Online Proceedings

2D

CURRENT TOPICS IN BIOENGINEERING

Session Moderator: Elain Fu, Bioengineering
231 MGH
3:45 PM to 5:15 PM

* Note: Titles in order of presentation.

Quantifying Variations in Prosthetic Sock Thickness with Use
Krittika Joannah (Krittika) D'silva, Sophomore, Bioengineering
Mary Gates Scholar, Undergraduate Research Conference Travel Awardee
Mentor: Joan Sanders, Bioengineering
Mentor: John Cagle, Bioengineering

One of the most universal problems faced by persons with transtibial amputations is volume fluctuation of their residual limb. Since the shape and size of a prosthetic socket stays the same, fluctuations in limb volume affect the fit of a socket. For example, if a prosthesis is too tight; pressure spots, skin irritation, and muscle atrophy can occur. Conversely, a loose prosthesis creates gait instability and compromises the comfort of a patient's prosthetic. Prosthetic socks of different materials and thicknesses are worn to compensate for the changes in volume and manage the discomfort created by daily and monthly volume changes. Properly fitting a residual limb to a socket is further confounded since the industry standard measurement of sock thickness is Ply, a non-linear unit of measurement. Our research examines how absolute thickness and material properties of prosthetic socks change with regular use. We measured the thickness and compression response of new out-of-box socks at three distinct points while in a donned condition. Measurement locations corresponded to area traditionally related to high interface stresses. Thickness and compression response were measured by a custom instrument. Participants walked for two hours while wearing a new sock, after which thickness was measured again in all three locations. Afterwards, volunteers took the socks home, along with a activity monitor, for regular use and returned every two days for one week, and then weekly for a month to re-assess sock thickness and response. The compression response after two hours of walking was used to validate cyclic testing conducting on an Instron material testing machine. Thickness response over long periods of normal use was used to characterize sock fatigue. We hope our study will help practitioners create more accurate volume management recommendations for their patients with a new understanding of the sock stiffness and durability.

The Distribution and Influence on Properties of Small Levels of Organic Materials in Glass Sponges
John Jinwoo (John) Park, Senior, Materials Science & Engineering
Mentor: George Mayer, Materials Science & Engineering

Glass sponge spicules (elements of the skeleton) have been shown to exhibit unique energy dissipating characteristics which may be extendable to applications such as earthquake protection, deep-sea fiber optics, and ceramic implants. Previous studies have revealed that a small volume (less than a few percent) of viscoelastic organic constituent is present throughout the spicule and acts as a key component in controlling the spicule's mechanical behavior. However, the spatial distribution of the organic component within the biomineralized glass material has yet to be identified. This information may be critical to understanding the spicule's energy dispersive behavior and, by extension, influence the design of new glass- or ceramic-based composites. Through the use of high resolution microscopy and other microscopic analysis techniques this study investigates the presence of organic material within the glass phase of these structures as a precursor for developing spicule-inspired synthetic composites.

Nanoengineered Three-Dimensional Skeletal Muscle Patch: Fabrication and Characterization
Nicole E. (Nicole) Trosper, Senior, Bioengineering
Mary Gates Scholar
Mentor: Deok-Ho Kim, Bioengineering
Mentor: Alex Jiao, Bioengineering

The field of tissue engineering is becoming increasingly aware of the role that the extracellular matrix (ECM) plays in driving cellular structure and function, especially in highly

anisotropic skeletal muscle. Skeletal muscle is a cell dense tissue composed of bundles of aligned myotubes responsible for lateral contraction. Replication of this organization is critical for engineering physiologically-relevant tissue constructs. The fibrous nature of the ECM has led us to the use of bio-inspired topographical line patterns on the nanoscale. We employ UV-assisted capillary force lithography to generate polyurethane-based substrates which stimulate cell elongation and alignment. By incorporating glycidyl methacrylate into our substrates, we present a novel method for engrafting a brush polymer coating of the temperature responsive polymer p(N-isopropylacrylamide) (NIPAAm) onto nano-topographically defined substrates. Seeded with C2C12 mouse skeletal myoblasts, these substrates allow for the harvest of intact cell sheets without the use of enzymes. Using a gelatin coated plunger, these cell sheets are stacked to form tri-layer thick tissue constructs. This study explores the effects of a 3D microenvironment on mature myotube formation and the ability of our NIPAAm-based system to control myotube dimension in 3D by altering nanotopography dimension as well as layer number and the timing of differentiation, contributing to the understanding of the 3D microenvironment in regulating the skeletal muscle cell niche. In addition to paving the way for clinically-significant cell-based therapies, this work may prove vital to the development of advanced in vitro drug screening platforms for patients suffering from muscular dystrophy.

