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the Columbia Undergraduate Scholars Program present
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Research
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Lily Zhao, SEAS '19, Mechanical Engineering

SilenshR: Bacteria-Mediated Oncogene Silencing as Living Cancer Therapeutic

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Abstract:

RNA interference (RNAi) therapies modulate endogenous gene expression in target cells through introduction of exogenous short interfering RNAs (siRNA) or their precursors, short hairpin RNAs (shRNA). Challenges for efficient and cell-specific RNAi therapies abound, like rapid renal clearance, degradation by serum nucleases, traversing the lipid bilayer and escape from the intracellular endosome. Bacteria innately colonize the hypoxic and immune-privileged cores of tumors and as such have been explored as potent delivery systems for RNAi-based cancer therapeutics. We are engineering an RNAi gene therapy, utilizing recombinant *E. coli* that invade mammalian cells and deliver an shRNA payload

targeting the aberrantly expressed receptor tyrosine kinase *EGFR* and transcription factor *c-Myc*. Bacterial uptake by mammalian cells and endosomal breakdown are mediated by a quorum-inducible *Invasin-HlyA* operon. We are characterizing the circuit via gentamicin protection assays *in vitro* using HeLa and prostate cancer lines, and assessing target oncogene knockdown through flow cytometry and qRT-PCR.

Keywords:

EGFR, c-Myc, *Invasin-HlyA*, shRNA

Silicon Oxide Nanofilms for Energy and Water Applications

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Since the mid-twentieth century, the global average surface temperature has risen by 1°C and is projected to continue to increase in the coming decades. Renewable energy is a crucial solution, but it can only be produced intermittently and in limited locations. To overcome this issue, fuel cells can convert renewable energy into solar fuels to be stored and transported, where electrolyzers revert the fuel to electricity. However, these technologies are not yet efficient enough to be widely implemented. A second issue this project addresses is water scarcity; one in ten people worldwide lack access to clean water, and these conditions will worsen as global warming progresses. Reverse osmosis (RO) desalination, involving the membrane-based separation of ions from water, can produce clean water sustainably, but inefficiencies make large-scale use of the process difficult.

Research in Esposito lab uses an ultrathin silicon oxide (SiO_x) overlayer on catalytic nanoparticles in fuel cells and electrolyzers to improve stability of the devices. Within this context, a SiO_x overlayer seems to enhance selectivity against metal ions. Better understanding the transport properties of silicon oxide could inform further development of the SiO_x overlayer model. As such, one goal of this study is to characterize and analyze the transport of water and solutes across a membrane with a SiO_x overlayer deposited upon it. If SiO_x proves to be sufficiently selective against solutes while maintaining adequate water permeability, the overlayer could also improve the filtration properties of membranes for RO desalination.

In RO desalination, SiO_x may also solve the issue of biofouling on the RO membrane surface, and damage to the membrane from chlorine used to clean it. Our second goal is to determine whether the SiO_x overlayer confers fouling-resistant or chlorine-resistant properties on the membrane. In this study, we tested different methods of deposition of SiO_x to achieve a uniform layer. Then, we used a diffusion cell and RO system to characterize the transport properties of SiO_x . Preliminary results from the diffusion cell suggest the SiO_x overlayer decreases permeability of the membrane to NaCl. We will continue by fine-tuning our deposition process, measuring transport for various solutes, and testing SiO_x resistance to biofouling and oxidizing agents.

Keywords

Silicon oxide, fuel cell, electrolyzer, desalination, reverse osmosis, diffusion cell

Bayesian inference and model selection for physiologically-based pharmacokinetic modeling of superparamagnetic iron oxide nanoparticles

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Abstract

The growing use of superparamagnetic iron oxide nanoparticles (SPIONs) in early cancer detection technologies has created a demand for physiologically-based pharmacokinetic (PBPK) models that accurately model and predict the biodistribution of SPIONs in the mouse and human model. The objective of this work is to use a Bayesian approach built upon nested-sampling to select a model based on qualitative criteria of the fit of the model and the likelihood function landscape, as well as quantitative criteria of the evidence and maximum likelihood values.

Four linear PBPK compartmental models of ranging complexity are considered. Compartments included in the models comprise of a combination of the plasma, liver, spleen, tumor, and “other” (the remaining body tissue), with parameters including the volume, blood flow rate, and plasma:tissue distribution ratios. The model parameters for each model are evaluated using

Bayesian inference, in addition to the respective evidence integrals, maximum log-likelihoods, and Bayes factors.

In contrast to the other models, the model containing all compartments and the model containing the plasma, liver, tumor and other has the highest log-likelihood and evidence values, indicating both a high goodness-of-fit and a high likelihood of the model given the data. This is similarly reflected in a faithful quality-of-fit and non-flat log-likelihood landscapes. Overall, these findings illustrate the strength of the Bayesian model selection framework in ranking different models to determine the best model that accurately represents the experimental data.

Origin and measurement of unknown O₂ transport resistances in ionomer thin films

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

In 2017, we saw the introduction of the first hydrogen fuel cell car with the Toyota Mirai. As polymer electrolyte fuel cells (PEFCs) approach mass commercialization in a sustainable energy future, research is needed to improve the efficiency of the chemical reaction known as the oxygen reduction reaction that occurs in the catalyst layer region of the fuel cell. The catalyst layer consists of three major components: a carbon microporous electrode, platinum (Pt) nanoparticles, and an ion-conducting polymer (ionomer) thin film. Recent studies have shown that the key source of efficiency losses is O₂ permeation resistance in the ionomer thin film region of the catalyst layer. In this study, we sought to quantify this transport resistance. This was accomplished by the modeling of a Pt nanoparticle with a 10-micron diameter microelectrode.

Chronoamperometry and cyclic voltammetry were utilized to determine the impact of environmental oxygen and film thickness on the transport of oxygen through the catalyst layer. We found that

environmental oxygen levels greatly influenced the efficiency of our cell. Most interestingly, we found that permeation resistance was greater with bulk films than with nanoscale thin films. We hypothesize that this loss of permeability at nanoscale demonstrates nanoscale confinement effects within the ionomer, potentially delineating that the polymer has drastically different morphologies between bulk and nanoscale. With this work, we hope to provide insights on the catalyst layer, an area of particular interest in modern PEFC research. These insights will be instrumental in moving hydrogen fuel cells closer to mass commercialization.

