Boston University College of Engineering
Department of Biomedical Engineering

BME

25th Annual Senior Design Project Conference

Friday, April 30, 2010
Cover photo credits - clockwise starting at top-left:

Derek Lee, Vidhya Kumar, Jesse Szatkowski; Samantha Byrnes, Barrett Steinberg; Jeffrey Chagnon, Michael de Mello; Karen Go, Jill Wolfson, Elizabeth Zamora; Alexina Fredman, Alyssa Trigger
Welcome from the Chair

It is my distinct pleasure to welcome our guests, our alumni, the biomedical industry, our faculty and our students to Boston University’s 25th Annual Biomedical Engineering Senior Design Project Conference. This conference has been a hallmark of the BU BME undergraduate experience for 25 years, and culminates our year-long Senior Design Project Program. This program is recognized as a national model for providing the culminating independent design and communication experience for BME undergraduates, and helps us train the future leaders and innovators in bioengineering. Over the course of the day, our talented students will present their state-of-the-art design and research activities, as they complete their BS degrees from one of the top Biomedical Engineering programs.

Biomedical Engineering synthesizes engineering, computation, math and physical sciences with the life sciences to advance our understanding of biology and physiology. This understanding is then exploited to develop new devices and methods to improve medical care. The BU BME BS degree program is one of the oldest such programs in the country. We are also one of the largest BME Departments, with a faculty of 32 primary tenured and tenure-track professors and over 70 affiliated faculty members.

Our ABET accredited BS degree program in Biomedical Engineering is designed to provide integrated training in life, physical, and engineering sciences as preparation for a variety of careers in bioengineering, applied biotechnology, and medicine. We also offer an Industrial Internship Program that can place students in companies for up to a year.

Seniors must also engage their projects via a course called “Product Design, Development and Entrepreneurship in Biomedical Engineering” taught by members of our Industrial Advisory Board and faculty from the School of Management. The course teaches students concepts of design, intellectual property, patents, regulatory issues, marketing, and entrepreneurship, all in the context of their projects.

This year’s senior design project program was directed by Professor Irving Bigio. He invested much energy and organizational skills to sustain the level of excellence and impact for which this program is renowned. Professor Bigio was assisted by Professor Tom Szabo, who helped coordinate the design and entrepreneurship portions of the program. I also want to thank the team of BME faculty who read, graded and commented on all written assignments, proposal drafts, oral proposal defenses and progress reports. Their efforts helped ensure that the program continued to sustain its level of excellence. The assistance of Professors Jackson, Passaglia, Suki, Tien, Vajda and Zaman was invaluable. I also served as part of this team and was fortunate to enjoy the program in all of its dimensions. Our students are remarkable at rising to the challenge and I have no doubt that their presentations will impress and entertain you today. Enjoy!

Solomon R. Eisenberg, ScD
Professor and Chair, Department of Biomedical Engineering
Associate Dean, College of Engineering Undergraduate Programs
### 25th Annual Senior Project Conference

Friday, April 30, 2010

<table>
<thead>
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<th>Time</th>
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<tr>
<td>7:15 – 8:00 AM</td>
<td>Continental Breakfast</td>
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<tr>
<td>8:00 AM</td>
<td>Welcome and Opening Remarks: Professor Irving Bigio</td>
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</tbody>
</table>
| 8:10 – 10:10 AM | SESSION I  
PHO 206    | Small Things: Nanotechnology, Molecules and Cells                       |
| Session Chair: Professor Muhammad Zaman  |
| Cell Electrofusion  
Nicholas Casciani, Kristen Pamper  |
| Utilization of Bacterial Proteins to Manipulate Intracellular Transport and Apoptosis  
Samantha Byrnes, Barrett Steinberg  |
| Single Molecule Mapping of Transcription Factors Using Solid State Nanopores  
Neraj Bobra, Izzuddin Diwan  |
| A Microchip System for Cardiac Myocyte Contractile Studies  
Karen Go, Jill Wolfson, Elizabeth Zamora  |
| Development of SPR Detection Method for Small Molecule Binding to EGFR in Supported Lipid Bilayers  
Alexander Razon, Tony Tam  |
| Fibronectin Fiber Strain Gradient  
Edeliz Flores, Ana Lara Alvarez  |
| Universal Interface for the Bi-stable Genetic Toggle Switch  
Douglas Flood, Leah Lemont, Kieran Mace  |
| 10:10 – 10:25 AM | BREAK       |
10:25 – 12:25 PM SESSION IIa
PHO 206
Fooling Mother Nature: Tissue Engineering and Tissue Properties

Session Chair: Professor Joe Tien

Designing an Approach to Probe How Airway Smooth Muscle Plasticity Impacts Airway Responsiveness
Robert Nims, Elena Simoncini

Design of a Device for Mechanical Stimulation of a Tissue-Engineered Construct
Jasmin Imsirovic, Kim Vo

Bioprinting of Neural Tissue for FUS-mediated Neuromodulation
Shiori Ensako, Adra Long, Jessica So

Computational Design of Microvascular Networks for the Oxygenation of Engineered Tissue
Constantinos Katevatis, Matthew Lough

The Effect of Humeral and Scapular Positioning on Superior Labral Strain in Simulated Pitching
William Dow, Daniel Li, Stacey Stanton