A Device to Promote Contractility of Engineered Cardiac Tissue

Khue An (Khue) Dao, Senior, Biochemistry, Bioengineering
Mary Gates Scholar
Mentor: Charles Murry, Pathology
Mentor: Kareen Kreutziger, Pathology

Stem cell based therapeutics is a promising venture to regenerate a damaged heart after a myocardial infarction and to prevent the progression to heart failure. However, we currently do not have a clear understanding of the maturation processes of cardiomyocytes, and this has been one of the main obstacles limiting progress in the field. Here, we develop a device that simulates the mechanical conditions that human cardiomyocytes experience during their growth phase. The aim of the device is to apply a constant mechanical stress on cardiac tissue to test the effects of creep on cardiomyocyte size and alignment. Cardiac tissue used in this study is obtained by mixing a collagen solution with cardiomyocytes derived from the directed differentiation of human embryonic stem cells and pipetted into PDMS molds held in 6-well plates (6wp). Testing of initial designs incorporating a moving magnet below the 6wp coupled with a metallic base within the plate have resulted in too much friction, leading to uneven stretching of the cardiac tissue and the breakage of all constructs tested within 10 days. In response, a revised design is utilized, where a direct screw-driven platform suspended on top of the 6wp controls the mechanical stress applied to the cardiac tissue. This device effectively stretches the constructs to 110% of their initial length over a period of 14 days, without the breakage of any of the four constructs tested. Here we show that mechanical creep over an extended period of time affects cardiac morphology, where increased cardiomyocyte size and a greater degree of cell alignment within the cardiac tissue are observed with stretch versus non-stretched controls. This project provides insight on the mechanical cues involved in the maturation of cardiomyocytes, with the device offering a platform for in vitro modeling of human cardiac tissue.

Biologically Active Polymer-Binding Peptides: A Novel Platform for Biomaterials Interaction

Cameron Lee (Cameron) Nemeth, Senior, Bioen: Nanoscience & Molecular Engr
Mary Gates Scholar
Mentor: Deok-Ho Kim, Bioengineering
Mentor: Candan Tamerler, Materials Science & Engineering

Polymers represent a versatile class of chemical compounds that have a wide range of impact in the field of medicine as implantable devices, tissue engineering scaffolds, and drug delivery vehicles. Synthetic polymers such as polyurethane acrylate (PUA) have been used to provide mechanistic cues in the form of altered nanotopography to help guide migration and differentiation in stem cells. To promote cell-biomaterial interactions to elicit desired cellular responses, these surfaces still must be modified. Chemical crosslinking reagents have been applied to engineer surfaces to enhance biological performance; however, they have limitations due to non-ideal reaction environments as well as their low coupling efficiencies with bioactive molecules and their potential converse effects under physiological conditions. Therefore, controlling the surface properties remains a challenge to induce enhanced interaction at the biomaterial interface. Material binding peptides were shown to possess specificity and high affinity to several inorganic surfaces such as gold or silica while offering easy conjugation with biomolecules. This peptide-based surface functionalization, if applied to polymers, can provide a more efficient and robust method of providing biological cues to synthetic polymers. Herein, we demonstrate a simple single-step incubation process that promotes non-covalent binding of bifunctional peptides on polymer surfaces. One end of the peptide possesses high binding affinity for the polymer substrate while the other end contains a bio-functional motif such as the RGD domain, which allows integrin-mediated cell adhesion. When combined with the topographical cues of an anisotropically nanopatterned polymer substrate, a flexible platform can be established to pursue many different research thrusts, such as enhanced stem cell differentiation. Specifically, we plan to use the established platform to uncover the underlying mechanisms of adhesion,

morphology, and differentiation in C2C12 mouse myoblasts.