Keywords

Polymer Electrolyte Fuel Cells (PEFC), Ionomer, Nanoscale, Thin Films, Microelectrodes

Modelling the Development of Numerical Intuition

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Numerical abilities exist in brains of animals with no language abilities. How does mathematical cognition come about? Developmental psychologists debate whether human mathematical cognition arises from a series of discoveries of fundamental principles, such as the Cardinality Principle (CP), or by the gradual acquisition of mathematical intuition. Parallel distributed processing models, implemented as artificial neural networks, demonstrate the gradual acquisition of knowledge. A network learns incrementally and builds an intuition system of its own, without regard to rules or principles. Artificial intelligence researchers have developed deep recurrent neural network (RNN) models with attention mechanisms for applications in Computer Vision and Natural Language Processing. The aim of this research was to use RNN models to characterize how numerical cognition arises. By designing a biologically-inspired artificial neural network able to do number estimation and counting, we demonstrate that these numerical abilities come from subtle adjustments in the intuition system.

We designed networks with Long Short-Term Memories (LSTMs), a sense of time, and a retina to mimic human visual attention. We were able to design a model with a fully differentiable window movement strategy that enabled the network to focus processing power on specific regions in the input image for the network to count. The model was trained using backpropagation. Our estimation model's outputs mirrored the distributions of neuronal activations of number classifications on the mental number line observed in monkeys, showing that an approximate number system (ANS) can be achieved by a neural network. Our counting model demonstrates a human-like point-and-count routine. These preliminary findings illustrate that mathematical cognition can arise from changes in connection weights of a neural network, indicating that human mathematical cognition arises gradually, with experience, much like intuition.

Keywords

mathematical cognition, parallel distributed processing (PDP), recurrent neural network (RNN), approximate number system (ANS)

Stationary Chamber-Based PCR on a Chip: Liquid Biopsy Detection of Circulating Tumor DNA

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Supervising Faculty, Sponsor, Location of Research

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Abstract

Cancer impacts more than 38% of the US population. At present, the methods used in healthcare can take at least 2 weeks from tissue biopsy to result reports. While this length of time is not an issue for most forms of cancer, it can be a matter of life or death for rapidly progressing cancers such as non-small cell lung cancer (NSCLC). NSCLC is one of the most prominent forms of cancer in the US and is often not diagnosed until late-stage. The objective of this project is to reduce the turnaround time from sample collection to results, as well as to enable serial monitoring to detect changes in therapy resistance over time. We do this through a liquid biopsy that can be performed rapidly, in the hospital. Unlike traditional methods of biopsies that require tissue samples from tumors, our method targets the cell-free circulating tumor DNA (ctDNA) cancerous cells release. As ctDNA is present in blood at very low concentrations, we require amplification for proper detection. We aim to meet that need through a rapid and cost-effective PCR on a chip.

We identified and met three central goals for the chip: material compatibility, a proper seal to withstand

the high pressures induced by high temperature cycling of PCR, and temperature control. We confirmed polymethyl methacrylate (PMMA) is compatible with PCR reaction with the assistance of BSA. We used isopropyl alcohol's solvent properties for an irreversible PMMAPMMA seal. We built a custom Arduino circuit containing Peltier heater and thermocouple for temperature control. The control drastically improved upon optimizing chip's design. At present, we have the main components needed for the PCR reaction work. The last step is to determine the optimal concentration of BSA. The PCR on a chip is one element of a larger, integrated device. Once PCR on a chip is fully functional, we will incorporate it into a standalone device that can perform the liquid biopsy.

Keywords

circulating tumor DNA (ctDNA), PCR on chip, liquid biopsy, non-small cell lung cancer (NSCLC), fully integrated diagnostic device

Energy Efficiency of Copper Mining

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Copper has been key to economic and societal growth for over 5000 years; it is abundant, ductile, corrosion resistant, and a good conductor of heat and electricity. Copper demand continues to increase, but the grade of available ore is decreasing. Since the mid-20th century, this has necessitated extraction techniques that are environmentally harsh – primarily pyrometallurgical smelting. Hydrometallurgical extraction techniques inflict significantly less pollution and energy usage by comparison. However, they are not yet viable for Chalcopyrite (70% of all available ore), due to its formation of extreme passivation layers during leaching. The design of a low-cost, environmentally-friendly hydrometallurgical process for Chalcopyrite would be a pivotal success of the 21st century in mining.

Recently, an innovative electrochemical pretreatment of Chalcopyrite was proposed. The process was not yet well understood, and its low efficiency made it unviable. The present research aims to: improve the efficiency so that the electrochemical reduction step is viable; couple it with an efficient oxidation step for a complete process; and explore both steps' mechanisms. The effects of cathode

material, pulp density, current, reactor size and reactor cycling were studied. The results revealed that the cathode material, current and reactor cycling had the greatest effect on performance. It was also found that industrially viable pulp densities (>50g/L) can be achieved, but that the reduction step becomes significantly limited by diffusion through a passivating layer. The oxidation step was rapid, but also met with considerable passivation beyond 50-70% Copper release.

Repeated cycling through both reactors appears to break down the passivation layer in each step, thereby improving efficiency and performance. This has prompted further future exploration into a cyclical, two-reactor process. The mechanisms are also currently being researched through solid characterization with XPS, XRD, SEM/EDS and Cyclic Voltammetry.

