, which are responsible for physiological and pathological mineralization, osteoblasts and VSMCs, respectively. These cells were cultured in pro-calcific media and co-treated with either Src tyrosine kinase inhibitor, EGFR inhibitor, or RhoA protein kinase inhibitor. To characterize the released EVs, the media from these cultures was collected and analyzed for tissue non-specific alkaline phosphatase activity, an enzyme required for calcification. Furthermore, tunable resistive pulse sensing (TRPS) will be used to quantitively asses the properties of calcifying EVs released by osteoblasts and VSMCs. The use of TRPS can aid in the differentiation of unique calcifying EVs properties that contribute to disease and potentially lead to develop better treatment options through development of vesicle-specific therapies.



Density-dependent color SEM indicates extracellular vesicles composing large calcifications within human plaque sections



Probable mechanistic pathway of calcific EV formation

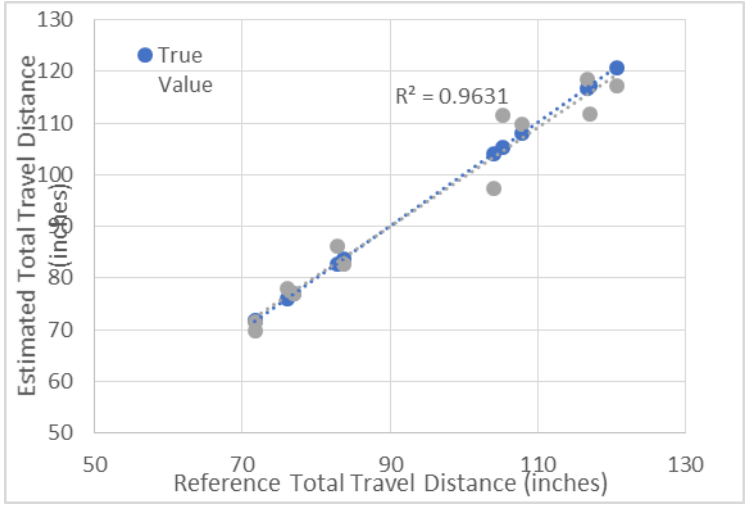


TRPS measures current disruption within a pore to measure EV size and charge

Wearable Wireless Sensors for the Real-Time Acquisition of Physiological Signals and Analysis of Movements

Authors: Angela Wong Lau, Sean Miller, Wei-Chiang Lin
Faculty Advisor: Wei-Chiang Lin, Ph.D.

Gait analysis is a method used to identify biomechanical parameters in the gait cycle, such as stride frequency, stride length and step size. Through gait analysis, we can detect some important abnormalities that include gait asymmetry, parkinsonian gait or sensory gait. The existing technologies for the gait analysis are costly, inaccessible, bulky and difficult to use. To overcome such limitations, we propose to develop a low-cost gait analysis system based on wireless inertial measurement units (IMUs). The prototype portable gait analysis system developed in house uses a total of 6 virtual reality (VR) IMUs (BNO080, Bosch), which can register the spatial orientation of the lower limbs of a body including the tights, lower legs, and feet. The accuracy of the measurements and the algorithms of the system have been validated and optimized using the existing technologies such as an instrumented walkway system.

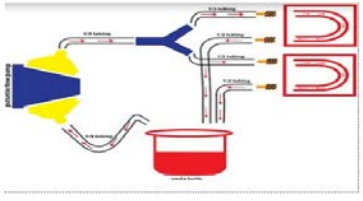


Scatterplot showing the linear relationship between the estimated and the reference total travel distance

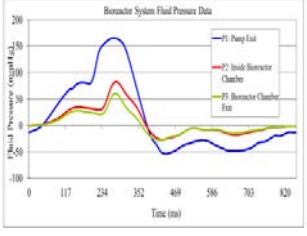
Validation of a Physiologically Relevant Pulsatile Bioreactor System for Cardiovascular Tissue

Authors: Marcos Gonzalez Perez, Manuel Perez, Elnaz Pour Issa, Sharan Ramaswamy
Faculty Advisor: Sharan Ramaswamy, Ph.D.

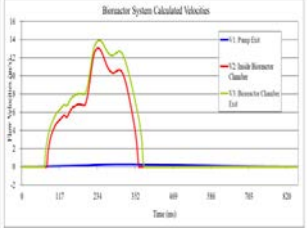
Cardiovascular Regenerative therapeutics may be the future for heart valve surgery due to their ability to restore sustained function. In previous studies in our laboratory, it was demonstrated that engineered cardiovascular tissue in a bioreactor promote changes in the tissue's characteristics, especially phenotypic development, as well as its growth and extracellular matrix (ECM) constituents, due to mechanical conditioning. In the current study a bioreactor system was assembled to apply in-vitro physiologically-relevant pulsatile flow induced shear stresses to human bone marrow derived from mesenchymal stem cells (BMSC) seeded tissue specimens. To assess if bioreactor-housed specimens were receiving the shear stresses, flow and pressure was measured at multiple locations within the flow circuit (pump exit, bioreactor inlet, bioreactor scaffold location, and bioreactor outlet; Fig. 1), by using transducers embedded in the flow loop, while the pump was set to deliver a physiologically-relevant pulsatile flow profile. Results demonstrated that the flow and pressure waveforms measured at the sample vicinity deviated slightly from the pump exit location (Fig. 2A,B). These results demonstrate that the samples are receiving the requisite physiologically-relevant flow patterns that would in turn, induce a potentially desirable specimen shear stress and an oscillatory shear pattern (oscillatory shear index/OSI), biomechanical triggers for de novo cardiovascular tissue formation. However, whether a selected flow profile provides the expected shear stress or OSI would have to be quantified via a computational fluid dynamic model. In conclusion, we were able to verify that the integrity of a physiologically-relevant flow profile was fairly well-maintained from the pump to the specimen locations, which establish the foundation for future fluid-induced mechanobiological investigations in cardiovascular regenerative medicine.