Design of Instrumentation for Simulated ACL Environment
Atiya Mahmud, Sarah Murray, Karen Smith

Biomechanical Health of the Intervertebral Disc
Alexina Fredman, Alyssa Trigger

10:25 – 12:25 PM SESSION IIb
PHO 205
Can You Hear Me Now?: Hearing Research and Visual Research

Session Chair: Professor Herbert Voigt

Designing an EEG Experiment to Find the Neural Signature of Source Segregation
Nicholas Kurkji, Yu Jie Shui

The Analysis of the Effect of Jitter on Localization Ability of Normal Hearing Listeners with Simulated Cochlear Implants
Roman Bokhenik, Michael MacDonald, Mikhail Makalski

Hearing Aid Feedback Alarm System
Viral Doshi, Fahad Memon

The Behavior of Sensitivity and Response Bias in Auditory Masked-Detection Experiments within a Critical Band
Akash Sheth

Ultrasonic Travel Aid for the Visually Impaired
Thomas Hagedorn, Christopher Mattaboni

Tooth Phone: Design of an Audiodontic Hearing Aid
Dana Jaeger, Jared Saffie

Behavioral and Neural Correlates of Visual-Guided Navigation, Healthy Subjects and Stroke Patients
Benvy Caldwell, Balaji Goparaju, Megan Menard

12:25 – 1:05 PM LUNCH
### SESSION IIIa

**PHO 206 Seeing is Believing: Imaging Technologies and Imaging Agents**

**Session Chair: Professor Thomas Szabo**

- **Localized, Dynamic Measurements of Intracapillary Blood Pressure in Live Mice during Intravital Microscopy**
  *Felita Agus, Lawrence Yu*

- **Enhancement of Microscope Image Resolution through Dithering and Multi-frame Restoration**
  *Eugene Grigortsevich, Cheng Bin Zhang*

- **Micro-Engineered Multispectral MRI Contrast Agent**
  *Amr Aly, Maggie Cox, Rachel Horenstein*

- **Image-able Thermometer for Magnetic Resonance Imaging**
  *Brian Chan, Nicholas Labriola, Matthew Lawrence*

- **Cell Programming using Small Compound Libraries and High Throughput Imaging**
  *Scott Chappell, Leon Hulli*

- **Phantom Design for Diffusion Tensor (DT) MR Imaging**
  *Vidhya Kumar, Derek Lee, Jesse Szatkowski*

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### SESSION IIIb

**PHO 205 NUMB3RS: Computation, Simulation, Analysis, Sequencing**

**Session Chair: Professor Bela Suki**

- **3D Avatar for the Representation of Physiological Data**
  *Aneesh Acharya, Maisam Dadgar*

- **Personalized Genomic Medicine: Length Variation in Short-Tandem Repeats**
  *Evan Appleton, Prabhat Dhar*

- **Genomic Drug Response Signatures for Personalized Treatment of Cancer**
  *Courtney Conley, Emily Palmer*

- **DNA Sequence Analysis of Genes Associated with Schizophrenia**
  *Jason DeBoer, Heather Macken*

- **An In Silico Operon Model of M. tuberculosis Utilizing RNA-Seq Evidence**
  *Dmitri Boulanov, Nicholas Kaiser*
Development of Multiplexed, Label-Free Hepatitis Assay for Clinical Diagnostics
Leslie Baggesen, Chelsea Pereira

Design of a System for the Injection of Glucose-Sensitive Nanoparticles into Murine Skin
Jeffrey Chagnon, Michael de Mello

Design of a Portable Optical Reader for Measuring Fluorescence Signal from Nanoparticle Sensors for in vivo Glucose Monitoring
Andrew Keiser, Kevin Yu

A Dielectrophoresis-based Microfluidic Delivery System for Single Cell Trapping
Aleksander Jonca, Matthew Lee, Jeremy Levesque

Optical Characterization of Mechanical Properties of Ultrasound-Stimulated Biological Cells
Max Jativa, Doris Ling

Origami Microfluidics: A Novel Rapid-Prototyping Technique
Andrew Fisher, Charles Jahnke

Design and Manufacture of a Robust, Solar-Powered Pulse Oximeter
Max Condren, Matthew Fleming, Bryan Lublin

Portable, No-Power, Nucleic Acid Extraction Device
Francis Jareczek, Mark Mazochette, Sean Moser

5:20 PM Final Conference Comments: Professor Irving Bigio
25th Annual Senior Design Project Conference

Visiting Companies, Institutions and Laboratories
## Visiting Companies, Institutions and Laboratories