Keywords

Copper, Energy, Electrochemistry, Chalcopyrite

Designing Environmental Sensors for Living Biomaterials

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

We aim to design environmental sensors to be integrated into a living biomaterial made from plant refuse. This structural composite can be shipped flat across the world and grown from local resources at a fraction of the cost of the transport of conventional materials to provide affordable, biologically-adaptive, and environmentally-conscious refuge worldwide. We hypothesize that we can utilize the promoters of yeast strain *S. cerevisiae* combined with a fluorescent readout to design these sensors. Due to the well-elucidated yeast genome, previous literature points to different repair pathways that include promoters whose protein transcriptions are sensitive to each of the environmental stimuli of interest. For this project, we aim to design sensors for UV toxicity, heavy metal poisoning, and heat stress, and, to do so, we used the promoters of RNR3, HUG1, and HSP104, respectively. We used Gibson Assembly to fuse each of these promoter sequences into a core acceptor plasmid directly upstream of a red fluorescent mCherry readout and a terminator sequence from the CYC1 gene. We then transformed each plasmid construct into a laboratory

yeast strain that had already undergone CRISPR with a promoter associated with glycolysis fused with a green fluorescent readout. The green fluorescence served as a model for basal cellular protein transcription and the red fluorescence served as a model for the transcription as driven by our new construct. This allows us to standardize the two fluorescence values by optical density (OD) and then compare the red fluorescence per cell to the green fluorescence per cell to ascertain the specificity of our construct to its respective stimulus.

So far, we have tested 2 of the 3 sensors we have designed. For the heat stress sensor, we chose to incubate cultures at 25, 30, 37, and 42 degrees, measuring fluorescence and OD every hour. We used the optimal growth temperature of 30 degrees as our control. For the UV toxicity sensor, we exposed samples to direct outdoor sunlight for 30 minutes, 1 hour, and 2 hours, using a sample that received no exposure as our control and taking the same measurements post-exposure every 30 minutes. For the heat stress sensor, we noted a 2.5 times increase in protein expression after 8 hours at 42 degrees and after 12 hours at 37 degrees. For the UV toxicity sensor, we discovered that the UV irradiance provided by ordinary sunlight was not intense enough to drive a marked response with this promoter.

Though we saw promising results for the heat stress sensor, we plan on assaying constructs with 6 other heat-sensitive promoters to ensure we have designed the sensor with the highest specificity. Additionally, although the UV sensor construct did not yield significant results, cells did show trends of lower growth at longer exposures. Therefore, we are currently

researching other promoters associated with the DNA damage repair pathway that may yield better results.

Keywords

S. cerevisiae, promoters, genetic engineering, biomaterial, repair pathways

Graphene Synthesis Via Chemical Vapor Deposition

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Supervising Faculty; Sponsor; Location of Research

Christopher DiMarco, Shruti Rastogi, Arnuparp Santimetaneedol, Alan West, James Hone, Jeffrey W. Kysar; National Science Foundation, Undergraduate Research Involvement Program; Hone Laboratory, Kysar Laboratory; Columbia University

Abstract

Graphene is a single layer of carbon atoms bonded together in a hexagonal honeycomb lattice. It is an area of great interest due to its excellent thermal, electrical, and mechanical properties. It is the strongest material ever characterized - 100X stronger than steel. Utilized properly, graphene has the potential to enhance many products, as well as fabricate new ones. It becomes essential to develop industrially scalable techniques to synthesize graphene. Chemical vapor deposition (CVD) has been shown to produce large area continuous sheets of monolayer graphene. While CVD introduces grain boundaries into the sheet, making it polycrystalline, these defects only slightly diminish the fracture strength. Copper foil, in particular, is used as a catalyst due to its low solubility of carbon. In order to synthesize high-quality graphene, minimal surface roughness of the copper substrate is essential. This is because increased surface roughness enhances increased nucleation density, therefore increasing the

density of grain boundaries and decreasing the overall strength. Herein, we study the effects of a smooth copper surface, with a roughness as low as a few nanometers, through rotating disk electropolishing. The minimization of the surface roughness has resulted a decrease in nucleation density, as well as an increase in grain size uniformity. Additionally, we discovered that treating the copper foil with acetic acid after electropolishing is necessary to avoid corrosion caused by phosphoric acid residue. Overall, we have successfully achieved large area continuous graphene growth on ultra-flat copper substrates by employing rotating disk electropolishing techniques.

Keywords

graphene, low pressure chemical vapor deposition, rotating disk electropolishing

Modeling cellular and tissue specific phenotypic changes in osteoarthritic synovium using a tissue engineered co-culture system.

Saiti S Halder SEAS 2019 Biomedical engineering
Robert M Stefani, Dr. Clark T Hung

Supervising Faculty, Sponsor and Location of Research

Robert Stefani (my mentor, PhD candidate), Clark Hung (principal investigator, faculty)

Sponsor/Location: biomedical engineering department, Columbia University (361 engineering terrace). Supported by NIH grants

Abstract

Osteoarthritis (OA) is a common disease, affecting more than 3 million people in the US per year. Although cartilage degeneration has been a key focus of OA research for years, recently there is growing appreciation for the intimate role that synovium plays in diarthrodial joint health. Despite the critical role of the synovium in governing joint homeostasis, there is surprisingly little known about the mechanisms that underlie this function. Previous research has led to the creation of tissue engineered synovium that primarily contains fibroblast-like synoviocytes (FLS). While it is clear that FLS are able to organize into a synovium-like architecture and perform other critical aspects of the native synovium, our previous research on native synovium explants has indicated that macrophages are a critical part of this model. In this project, we build upon the previous model by incorporating both macrophages and fibroblasts. Our results indicate that

it is possible to co-culture FLS and macrophages in the same tissue engineered construct. To compare the behavior of the tissue engineered synovium to the native synovium, we treated the tissue engineered synovium with different inflammatory cytokines and anti-inflammatory drugs that we previously used to characterize the explants. It was observed that interleukin-1 and/or dexamethasone treatment differentially modulates FLS and synovial macrophage (SM) content in a tissue engineered synovium model.

Keywords

Fibroblast-like synoviocytes (FLS), synovial macrophages (SM), cytokines, osteoarthritis (OA), tissue engineered model.

Can Barefoot Walking Simulations Estimate Ankle Foot Orthoses Impact on Muscle Activity?

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Passive ankle foot orthoses (AFOs) are frequently prescribed to assist locomotion for children with cerebral palsy (CP). However, it is difficult to estimate how an AFO impacts muscle activity. Simulation has previously been done to examine changes in muscle activity with an AFO using barefoot walking data, but walking kinematics often change with AFOs. This study evaluated the accuracy of simulation using barefoot walking data to estimate impacts of walking with AFOs. We simulated gait with passive AFOs for two children with CP: one simulation using barefoot walking data and the other using walking data with AFOs. We compared simulated activations with experimental activations from electromyography (EMG). Neither simulation paradigm produced consistently more accurate results, as quantified by portion of overlap between simulated and experimental EMG and zerolag crosscorrelation. Simulations tended to be more accurate and less variable for more proximal muscles.