Flow diagram of pulsatile-flow bioreactor system



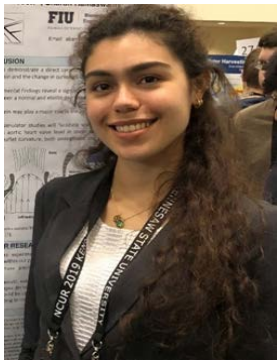
Pressure values at pump outflow and bioreactor chamber



Flow velocities generated at the Bioreacto

Regional Curvature Alterations in Human Aortic Valve Leaflets after Calcification

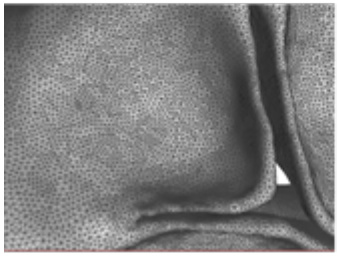
Authors: Amanda Barreto, Asad M. Mirza, Sharan Ramaswamy
Faculty Advisor: Sharan Ramaswamy, Ph.D.



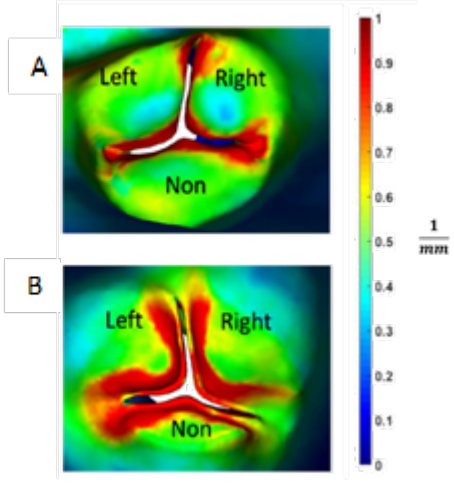
Calcific aortic valve disease (CAVD) is a health condition which requires prosthetic valve replacement. The disease is expected to increase from 2.5 million cases in 2000 to 4.5 million in 2030 worldwide. The expression of the MMP-12 gene activates inflammation in the valves leading to the fragmentation 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.

$$k(\varphi) = \frac{e\varphi^2 + 2f\varphi + g}{E\varphi^2 + 2F\varphi + G}$$

$$k_{mean} = \frac{k_{min} + k_{max}}{2}$$



Mesh subdivided by midpoint scheme

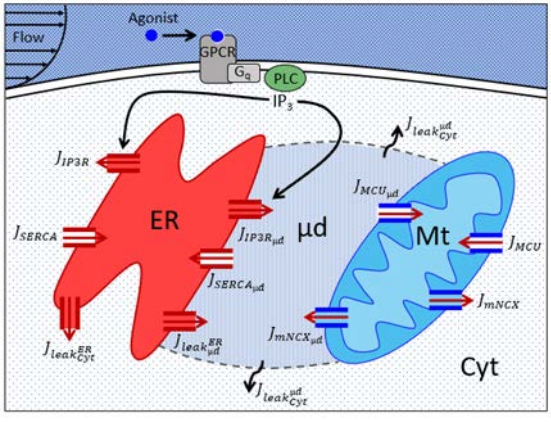


Mean curvature maps across all three leaflets (A) Ventricularis (B) Fibrosa

Modeling the Role of Endoplasmic Reticulum-Mitochondria Microdomains in Endothelial Calcium Dynamics

Authors: Baarbod Ashenagar, Arash Moshkforoush, Nikolaos Tsoukias, B. Rita Alevriadou
Faculty Advisor: Nikolaos Tsoukias, Ph.D.

Upon inositol trisphosphate (IP3) stimulation of non-excitable cells, including vascular endothelial cells, calcium (Ca2+) shuttling between the endoplas¬mic reticulum (ER) and mitochon¬dria, facili¬tated by complexes called Mitochon¬dria-Associated ER Membranes (MAMs), is known to play an important role in the occurrence of cyto¬solic Ca2+ concentration ([Ca2+]Cyt) oscil¬lations. A mathe¬matical compartmental closed-cell model of Ca2+ dy¬namics was developed that accounts for ER-mitochondria Ca2+ microdo¬mains as the µd compartment (besides the cy¬tosol, ER and mitochon¬dria), Ca2+ influx to/efflux from each compartment and Ca2+ buffering. Varying the distribution of functional receptors in MAMs vs. the rest of ER/mitochon¬drial mem¬branes, a parameter called the channel connectivity coefficient (to the µd), allowed for generation of [Ca2+]Cyt oscilla¬tions driven by distinct mechanisms at various levels of IP3 stimulation. Oscillations could be initiated by the transient opening of IP3 receptors facing either the cytosol or the µd, and subsequent refilling of the respective compartment by Ca2+ efflux from the ER and/or the mitochondria. Only under con¬ditions where the µd became the oscillation-driving compartment, silencing the Mito¬chondrial Ca2+ Uniporter led to oscillation inhibition. Thus, the model predicts that alternative mechanisms can yield [Ca2+]Cyt oscillations in non-excitable cells, and, under certain conditions, the ER-mitochondria µd can play a regulatory role.

