Poly(ethylene glycol)-block-poly(L-lactide) (PEG/PLA) Encapsulation of Oral Antibiotics for Drug Delivery into Dentin Tubules

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Aim: To encapsulate an effective drug in oral applications with PEG/PLA diblock copolymer into microparticles for infected root canals and dentinal tubules. To maintain drug release for extended periods to prevent bacterial regrowth after root canal treatment.

Methodology: Drug encapsulation was carried out through an oil-water emulsion-solvent evaporation method. In summary, the PEG/PLA copolymer and the oral drug were dissolved in an oil phase (dichloromethane), which was combined and emulsified with a water phase (polyvinyl alcohol and de-ionized water). The resultant solution was stirred, centrifuged, washed, and lyophilized. Particle size was determined using digital microscopy. Antimicrobial effectiveness was assessed *in vitro* by placing small amounts of encapsulated particles on bacterial (*Enterococcus faecalis* OG1RF) agar plate cultures and monitoring growth inhibition.

Results: Encapsulated particles ranged in size from 2.0 μm to 6.5 μm, which depended on the homogenization speed employed. Only particles with diameter ≤2.0 μm were used for further testing. A preliminary 24-hour bacterial inhibition test showed that the particles exhibited zones of inhibition between 3 mm and 5 mm.

Conclusion: The proposed method with the PEG/PLA copolymer effectively encapsulates the oral antibiotic producing particles with size distribution that may penetrate the dentin tubules (2.5 μm in diameter). Bacterial inhibition tests showed that the particles inhibited bacterial growth after 24 hours. Ongoing bacterial inhibition tests will determine the extended release profile of the microparticles.

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John Corbett

IEEE Medical Device Symposium 2013 Abstract

Lipocalin-type prostaglandin D synthase (L-PGDS) in cerebrospinal fluid (CSF) contributes to the maturation and maintenance of CNS. L-PGDS post-translational dysregulation may contribute to pathobiology of different CNS diseases, but methods to monitor its proteoforms are limited. In this report we combined in-solution isoelectric focusing (IEF) and superficially porous liquid chromatography (SPLC) with Fourier transform mass spectrometry (FTMS) to characterize common CSF L-PGDS proteoforms. Across 3D physiochemical space (*pI*, hydrophobicity, and mass) 217 putative proteoforms were observed from 21-24 kDa and *pI* 5-10. Glycoprotein accurate mass information, combined with tandem MS analysis of peptides generated from 2D fractionated proteoforms, enabled the putative assignment of 208 proteoforms with varied PTM positional occupants. 15 structurally-related N-glycans at N29 and N56 were observed, with results that suggest distinct N-glycan compositional variants are preferred on each amino acid, and that sialic acid content was a determinant of proteoform *pI*. Other PTMs characterized include a core-1 HexHexNAc-O-glycan at S7, acetylation at K16 and K138, sulfonation at S41 and T142, and dioxidation at C43 and C145. The IEF-SPLC-MS platform presented provides 30-40× improved peak capacity versus conventional 2D gel electrophoresis and shows potential for repeatable proteoform analysis of surrogate PTM-based biomarkers from biofluids.

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Development of methodologies to evaluate the effect of bacterial biofilm and micromotion on corrosion of dental implants

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Introduction: Bacterial biofilms on the surface of dental implants can create byproducts that are acidic in nature. This along with micromotion from occlusal loading, can cause the dissolution of titanium, which is a primary factor of peri-implantitis (PI).

Aims & Methods: This study will discuss a novel testing method that will enable the accruement of knowledge on the effect of bacterial biofilm and occlusal forces in the failure of dental implants. Different bacterial strains pertaining to PI, such as *E. faecalis, S. sanguinis, S. gordonii,* etc., were tested for their growth and pH. The strain capable of providing a good growth rate and an acidic pH, was used for the immersion tests and mechanical testing. In the immersion tests, dental implants were immersed in broth containing the bacterial strain. For mechanical testing the dental implants were placed under fatigue cycles in the presence of bacterial biofilm in a chamber with ample flow of broth and bacteria. The testing conditions were guided by ISO standards which required an inclination of the implant setup at a 30_0 angle and representation of 3mm bone loss. During immersion and mechanical testing, aliquots from fixed intervals were extracted to quantify the dissolution of titanium ions using Electrical Impedance Spectroscopy and Voltammetry. Surfaces of implants were imaged using a Keyence microscope, and analyzed by Scanning Electron Microscopy equipped with Energy Dispersive X-ray Spectroscopy detector, before and after testing.

Results & Conclusion: This experimental setup enacts relevant physiological conditions and forces met in the oral cavity by the implants. Analysis of results show the corrosive nature and forces implants have to endure. The results concluded provides more insight on the contribution of bacterial biofilms and occlusal forces on the integrity of dental implants. Furthermore, targeted measures on how to prevent such factors can also be inferred.

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Nanomics: Proteomic platform based solution for point of care quantification of cancer stem cell activity

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The goal of the project is the demonstration of a bio-electrochemical solution for quantification of protein biomarker activity from cancer stem cell lysates. This quantification is essential for cancer risk assessment, prognosis study, early diagnosis and phenotype classification.

Introduction: Cancer stem cells have been identified as critical cues for detection and analysis of primary cancer metastasis and distant metastasis. It was recently demonstrated that cancer stem cells are rich in aldehyde dehydrogenase isozymes. Current detection/quantification techniques such as western blotting and flow cytometry are not geared for this task due to (1) low concentration of activity markers corresponding to cancer stem cells in a tumor mass (2) lack of robust surface markers.

Aims and Methods: This project innovatively combines a nano-porous sieve and micro-metal electrodes for protein biomarker quantification from cancer stem cell lysates. An affinity immunoassay is used to capture specific protein biomarkers and electrochemical impedance spectroscopy is used to quantify these protein-binding events. The nano-porous sieve is overlaid on the electrodes and the resulting innovation (1) achieves improved macromolecular crowding to enhance protein-protein interaction (2) functions as a molecular sieve to filter cell debris, thus reducing non-specific binding/signal (3) achieves an amplified signal response enabling low detection limits. By tuning the frequency of applied voltage, we selectively study the nano-confined spaces where protein binding happens and this additionally helps to achieve low limits of detection.

Results: We present our work for quantification of two isozymes of aldehyde dehydrogenase: ALDH1A1 and ALDH1A3 from lung cancer stem cell lysates. The sensor has demonstrated low detection limits of 10 pg/mL for both the protein biomarkers ALDH1A1 and ALDH1A3. This high sensitivity and robust operation showcase the ability of the technology to be used as a point-of-care solution for quantification of cancer stem cell activity

Preventing Operating Room Fires: Development of an Operating Room Fire Prevention Device

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Introduction

Operating room (OR) fires present a real danger to surgical patients and is estimated to occur over 600 times annually. For fire to occur, the three points of the fire triad must be present: an oxygen source, ignition source, and fuel source. The electrosurgical unit (ESU) pencil triggers the vast majority of OR fires. Carbon dioxide (CO_2) is a gas proven to prevent ignition and suppress fire by displacing oxygen.