The vastus intermedius had an average crosscorrelation of 0.88 ± 0.04 while the gastrocnemius had an average crosscorrelation of 0.59 ± 0.16 . Simulation using AFO walking data may give better estimates of muscle activity magnitude for the gastrocnemius, since the portion of overlap between estimated gastrocnemius activity and experimental EMG increased from 0.37 ± 0.08 to 0.55 ± 0.13 when using AFO walking data rather than barefoot walking data. These results indicate that common model parameters or the optimization method hinder accurate simulation, and that barefoot walking data may not be suitable for simulation estimating distal muscle activity with AFOs. Improvement in model development and simulation method and using AFO walking data may improve simulation accuracy for walking with orthoses, informing AFO design and prescription.

Characterizing force-strain relationships in *ex vivo* Balb/c mice tibia

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Osteocytes make up almost 95 percent of the bone cell population. They are characterized by the dendrites that form a network with other osteocytes and cells on the bone surface. This extensive cellular network allows for the osteocytes to be ideal mechanosensors, able to sense the local mechanical environment and respond to changes. A loss in the osteocyte's mechanosensitivity may lead to bone diseases such as osteoporosis. A promising treatment for bone loss is the administration of a monoclonal antibody against sclerostin (Scl-Ab), a protein produced by osteocytes that inhibits bone formation. Scl-Ab has been shown to increase bone mineral density by increasing bone formation, subsequently altering the mechanical environment of the osteocytes. However, osteocyte responses are dependent on the strain it experiences, and a change in mechanical environment may change the response of the osteocytes.

To better understand how the Scl-Ab treatment will affect the osteocyte's mechanosensitivity, a strain gauging protocol needed to be developed to test the

strain on mice bones that have received treatment. Tibia from three female Balb/c mice were cyclically loaded and strain gauged, and compared to a previous study that measured the force-strain relationship of C57BL/6 mice. Ultimately, the preliminary data from the strain gauging proved to be similar to the previous study. The next steps will be to compare the mechanosensitivities of long term verses short term Scl-Ab treatments on Balb/c mice.

Keywords

Osteocytes, mechanosensitivity, strain gauging, Scl-Ab, Balb/c mice

Initiation and Visualization of Neurovascular Coupling in Alzheimer's Disease Mice Models

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Supervising Faculty, Sponsor, Location of Research:

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Abstract

Alzheimer's disease is a catastrophic, fatal disease in which patients experience loss of body functions, memory loss and confusion that gets worse as the disease progresses with time. With a rapidly aging population, and an increasing life-span, the number of those suffering from Alzheimer's disease is only expected to grow, allowing it to become an even more devastating disease than it already is. There is currently no cure for Alzheimer's disease. A key marker of this disease is amyloid-beta protein, a sticky protein which lays on the brain's surface and builds atop each other to eventually form plaques on the brain, leading to neuronal synapse degeneration and eventually nerve cell death in the brain. The aim of this research was to analyze neurovascular coupling, which is the phenomena in which neuronal activity is followed by changes in cerebral blood flow in the same region, in both control and diseased mice, to establish the effect, if any, plaques have on neurovascular coupling. We would then be able to hypothesize whether blood flow changes may play a role in brain degeneration in those who suffer from this disease, if hemodynamic response is eventually seen to be atypical. Utilizing fluorescent

imaging techniques, mice cortexes were observed under resting and stimulatory conditions. Data involving the hemodynamics of the brain, including oxygenated and deoxygenated hemoglobin levels present at any point in time, and calcium levels, using calcium indicator GCaMP, which tells us about the neuronal activity of the brain, was collected. Using MATLAB, analysis was done to visualize experimental data to compare the neuronal and hemodynamic response in control and diseased mice. This research is imperative in understanding how we could potentially combat this disease, in terms of understanding how vasculature changes may potentially be accompanying neuronal changes we know occur and causing further progression or aiding in the rapid degeneration of the brain.

Keywords

Alzheimer's Disease, neurovascular coupling, amyloid beta, hemoglobin, GCaMP

Testing and Modeling Soft Tissue

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Supervising Faculty, Sponsor, Location of Research

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Abstract

Addressing complex biomechanics problems such as pre-term birth requires an understanding of the mechanics of soft tissue. Designing and effectively implementing tests for complex and often delicate biological materials proves challenging, and ensuring accurate characterization of these complex materials requires data from many samples. Human tissue can be difficult to obtain, and rodent tissue provides a far more attainable alternative. In an ongoing study aimed at understanding the mechanical environment of pregnancy, cervical tissue from mice is mechanically tested and results are compared with chemical composition data and microscopy data to characterize the material and to attempt to identify mechanisms by which the tissue remodels.

For another related project, it was desired to determine via a computer model how alterations to a collagenous fiber mesh were likely to influence its mechanical behavior. The fiber mesh was modeled as a continuous circular fiber distribution imbedded in a very soft neo-hookean ground substance. The elastic fiber modulus was adjusted to roughly simulate the

effect of mixing calcium deposits into the mesh in different ratios, and the mesh was modeled in contact with substrates having two different geometries. Simulation supported the hypothesis that the fiber mesh would become firmer with higher calcium concentrations, and when attached to an undulated vs a flat substrate.

Keywords

soft tissue mechanics, preterm birth, modeling biological tissue, collagen fiber

Nanosphere Lithography on MoS₂ Monolayers for Enhanced Hydrogen Evolution Catalysis

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Low cost and efficient catalysis for hydrogen evolution reaction (HER) is significant for hydrogen production and energy storage. Two dimensional MoS₂ is a well-studied HER catalyst that can be a prominent alternative to Platinum for HER. However, the active sites of MoS₂ are mostly located on edge rather than the basal plane. Thus, large area MoS₂ with high edge site density is essential for enhanced HER catalysis. One method to create highly edge dense samples is by patterning MoS₂ to expose edges. Nanosphere lithography is a scalable and cost-effective solution for material patterning that uses the self-assembly of polystyrene nanospheres (PSN) to form uniform plasma etching masks of hexagonally closed packed (HCP) sphere patterns. This study focuses on laying the preliminary groundwork for creating a nanosphere patterned MoS₂ device. The first part of this study focuses on mask formation by dip coating a monolayer film of PSN on a target substrate. The second part of this study focuses on testing the functionality of the PSN mask by plasma etching Platinum control samples. Future work will focus on patterning MoS₂ for HER catalysis.