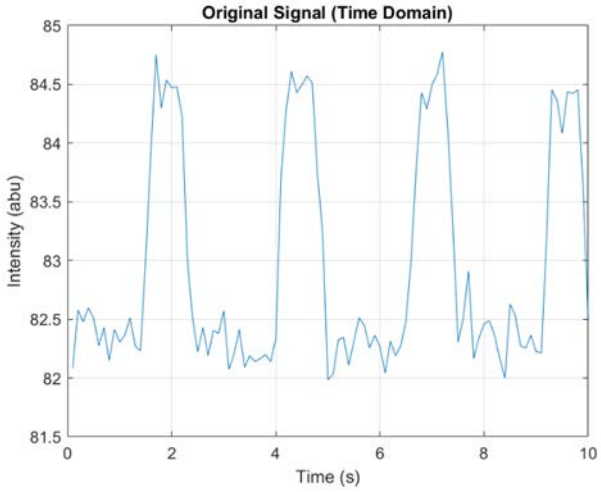


Schematic representation of the cell model. Either chemical stimulation or flow-induced shear stress results in increased intracellular [IP3]. IP3 binds to IP3R triggering ER Ca2+ release. Ca2+ is pumped back into the ER via the SERCA or is taken up by the Mt via the MCU. Ca2+ is also extruded from the Mt into the intracellular space via the mNCX. IP3R, MCU, SERCA and mNCX channels face either the µd or Cyt (channels inward to the respective compartment are filled with color; outward channels are not filled). All fluxes, including leaks, are shown.Each compartment contains Ca2+ buffering proteins (not shown)

Non-contact Pulse Measurements using a Near-infrared Optical Imager

Authors: Daniela Leizaola, Kevin Leiva, Anuradha Godavarty
Faculty Advisor: Anuradha Godavarty, Ph.D.

The gold-standard Doppler ultrasound is used to measure the pulse at the ankle in order to determine wound healing potential. It is a contact-based approach and distanced from the wound site in order to assess healing potential. There is a need for a non-contact-based imaging approach to measure pulses closer to the wound site for improved diagnosis. A non-contact near infra-red optical scanner (NIROS) has been previously used to measure tissue oxygenation changes in ulcers across weeks of wound treatment process. Herein, NIROS was modified to acquire real-time optical measurements and extract pulse information as a non-contact imaging approach. Initially, the accuracy and stabilization of NIROS was determined to differentiate the noise floor, prior to extracting the pulse. Following this, in-vivo studies were performed to dynamically image the changes in diffuse reflectance signal for extraction of pulse information via fast Fourier transforms. Pulse frequency extracted from NIROS was further compared to pulse oximeter-based measurements for its correlation.



Pulsatile NIR signal captured at 10 Hz frequency using NIROS

LED Optimization of An Integrated Near Infrared Optical Scanner for Wound Imaging

Authors: Jorge Barter, Nicole Sevilla, Kevin Leiva, Edwin Robledo, Anuradha Godavarty
Faculty Advisor: Anuradha Godavarty, Ph.D.

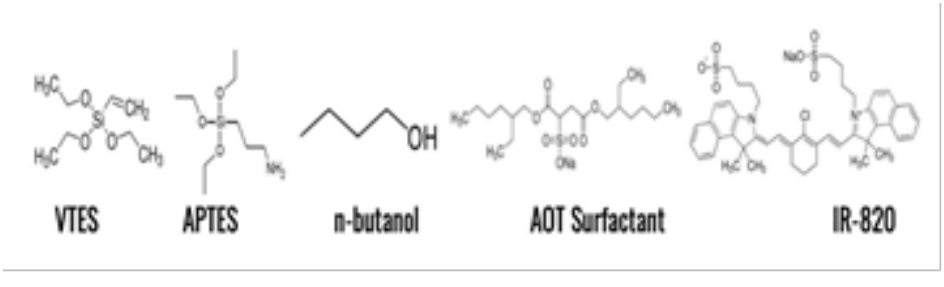
At our Optical Imaging Laboratory, a hand-held near-infrared optical scanner (NIROS) has been developed for real-time oxygenation imaging of wounds. NIROS has been operated by a laptop for data acquisition and analysis, which adds substantial bulk and difficulty of use in clinical settings. Thus, an 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.

I-NIROS, an integrated version of NIROS

Techniques in the Ranostic ORMOSIL Nanoparticles for Cancer Therapy

Authors: Romina Doubnia, Anthony McGoron
Faculty Advisor: Anthony McGoron, Ph.D.

Organically Modified Silica (ORMOSIL) nanoparticles have been studied for chemotherapeutic, photodynamic, gene delivery and bioimaging applications, and have improved pharmacokinetic properties, controlled release of the drug and lowered toxicity. This project emphasizes on the fabrication of ORMOSIL nanoparticles through a nanoemulsion technique to generate drug encapsulating medium for theranostics and include an optic imaging agent that allows tracing the drug from the time is administered to the time it reaches the target.. The quality of these nanoparticles is determined by measuring the size, polydispersity index (PDI), and the quantity of functional groups on the surface. The size of nanoparticles is critical to take advantage of the Enhanced Permeability and Retention Effect (EPR) of most tumors, which makes size optimization an integral aim for this project. These nanoparticles are synthesized within an oil-in-water nanoemulsion medium. Once the optimal synthesis has been achieved, the second phase of the project can start which involves amine functionalization by addition of APTES for later labeling with an optical imaging agent using a near infrared element further up on the spectrum. Expected results involve an average nanoparticle population of ~50 nm, with a PDI below 0.200 an indication of high particle homogeneity. Dynamic Light Scattering (DLS) is used to characterize the synthesized nanoparticles. The concentration of surfactant played an important role in the effect to drug delivery applications.