Aims and Methods

We hypothesize that a device can be created to produce a cone of CO_2 around an ESU pencil tip, thus reducing OR fire risk. A divergent nozzle was connected to a CO_2 source via silicon tubing, which was then secured to an ESU pencil (Figure 1). This device was tested in a flammability testing chamber in which the ESU pencil was activated for sustained current delivery to an aluminum plate holding a laparotomy sponge. Each test was performed in various oxygen environments with the device turned on (CO_2 flow) and with the device turned off. Additionally, 4D contour mapping of CO_2 concentrations was performed with a micro-CO_2 sampling device using a 6x3x3cm matrix to depict CO_2 concentrations in 3D space.

Figure 1

Results and Conclusions

The median ±SD [range] ignition time of the control group in 21% oxygen was 2.9s±0.44 [2.3 – 3.0], in 50% oxygen 0.58s±0.12 [0.47 – 0.73], and in 100% oxygen 0.48s±0.50 [0.03 – 1.27]. No fire was observed when CO_2 was applied through the device in all oxygen concentrations (Figure 2). The CO_2 concentration at the end of the ESU tip was 95% while the average CO_2 concentration one centimeter away was 64% (Figure 3). Therefore, pumping CO_2 through the device effectively displaced enough oxygen around the ESU tip to prevent ignition.

Gecko Hands: Novel cardiothoracic forceps for prevention of mechanical damage during CABG surgery

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Introduction:
Coronary heart disease (CHD) is a chronic disease affecting millions of Americans. For individuals with severe CHD, coronary artery bypass graft (CABG) surgery is often the only effective intervention. During a CABG procedure, cardiothoracic surgeons use forceps with broad blades mainly used for tissue manipulation via a compressive force. When manipulating fragile tissues encountered in CABG surgery, forceps can cause unintended damage to the tissue. In this study, novel cardiothoracic forceps which circumvent the application of compressive force to cardiac tissue were explored and prototyped.

Aims and Methods:
The functional redesign of the cardiothoracic forceps calls for a device with similar design parameters. Novel improvements should ensure the release of tissue in the event of a major displacement (aberrant beat, etc.) to avoid forces above the burst limit of the vessel. Surgeons at Emory University Hospital at Midtown were contacted for input on design parameters and functionality. Calculations on blood vessel rupture force were derived from literature and a handicap factor (E' = E*0.5) for the stiffness of the compromised vessels was used as a threshold for the maximal output force. Finally, finite element analysis (FEA) was conducted to study the stress distribution in the first design. A sample prototype was then printed and assembled for initial testing.

Results:
The Gecko Hands design was chosen for its minimization of compressive force, as well as its integration of aspiration. The proposed design meets the selection criteria of current forceps (21.6cm, 24g, < 10N applied force) and also employs the use of suction to remove excess fluid in the surgical space. In doing so, the Gecko Hands vacuum forceps also replaces the surgical aspirator, another commonly used surgical device. The use of this multi-tool in CABG surgery could eliminate surgical clutter during openheart procedures while also reducing the duration of surgery

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Metal-on-Metal Total Hip Implants: A Study Their Failure Modes in Relation to Adverse Local Tissue Reaction

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Introduction: The use of metal-on-metal (MoM) total hip arthroplasty (THA) has decreased recently due to concerns of high failure rates. MoM hip implant designs have shown to generate metal debris particles that are released into the surrounding soft tissues. These released contaminants have caused inflammatory reactions in the patients know as adverse local tissue reactions (ALTR).

Aims and Methods: The purpose of this study was to characterize failure patterns in retrieved MoM THA components revised for ALTR. Four retrieved MoM THA components were selected for analysis from an ongoing retrieval study due to the presence of ALTR. All specimens were analyzed using digital microscopy. Particularly corroded and scratched areas were further analyzed under Scanning Electron Microscopy (SEM), and Energy Dispersive X-ray Spectrometer (EDS).

Results and Conclusions: All patients were revised for pain and presence of ALTR (range 23-134 months *in vivo*). Surface analysis revealed three distinct failure mechanisms: 1) corrosion at the head-neck junction, 2) mechanical wear at the head-cup bearing surface with severe scratching, and 3) pitting attack, induced by reduction in surface potential due to scratching. The implant with the most severe wear had a cup abduction angle of 57 degrees. The implant with the most significant corrosion at the head-neck junction was a 32-mm CoCr head on a titanium alloy stem.

Multiple failure mechanisms of MoM THA implants exist, including corrosion, mechanical wear, and pitting. Increased metal ion levels and ALTR were present in patients with these failure mechanisms. In response to clinical observations of implant performance, a novel surface treatment technology to improve lubrication and corrosion properties of these MoM implants is under investigation.

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A Software for Analyzing Brain's Dynamic Functional Connectivity from Functional Magnetic Resonance Images

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I. Introduction

Functional magnetic resonance imaging (fMRI) is a medical imaging method which measures brain activity by detecting changes in blood-oxygenation levels. Functional connectivity analyses investigate interactions among different brain regions using fMRI data. These interactions are very dynamic; this necessitates the use and implementation of dynamic functional connectivity (DFC) methods. There is need for user-friendly software which implements these methods.

II. Aims And Methods

The software is implemented as a graphical user interface (GUI) written in MATLAB. It can read 4D-Nifti fMRI data, different brain maps and atlas files which labels different anatomical regions and it can do co-registration between atlas and data. Functional connectivity among different networks or regions from the data are calculated dynamically by calculating the correlation among time-courses using a sliding time-window. The window step size and width are adjustable through the GUI. The dynamics of the connectivity can be plotted, along with any experimental tasks/stimuli. This allows quantification of how connectivity is modulated by task/stimuli, if any.

The GUI allows the user to identify functionally connected brain networks or regions both visually and numerically. Numerically, it can list highest correlated brain network/region combinations. Visually, it can show the brain images with the highlighted networks/regions.

DFC analysis can be applied to any fMRI data directly; however, it can also be applied to networks found by independent component analysis (ICA). ICA is a blind source-separation technique used for separating independent brain networks. ICA results can be also be loaded and analyzed with our software which can identify the most significant connections among brain networks.

III. Results And Conclusions

The user-friendly DFC GUI implements analysis methods for quantifying the dynamics of the brain's functionally connected regions or networks from fMRI data. It also features tools for visualizing functionally-connected networks, functional connectivity dynamics and task-modulation.

A Software for Multivoxel Pattern Analysis of Functional Magnetic Resonance Imaging Data

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I. INTRODUCTION

Functional magnetic resonance imaging (fMRI) is a medical imaging method which indirectly measures brain activity by measuring changes in blood-oxygenation levels from 3D snapshots of the brain every few seconds. Exposing a subject to different kind of stimuli or tasks systematically during the fMRI scan causes different parts of the brain to activate. FMRI signal can be analyzed to find out the characteristics of these activations and any systematic activation differences under different stimuli/tasks. Multivariate pattern recognition and classification algorithms, as known as multivoxel pattern analyses (MVPA) methods in the neuroimaging community, have been recently applied to fMRI data to classify between different brain "states" or "conditions" resulting from different stimuli/tasks. MVPA methods have been gaining popularity in neuroimaging and there is need for user-friendly graphical user interface (GUI) software which implements these methods.