Keywords

hydrogen evolution reaction (HER), energy storage,
nanosphere lithography, MoS₂

Building a Better Lab: Future Directions of Display Science Instruction

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Supervising Faculty, Sponsor, and Location of Research

Professor John Kymissis, Sponsored in Part by Johnson and Johnson, Columbia Laboratory for Unconventional Electronics

A common issue faced by students in electrical engineering classes is the need to a great deal of time soldering and trying to get devices to function, which limits the amount of time that can be spent in lab learning the material of the class. Classes in display science can be notably difficult in this regard; while instruction is primarily focused on the composition and behavior of the displays, screens must be appropriately powered and have the correct means for communication with software for the observer to be able to obtain meaningful information

In recent years, advances in automated assembly technologies have allowed companies to have in-house machines that can not only print electric connections onto circuit boards, but can also expedite or even completely automate the placement of components such as resistors, capacitors, and microprocessors. However, such equipment is expensive and impractical for small-scale university use. Several pioneering new companies have recognized the demand of small-scale makers to have the ability to create uniform, replicable devices at a low cost and have begun contracting out their fabrication services.

By working with one such company called Macrofab, our lab has been able to remove the time hurdle for students and instructors in Columbia's ELEN4193 Modern Displays Class by providing pre-made devices that connect student created display projects to personal computers for control and observation. Our devices:

- Eliminate the need for an Arduino or other small processor, thus reducing the net cost to below that of the components that made up the original hand-assembly kits
- Utilize open-source PCB design software to translate the existing labs into files that can be interpreted by Macrofab to create a finished product

The success of this project is indicative of the changing climate of who is creating and popularizing new devices. Macrofab is only a complement to the huge creator culture online. Innovators everywhere can now not only share their designs, but also manufacture and capitalize on them with very little start-up cash; our group hopes to publish our lab designs for order by other academic institutions on a public sharing platform.

Keywords: Printed Circuit Board (PCB), Arduino, microprocessors, maker, Macrofab

Therapeutic Variability of Bevacizumab in Non-Small Cell Lung Adenocarcinoma

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Lung adenocarcinoma is the uncontrolled growth of cancer cells originating in the mucus-producing glands of the lungs, resulting in nearly 1.7 million deaths globally each year. Non-small cell lung adenocarcinoma (NSCLA) has spurred the creation and testing of first-line chemotherapy drugs like bevacizumab (Avastin). Bevacizumab acts as an antibody to the upregulated levels of Vascular Endothelial Growth Factor (VEGF) in lung tumors, as this growth factor encourages tumor growth through new blood vessel recruitment. Despite a singular proposed mechanism of action, there has been significant variability in patients' response to the drug. The aim of this project is to quantify how interpatient variability affects bevacizumab's **pharmacokinetics** and **pharmacodynamics**—how each body acts on the drug, and how the drug acts on each patient's body. First, a computational model describing the somatic movement of bevacizumab was created. This computational model was then modified to incorporate variability into aspects related to the drug's predicted therapeutic effect in a patient, such as an

individual's body weight and expression of the target VEGF-A gene. The distribution of patient characteristics used in the model were based on existing populations of NSCLA patients. Preliminary findings indicate that variability in pharmacodynamic factors—like target gene expression—has a much larger impact on predicted therapeutic effect than variability in the pharmacokinetic factors of bevacizumab. Biologically-based computational models like the one used in this project may provide insight into how specific patient populations will respond to existing and potential chemotherapy treatments for NSCLA.

Keywords

Non-small cell lung adenocarcinoma (NSCLA),
computational modeling, patient variability,
pharmacokinetics, pharmacodynamics

Mechanics of Hemocyte Cell Migration in the Developing *Drosophila* Embryo

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Hemocytes are the fruit fly's macrophage and are found within the cell. Myosin II is said to act as a protein in the hemocytes that helps generate mechanical forces so that the hemocytes can migrate across the embryo and disperse into a set pattern. Fruit fly mutations are similar to those found in humans and their genes are amenable to genetic manipulation. We can therefore try to understand how these mechanical forces work by genetic manipulation. We first generate fruit fly embryos expressing GFP-tagged myosin II in hemocytes so that we can use live confocal fluorescence microscopy to observe myosin localization and dynamics during hemocyte migration. Second, we compare migration of hemocytes expressing normal myosin II to those expressing mutant myosin II. We have found that cells with mutant myosin II appear to move slower than those with normal myosin II, yet appear to travel greater distances across the embryo. We have also found that cells with mutant myosin II tend to stay in clusters longer than cells with normal myosin II. As we observed differences in the way cells with mutant myosin II behave compared to cells with normal myosin II, we believe that myosin II plays an integral role in cell migration and dispersal. As we move

forward, we hope to track all cell migrations so that we can quantify cell migration speeds and distances, investigate cell-cell collisions, and analyze the final cell dispersal pattern.

Key Words

Myosin II, cell migration and dispersal, hemocytes

Prototyping a Bidirectional Pulling Apparatus for Manufacturing Soda-Lime Silica Glass Nanowires

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Supervising Faculty, Sponsor, and Location of Research

Dr. Arvind Narayanaswamy Ph.D. and Arvind Srinivasan M.S., Johnson and Johnson Scholarship, and Swamy Group at Columbia Engineering

Abstract

A recent article by Ordonez-Miranda et. al. [1] has theorized that quantized thermal transport by Zenneck surface-phonon polaritons (SPPs) is achievable at room temperature through nanowires due to the independence of SPPs on temperature. It is the intention of the Swamy Group at Columbia Engineering to further examine this concept by measuring the thermal conductance of nanowires through dual cantilever thermal metrology. In order to conduct these experiments, wires less than 50 nanometers must be manufactured such that they can be easily strung across cantilevers 130 nanometers apart without mechanical interference overpowering the measurements of thermal conductance. The production method that would produce such wires and that appears to be most achievable in the Swamy lab consists of symmetrically pulling soda-lime silica glass wires in a furnace to reduce the wires' diameter through viscoelastic effects. The initial mechanism of pulling used two independently-controlled and loosely-constrained linear actuators using a PID control law implemented by an Arduino to govern their movement.