1. 3M Health Care  
   St. Paul, MN
2. 3Wave Optics  
   Boston, MA
3. Abiomed  
   Danvers, MA
4. Advanced Instruments  
   Norwood, MA
5. Angell Medical Center  
   Scituate, MA
6. ArQule, Inc.  
   Woburn, MA
7. Arrow International  
   Everett, MA
8. Aspect Medical Systems  
   Norwood, MA
9. Atrium Medical Corporation  
   Hudson, NH
10. BAMM Labs  
    Cambridge, MA
11. BD Medical  
    Waltham, MA
12. Beth Israel Deaconess Medical Center  
    Boston, MA
13. Biotrove, Inc.  
    Woburn, MA
14. Bolton Chiropractic  
    Bolton, MA
15. Boston Scientific  
    Natick, MA
16. Boston University Center for Nanoscience  
    Boston, MA
17. Boston University School of Medicine  
    Boston, MA
18. Brigham and Women’s Hospital  
    Boston, MA
19. Bruker Daltonics  
    Billerica, MA
20. Charles Stark Draper Laboratory  
    Cambridge, MA
21. Children's Hospital Boston  
    Boston, MA
22. CIMIT: Center for Integration of Medicine & Innovative Technology  
    Cambridge, MA
23. Cleveland Clinic  
    Cleveland, OH
24. Comprehensive Health Management, Inc.  
    Tampa, FL
25. Corning, Inc.  
    Corning, NY
26. Covidiene  
    Mansfield, MA
27. Davol, Inc.  
    Warwick, RI
28. Delsys, Inc.  
    Boston, MA
29. Essex Orthopaedics and Optima Sports Medicine  
    Andover, MA
30. Ethicon  
    Somerville, NJ
31. Fraunhofer USA  
    Brookline, MA
32. Gems Sensors- Controls  
    Plainville, CT
33. General Electric-Healthcare  
    Lawrence, MA
34. Genzyme Corporation  
    Cambridge, MA
35. Glemser Technologies  
    Woburn, MA
36. Harvard Medical School  
    Boston, MA
37. Harvard-MIT Division of Health Sciences and Technology  
    Cambridge, MA
38. Harvard School of Dental Medicine  
    Boston, MA
39. Harvard University  
    Cambridge, MA
40. Hologic  
    Marlborough, MA
41. Infoscitex  
    Waltham, MA
42. InfraReDx  
    Burlington, MA
43. Instrumentation Laboratory  
    Lexington, MA
44. Integra LifeSciences  
    Burlington, MA
45. I-Therapeutix  
    Waltham, MA
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<td>US Army Research Institute of Environmental Medicine</td>
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<td>Worcester Polytechnic Institute</td>
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25th Annual Senior Design Project Conference

Technical Advisors and Faculty Profiles
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<tr>
<td>Nicholas Casciani &amp; Kristen Pamper</td>
<td>Mario Cabodi, Selim Ünlü &amp; Orian Shirihai</td>
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<tr>
<td>Samantha Byrne &amp; Barrett Steinberg</td>
<td>Horacio Frydman &amp; Mark Grinstaff</td>
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<td>Neraj Bobra &amp; Izzuddin Diwan</td>
<td>Amit Meller</td>
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<td>Karen Go, Jill Wolfson &amp; Elizabeth Zamora</td>
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<td>Alexander Razon &amp; Tony Tam</td>
<td>Ragnhild Whitaker &amp; Joyce Wong</td>
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<td>Edeliz Flores &amp; Ana Lara Alvarez</td>
<td>Michael Smith</td>
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<td>Douglas Flood, Leah Lemont &amp; Kieran Mace</td>
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<td><strong>Session IIA</strong></td>
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<td>Robert Nims &amp; Elena Simoncini</td>
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<td>Jasmin Imsirovic &amp; Kim Vo</td>
<td>Bela Suki</td>
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<td>Shiori Ensako, Adra Long &amp; Jessica So</td>
<td>Seung-Schik Yoo</td>
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<td>Constantinatos Katevatis &amp; Matthew Lough</td>
<td>Joe Tien</td>
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<td>Martha Murray</td>
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<td>Alexina Fredman &amp; Alyssa Trigger</td>
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<tr>
<td>Nicholas Kurkjy &amp; Yu Jie Shui</td>
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<td>Roman Bokhenik, Michael MacDonald &amp; Mikhail Makalski</td>
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<td>Thomas Hagedorn &amp; Christopher Mattaboni</td>
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<td>Dana Jaeger &amp; Jared Saffie</td>
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<td>Felita Agus &amp; Lawrence Yu</td>
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<td>Vidhyaa Kumar, Derek Lee &amp; Jesse Szatkowski</td>
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<tr>
<td>Aneesh Acharya &amp; Maisam Dadgar</td>
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<td><strong>Session IV</strong></td>
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<td>Leslie Baggesen &amp; Chelsea Pereira</td>
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<td>Max Jativa &amp; Doris Ling</td>
<td>Irving Bigio</td>
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<td>Max Condren, Matthew Fleming &amp; Bryan Lublin</td>
<td>Muhammad Zaman</td>
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<td>Francis Jareczek, Mark Mazzochette &amp; Sean Moser</td>
<td>Catherine Klapperich</td>
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Primary Faculty

IRVING J. BIGIO
Professor, Biomedical Engineering, Electrical & Computer Engineering, Physics, Medicine Ph.D., Physics, University of Michigan
Research Interests: Medical applications of optics, lasers and spectroscopy; biomedical optics and biophotonics; biomolecular dynamics; applied spectroscopy, especially to biomedical problems; nonlinear optics, quantum electronics and laser

CHARLES R. CANTOR
Professor, Biomedical Engineering & Pharmacology AB, Chemistry, Columbia Univ, PhDBiophysical Chemistry, Univ of California, Berkeley LOA, CSO Sequenom
Research Interests: Human genome analysis; molecular genetics; new biophysical tools and methodologies; genetic engineering