II. AIMS AND METHODS

In this project, we implemented in MATLAB a GUI tool which can read 4D-Nifti fMRI data from the brain, and does classification of different brain "states" or "conditions" using various supervised machine learning algorithms. The algorithms which are implemented in the toolbox include linear discriminant analysis, neural networks, logistic regression, sparse multinomial logistic regression, ridge regression, and support vector machines. The toolbox allows the user to mask the brain and focus on only the anatomical parts she/he is interested in. The tool accommodates choosing between various types of inputs which describe the fMRI experiment stimuli/tasks and it provides a detailed visualization of results.

III. RESULTS AND CONCLUSIONS

A user-friendly GUI software which implements multivoxel pattern analysis or machine learning methods for classifying different brain states or conditions from the fMRI data is developed. It enables fast and efficient classification analysis of large-scale fMRI data from multiple subjects and it provides effective visualization of these classification results for better interpretation.

Title: Stimuli-Responsive Polymer Substrates for Improved Neural Interfaces

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Introduction: Implantable microelectrode arrays (MEAs) enable neuroscientists to record single unit action potentials to gain a better understanding of neurological processes and develop therapies to treat those suffering from neurological diseases such as Parkinson's disease, Alzheimer's disease and stroke. However, microwire and planar silicon MEAs are limited to acute implantation because devices either evoke a chronic immune response that electrically isolates the device or the electrode passivation materials degrade in physiological conditions. Both of these failure mechanisms prevent MEAs from providing long-term recording of neural activity.

Aims and Methods: This work aims to engineer high density penetrating microelectrodes with materials that evoke an appropriate response from the local neuronal population and withstand the dynamic physiological environment in both the central and peripheral nervous system. A thiol-ene/acrylate polymer is developed as a novel substrate material that is compatible with photolithography processing, has the requisite stiffness to penetrate soft neural tissue and softens in response to physiological conditions. The polymer substrate provides a platform for fabricating novel neural interfaces that can be laser-micromachined to incorporate sub-cellular features and offer improved encapsulation with amorphous silicon carbide thin-films. Softening thiol-ene/acrylate MEAs are compared in vivo to stiff Parylene-C MEAs with the same geometry to understand the relationship between device stiffness and recording longevity and quality.

Results and Conclusions: After 4 weeks of implantation, the thiol-ene/acrylate MEA enabled a decrease in reactive astrocytes surrounding the implant compared to Parylene-C implants. Thiol-ene/acrylate MEAs with 20 μm laser-micromachined pores displayed an increased in neuronal density surrounding the implant compared to non-porous implants. Recording of driven multi-unit neural activity has been demonstrated for up to eight weeks. Future work consists of establishing the chronic immune response to stimuli-responsive neural interfaces as a function of device stiffness as well as developing a fullyimplantable wireless recording system.

Mechanically Adaptive Organic Transistors Enabled by Physiologically Responsive Shape Memory Polymer Substrates

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Future biomedical devices may enable chronic sensing or stimulation of body tissue through stable interfaces between soft tissue and high-performance electronics. We demonstrate flexible organic thin-film transistors (OTFTs) on physiologically-responsive smart polymer substrates with shape-changing and softening properties that can mechanically-adapt after implantation for creating soft bioelectronic interfaces.

Shape memory polymers (SMPs) are smart polymers which respond to stimuli, such as a temperature change, to soften and change shape. Here, we synthesize SMP substrates which can adapt *in vivo* to autonomously form secure interfaces with target tissue. The thiolene-acrylate shape memory polymer (SMP) substrate exhibits a drop in modulus of over two orders of magnitude when exposed to physiological conditions, reducing the modulus mismatch with soft tissue. Reduction in the mechanical mismatch between biomedical implants and soft tissue through soft materials has been shown to extend the long-term viability of biotic/abiotic interfaces. Additionally, large 3D shape changes are enabled based on the release of stored applied stresses for creating deployable structures, or the conforming of films to 3D geometries.

OTFTs fabricated on SMP substrates are demonstrated which can autonomously deploy to programmed 3D shapes 15× larger than the insertion footprint of the device, as well as conform to 3D surfaces with radii as small as 500 µm. Acute *in vivo* stability of a conformable OTFT is shown with only small changes in device performance after implantation for 24 hours. Flexural stability of the OTFTs is demonstrated down to 1 mm radius for four bending configurations; with some devices remaining operational at radii as small as 100 µm. The flexible low-voltage transistors (3 V) based on the air-stable organic semiconductor, dinaphtho[2,3-b:2’,3’-f]thieno[3,2-b]thiophene (DNTT), are demonstrated with a measured average mobility of 1.5 $cm^2V^{-1}S^{-1}$ and an on/off current ratio of 10^4, which is suitable for sensing small biosignals at low operating voltages.

Abstract:
Traumatic Brain Injury (TBI) is one of the largest health problems in the United States, and affects almost two million people every year. The effects of TBI include weakness and loss of coordination, and these effects can be observed even years after the initial injury. We have developed a method by which we drive cortical plasticity through stimulation of the vagus nerve during rehabilitative therapy to assist recovery from TBI. We trained rats to perform the isometric pull task – a skilled reaching and strength task. After training, all animals received a controlled cortical impact in the forelimb area of left motor cortex. After injury, one group of animals received vagus nerve stimulation (VNS) paired with rehabilitative therapy, while another group received rehabilitative therapy alone. We found that animals that received VNS paired with therapy achieved a full recovery of their forelimb strength, while animals that received only rehabilitative training did not significantly recover forelimb strength.

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Vagus nerve stimulation paired with rehabilitative training improves recovery of forelimb function in two clinically relevant models of stroke.

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Introduction:

Stroke is a debilitating neurological disease that affects 800,000 individuals in the United States each year, with many of these patients suffering chronic motor impairments. The development of treatment strategies to restore motor function after stroke represents a significant unmet clinical need. We have recently developed a technique to improve motor function after stroke based on stimulation of the vagus nerve paired with rehabilitative training. Our previous studies have demonstrated that vagus nerve stimulation (VNS) paired with rehabilitative training improves recovery of multiple parameters of forelimb function in a model of ischemic stroke in young rats.

Aims and Methods:

We sought to evaluate if VNS paired with rehabilitative training would improve recovery of forelimb function in two models of stroke that share more characteristics with the clinical population of stroke patients, including subcortical brain damage and in the context of advanced age. In the first experiment, a cohort of rats was trained to proficiency on the bradykinesia assessment task, a novel behavioral task that measures multiple parameters of forelimb function, and then underwent a unilateral hemorrhagic stroke to severely impair function of the trained limb. Subjects subsequently received rehabilitative training with or without VNS and recovery of skilled forelimb function was measured. In the second experiment, a cohort of aged rats (18 months old) were trained to proficiency on the isometric force task and then underwent a unilateral ischemic stroke to impair the trained forelimb. Subjects subsequently received rehabilitative training with or without VNS and recovery of forelimb strength was measured.