The resulting motion was inconsistent, asymmetric, and difficult to control by desired velocity. As a result, the specimens broke within the furnace before pulling was completed, thereby making it difficult to isolate the smallest portion of the wire and also preventing the wire from being pulled for the entire length of actuation. The goal of this project is to prototype a new mechanism of pulling that minimizes vibration and improves the likelihood of producing unbroken wires. I found that by using a single rotary motor to translate two stages along a lead screw shaft in opposite directions, I improved the consistency of the pulling mechanism considerably, reducing vibrations and enabling speed control. Furthermore, in furnace temperature ranges between 600 and 800 degrees Celsius I was able to produce unbroken wires with diameters at least as small as 101 nanometers. I also observed I was able to produce unbroken wires more repeatably closer to the glass's transition temperature when pulling at a speed of 5.2 mm/s. However, it cannot be stated with certainty that the smallest diameter measured is the smallest diameter achieved, because although the wires stayed continuous throughout the pulling process, removing the wire from the pulling apparatus unbroken has yet to be accomplished. Further efforts must be made to extract the smallest portion of the wire.

[1] Ordonez-Miranda, J., Tranchant, L., Kim, B., Chalopin, Y., Antoni, T., and Volz, S., 2014. "Quantized Thermal Conductance of Nanowires at Room Temperature Due to Zenneck Surface-Phonon Polaritons". *Physical Review Letters*, 112, Feb., p. 55901.

Keywords

*Nanowires, viscoelastic, soda-lime silica glass,
quantized thermal transport,*

Open Source Ultrasound

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Acquiring large amounts of medical imaging data for training machine learning algorithms is an expensive and time consuming process. In order to make this easier an open source ultrasound device is being designed in order to make acquiring medical imaging data easier as well as make ultrasound devices cheaper and more widespread, especially in the developing world. As part of this project it is necessary to build a low cost transducer and corresponding probe as an alternative to complex commercial solutions. Historically mechanical probes were used to direct ultrasound waves without the use of phased arrays, a solution which we adapted into an open source design. This design mechanically changes the angle of the piezoelectric device we are using as a transducer while tracking its position at each pulse.

To facilitate easy replication of our probe we 3D printed all structural components and used commonly available hardware for the remaining components. To actuate the transducer we used a scotch-yoke mechanism that rotates an arm connected to the transducer. The transducer rotates about its central axis, creating a cone of vision from the head of the probe. The advantage of using the scotch-yoke is that it allows us to use a very simple motor that can

continually rotate without ever needing to change direction. This significantly improved the scan speeds of the probe as opposed to an earlier prototype which used a servo motor. Furthermore the precise angle of the transducer can be tracked with an encoder attached to the case of the probe. In addition to the scotch-yoke an important innovation was the creation of a flexible silicone buffer between the transducer and face of the probe which allowed for a consistent connection without the use of any lubricating fluid inside the case itself. The probe we built can be modified and improved by a larger community now and provides a base for the rest of the open source ultrasound project.

Keywords:

ultrasound, open source, mechanical probe

Impact of Radiofrequency Ablation Geometry on Electrical Conduction

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Supervising Faculty, Sponsor, Locations

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Abstract

The gold standard of current treatment for atrial fibrillation is radiofrequency ablation (RFA). Single RFA procedures have low single-procedure success rates, which can be attributed to factors including inability to measure and visualize lesion depth in real time and incomplete knowledge of how atrial fibrillation manifests and persists. One way to address this problem is to develop a heart model that accurately fits lesion dimensions and depth using OCT to extract structural information.

Seven lesions of varying transmuralities in left and right swine atrial tissue have been imaged with a Thorlabs OCT system with 6.5 micron axial resolution and a custom Ultra High Resolution system with 2.5 micron axial resolution. The boundaries of the ablation lesions were identified by the appearance of the birefringence artifact to identify areas of normal tissue and by decreased intensity contrast observed between the endocardium and myocardium within the ablation lesion.

Using these two features the lateral positions of the lesion boundaries were identified. An algorithm that fit

ellipses to the lesion contours modeled the ablation geometry. Lesion dimensions and shape were confirmed by comparison with trichrome histological processing. The mesh models were fitted with these parameters and refined with Continuity 6 software. Next steps include correlating lesion geometry to conduction velocity, and including tissue architecture (composition and fiber orientation). Additional models of linear lesions with gaps and lesions created with non-perpendicular contact will be created. This work will provide insight into how lesion geometry, tissue composition, and fiber organization impact electrophysiological propagation.

Key Words

Optical Coherence Tomography, Imaging, Cardio electrophysiology, Computational Modeling,

Investigating the mechanical environment of pregnancy using finite element models

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Preterm birth affects about 10% of pregnancies and is a major cause of neonatal mortality and morbidity, as well as a major cause of long-term morbidity. Despite the role of the cervix as the final barrier in birth, little is known about the physics behind its functions. The aim of this study was to apply engineering principles to understand the mechanics of the cervix within the protected environment of pregnancy. Ultrasound measurements of the uterus and cervix of women at low risk (n=2) and high risk (n=3) for preterm birth were inputted into a parameterized script to create a CAD model of the approximated physiological geometry. Intrauterine pressure was applied on the inner surface, and finite element analyses were performed. Despite widely varying maternal geometries, minor edits in the parameterized script allowed each step in the workflow to converge, and a final simulation was produced in which the tissue stretch could be easily visualized. The resulting models serve as a proof of concept that patient-specific finite element models of the uterus, cervix, fetal membranes, and surrounding tissues can be made using measurements obtained from ten to twenty minutes of ultrasound scans. Our method brings

us one step closer to our ultimate goal of creating a diagnostic tool for preterm birth as well as an ex vivo workspace to evaluate treatments.