H. STEVEN COLBURN
Professor, Associate Chair for Undergraduate Programs Biomedical Engineering, Director, Hearing Research Center S.B., S.M., Ph.D., Electrical Engineering, Massachusetts Institute of Technology
Research Interests: Measurement and modeling of binaural hearing performance. Modeling the activity of auditory brainstem neurons and measurement and modeling of spatial attributes of sound perception

JAMES J. COLLINS
Professor, Biomedical Engineering; University Professor, Co-Director, Center for BioDynamics, Investigator, Howard Hughes Medical Institute, A.B., Physics, College of the Holy Cross; Ph.D., Medical Engineering, University of Oxford
Research Interests: Synthetic biology; systems biology; engineered gene networks

EDWARD DAMIANO
Associate Professor, Biomedical Engineering Ph.D., Applied Mechanics, RPI; M.S., Mech Eng, Washington Univ; B.S., Biomedical Engineering, RPI
Research Interests: Integrated cellular and extracellular biomechanics; biofluid dynamics; microhemofluidics; microcirculation; vestibular biomechanics; non-Newtonian rheology; closed-loop blood-glucose regulation

CHARLES DELISI
Metcalf Professor, of Science and Engineering; Dean Emeritus, College of Engineering B.A., Physics, City College of New York, Ph.D., Physics, New York University
Research Interests: Developing and applying computational/mathematical methods, and high throughput experimental methods for inferring the structure and function of protein networks

CARLO J. DE LUCA
Professor, Biomedical Engineering & Neurology, Research Professor Electrical and Computer Engineering; Director, NMRC; BASc, U of British Columbia, MSc, U of New Brunswick, Ph.D., Queens University (Canada)
Research Interests: Motor control of normal and abnormal muscles; objective evaluation of muscle fatigue, objective assessment of functional activities in humans; biosignals

MICAH DEMBO
Professor, Biomedical Engineering B.S., Mathematics, Allegheny College, Ph.D., Biomathematics, Cornell University
Research Interests: Statistical mechanics in biological systems; cell information processing and signal transduction; thermodynamics and mechanics of cell adhesion; biophysics of cell deformation, active motility
SOLOMON EISENBERG  
Professor, Chair Biomedical Engineering; Professor, Electrical and Computer Engineering, Assoc Dean for Undergrad Programs, College of Engineering S.B., S.M., Sc.D., Electrical Engineering, MIT  
Research Interests: Electrically mediated phenomena in tissues and biopolymers; cartilage biomechanics; computational modeling of electric field distributions in the human thorax and heart during defibrillation; transcranial magnetic stimulation

MAXIM D. FRANK-KAMENETSKII  
Professor, Biomedical Engineering, M.Sc., Ph.D., Biophysics, Moscow Physical-Technical Institute, Sc.D. (IVth degree), Physical and Mathematical Sciences, Institute of Chemical  
Research Interests: DNA structures; DNA topology; DNA functioning, PNA (peptide nucleic acid)

MARK GRINSTAFF  
Professor, Biomedical Engineering & Chemistry Ph.D., University of Illinois at Urbana-Champaign; A.B., Chemistry Honors, Occidental College  
Research Interests: Biomaterials, tissue engineering, drug delivery, macromolecular chemistry and engineering, self-assembly, nanodevices

SIMON KASIF  
Professor, Biomedical Engineering B.Sc., Mathematics, Tel Aviv University; M.S. & PhD, Computer Science, University of Maryland  
Research Interests: Bioinformatics, Computational Genomics, Algorithm Design, Artificial Intelligence, High Performance Systems

EVAN EVANS  
Professor, Biomedical Engineering  
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SESSION I

Small Things: Nanotechnology, Molecules and Cells
Cell Electrofusion

Nicholas Casciani, Kristen Pamper

Diabetes is a chronic disease that is characterized by the inability of insulin-producing β-cells in the human pancreas to maintain homeostatic blood glucose levels. Recently, a new hypothesis has been proposed, which correlates mitochondrial activity within the β-cells directly to their insulin producing capabilities. With the ultimate goal of introducing mitochondria into INS-1 cells (a clone of insulin producing β-cells), an experiment was designed to fuse individual cells using an electric stimulus. Two main components comprised the majority of the project: patterning INS-1 cells in a specific manner and developing an electrofusion apparatus and protocol. The goal of the patterning segment of the project was to obtain electrically conductive adhesive regions to which individual cells bind. A gold substrate was used as the conductive material and was patterned by standard photolithography and etching procedures. The pattern consisted of a conductive grid which would deliver the pulse stimulus to each adhesive island located at grid intersections. The conductive nature of the gold substrate allowed each island to serve both as an electrode and a cell adhesive region, while the grid ensured uniform electric field across all islands. A non-fouling polymeric coating outside the gold pattern ensured that cells would only adhere in pre-determined areas. The electrofusion apparatus consisted of two of these gold chips positioned with electrically conductive surfaces facing one another. The chips were separated by a metal tape that served as the electrical contact with the pulse generator which delivered the electrofusion stimulus. Combining the successfully demonstrated patterning and electrofusion procedures produces a tool that can be used for a range of applications in which specific cell fusion is required.
Utilization of Bacterial Proteins to Manipulate Intracellular Transport and Apoptosis