Results and Conclusions:

Here we show that VNS paired with rehabilitative training improves recovery of forelimb function in a model of severe hemorrhagic stroke. Additionally, preliminary findings suggest that VNS paired with rehabilitative training improves recovery of forelimb strength in aged rats. Our results indicate that VNS enhances recovery after stroke in two models that bear similarity to the clinical population of stroke patients; therefore, VNS represents a potential therapy to increase motor recovery in stroke patients.

Zinc Oxide-based Nanosensor for the Ultra-sensitive Detection of Troponin-T

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Introduction

This project demonstrates the development of a zinc oxide based microelectrode sensor for the ultra-sensitive detection of protein biomarkers. Biomarkers are unique biological macromolecules that may indicate the presence or risk of certain developing ailments. Point-of-care, rapid quantification of these molecules is essential to disease identification, monitoring, and analysis. Currently employed technologies for quantitative detection of protein biomarkers suffer from problems such as a lack of sensitivity/selectivity, dominance of signal noise, adaptability of detection to a wide range of biomolecules, and are not geared for rapid detection. Our research focuses on utilizing a materials-based approach to overcome these problems often associated with the detection of biomarkers by utilizing zinc oxide as part of our biosensor for (1) improved binding surface area for enhancing sensitivity and (2) creating nano-structures for biomolecule confinement that can enhance output signal response.

Aims and Methods

This study integrated nanotextured zinc oxide thin films onto printed circuit boards using RF magnetron sputter deposition at room temperature. By manipulating zinc oxide deposition conditions, certain properties of the material can be tuned to increase the efficacy of signal transduction. These fabrication conditions not only dictate the number of oxygen vacancies within the film but also regulate the amount of zinc and oxygen terminated ends occurring on the material surface. Zinc oxide films sputtered with and without the presence of oxygen were examined for possible differences in biosensor efficacy. Evaluation of the cross-linkers dithiobis succinimidyl propionate and (3-aminopropyl)triethoxysilane for binding to these two different surfaces was achieved through fluorescent studies. Qualitative and quantitative assessment of cross-linker binding was accomplished using microscopy and fluorescent intensity measurements. Impedance spectroscopy was used as the electrical transduction mechanism for detection of the well-established cardiac biomarker, troponin-T, whose presence in trace quantities is indicative of multiple cardiovascular ailments.

Results and Conclusion

This study focuses on the correlation between the effect of physical confinement and surface termination of nanotextured zinc oxide to its performance as a biosensor. Troponin-T was detected as low as 10 fg/mL in purified buffer media and 100 fg/mL in human serum. The zinc oxide films sputtered without the presence of oxygen showed enhanced detection due to oxygen vacancies within the film and a greater amount of cross-linker binding to the surface of the sensing site. This platform demonstrates applicability as a sensitive, low-cost, rapid and easy to use tool that can be integrated as a point-of-care diagnostic device.

Movement-paired vagus nerve stimulation improves motor recovery following ischemic brain damage

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Abstract

Stroke is the second most common cause of disability and death worldwide (Leary 2003). A variety of physical rehab methods have been developed to improve recovery of motor function following stroke. These methods usually do not generate sufficient neural plasticity to provide a complete recovery. New approaches are being developed to enhance physical rehab by activating brain mechanisms to direct more effective neural plasticity. Stimulation of the left vagus nerve triggers a precisely timed burst of neuromodulators and enhances neural plasticity. Repeatedly pairing vagus nerve stimulation (VNS) with two distinct forelimb movements resulted in movement-specific map plasticity within primary motor cortex (Porter et. al.). VNS is well-tolerated in patients with a variety of neurological diseases and could be added to physical rehab to improve recovery. In this study, we evaluated whether the addition of VNS to motor rehab can enhance recovery from cortical ischemia. In the current study, VNS repeatedly paired with successful forelimb movements can improve recovery after motor cortex ischemia and may be a viable option for stroke rehabilitation.

SWITCHING BASED HYBRID DEVICES FOR CLINICAL DIAGNOSTICS

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Recent advances in semiconductor nanotechnology have resulted in the development of bottom-up manufacturing of hybrid devices. These devices incorporate organic as well as inorganic components. These devices are engineered to function as silicon based two terminal and three terminal structures but with enhanced functionality. In our work, the device has been fabricated using polymer/metal hybrids due to their mechanical flexibility, scalability, cost effectiveness and suitability to form thin films.

The crossbar array configuration has been adopted in the design of these diode (2 terminal) /field effect transistor (3 terminals) devices. In these devices, the biomolecules with surface charge have been selected to interface with the polymer/metal nanocomposites in isotonic buffers. The change in electrical properties due to modulation in charge transport at the crossbar junction is used to obtain switching behavior that can be leveraged as an electrical signal for designing sensors.

The device designed in this research comprises of a glass substrate with a metal microelectrode array used for electrical characterization of polymer cross bar junction. The active sensing area comprises of gold nanoparticle embedded in polypyrrole (PPy) matrix. The target molecule on attaching on to the crossbar junction potentially modulates the charge transfer kinetics and modifies junction characteristics due to the surface charge associated with these charged molecules. The net change in the surface charge is investigated by using square wave voltammetry technique. The device performance is demonstrated for detection of the cardiac biomarker troponin-T. The voltammetric current response (in microamperes) was measured between -3V and 3V with protein concentration in the range of 1fg/mL to 100ng/mL. The switching behavior is observed when the change in the measured current is higher than three orders of magnitude.

Electrokinetically assisted drug targeting using lab on a chip technology

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As a prerequisite for efficient drug targeting systems, techniques are required for rapid entrapment of desired drug and its delivery with minimal adverse effects to both the drug and the target. However, complex nature of dynamic diseases such as cancer demands extensive drug delivery with high throughput and precision. Motivation behind advanced drug targeting systems is the increasing necessity for targeting specific areas with controlled drug delivery. This can be achieved by using external cues such as alternating current electric fields to encapsulate, characterize and administer drugs to targeted locations. Current research focuses on non-electrokinetic methods such as chemical modification and invitro approaches to deliver drugs. The major limitation of such systems is its inability to protect the drug from degradation and mismanagement of medication leading to drug distribution throughout the area.

AC electrokinetic techniques offer contactless method of manipulating biological particles through electric fields. In this work, liposomes response to applied electric field and their application in drug targeting solutions are emphasized. Inherent dielectric properties of biological molecules and their response to applied field were extensively studied. The electrical properties such as permittivity and conductivity of liposomes vary with respect to the drug content present within the vesicle. We have developed a prototype lab on a chip device capable of transporting and manipulating encapsulated drug using non-invasive application of AC electric fields such as dielectrophoresis and electrorotation to sort and separate the mixture of loaded and unloaded drug encapsulated vesicles.

The project demonstrates greater resolution with non-uniform electric fields to sort, manipulate and transport vesicles by using a combination of translational and rotational motion. This platform involves micro-fabrication semiconductor techniques to pattern microelectrodes that are capable of implementing the desired workflow. Incorporation of microfluidics provides the critical interface between fluid transport and real time delivery process and can be made flexible to satisfy the needs in both diagnostics as well as in therapeutics.