A Novel Paper-Based Diagnostic Test with Improved Sensitivity and Usability for Low-Resource Settings

Tinny Liang, Senior, Bioen: Nanoscience & Molecular Engr
Levinson Emerging Scholar, Mary Gates Scholar
Mentor: Elain Fu, Bioengineering

Millions of people in developing countries die from infectious diseases(e.g. malaria and tuberculosis), yet many of these deaths could be prevented if tools for accurate diagnosis were available. The current method for diagnosis of infectious diseases in low-resource settings is the lateral flow test (LFT), which has the appropriate usability (i.e. equipment-free, rapid, and easy to use), but lacks the required sensitivity to have clinical utility for some disease targets. Thus there is a need for diagnostic tools with improved clinical sensitivity and with the appropriate characteristics for use in low-resource settings. I have designed a novel two-dimensional paper network (2DPN), which enables more sophisticated chemical processes for improved sensitivity and usability in low-resource settings. The novel device utilizes commercial enhancement solutions for signal amplification via a metal catalytic reaction to increase sensitivity. The set of reagents and reagent volumes have been optimized for sensitivity and incorporated into a 2DPN assay device, where the programmed delivery of reagents is achieved through the design of the paper geometry and a fluidic on-switch.

Fluorescent Detection and Image Guided Photodynamic Therapy of Cancer Using 5-Aminolevulinic Acid Induced Protoporphyrin IX and a Scanning Fiber Endoscope

Mikias Habteab (Mikias) Woldetensae, Sophomore,
Pre-Major (Arts & Sciences)
Mentor: Eric Seibel, Mechanical Engineering

The National Cancer Institute estimated that there will be approximately 72,570 new cases of bladder cancer in the United States during the year 2013, and 15,210 deaths due to the disease. The high recurrence rate of 50-70% of treated bladder cancer creates a necessity for life long surveillance, which in turn makes bladder cancer the most expensive cancer for a per-patient cost—89,000 to 202,000 USD per patient—from diagnosis to death. This research aims to combine the cancer specific biomarker 5-Aminolevulinic acid (5-ALA) and the Scanning Fiber Endoscope (SFE) to fluorescently detect and treat cancerous legions in a controlled setting within the bladder, and to find any correlations that might exist between our dependent and independent variables, allowing us to optimize cell death. The Scanning Fiber Endoscope (SFE) created in the Human Photonics Lab (HPL) at the University of Washington was used to apply therapy at 405 nm to A549 cancerous cells previously administered with 5-ALA. Cells were stained with LIVE/DEAD®stain and analyzed under a confocal microscope. The results show that PDT of A549 cancer cells with 405nm light and 5-ALA induces Protoporphyrin IX (PpIX) was successful. Varying sizes in cell death were produced when varying combinations of duration of therapy and light intensity were applied. A correlation between light intensity and duration of therapy was found. An increased time of exposure and a decreased light intensity yields a larger area of cell death than a decreased time of exposure and an increased light intensity. Recurrence of cancers is mediated by cancerous cells that are overlooked in the treatment process, therefor optimizing cell death will allow for a decrease in costs associated with bladder cancer due to a decrease in recurrence rate.

The Smart Shunt: A Smarter Way to Drain Excess "Water in the Brain"

Pranav Venkataraman, Senior, Bioengineering
Howard Hughes Scholar, Mary Gates Scholar
Mentor: Barry Lutz, Bioengineering

Hydrocephalus is a pathology characterized by the accumulation of excess cerebrospinal fluid (CSF) within the brain, which can lead to dangerously high intracranial pressure (ICP) and brain tissue damage. Surgically implanting a cerebral shunt, which keeps ICP under control by mechanically draining the excess CSF, is the most common method of treating hydrocephalus, but these shunts are plagued with problems. Roughly half of all shunts fail within the first two years of implantation, with 98% failing within ten years. Through a collaboration with pediatric neurosurgeon Dr. Sam Browd of Seattle Children's Hospital, Dr. Barry Lutz's laboratory is developing the "smart shunt" – an electromechanical shunt which uses electronic feedback control of ICP and a simpler valve design to regulate CSF drainage. The goal of my research is to design a testing platform for the smart shunt, which will be used to simulate CSF and ICP dynamics caused by the respiratory and cardiac cycles, changes in patient posture, and other physiological phenomena that are typical of the daily lives of patients. Since the smart shunt must function on battery power for several years, it needs to be tested with a physiologically accurate simulation system in order to produce an optimal balance between ICP control and energy efficiency. To maximize simplicity and flexibility, the system will be computer controlled and operated through virtual representations of ICP and brain compliance modeled from patient data. The physical portion of the simulation system consists of regulators which stabilize pressure within fluidic reservoirs representing the brain and abdomen, speakers which produce physiological pressure oscillations within these reservoirs, and a pump which circulates mock CSF through the system. Apart from testing shunt performance, the ultimate objective of the testing system is enabling physicians to optimize the smart shunt to suit the unique brain physiology of each patient.