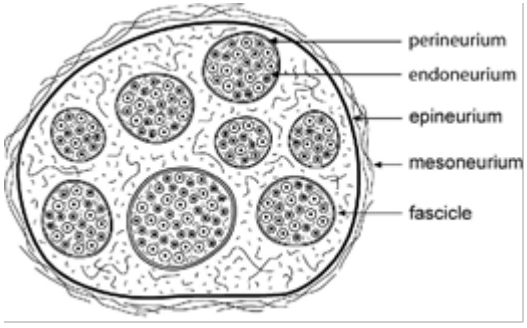


Chemical structures of used elements

Morphometric Study of the Sciatic Nerve

Authors: Brigette Manohar, Jefferson Gomes, Ranu Jung
Faculty Advisor: Ranu Jung, Ph.D.

Neural interface technology has been used to alter patterns of neural activity in different peripheral nerves by the use of intraneural electrodes. Peripheral nerves consist of fascicles of nerve fibers. By stimulating different fascicles with intrafascicular electrodes, the electric field within the fascicle can be modified and different nerve fibers recruited. Computational models of the peripheral nerve could be utilized to determine the best stimulation parameters in order to activate different portions of the peripheral nerve. To create a realistic, biophysical model of the nerve, morphometric analysis of the peripheral nerve sections will be used to determine the fascicular organization. The morphology and geometry of the nerve fibers within the fascicles will be determined by the use of histological staining methods and analyzed by the use of the Neurolucida software and the Leica Light Microscope respectively. The size of the fascicles, the shape of the fascicles and the number of fascicles within the nerve section will be identified along with the type of nerve fibers and the number of nerve fibers within the fascicle. The histological staining methods include the immunohistochemical detection of choline acetyltransferase (ChAT) to identify sensory fibers and counterstaining with hematoxylin to identify motor axons. Toluidine blue staining will be used to identify the number of axons and the degree of myelination of the nerve section. The tracing of these fibers will be done using the Neurolucida software to create a three-dimensional reconstruction of the peripheral nerve section. Sections of the peripheral nerve in rats have been collected and have been prepared and preserved through paraffin embedding or cryopreservation. This tissue was then cut into 4-6 mm sections to obtain serial sections in steps of 200 mm or 500mm on a microtome. After cutting, slides were stained and the Neurolucida software has been used to perform morphometric analysis of the fascicles and fibers within peripheral nerve sections that were collected.

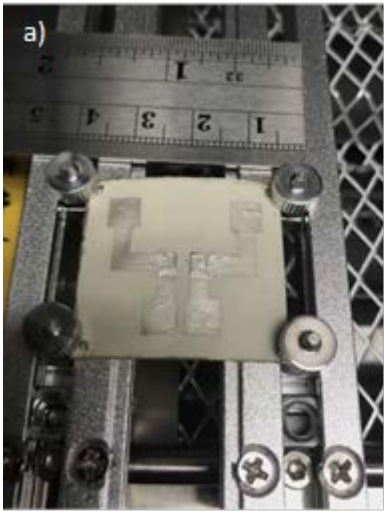


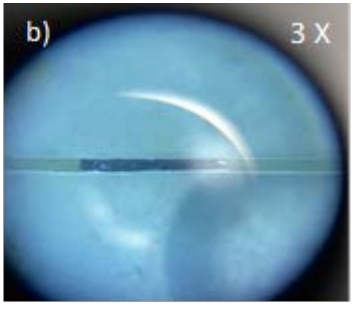
This illustrated diagram shows the cross-section through a myelinated nerve such as the sciatic nerve , clearly indicating the various components of the nerve as well as the fascicles of the nerve. The axons of the nerve are illustrated as distinct circular structures within the fascicle

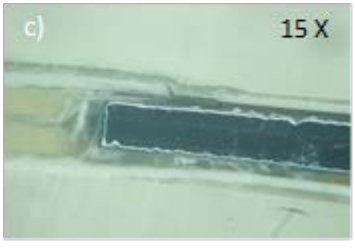
Embedded Die Flexible Fan-Out Packaging

Authors: Jose F. Solis-Camara, Juan Bermudez, Daniel Wilding, P. M Raj
Faculty Advisor: P. M Raj, Ph.D.

Vertical or 3D integration of devices and other system components is the key to achieve smaller systems and is hence the primary driver for future packaging. Die-embedding with chip-first assembly is, therefore, emerging as a major alternative to the existing flip-chip assembly technologies with thick solder joints. Packaging with embedded-die interconnects will lower the package thickness and the package stresses in the interconnects, thereby increasing the system flexibility and reliability. This presentation demonstrates fan-out packaging technologies with flexible substrates to embed active devices in packages. For the initial technology demonstration, a flexible sheet was used as the flexible package core, A die was assembled in the cavity and feedthroughs were drilled to provide interconnections between the layers. The key process steps are: laser drilling of cavities and alignment holes, lamination of backing LCP layer, die assembly into the cavities, LCP top layer lamination, via drilling and interconnect trace printing. In order to evaluate the mechanical performance of the traces, a Keysight U1242B multimeter will be used to measure the resistance before and after bending over a one 1-cm radius cylinder. Kelvin probe structures were designed to extract the interconnection resistance without the effect of contact resistances. The stability in interconnection resistance was characterized after bending to less than 1 cm of curvature.







a) Flexible Package with embedded die undergoing testing. c) 3X magnification of embedded die and substrate. c) 15X magnification of embedded die and substrate