In-situ Observation of Deformation Behavior of NiTiCu Foams for Implant Applications

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Introduction

NiTi-based shape memory alloys (SMAs) have been successfully used in the biomedical field due their good biocompatibility, high corrosion resistance and superelasticity. The addition of Cu to NiTi is known to narrow the thermal hysteresis and improve fatigue behavior. The addition of porosity to SMAs decreases the stiffness, increases the damping capacity, and allows for bone tissue ingrowth, leading better stability and compatibility with the body, and thus making it ideal for biomedical applications.

Aims and Methods

Our research is focused on the cyclical loading/unloading compressive behaviors of porous SMA foams during *in situ* X-ray tomography. A superelastic $Ni_{40}Ti_{50}Cu_{10}$ SMA with ~60 % porosity was prepared for cyclical loading/unloading compression testing. Samples were prepared by pressure infiltration melting of the alloy into a porous salt preform (i.e. a space-holder consisting of SrF_2). The salt was subsequently dissolved in nitric acid. The resulting porous NiTiCu foams were wrapped in Ti foil and homogenized. The $2 \times 2 \times 4$ mm^3 compression samples were then heat treated. Differential scanning calorimetry (DSC) was used to characterize the phase transformation temperatures. Optical microscopy and scanning electron microscopy (SEM) were used to characterize the microstructure. Micro-Computed tomography (μCT) scanning was performed using a Skyscan 1172 during *in situ* cyclical loading/unloading for 10 cycles each up to 2.5%, 3.5%, 4.5%, and to failure.

Results and Conclusions

DSC results show the austenitic transformation starts at 2.5 ºC and finish at 26.4 ºC, and the martensitic transformation starts at 9.4 ºC and finishes at -18.9 ºC. Thus, at just above room temperature, the NiTiCu foam is fully austenitic (i.e. superelastic). μCT results confirm that the salt is removed completely. The fatigue behavior and superelastic effect were observed during compression testing with *in situ* X-ray tomography and exhibited lower stiffness than bulk material as expected.

Keywords: Nitinol, shape-memory alloys, metallic foams, processing, compression testing, X-ray tomography

Local Brain Sonication Simulation with Gel Phantom by Stereotaxic Apparatus Guided HIFU

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Introduction:

High-Intensity Focused Ultrasound (HIFU) can deliver energy noninvasively to focal regions within tissues to generate lesion or ablation. To acquire an accurate targeting, MRI is often used for guiding HIFU to perform the task. In this paper, a stereotaxic apparatus was introduced as a cheaper method to replace MRI for targeting the specific region in the brain.

Aim & Method:

The overall goal of this project was to evaluate the feasibility of controlling HIFU exposures with a modified stereotaxic system to perform ultrasound sonication within a specific region in the brain. A tissue mimicking material (TMM) developed based on Gellan Gum and dissolved albumin was used in this project as a gel phantom. In this project, a focused ultrasound transducer was built to integrate into the stereotaxic system. A water tank was developed by a 3D printer to enable transmission of ultrasound. Using stereotaxic apparatus system, the focal point of transducer was targeting at the specific region with the gel phantom. The transducer was excited with 400mV peak to peak voltage and set to be working at its 3rd harmonic frequency (4.86MHz). A continuous sine wave was generated for sonication and the total exposure time was 20 seconds.

Results & Conclusions

The spatial accuracy of individual sonications was approximately +5% (of 7-8mm target ranges) for XYZ. The ability to expose specific regions of the brain was demonstrated. The gel phantom developed accurately represents the focal volume of the focused transducer and is useful for evaluating the spatial accuracy of the apparatus. Combining ultrasound with stereotaxy for precise exposure of brain regions is feasible on a mechanical level. Compared with MRI guided HIFU, the stereotaxic apparatus is cheaper and more compatible with neuroscience experiments. This system could be used in a higher level HIFU project such as blood-brain barrier disruption.

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An automated supination assessment task

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Introduction:

Loss of motor function following stroke affects hundreds of thousands each year. Many stroke patients who have motor loss experience some level of impaired distal wrist rotation. The current gold standard tasks of measuring distal rotation in rodents are prone to human error and problems in different scoring systems. There is currently no task that allows a quantitative measurement of supination and pronation in rodents.

Aims and Methods:

We have developed a novel behavioral task that allows us to automate and quantitatively measure distal forelimb supination in rats. The task requires animals to reach through a small aperture in a clear acrylic cage, grasp a spherical knob, and then supinate. The knob is attached to a rotary encoder and allows measurements of ¼" of a degree. When the user defined threshold is reached, the animal is rewarded with a pellet. The data is displayed in real time and recorded automatically. With a rich dataset of 300-400 trials a day per animal, we can quantitatively analyze each rat's performance free from human bias. Due to the automation of the program, and implementing adaptive hit thresholds, we are able to train animals to proficiency within two weeks. Once the animals trained to the specified degree threshold, unilateral motor cortex ischemic lesions are administered.

Results and Conclusions:

Animals exhibit a sustained supination deficit following motor cortex ischemia. All relevant calculated parameters show a drop in performance, including total degrees turned, velocity, acceleration, and inner spin times. Our results show that our task isolates distal rotation and is a sensitive measurement of supination loss.

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Abstract:

Unilateral neglect is an attention deficit disorder often seen in stroke victims that have right parietal damage. It is hallmarked by the inability of patients to respond to activity or cues on their left side. At present, very few rehabilitative therapies exist for neglect, and full recovery is sparse among patients. Unfortunately, the animal literature has failed to provide any successful pre-clinical therapies that may be able to transfer to the clinic. In this study, we have developed an animal model of unilateral neglect as well as a new method to measure neglect in animals. Rats were trained to enter a nosepoke and wait for a visual light cue. After responding to the cue by exiting the nosepoke, rats were rewarded with a food pellet. After training on this task, each rat received injections of the vasoconstrictor endothelin-1 (ET-1) into right parietal cortex as a model of ischemic stroke and in order to induce unilateral neglect. We then tested animals post-surgically and measured their deficit in responding to cues in the contralesional space. This new behavioral measure and animal model of neglect could be helpful in promoting research into pre-clinical and clinical therapies for unilateral neglect.

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Measuring Forelimb Speed on a Skilled Reaching Task in 6-OHDA lesioned rats

Anthony Nguyen, Seth Hays Ph.D., David Pruitt, Michael Kilgard Ph.D., Robert Rennaker Ph.D.

Introduction

The bradykinesia assessment task, is a modified appetitive skilled reaching task in which rats are trained to press a lever twice in rapid succession. The bradykinesia assessment task demonstrates a reduction in performance of multiple parameters of forelimb function, including a decrease in forelimb movement speed, resulting from both hemorrhagic striatal lesions and ischemic lesions to the motor cortex.
Rat models of PD utilize the stereotaxic administration of the neurotoxin 6-OHDA into the medial forebrain bundle to cause extensive damage to the dopaminergic neurons of the substantia nigra. We hypothesized that 6-OHDA lesioned animals would show deficits in multiple parameters of forelimb function on the bradykinesia assessment task.