Samantha Byrnes, Barrett Steinberg

Intracellular transport and apoptosis are two vital biological processes that control movement of raw materials and provide healthy cellular renewal. The bacteria *Wolbachia* are endosymbiotic to most arthropods and have recently become a prominent tool in combating tropical diseases such as filariasis and malaria, but also have strain-specific effects on apoptosis, intracellular transport, fecundity, and other characteristics of its host that correlate to specific homologs of *Wolbachia surface protein* (*wsp*). Despite the evidence for *wsp* affecting host processes and characterizing *Wolbachia* strains, its molecular role has not been confirmed. Using the Gateway and PhiC31 expression systems, our study is expressing *wsp* independently of *Wolbachia* in *Drosophila* cell lines and within transgenic flies *in vivo* to isolate and study its effects. By designing separate homologs of *wsp* with added fluorescent tags and evaluating their effects in host cells, we are testing the effects and localization patterns of each *wsp*. To manipulate bacterial levels and evaluate their effects, a novel antimicrobial agent has been developed that facilitates selective and quantitative bacterial killing while remaining non-cytotoxic to normal, healthy cells. *Wolbachia* levels were manipulated by an ionic liquid-based antimicrobial agent designed using click chemistry. Following two weeks of antibiotic exposure, the host DNA was analyzed through PCR to test for the presence of *wsp*. At concentrations of 0.15 mg/mL and above, the flies died before the end of the experiment, and at concentrations below the flies survived and levels of *wsp* were reduced. The new antimicrobial agent provides selective killing of *Wolbachia* without harming the hosts, and at concentrations below the minimum bactericidal concentration (MBC) of 0.12 mg/mL, specific levels of bacteria can be achieved. By controlling *Wolbachia* levels and expressing *wsp* in the host, our work hopes to confirm the role of live *Wolbachia* and both wMel and wMau07 homologs of *wsp* in significantly lowering rates of apoptosis. Additionally, we hope to confirm the effects on similarly associated intracellular localizations within host cells to the respective *Wolbachia* strain. These effects should be noted both in germline cells *in vivo* and *in vitro* *Drosophila* cell lines. The knowledge of the role of *wsp* and *Wolbachia* as well as the ability to control infection may directly benefit treatment of tropical diseases such as malaria and filariasis as well as identify a platform for potential intracellular delivery mechanisms or apoptotic controls.
Transcription factors (TFs) are required to initiate RNA synthesis in eukaryotic cells. It is a central problem in biology to decipher the locations, affinities and binding motifs of TFs. Current in vitro methods to detect DNA-TF complexes involve laborious sample amplification and labeling. The solid state nanopore is an emerging label-free, single molecule technique to investigate DNA structure and DNA-protein interactions. In this study, we extend the utility of nanopores to probe the DNA-TF binding interaction. Specifically, the DNA sample is a PCR amplified 960 base pair human genomic DNA fragment, and the TF is Early Growth Response Protein I (EGR1) expressed and purified from E. Coli. The binding activity of EGR1 is verified using a standard Electrophoretic Mobility Shift Assay. Nanopore translocation experiments are carried out for both free DNA and the DNA-EGR1 complex. We expect to show significant change in current blockage and translocation time for the DNA-EGR1 complex as compared to free DNA, where the change can be understood in the context of protein size, its net charge, and interactions with the nanopore. This study demonstrates the feasibility of label-free electronic recognition and characterization of DNA-TF binding complexes at the single molecule level.
Detection of cardiomyocyte cell contractility has become a necessary technique in the process for developing drugs that can treat cardiac myocyte cell abnormalities. Specifically, hypertrophic myopathy is the thickening of heart muscle, which directly corresponds to cardiomyocyte contractility. As this medical condition presently affects 1 out of every 500 Americans, the need to quantify cell contractions has increased. This project addressed this necessity through the design, development, and use of a biocompatible polymeric microchip made of polydimethylsiloxane, as well as image analysis through a MATLAB algorithm—which provides preparation for any experimental tests completed on cell cultures. Through Computer-Aided Design Solidworks, and photolithography and soft lithography techniques, the biocompatible microchip that is capable of quantifying cell contractility was designed and developed. Image analysis through MATLAB programming allowed for the quantization of displacements of micropillar arrays embedded within the chip, which directly correlates to the contractility of single cells. Experimentation with mice cardiomyocytes proved this technique to be valid, as the displacement of cell cultures on the microchip was successfully quantified. The image analysis algorithm showed the direction and region of greater cellular contractility forces. Thus, this technique can be used to detect cardiac myocyte cell contractility for the purpose of better understanding cardiac hypertrophy and other medical conditions. Learning more about hypertrophic myopathy and other illnesses can lead to pharmaceutical development and can provide solutions to the thousands of Americans affected by these conditions.
Development of SPR Detection Method for Small Molecule Binding to EGFR in Supported Lipid Bilayers