Oscillatory Shear Stress Effects on Mesenchymal Stem Cells in Monolayer Culture

Authors: Elizabeth Cheng, Denise Hsu, Alexandra Tchir, 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.. However, the cells that are used must be able to express certain genes to promote the valve phenotype. Human bone marrow stem cells (BMSCs) 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 BMSCs towards cardiovascular lineages. The oscillatory shear index (OSI) is a measure of the shear stress placed on a system, ranging from a steady flow of zero to a maximum oscillatory flow of 0.5. Previous computational research conducted in determining the most effective range of OSI necessary for favorable gene expression garnered a range of 0.18 to 0.23. Thus, human BMSCs were cultured and plated into separate wells for introduction into a shear stress cell assay system (BioFlux 200, Fluxion Biosciences, San Francisco, CA) system for the purpose of exposing the cells to different OSI environments from 0 to 0.5. Each sample consisted of roughly 8 x 105 BMSCs and the duration of exposure/group was 48 hours after an initial 24 hour static culture period to ensure proper adhesion to the walls of the device. RNA from the human BMSCs was then extracted in order to analyze the cell's gene expression of specific heart valve genes using real-time polymerase chain reaction (PCR). To expand on previous research, a larger sample size will be tested, along with a different set of genes evaluated, as well as additional OSI conditions (0, 0.1, 0.2, 0.3, 0.4, 0.5).

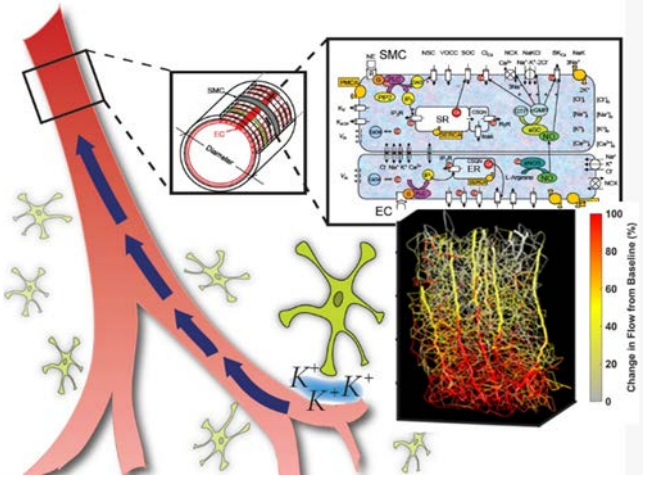
$$OSI = 0.5 \times \left(1.0 - \frac{\left| \int_0^T W\vec{S}S\,dt \right|}{\int_0^T \left| W\vec{S}S \right| dt} \right)$$

Quantification of fluid oscillations with oscillatory shear Index (OSI) formula

Mathematical Model of Blood Flow Control in Brain during Neurovascular Coupling

Authors: Tisha Boodooram, Baarbod Ashenagar, Arash Moshkforoush, Nikolaos Tsoukias
Faculty Advisor: Nikolaos Tsoukias, Ph.D.

Neurovascular coupling (NVC) is the phenomenon by which neuronal activity is rapidly accompanied by elevated local blood perfusion. Impairment of NVC has been associated with several pathological conditions, including stroke, dementia, and Alzheimer's disease. Prior literature has mainly focused on NVC pathways involving penetrating arterioles (PAs), attributing a more passive role to the capillary network in the distribution of oxygen and nutrients in different regions of the brain. Recent evidence, however, has shown an active role of capillary endothelial cells in NVC through inwardly rectifying potassium dependent pathways. Using mathematical models of cell electrophysiology developed in the lab, the changes in membrane potential of PAs, and the corresponding change in the diameter of these vessels, are predicted when a local capillary region is subjected to high extracellular potassium concentration [K+]o. Here, we provide a detailed mathematical model of blood flow dynamics in a reconstructed network of brain vasculature from the mice cortex which considers the interaction between individual red blood cells with the inner walls of rigid capillary vessels and the non-continuum nature of blood when flowing through narrow vessels. We analyze how blood is distributed in the network following a localized potassium stimulation at the capillary level.

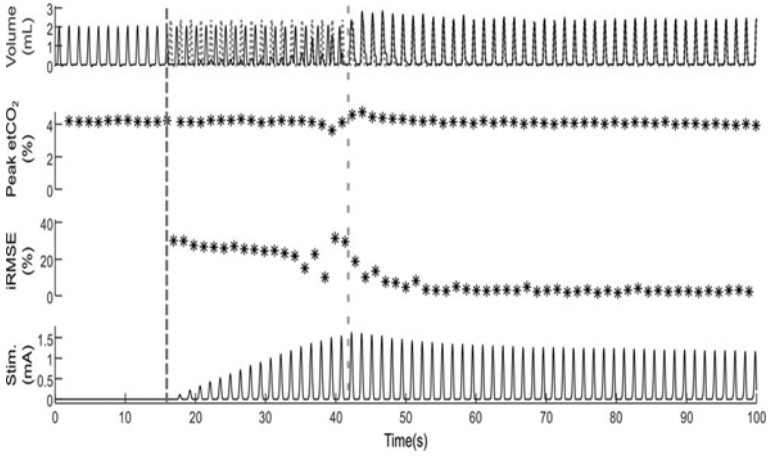


Schematic of the multiscale modelling of Neurovascular Coupling

Novel Implementation of Whole-Body Plethysmography for Chronic Closed-loop Respiratory Control Studies

Authors: Sepehr Soroushiani, Ranu Jung
Faculty Advisor: Ranu Jung, Ph.D.