Aims

To assess the sensitivity of the bradykinesia assessment task to a unilateral 6-OHDA lesion to the medial forebrain bundle (MFB), the predominant model for preclinical research of Parkinson's disease.

Methods

After training the animals to task proficiency, unilateral infusions of 6-OHDA into the medial forebrain bundle were performed to induce Parkinson’s disease. Motor performance on the bradykinesia assessment task was continued for 6 weeks post-lesion.
The lever was attached to a electrical potentiometer. This allowed us to obtain an analog signal of the position of the lever. Using custom software, we were able to quantitatively analyze multiple parameters of forelimb function.

Results

After administration of 6-OHDA, the rats showed an impairment in forelimb speed, and marked reduction in successful trials, total presses per trial, and total trials per session.

Discussion

This study assessed the sensitivity of the bradykinesia assessment task on unilateral 6-OHDA lesions to the medial forebrain bundle. The 6-OHDA lesioned rats showed marked declines in multiple parameters of forelimb function. This task produced deficits in rats with sub-maximal nigral damage, which could be analogous to subclinical neuronal changes in the Parkinsonian brain and warrants further investigation.

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Characterization of Two-Solution Bone Cements (TSBC) with Calcium Phosphate (CaP)

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Introduction: Acrylic bone cements are used in orthopedics for a variety of applications including vertebral disk decompression, implant augmentation, and fracture fixation. However, traditional acrylic bone cements are bioinert and will neither integrate with the surrounding bone nor be resorbed. This can be remedied by adding a calcium phosphate filler such as Brushite to the cement composition to provide a porous scaffold in which the bone may interdigitate.

Aims and Methods: The aim of this study was to engineer partially resorbable bone cement for orthopedic applications by substituting the plastic phase with various concentrations of calcium phosphate filler (Brushite) while retaining desirable mechanical and rheological properties. To accomplish this, TSBC was prepared by mixing poly (methyl methacrylate) (PMMA), methyl methacrylate (MMA) and Brushite in various concentrations yielding a pre-mixed composite bone cement with up to 75% of the original polymer replaced by filler. N,N-dimethyl p-toluidine (DMPT) and benzoyl peroxide (BPO) were utilized to initiate free radical polymerization of setting cements. Viscosity, storage moduli, and extrusion stress were assessed using dynamic rheological characterization of non-setting cements on a DHR-3 Rheometer. Mechanical compression tests followed the ASTM F451 standard using a Bionix Mechanical Testing System (MTS 370). For injectability characterization, a pneumatic gun (Ellsworth, Germantown, WI) was used to extrude the cement through the system and injectability rate was assessed.

Results and Conclusions: Results demonstrated that replacing the polymer concentration with CaP did not detrimentally affect the mechanical properties of the cement compositions investigated. Rheological characterization was performed to determine the feasibility of utilizing these compositions for various orthopedic applications. The injectability of the various concentrations of cement varied considerably, while the pseudoplasticity of the cements was not detrimentally affected.

Source of Funding: University of Texas System, UT Transform Award (Dr. Rodrigues)

Presentation Title: A Wireless Transponder for Smart Shoe

Authors: Shahrzad Sheibani[1], Bhaskar Banerjee[1], Haiying Huang[2], Rashaunda Henderson[1]

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Introduction:

The research objective is to design a wireless transponder for antenna-based sensors used to simultaneously measure shear and pressure forces for diabetic foot diagnosis. The transponder is placed on the top surface of a shoe and consists of sensors and an interrogation system that transmits information to a receiver by modulating the interrogation frequency. The identification system includes an energy harvester, crystal oscillator and a passive mixer. A single chip interrogation circuit has been designed in CMOS to reduce size.

Aims and Methods:

The sensors can be interrogated based on the principle of backscattering. A Rx/Tx antenna connects to the sensor via a switch. The Rx/TX antenna receives an interrogation signal that is either reflected by the switch or antenna sensor. When the switch is controlled using an oscillator, the reflected signal will be amplitude-modulated at the oscillator frequency. The RF energy harvester IC consists of a rectifier, limiter, reference and voltage regulator designed to power up the oscillator since it is the only device which needs an external power source. The rectifier converts the RF signal to DC and powers up the entire identification blocks. The voltage regulator generates a clean and regulated signal for the crystal oscillator.

Results:

The proposed identification system was fabricated in IBM 130nm CMOS technology. The rectifier generates a DC voltage up to 1.75V with an applied

7dBm signal at 5.8GHz. The limiter maintains DC voltage to 1.2V and powers up the entire system. The limiter is followed by a voltage reference and regulator circuits to provide 0.6V supply voltage for the crystal oscillator. The crystal oscillator, including the output buffer and level shifter, generate 4MHz signals with 0.8 V_{p-p} amplitude for the passive mixer with 15dBm of conversion loss. The identification system including bond pads has a size of 1.2mm × 0.8mm.

I. E-VEST: Athletic Heart Monitoring System

By Rizan Shrestha, Jeff Smith, Miguel Ysuhuaylas, and Ryan Johnson

II. Introduction

Sudden cardiac arrest is a condition in which proper heart function seizes unexpectedly (often due to ventricular fibrillation) and often results in death without immediate medical attention. When an athlete performs vigorous workout sessions, a sudden cardiac arrest could happen, resulting in sudden cardiac death (SCD).

III. Aim and Method

The aim of our project is to design and implement an electrocardiogram (ECG) monitoring device, which monitors athletes' ECG signals autonomously. The system is latched inside a wearable vest which monitors the signal from an athlete. It processes the analog signal through a microcontroller and then sends the collected real time data wirelessly to a base station. The base station will further process the digital signal through various filters to acquire a reasonably clean ECG signal while checking for any sort of abnormality, which can trigger an alarm to the nearest emergency unit from where the athlete is located.

IV. Results and Conclusion

Modern automatic external defibrillators (AEDs) substantially increase the survival rate from sudden cardiac arrest during marathon runs, but current responses are typically 'de facto' and require experienced EMS personnel to identify and then treat sudden cardiac arrest. Therefore, athletes may be willing to wear an E-vest that can automatically recognize a cardiac event and immediately alert EMS and/or exercise event emergency personnel.

We are currently working on reducing the noise on the transmitted signal in the analog domain via notch-filtering. We are also working on further noise reduction in the digital domain using various finite impulse response (FIR) filters. The end goal is to attenuate noise and produce a clean signal. Once we achieve this goal, we will perform multiple analysis tests on multiple human cardiac signals. We are expecting to minimize the size and weight of the circuit for minimal intrusion and maximum comfort.

DESIGN AND FABRICATION OF NANOGAP FOR BIOSENSING APPLICATIONS

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Nanogap biosensor comprises of nanometer-scale detection region sandwiched between two electrodes. The nanogap biosensor leverages overlapped Electrical Double Layer (EDL) formation as the nanogap is smaller than the debye length of a single double layer. The purpose of the nanogap is to immobilize the DNA of similar dimensions for biological detection. Nanogap biosensing aids in amplified electrical signal detection and specific detection, however due to difficulty in fabrication, it is a newly emerging area of study. Biomolecular immobilization, within the gap, detected by electrical measurements makes it a label-free, ultra-sensitive and rapid biomolecular detection technique. The detection modality results in an amplified signal owing to the overlapped electrical double layers of the two electrodes.