Alexander Razon, Tony Tam

Epithelial growth factor receptors (EGFR) are transmembrane proteins that are involved with the reproduction and apoptosis of cells. While irregular activation of EGFR receptors is present in cancer, antibodies that are specific to these receptors have been used therapeutically to inhibit receptor function. In order to identify both antibodies and small molecule ligands, a highly sensitive device that can detect ligand-receptor interactions is of great importance. We propose a sensing device that employs receptors embedded in a supported lipid bilayer (SLB) where potential EGFR ligands are presented to the receptors in a flow channel. Static receptor binding and binding under flow can then be probed using different detection methods as described below. By incorporating the receptors into a SLB, they retain their native conformation and will be compatible with surface plasmon resonance (SPR). SPR can detect the small changes that occur in ligand-receptor interactions, enabling the identification of EGFR ligands with high sensitivity. Parallel lanes of planar SLBs that mimic the surface of natural bilayers are created via vesicle fusion in microfluidic PDMS channels produced using soft lithography. Developing a means to safely transport these ligands in vivo is also important and the proposed method involves attaching the ligands to iron-oxide nanoparticles coated with poly(ethylene glycol) (PEG). PEGylated iron-oxide nanoparticles are favorable in that they are useful carriers, FDA approved, and excellent contrast agents in magnetic resonance imaging (MRI). Binding between monoclonal antibodies and EGFR was simulated using NeutrAvidin and biotin. The high affinity and selectivity of the NeutrAvidin-biotin complex was employed as a proof of concept for molecular binding interactions, such as those presented amongst small molecules and EGFR. An optimum configuration will be found that will maximize the amount of NeutrAvidin on the surface of the nanoparticles by varying the distribution of different PEG types (2000 Da and 3500 Da). PEG 2000 will serve as a support layer for bifunctionalized PEG 3500 with COOH ends. PEG 3500 will hold the proteins of interest and it is expected that the use of an EDC-NHS coupling mechanism will conjugate PEG 3500 with NeutrAvidin. EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) and NHS (N-Hydroxysuccinimide) are used together to form covalent linkages between the carboxylic acid terminated PEGs and proteins that have primary amines. Furthermore, results should indicate that the incorporation of NeutrAvidin onto PEGylated iron-oxide nanoparticles will facilitate binding with biotinylated SLBs. The proposed method will allow for the identification of EGFR inhibitors with high sensitivity. The procedure also provides a novel means of studying molecular interactions for a wide range of ligands and receptors via fluorescence spectroscopy, MRI, and SPR.
The extracellular matrix (ECM) controls vital cell functions by providing cells with structural support, influencing cell differentiation and therefore contributing to a tissue's overall functionality. More specifically, mechanical properties of the ECM, such as strain, act as a mechanical signal to control cell behavior. Cell response to strain has been studied over multiple substrates and it is known that cells move towards regions of increased stiffness, a concept known as durotaxis, but has yet to be understood over the extracellular matrix protein fibronectin (Fn). Studies have shown that Fn fibers form gradients in stiffness along their length when the fibers are stretched. The knowledge that fibronectin can strain harden and cells move up a stiffness gradient leads to the investigation of cell response to gradients of stiffness across fibronectin. Cell response was quantified as two forms of measurements: cell movement, and cell proliferation. Fibronectin can adopt the strain gradient of a polydimethylsiloxane (PDMS) substrate after fiber deposition. Therefore, to observe optimal results, the strain gradient across a PDMS substrate was maximized by analyzing the stress-strain curves across substrates of different shapes. Once a desirable shape was determined, fibronectin fibers were deposited. A strain device was designed to accommodate cells for durotaxis analysis and cell culturing. Cell movement was observed through time lapse microscopy and cell proliferation was assessed using a Bromodeoxyuridine (BrdU) incorporation assay. Further investigation is expected to show cell movement towards regions of higher stiffness on a single fibronectin fiber. Additionally, a confluent line of cells on a single fiber is expected to show a heterogeneous pattern of cell proliferation, with proliferating cells often attached to the stiffest region of the fiber. These experiments will verify the contribution of durotaxis onto cell response and provide insight into the mechanisms of cell behavior.
Universal Interface for the Bi-Stable Genetic Toggle Switch