Positive pressure mechanical ventilation (PPMV) tends to cause alveolar damage and diaphragmatic muscle atrophy. Respiratory pacing has helped patients to wean and avoid the drawbacks inherent in PPMV. An adaptive, closed-loop, and neuromorphic controller has been developed that can automatically modulate stimulation to maintain a desired ventilatory pattern on a breath-by-breath basis. Previous studies assessed controller performance acutely on spinally-injured anesthetized rats. The controller was able to achieve a desired ventilatory pattern that led to a reduction of end-tidal CO2. However, an invasive tracheostomy procedure had to be performed to accurately measure the respiratory flow, volume, and end-tidal CO2. Due to its invasiveness, tracheostomy is not suitable for chronic studies. Therefore, usage of whole-body plethysmography (WBP) has been proposed to measure breath volume noninvasively. C2-spinally-hemisected rats will be used to assess the adaptive controller in a chronic setting. Anesthetized rats will undergo diaphragm pacing for 3 weeks, 15 minutes a day; breath volume will be measured using WBP. A control group will undergo C2-spinal hemisection but will not be paced. After the studies, the diaphragms will be extracted to assess muscle conditioning, and the spinal cord will be harvested to confirm injury and to assess biomarkers of upregulation of neuroplasticity.

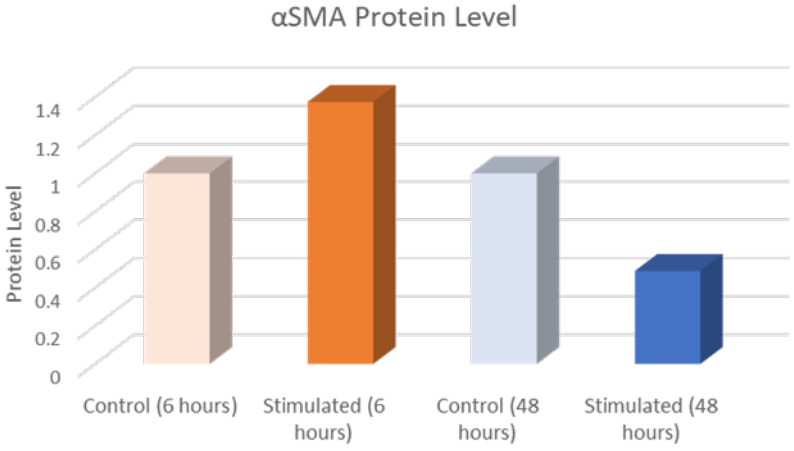


Adaptive PS controller implementation in hemisected animal for the initial 100 seconds of the trial

Quantifying Biological Response of Valve Interstitial Cells Under Nano-vibrational Stimulation

Authors: Jay Yeung, Mohammad Shaver, Daniel Chaparro, Joshua Hutcheson
Faculty Advisor: Joshua Hutcheson, Ph.D.

This project investigates the influence of mechanical vibrational stimulation on aortic valve interstitial cell (VIC) phenotype.
When aortic valves close during diastole, the leaflets vibrate. This produces the S2 sound- the same sound a doctor hears in a stethoscope. In this preliminary study, we used a nano-vibrational bioreactor to study the effects of vibration on VIC phenotype. Porcine VICs were introduced to an in vitro environment for 6 and 48 hours with a frequency of 150 Hz and amplitude of 100 nm, which emulates the cardio-mechanical frequencies experienced by valves in vivo. Nonstimulated VICs were used as a control. Western Blotting with an Alpha SMA primary antibody was used to determine change in Alpha SMA protein expression, which correlates to changed in VIC phenotype during remodeling.
Results show a 37% increase in smooth muscle alpha-actin (alpha-SMA) protein expression for the stimulated VICs after 6 hours compared to the control. However, after 48 hours, the stimulated sample shows a 53% decrease in alpha-SMA protein expression compared to the control.
These preliminary results indicate that the vibrational stimulation may result in a change in phenotype. To understand the relationship between valvular frequency and extracellular matrix remodeling of the aortic valve, future studies will investigate the role of other frequencies and amplitudes on VIC phenotypes.

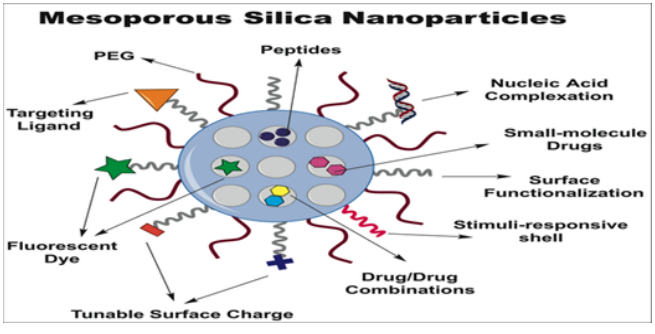


Expression of Alpha SMA protein levels in porcine VICs between control and stimulated groups. A significant decrease in expressed protein levels was observed in the stimulated 48-hour group

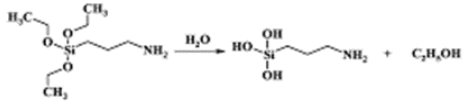
Functionalization of Silica Nanoparticles for Drug Delivery and Optimization of Synthesis Methods

Authors: Carolina Guillen, Anthony McGoron
Faculty Advisor: Anthony McGoron, Ph.D.