The aim is to fabricate and optimize a nanogap biosensor on varied substrates such as glass and a porous film. Since the fabrication of nanogap below 50nm regime requires complex fabrication, we demonstrate the fabrication and testing of a nanogap biosensor of dimensions 50nm using a combined technique of thin film deposition of metal precursor, using sputter coaters, Atomic Layer Deposition (ALD) of alumina that acts as a sacrificial layer and etching off alumina layer to allow for formation of nanogap. The electrodes were fabricated and tested in the micrometer regime, specifically from 500 microns to 125microns. The presence of the nanogap was tested using a micromanipulator probe system to measure the I-V characteristics of the proposed electrode design. The results of the nanogap biosensor fabrication comprise of I-V characteristics of the fabricated nanogap with varying frequency and temperature. The presence of the nanogap is shown through the SEM images generated.

Design and optimization of Electrical Cell-substrate Impedance Sensing (ECIS) biosensor for real time cellular monitoring

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Introduction:

Seamless integration of biological components with electrochemical sensors is critical in the development of microdevices for cell analysis. Cell-based impedance biosensing is an emerging technology that can be used to non-invasively and instantaneously detect and analyze cell responses to chemical and biological agents. The use of bioimpedance measurements allows for the in vitro monitoring of cellular adherence, proliferation, viability, and morphological changes.

Aims and Methods:

We are developing and optimizing a biosensor platform that is capable of detecting cellular changes caused by reagents down to the single cell level. The optimization of the electrode design provides the ability to monitor the changes of cell kinetics while reducing the background noise often seen in other impedance based sensors. Cells added to a microfluidic reservoir of a micro electronic device will settle to the bottom and can attach when given an appropriate substrate for binding. The addition of electrodes to the bottom of the well allow for the cells to bind and cause a quantifiable change in impedance which provides real time indications of cellular changes. This project uses Electrical Cell-substrate Impedance Sensing (ECIS) to measure cellular adherence to gold electrodes and to monitor changes in adherence and to the cellular environment. For this mammalian Human Embryonic Kidney cells were used as the target cells. The ability of ECIS to give real time information about the cellular environment also presents the possibility for the detection of cellular biomarkers as a reference to test for the ability to monitor cells in-situ for the release of specific biomarkers. Readings are attained using a multiplexed potentiostat to measure changes in the impedance of the cellular environment in each microfliudic well individually and simultaneously.

Results and Conclusions:

The biosensor provides strong detection readings caused by cellular adherence. The current multiplexed design offers a platform for real time detection of cellular changes.

Authors: Ridhima Chadha, Shalini Prasad

Title: Rare Cell Separation Using Dielectrophoresis

Cancer affects 7.6 million people worldwide according to the Center for Disease Control. In order to more effectively treat cancer patients the cause of heterogeneity in the disease must be fully understood. It has been recently hypothesized that select subpopulations of cancer cells have tumorigenic properties similar to embryonic stem cells. These cells are thought to be associated cancer proliferation .The goal of our project is sorting and identifying rare cells such as cancer stem cells by designing label-free cytometry tools.

Currently cancer cells are sequestered through label-based and invasive techniques requiring a “tag” to be attached to the cell and a significant amount of time for separation to occur. Dielectrophoresis (DEP, gradient electric field based electro kinetic technique separates cells using non-invasive and label free method at a much faster rate. It is an accurate method that can be used for sorting biological cells with varying dielectric properties.

We have designed a microelectrode array based cytometry tool, working on the principle of dielectrophoresis. In DEP a specific voltage and frequency are applied to an electrode pattern creating a non uniform electric field. The applied field induces a dipole in the cells, which are suspended in a conductive medium, causing them to move toward specific areas on the electrode patterned chip based on their dielectric properties. The electrode design was a simple two by two array with alternating positive and negative terminals with a diameter of 250 microns and center to center distance of 750 microns creating an area of high electric flux between the electrodes for the target “rare” cells to gather. High throughput was achieved through micro fluidics. This project demonstrates the separation of cervical cancer cells (HeLa) from non-cancerous human kidney cells (HEK). Separation efficiencies of 90.5 % have been achieved. 500,000 cells are separated per minute.

Improved Cochlear Stimulation Based on Shape Memory Polymers

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Hearing loss is the most common chronic disorder in the world, impairing more people than blindness, heart disease and cancer combined. Currently, hearing can be partially restored through cochlear implants (CIs) which bypass cochlear dysfunction through direct electrical stimulation of spiral ganglion neurons (SGNs). These devices are limited by their low frequency and intensity resolution of sound coding, a result of inadequate electrode contact to stimulate the SGNs. Moreover, insertion of standard CI arrays cause trauma to both the basilar membrane and lateral wall of the cochlea, resulting in an inflammatory response and trauma which ultimately leads to fibrosis and neo-ossification.

We propose to utilize temperature dependent shape memory polymers to fabricate cochlear implants. Specifically, the shape memory effect allows for stiff insertion of cochlear implants that soften and coil during implantation, are chronically flexible and are compatible with photolithography. As the CI warms to body temperature, it transitions to the "remembered" coiled shape of the cochlea and atraumatically navigates the turns of scala tympani. Beyond improving substrate design to achieve enhanced stimulation of SGNs, we aim to overcome modern challenges to CI design regarding electrode size and charge injection capacity. By utilizing materials such as titanium nitride or PEDOT in order to increase the porosity of electrode surfaces, we seek to attain an electrochemical surface area many times larger than the geometric surface area. In this way, we can increase the number of electrodes within the same geometric area, maintaining comparable charge injection levels while increasing signal specificity to SGNs to improve sound coding.

The results of this study are intended to enable improved cochlear stimulation and can be applied to a host of flexible neural electronics such as cortical probes, regenerative nerve electrodes and nerve cuff electrodes.

Raising the Core Body Temperature by Heating Glabrous Surfaces During Vasodilation

By: Andrew Stier

Intro:

Anesthesia can prevent the blood vessels from constricting, increasing blood perfusion and allowing blood cooled by the cold ambient air to travel to and cool down the core. Operating on a patient with a hypothermic core can cause complications. This experiment involves a solution to this dilemma.

Aims and Methods:

This experiment aims to show experimental evidence supporting the theory that supplying a high amount of heat to the palms of the hands and the soles of the feet while inducing increased blood perfusion can raise the core body temperature and sustain it at a desired level. The palms and soles are glabrous skin surfaces which have been shown to be areas of great heat transfer during vasodilation and increased blood perfusion. This heat must be supplied with a heating device that is flexible, completely adhesive, and able to supply uniform heat to avoid burning the patient. This project involved fabricating a surface electronic heater that meets these criteria using nanofabrication techniques. A prototype of this device was created by spincoating polyimide (PI) onto a glass slide. Ultra thin titanium wires were then sputtered onto the slide using sputtering, photolithography, and a mask designed in SolidWorks. The wires were then bonded to an external voltage source using thin flexible cables, and produce heat when voltage is applied. Once perfected, this prototype can be used to test the theory.