Douglas Flood, Leah Lemont, Kieran Mace

The genetic toggle switch is a bi-stable gene network consisting of two mutually repressing proteins that can be "flipped" between stable states by the addition of inducers that target these proteins. The sharp switching threshold of the toggle switch could be of great utility in medicine, wherein the switch could respond to increased levels of molecules involved in pathologic processes. This ability could also be useful in biosensing or bioremediation applications. Each of the two current designs is sensitive to an inducer pair: isopropyl-β-thiogalactopyranoside (IPTG) and heat, or IPTG and anhydrotetracycline (aTc). The objective of this project was to construct a universal interface for the genetic toggle switch that confers sensitivity to a greater range of biological signals. This was achieved through the construction of a sensor plasmid into which a promoter sensitive to a desired biological signal can be inserted easily. When placed upstream of a duplicate copy of a toggle switch repressor gene, an activated sensor promoter will cause expression of that particular toggle gene and "flip" the switch located on another plasmid. As proof of concept, four inducible promoters (sensitive to zinc, copper, arsenic, or reactive oxygen species (ROS)) were selected and cloned into four sensor plasmids. Addition of the corresponding inducer should change the toggle state, which can be verified by flow cytometry measurements. A successful result would indicate that the utility of the genetic toggle switch can be expanded to a broad range of relevant signals, and this would represent one step towards a "plug-and-play" interface that couples the switch to virtually any natural or synthetic signaling pathway.
SESSION IIa
Fooling Mother Nature: Tissue Engineering and Tissue Properties
Excessive constriction of the lung’s airways, a hallmark of asthma, is a defect attributed to the surrounding airway smooth muscle (ASM). However, the exact origin of airway hyperresponsiveness (AHR) remains unknown. One theory is length adaptation, a smooth muscle property by which a muscle can adapt to produce maximal isometric force at a smaller length. This increases the ASM's functional range and may lead to AHR via a positive-feedback cycle of shortening and adaptation. The mechanical changes which occur during length adaptation, specifically the effect of stiffness on the passive and active ASM forces, remain unclear. The aim of this project was to investigate ASM's mechanical properties before, during, and after the length adaptation process. Bovine tracheal ASM strips were dissected, mounted in a tissue bath, and connected to a computer-controlled length-force transducer. The ASM was contracted isometrically with acetylcholine (ACh) at two lengths: its initial resting length ($L_{\text{ref}}$) and $2L_{\text{ref}}$. Small amplitude, high frequency length oscillations were used to measure stiffness over the contraction time course. To examine the muscle’s ability to contract, the shortening velocity was measured by switching to isotonic control after the plateau in active isometric force. Slow ramps in length were delivered to measure the full quasi-static stress-strain curves before and during contraction. To adapt the ASM to $2L_{\text{ref}}$, the ASM was held at this new length for 60 minutes and stimulated every 5 minutes with electric field stimulation (EFS). To partition the roles of active force generation via actin-myosin interactions from active ASM stiffness, a mechanical model of the ASM strips was proposed. Our results show that the length adaptation process cannot be solely attributed to alterations of the actin-myosin crossbridges as has been previously proposed. While a length adapted muscle can generate maximal isometric force, it has been shown that changes in stiffness prevent the conditions necessary for AHR and would therefore maintain viable airway conditions. Furthermore, shifts in both the passive and active force measured using a ramping length, illustrated and better explained the length adaptive changes of the ASM mechanical properties via the reference and adaptive stress-strain curves of the muscle. Therefore, despite the cytoskeleton and extracellular structures of muscle tissue strips often being regarded as static and passive, their dynamic characteristics and restructuring, induced either mechanically or chemically, is an essential factor in the mechanics of both passive and stimulated biological tissues and which must be considered in future studies on length adaptation.
Design of a Device for Mechanical Stimulation of a Tissue-Engineered Construct

Jasmin Imsirovic, Kim Vo

Biological tissues, such as those found in the lungs, vasculature and the muscular system, are under constant mechanical stimulation in vivo. In cases of disease, such tissues can become damaged with altered mechanical and physiological properties and eventually lose their functionality. Tissue engineering attempts to cure these diseases by replacing damaged tissues with constructs grown in the laboratory. Replacement constructs, however, are generally not submitted to the same mechanical environment as live tissue until they are implanted into the body; thus the grown constructs can become nonfunctional tissues. Therefore, the goal of this project was to design, manufacture and test a multi-well tissue stretching system capable of growing tissues under specific mechanical conditions. The design criteria for the device required a six well design in order to decrease the number of individual experiments. Furthermore, the system had to be small and noncorrosive so as to fit into a cell culture incubator, providing the appropriate temperature, humidity and CO₂ concentration. Finally, the system had to be able to run continuously for an extended period so as to provide the appropriate time scale for growing tissues. Such a system has been designed, constructed, tested and installed into an incubator. The system consists of a mechanical stretcher remotely actuated by a linear actuator via a hydraulic mechanism. An interface to control the linear actuator was also developed, which allows the user to input stretching parameters such as stretching duration, mean and amplitude of strain, and frequency. To test the system, tissue constructs (Gelfoam) seeded with neonatal rat lung fibroblast cells were stretched continuously for multiple hours. Following stretching, real-time polymerase chain reaction (RT-PCR) analysis will be used to determine the relative effects of mechanical stimulation on the regulation of collagen and elastin in the constructs. Following validation, the device can be a valuable research tool that can be used to mechanically stimulate tissues and tissue constructs for extended periods of time.
Bioprinting of Neural Tissue for FUS-mediated Neuromodulation