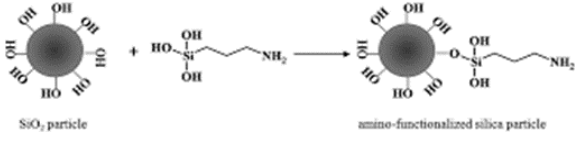
Cancer is one of the leading causes of death every year. Advancement of nanotechnology in the biomedical field could provide a solution by crafting an efficient drug delivery system consisting of organically modified mesoporous silica (ORMOSIL) nanoparticles that offer excellent target specificity, biocompatibility, biodegradability, and reduced side effects on healthy tissues while retaining and delivering the anti-cancer drugs for more extended periods. The outcome of this research could represent a turning point in the biomedical field because making the production of silica nanocarriers a cost-effective and optimal process would allow the silica nanocarriers to be taken to the larger, industrial scale and potentially reduce the number of deaths to cancer. Functionalization of the silica nanoparticles enhances their specificity and their resistance to the body's immune system. Successful attachment of functional groups to the surface of the nanocarrier while maintaining adequate particle size and zeta potential is crucial to optimal drug delivery. The grafting of amino groups is accomplished during the micro-emulsion synthesis process of the particles by adding APTES. Other variables, such as the nature of the surfactant used, the amount of time of dialysis, and the type of microemulsion performed to synthesize the particles are modified to find the optimal conditions and synthesis method that make the process more efficient.



Attachment of ligands, PEGylation and functionalization of the surface of nanocarriers enhance their efficiency



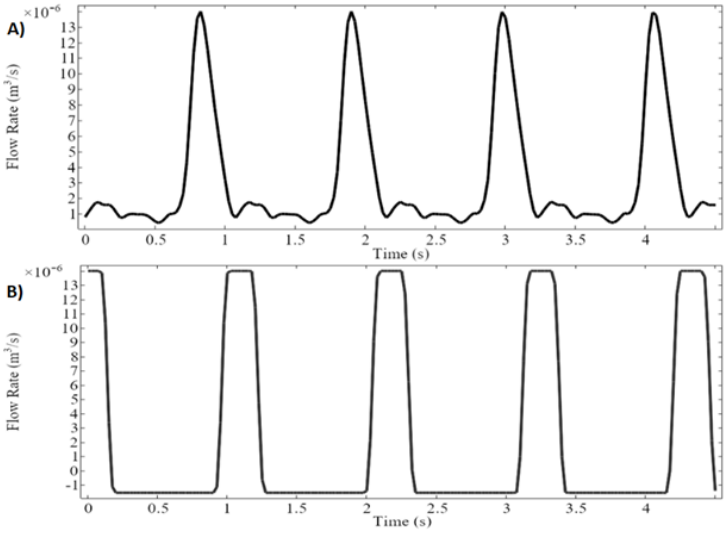
A silica precursor reacts with water and an amino source to yield a functionalized silica particle



Optimal Oscillatory Flow-Induced Waveform for Cell Conditioning via CFD Simulations: COMSOL vs ANSYS

Authors: Sergio Rodriguez, Asad Mirza, Manuel Perez, Brittany Gonzalez, Sharan Ramaswamy
Faculty Advisor: Sharan Ramaswamy, Ph.D.

Cell conditioning is a difficult procedure that involves many variables and factors in order to produce successful results. Cell media, mechanical conditions and other environmental factors control the degree of cell response in terms of its, growth, secretome and phenotype. Fluid-induced oscillations, measured with the oscillatory shear index (OSI), between 0.18 – 0.23, and wall shear stress (WSS) between 3 to 9 dynes/cm2 have been shown to previously be conducive to heart valve cell growth in our laboratory. To achieve these fluid parameters, an optimization study was conducted using the computational fluid dynamic (CFD) package COMSOL Multiphysics 5.4a (COMSOL, Inc, Burlington VT). Specifically, under the laminar flow domain, the inlet flow waveform was iteratively changed from an aortic to a square waveform in order to achieve the aforementioned OSI and WSS values in a pre-designed bioreactor geometry. The final values found were a time-averaged WSS of 3.1 dynes/cm2 and an OSI of 0.20. To better confirm our simulation results we will conduct an additional study whereby the iterative operations done in COMSOL software will be repeated in ANSYS Fluent environment (Ansys Inc, Canonsburg, PA) and their fluid dynamic results (WSS, OSI, Reynolds Number, pressure, velocity, etc.) will be compared.

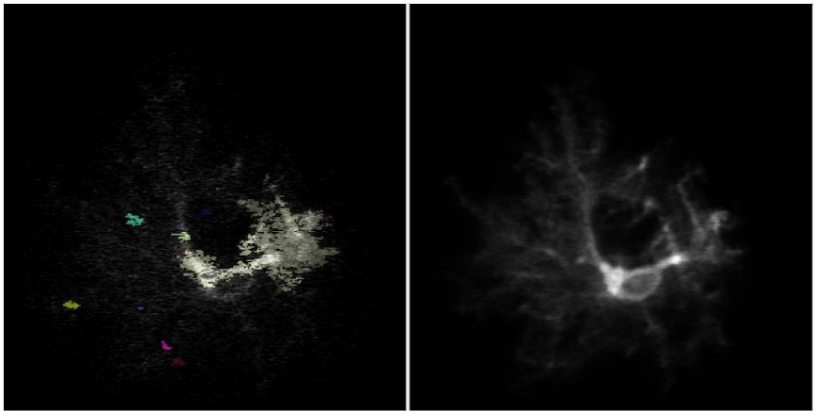


Inlet flow profiles A) Original aortic waveform B) Finalized square waveform with 10% duty cycle

Examine the Role of Astrocytes in Cortical Circuits with Novel Spatio-Temporal Event Detection Package

Authors: Tomas Suarez Omedas, Carlos Otero, Gerson Romero, Vered Kellner, Monica Lopez Hidalgo, James Schummers
Faculty Advisor: James Schummers, Ph.D.