Keywords

preterm birth, finite element model, cervix, biomechanics

Micropatterning of PDMS for Improved Adhesion of Acute Hippocampal Slices

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Traumatic brain injury (TBI) causes about 50,000 deaths and leaves 80,000 people disabled each year in the United States. The clinical situation greatly needs attention, as there are currently no drug treatments designed to address the underlying pathobiology of TBI. The Neurotrauma and Repair (NTAR) Lab studies the biomechanics of TBI and why brain cells die after such an injury using two different injury models: blast and stretch. In order to study the effects of stretch on brain tissue, the NTAR Laboratory cultures organotypic hippocampal brain slices on polydimethylsiloxane (PDMS) membranes and then places these in a stretch device for injury and observation. However, the stretch experienced by the substrate is often much greater than the stretch that is experienced by the hippocampal slices. There is previous data that cells adhere better to material with micropatterns and the NTAR Lab wanted to find out if tissues would experience a similar increase in adhesion if the PDMS membranes were micropatterned. Using a laser cutter we added micro grid patterns to the PDMS membranes and then used these membranes in the stretch device to see if the micropatterning improved tissue adhesion.

The preliminary findings suggest that micropatterning does improve tissue adhesion, however there is not enough data yet to make a concrete conclusion. We did see promising evidence of a much more biaxial stretch and a tissue stretch that follows the substrate stretch much more closely than hippocampal tissue cultured on non-patterned PDMS. Further experiments will involve investigating if there is a connection between the power setting of the laser cutter and an increased level of adhesion.

Keywords

tissue adhesion, organotypic hippocampal slices, polydimethylsiloxane (PDMS), traumatic brain injury, micropattern

Method for Flexible Imaging of *Drosophila* Embryos Using Microgel

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Currently, imaging *Drosophila* embryos in an angled or vertical position requires expensive and complicated equipment and therefore cannot be accomplished in most research laboratories. By using liquid-like pAAM/MMA microgels, we aimed to develop a simple and inexpensive method for researchers to obtain useful images of *Drosophila* development in different positions. In order to test the microgel's ability to support *Drosophila* embryos, we made three pAAM/MMA concentrations of microgel, 4%, 6%, and 10%. For imaging, embryos were glued within a Valap barrier on a coverslip and covered in microgel and a top coverslip. By taking photos and time-lapses on the stereoscope and confocal microscopes, we were able to observe how the embryos behaved in the microgel and note the differences between the multiple microgel concentrations.

We hypothesized that higher concentrations of microgel would be better at supporting the *Drosophila* embryos in place for longer periods of time. Additionally, we predicted that the microgel would not hinder the development of the embryos in the short-term, but it would not be able to support development into the larval or pupal stages.

We concluded that all microgels are capable of supporting embryos in place for varying lengths of time. Also, the higher the pAAM/MMA concentration, the thicker the microgel. Results from rheology testing indicated that the 4% concentration exhibited liquid-like properties and the 10% concentration solid-like properties. Regardless of concentration, the microgel is able to support embryo development until the larval stage. Microgel evaporation and lack of food in gel might be the cause of embryo/larvae death over long time periods. Based off of these conclusions, laboratories that use *Drosophila* embryos in their research now have an inexpensive and simple to use tool to image embryos in more complicated positions. Specifically, the microgels can be used for time-lapse imaging of vertically oriented *Drosophila* embryos to visualize development of head and tail regions that are difficult to view using traditional approaches.

Key Words

Drosophila, embryos, microgel, concentration, imaging

Resource Recovery in Source Separated Urine

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

Currently nutrients are currently produced in an unsustainable manner that uses finite resources and energy intensive methods. We generally use what resources are needed and then proceed to discard of them, which is extremely wasteful. This leads us to the thought of recycling these nutrients. A ready source of nutrients to be recycled is human urine. Currently most urine is diluted by over 100x once collected in restrooms. If urine was to be initially separate, the nutrients in the urine could then be recycled through direct contact membrane distillation. DCMD uses a temperature differential to transport certain substances through a membrane. Not only is DCMD highly effective but it also is highly autonomous so would be very simple to implement. The first step to this process was to research the previous systems designed to recycle nutrients from urine. After creating our own design that we felt would optimize performance, parts were ordered and it was assembled while research was compiled on synthetic urine recipes and membranes used in the system. Tests were done to analyze heat loss throughout the entire system and time lapsed to reach steady state.

Keywords

Direct contact membrane distillation (DCMD), source-separated, resource recovery

Integrated Stormwater Management

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

The city of South Bend, Indiana is one of many American communities with a combined sewer system (CSS). In such a system, industrial wastewater, stormwater, and raw sewage are all channeled through the same sewer main to be treated at the wastewater treatment plant. When a large rain event occurs, the CSS can be overwhelmed causing millions of gallons of this combined sewage to enter waterways and backup into citizens basements. Our team analyzed green infrastructure as a sustainable method to mitigate stormwater runoff and sewage overflows in South Bend. With a strong focus on improving human and environmental health, the team analyzed the performance of rain gardens and strategic placement to maximize their impact. First, the team monitored the eight engineered soil rain gardens installed in summer 2016 using soil moisture sensors to analyze how different soil types balance infiltration and storage of rainwater. The team first created simulated rain gardens in the lab to better understand water movement before installing sensors in the field. Data from field rain gardens was

then collected from simulated rain storms. Finally, a model was created using EmNet's smart sewer sensors, a company focused on integrating technology with water infrastructure, to visualize which rain events cause sewer backups. This will be used to inform placement of green infrastructure in the areas of highest concern.