Results and Conclusions: Applying 45V of voltage to the device allowed it to reach sufficiently high temperatures (up to 43$_{o}$C). In future prototypes, gold may be used in place of titanium as it has a lower resistivity constant and should reach higher temperatures at lower voltages. Future prototypes will be transferred to temporary tattoo adhesive sheets so that the device can be applied to the skin in a flexible, low pressure manner.

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The *In Vitro* Effects of Embryonic Stem Cell Paracrine Signaling on Macrophage Phenotype

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Introduction

Embryonic stem cells (ESCs) may play an important role in tissue regeneration. Differentiating ESC aggregates, referred to as embryoid bodies (EBs), secrete a number of growth factors involved in inflammation and tissue repair. Macrophages, a major cell type in inflammation and tissue repair, exhibit a pro-inflammatory M1 phenotype or a pro-wound healing M2 phenotype. Thus, EB paracrine secretions may induce a phenotypic change in macrophages.

Aims and Methods

The aim of this study was to gain a better understanding of how ESC paracrine secretions may affect the immune system *in vivo*, by examining the effects of EB conditioned media (EB-CM) on macrophage phenotype. EBs were formed from mouse ESCs, and EB-CM was collected on days 4 and 7. Simultaneously, human THP-1 cells were cultured in growth medium + PMA for 48 hours to form adherent macrophages. Macrophages were then cultured in polarization medium (M1: growth medium + LPS + IFN-γ; M2: growth medium + IL-4) or EB-CM for 48 hours. Fresh growth medium was used as a control. After 48 hours, these media samples were collected, and enzyme-linked immunoassays (ELISAs) were performed to analyze cytokine secretion (TNF-α to characterize M1 phenotype and IL-10 to characterize M2 phenotype).

Results and Conclusions

As expected with proper formation of EBs, macrophages activated by LPS and IFN-γ (M1) secreted high amounts of TNF-α and low amounts of IL-10 while macrophages activated by IL-4 (M2) secreted low amounts of TNF-α and high amounts of IL-10. Macrophages treated with EB-CM on days 4 and 7 showed increased secretion of TNF-α as compared to all other media samples but significantly less than M1 macrophages. Secretion of IL-10 was low compared to all samples. This suggests that EB-CM may induce a phenotype resembling M1, and inflammatory response may be enhanced *in vivo*.

(Melanie Maurer- melanie.maurer@utdallas.edu)

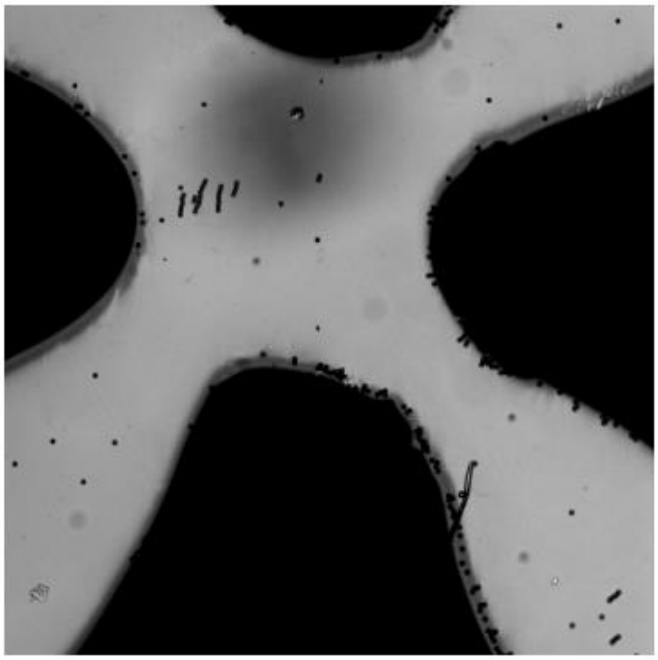
Application of Electrokinetics for Cell Separation

Cell separation usually consists of either fluorescence activated cell sorting or magnetic activated cell sorting. These methods are useful for cell separation/sorting but a more efficient way is there through dielectrophoresis (DEP) and electrorotation (ROT). This involves applying electrokinetics to manipulate the cell through the use of its dielectric properties.

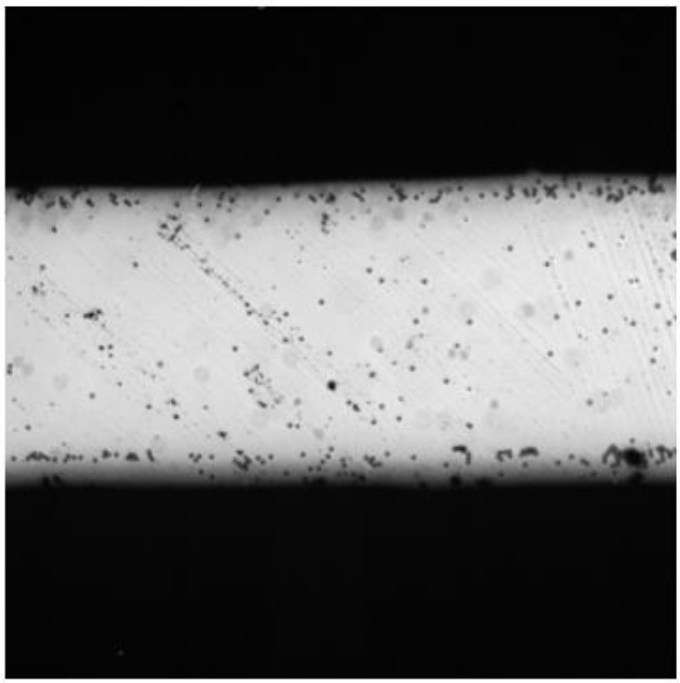
The device set up is on a glass substrate with gold electrode plated on the glass slide. For dielectrophoresis, the electrode applies a voltage (positive and negative) to the circuit. Based on the dielectric properties of the particle, the particle will either experience negative DEP or positive DEP depending on the frequency applied in the electric field. In negative DEP, the particle moves away from the flow of the electric field. In positive DEP, the particle moves towards the electrode. By utilizing the dielectric properties of the particle, we can accomplish negative or positive DEP so that cell separation is effective. In electrorotation, voltage is applied the same way as in DEP, but a phase lag is also applied to the rotating electric field to cause the circular motion. So far, our experiments have used polystyrene beads to optimize negative and positive DEP. We have used polystyrene beads suspended in diH2O and observe their movement when electric field is applied.

For the polystyrene bead experiments, the results we have gotten have shown that positive DEP can be achieved through low frequencies and negative DEP can be achieved through high frequencies. The main frequency range for positive DEP went from 100 Hz to 500 Hz. For negative DEP, the effects could be first observed around 500 kHz all the way to 1 MHz. For negative DEP, pearl chain formations could also be observed. Below are images of different electrode patterns and their results for negative and positive DEP.

Negative DEP: (pearl chains can be observed)



Positive DEP:



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