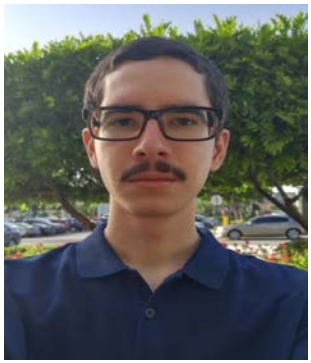
Astrocytes have been taken as only a supportive glial cell in the brain not related to higher brain functions. Recent evidence suggests that astrocytic Calcium activity may have an effect on cognition and visual stimulus processing. Tools for quantitative analysis of astrocyte calcium signaling are lacking. A recently developed algorithm package, AQuA (Astrocyte Quantitative Analysis) is capable of characterizing astrocyte calcium signals in the spatial and temporal plane simultaneously in an event-wise manner, which can help in understanding the physiology of these cells and the calcium signaling events within them. Calcium imaging of astrocytes has shown strong correlation between the astrocyte's activity and specifically designed visual input in ferrets. To assess astrocyte's activity in binocular mammals, we prepare ferrets with AAV virus that produces GCaMP, a substance that will emit fluorescence when Calcium concentration increases within the astrocyte. Two-photon microscopy is used to analyze single or multiple cells (astrocytes and neurons). The current goal of our team is to establish optimal parameters within AQuA that will allow us to process and delineate events within the cell to effectively analyze astrocytes in the visual cortex of ferrets. The future for the research will be to correlate astrocyte activity and the neurons' response to visual stimuli to assess its connection with cognition processes.



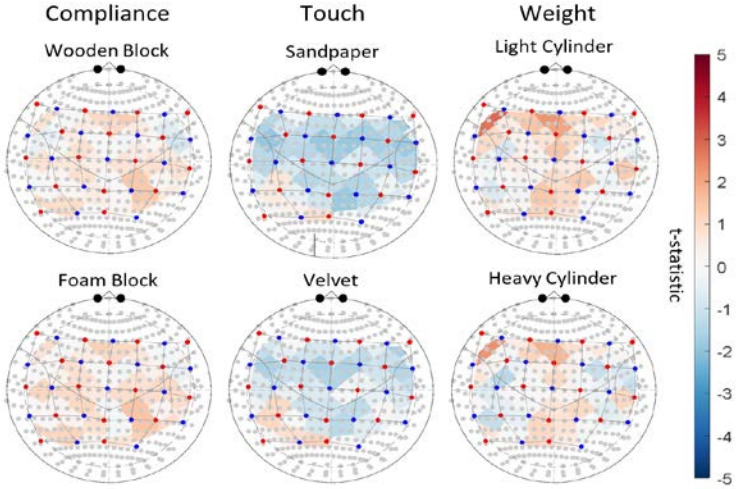
AQuA processed movie and average projection of one astrocyte

Evaluation of Brain Activity in Sensorimotor Regions during Activities of Daily Living Using Functional Near-Infrared Spectroscopy

Authors: Jonathan Cobos-Solis, Gianni Tipan, Miguel Perez, Anil Thota, Ranu Jung
Faculty Advisor: Ranu Jung, Ph.D.



Approximately 2 million people live in the U.S. with some form of limb loss. The loss of a limb, particularly upper limb loss, has a lasting impact on an individual both physically and emotionally because of reduced performance in executing activities of daily living (ADL) tasks such as gripping a cup to lift it due to loss of the sensory information. The sensorimotor brain activation patterns in people with upper limb loss are poorly understood. The knowledge of brain activation patterns is important in evaluating novel technologies that restore lost sensations. The goal of this study is to study brain activity in the sensorimotor regions using functional near-infrared spectroscopy (fNIRS) to understand the role of sensorimotor re-integration. To achieve this, an fNIRS head-cap with 32 optodes was constructed to record the brain activity from Brodmann Areas 3-1-2, 5, 7, and 40 during ADL tasks that simulated the differences in weight, compliance, and touch. In a study successfully conducted on one subject, the results indicate that the oxy-hemoglobin concentration levels are higher for the weight task, lower for the compliance task, and the least for the touch task. However, there are no discernable differences between weights, compliances, or textures.



Brain activity across sensorimotor tasks: The Oxy-hemoglobin (hbO) concentration was different across the different sensorimotor tasks. The t-statistic shows that hbO is highest for the weight task, lower for the compliance task, and the least for the touch task

BME ALUMNI PANELISTS

Michaela Mills (2nd year medical student, Herbert Wertheim College of Medicine, FIU)

Sebastian Marquez (Ph.D. candidate, Electrical Engineering, FIU)

Carolina Moncion (Ph.D. candidate, Biomedical Engineering, FIU)

Anthony Higgins (Senior manufacturing Engineer, Ortho Sensor, Miramar, FL)

Dr. Manuel Salinas, (Ph.D., Assistant Professor, Nova School of Engineering)

ABOUT OUR PROGRAM

The Department of Biomedical Engineering (BME) is part of the College of Engineering and Computing at FIU and is a prime resource for biomedical engineering education, training, research, and technology development. BME is an ever-evolving field that uses and applies engineering principles to the study of biology and medicine in order to improve health care.

Located in Miami, Florida, Florida International University, a Top 100 public university that is designated a Carnegie Highest Research (R1) and Carnegie Community Engaged institution is committed to high-quality teaching, state-of-the-art research and creative activity, and collaborative engagement with the local and global communities.

The Department of Biomedical Engineering is ranked among the Top 50 schools providing the best value to students nationally, #1 for bachelor's degrees awarded to Hispanics, and #3 in bachelor's degrees awarded to African-Americans. We are preparing a diverse community of biomedical engineers and are engaged in translation of research to health care applications through discovery, innovation, entrepreneurship, and community engagement.

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