Keywords

Green infrastructure, combined sewer system, combined sewer overflow, rain garden, engineered soil

Individualized Cortical Thickness Heatmaps for Improved Clinical Care in Neurodegenerative Disorders

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Supervising Faculty, Sponsor, Location of Research

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Abstract:

Neurodegenerative disorders are characterized by gradual atrophy in the brain, resulting in a decline in behavior, motor skills, and/or language. The disease progression often includes social impairments and difficulty with executive functioning, which necessitates capable caregivers. As part of treatment, patients are routinely given MRIs to assess brain condition. In clinic visits, it is often difficult to communicate to patients and their caregivers the results from MRI images due to their 3D nature and subtle differences to an untrained eye. Our objective was to develop a method to automatically render standardized images that would better communicate to patients their MRI results. We also aimed to offer caregivers and patients a better understanding of their disease progression and some explanation for symptoms. We developed a computer program that utilizes the open source visualization tool, Connectome Workbench, to display MRI values on a color scale. Using T1-weighted MRI scans from the Penn Frontotemporal Degeneration Center, cortical thickness measurements were calculated using Advanced Normalization Tools (ANTs). To provide patients and clinicians with understandable results, we

calculated z-scores of patients' cortical thickness values against healthy controls for every voxel in the MRI. Cortical thickness is an important biomarker that correlates with gray matter health and the number of neurons in the brain. The patient's z-scores, on a color scale were imposed onto a brain render such that significant brain atrophy could be easily visualized. Various disease phenotypes were tested and the resulting renders were visually powerful in identifying the characteristic areas of atrophy. Furthermore, the z-score heat maps could display disease progression and help evaluate prognosis. We hope to implement these individualized heatmaps for clinic use to improve MRI assessment for clinicians and understanding of the disorder for the patient and caregiver.

Keywords

frontotemporal degeneration, cortical thickness, patient care, z-scores,

Plasma Response to Driven Oscillations

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Supervising Faculty, Sponsor, Location of Research

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Abstract

Plasma makes up the entire visible universe and 99% of all ordinary matter in space. Plasma physics is a relatively new field which aims to study the interactions and properties of plasmas. One of the most significant goals of the field is the search for a clean and sustainable source of energy. Another is to further our understanding of the many astronomical bodies in space.

The Collisionless Terella Experiment (CTX) is a dipole-confined plasma experiment for investigating laboratory magnetospheric phenomena, specifically turbulence. This summer we were studying how launching oscillations into the plasma affects the frequencies in the plasma. In the CTX, the plasma is generated by Electron Cyclotron Resonance Heating (ECRH) and is confined by a mechanically supported electromagnet in a vacuum vessel. The plasma is investigated by a variety of diagnostics, including moveable, floating potential probes. These probes record the signals in a time domain. Using the Fourier Transform and Ensemble Averaging, these signals are converted into Power Spectra in the frequency domain. Using the power spectra recorded in the Spitzer terminal, I created various sets of graphs to observe and analyze the data we recorded from the probes.

From the density maps we realised that driven low frequency interchange modes result in multiple harmonics which weaken as they leave the actuators, going in the same direction as the electromagnetic drift. The vertical columns display the actual launched oscillations, whereas the diagonal lines represent the harmonics. We also observed when removing the background frequencies from the power spectra, that some of the values were negative. This usually occurred before large peaks, resulting in the possible explanation that energy is withdrawn from the surrounding plasma and into the surge. In the future, we plan to run the experiment again with a different range of driving frequencies.

Keywords

Collisionless Terella Experiment (CTX), dipole confinement, magnetosphere, turbulence

Engineering Bacterial Surface for Cancer Therapy

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Supervising Faculty, Sponsor, and Location of Research

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Abstract:

In vivo administration of bacteria has shown that bacteria selectively colonize the tumor necrotic core. Due to their selectivity for tumors, bacteria can be used as a natural platform for programmable delivery of therapeutics for cancer. However, the bacterial surface is highly immunogenic and can lead to septic shock when injected in large amounts into the human body. Since large amounts of bacteria is required in order to reach tumor site, bacterial cancer therapy is limited by its low tolerance. We studied the bacterial capsule and its role in reducing the immunogenicity of bacteria. We utilized two strains of bacteria, *E. coli K1* which is a virulent strain responsible for urinary tract infections, and *E. coli EV36*, a hybrid strain consisting of non-virulent *E. coli K12* with *E. coli K1* capsule, as our models of study. In order to make direct comparison between capsule vs non-capsule, we also knocked out the NeuC gene in *E. coli K1* and *E. coli EV36*, which is an important component of the biosynthetic pathway toward capsule production. Genetic deletion of capsule was confirmed through T7 phage assay in which T7 phage only lyses non-capsular bacteria. Intravenous injection of 10^6 bacteria into Balb C mice

reveals that capsular bacteria elicit a twofold lower TNF-alpha response compared to non-capsular bacteria, as well as more effectively limiting tumor growth. Further, capsular bacteria also survive longer in mouse serum in vitro, thus indicating effective immune system evasion. These preliminary findings indicate that coating bacteria with naturally produced capsule can effectively reduce the immunogenicity of bacteria, allowing for higher dosing tolerance for bacterial cancer therapy.

Keywords: synthetic biology, bacterial cancer therapy, bacterial capsule, immunogenicity

Characterizing the Mechanical Properties of Human Cervix Tissue using Indentation and Tension Tests

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Supervising Faculty, Sponsor, and Location of Research

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Abstract

During pregnancy, the human cervix must tolerate compressive and tensile forces created from the growing fetus. Alterations of cervical material properties that lead to premature cervix shortening are known to increase a woman's risk of preterm birth, the leading cause of death in newborns. Therefore, an understanding of the mechanical properties of the human cervix is vital to understanding and modeling the human cervix in pregnancy. Using samples from pregnant (PG) and non-pregnant (NG) patients, a spherical indentation method was first developed to characterize the compressive mechanical properties on the cervix as a whole. A displacement-controlled, multi-level ramp hold test was conducted. Tension tests were then conducted on the sample to gain a better understanding of the tensile mechanical properties of the cervix. Two rectangular slices of tissue were cut from the original sample on which to conduct tension tests. Digital image correlation was also used in indentation and tension tests to capture the real-time deformation data and create strain maps. Data from the Instron machine that indented and pulled the samples provided force and displacement data with

respect to time. The initial data gathered from these tests can be used to model compressive and tensile time-dependent behavior of the tissue. These models can fit material parameters to the data, allowing to compare differences in mechanical properties across multiple samples.

Keywords

reproductive biomechanics, human cervix, tension test, spherical indentation test, digital image correlation (DIC)

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