Shiori Ensako, Adra Long, Jessica So

Neurological disorders are mainly treated with invasive or non-localized methods. Focused ultrasound has recently become a major research field as a possible non-invasive method to treating neurological disorders. To understand its possible roles, a safety profile must first be created to ensure its safe use during sonication. This project aimed to understand the effects of low frequency low intensity focused ultrasound use on artificial neural tissue. The task was undertaken by first calibrating the transducers. 3D bio-printing of neural cells was then done to create multiple tissue constructs. Ultimately, the constructs were tested within a designed experimental apparatus using different frequencies and voltages of focused ultrasound. Results showed a variable sonication region between 4-7 mm^3. Viability of the tissue constructs were then tested using fluorescence staining techniques. We hope to show cell growth occurring at voltages ranging between 300 to 1000 mV as well as frequencies between 350 to 650 kHz. This project also aims to demonstrate that values above the aforementioned ranges can result in cell death, while values below did not significantly alter cell viability in the neural tissue. We will then be able to conclude that focused ultrasound is a safe alternative to invasive methods, and has a high potential for use in treatment once further testing is done. Furthermore, artificial neural tissue can be an efficient method to quickly obtain safety profiles, and therefore may have further use in other experimental settings.
Engineered tissues currently lack a vascular network to adequately perfuse minerals and compounds necessary for the cells to survive. Adding an efficient vascular network can increase the success rate of engineered tissues by increasing the perfusion of vital compounds, particularly oxygen. Currently, there is little computational research being conducted analyzing the relationship between vascular network geometry and oxygenation efficiency. The overall objective of this project was to study the effects different geometries of vascular networks have on the oxygenation of cells in a two centimeter cube of tissue. The ultimate goal was to design a microvascular network that limits hypoxic tissue and occupies a small percentage of the modeled cube. This was accomplished solely through computational methods using finite element analysis, which aided with the creation and analysis of the designs. Vascular geometries were created and solved using diffusion and convection principles in the Comsol Multiphysics software. Initial designs incorporated a constant concentration of oxygen on the outer wall of the vessels and only diffusion within the tissue domain. This simplification showed that increasing vessel size increased oxygenation of the surrounding tissue, but reduced the amount of existing tissue available for oxygenation. Convection and diffusion were then added to the vessel space for the remainder of the project with a constant oxygen flux at the inlet. The added complexity resulted in a finite range of radii with peak oxygenated efficiency. Navier-Stokes principles were used to solve for the velocity profiles within the vessels to solve the convection principles. Oxygenation efficiency for the vascular designs was determined using the percent of tissue with an oxygen concentration greater than zero. Geometries were optimized in an attempt to oxygenate at least 90% of modeled tissue. These geometries can be used as the framework for future research to construct microvascular networks to sustain in vitro engineered tissue.
Superior Labrum Anterior to Posterior (SLAP) lesions are a significant threat to overhead throwing athletes. Major League Baseball (MLB) pitchers are susceptible to SLAP lesions during the late cocking phase of pitching. A pitcher suffering from a SLAP lesion can spend eight months in recovery, and is unlikely to return to the optimum performance of the player prior to injury. This study investigated the strains experienced by the rotator cuff, the capsule, and the labrum in normal, replicated SLAP lesion, and repaired cadaveric shoulders. The testing apparatus was programmed to move a cadaveric torso through both the pitching motion and normal shoulder motion, defined as raising the arm from waist to the overhead position in the sagittal, coronal, and scapular planes. Strain was measured using strain gages implanted into the muscles, and motion was measured using motion-capturing cameras. Strain gages were placed in the rotator cuff during the pitching motion. Following testing, the rotator cuff was removed and the strain gages were placed in the capsule. After testing with strain gages in the capsule, the capsule was removed and testing was completed with the strain gages in the labrum. To measure the motion, bone-in markers were placed on the scapula, elbow, wrist, and shoulder joints. The movement experienced by these markers was recorded using the motion-capturing cameras. The data was collected for both the pitching motion and normal shoulder motion. Analysis of this data provided a further understanding of the effects of humeral and scapular positioning on the glenohumeral joint, specifically looking at the scapula-thoracic, glenohumeral, and clavicular motion.
The orthopedic community needs an effective method for generating viable Anterior Cruciate Ligament (ACL) tissue once it has been torn. Collagen serves as the dense connective tissue between individual ACL cells that ultimately organizes them into ligaments and supports their capacity to sustain load. Research has proven that fibroblast cells respond to mechanical stimulation by increasing collagen production, resulting in stronger ligament tissue. The objective of this project is to design an apparatus that would subject fibroblast hydrogels to strain rates similar to those of the knee, thereby optimizing the ligament’s capacity to promote mechanically stable ACL tissue. Using a design generated in Solid Works, a cell-stretching device was manufactured of medical grade Teflon. The device consists of eight wells, which hold and stabilize hydrogels composed of bovine ACL tissue and platelet-collagen rich slurry. Tissue samples were allowed to proliferate in an incubator over a 72-hour period so as to generate a sample size sufficient enough to undergo mechanical testing. During this time, tensile stresses were applied to the scaffold using a micro linear actuator at strain rates of 3%, 4% and 5% of their original length at a frequency of 1Hz. Once the gels had undergone cyclic strain, they were individually loaded onto an Instron machine to determine their yield and maximum strengths. The information from this project will be useful for rehabilitation methods in clinical applications with ACL scaffolds. Furthermore, it is believed that this enhanced functionality will reduce the incidence of osteoarthritis and ACL implantation failure seen throughout the orthopedic community.
Biomechanical Health of the Intervertebral Disc

Alexina Fredman, Alyssa Trigger

Healthy intervertebral discs facilitate uniform load transfer across adjacent vertebrae, whereas degenerate discs can cause pathological load transfer and may predispose other spinal structures to injury, including vertebral fracture. Thus, the biomechanics of vertebral fracture cannot be completely understood without investigating the correlation between the biomechanical health of the intervertebral disc and the mechanisms of vertebral failure. This project aimed to quantify biochemical and morphological indices of intervertebral disc health, and to correlate these indices with failure mechanisms in the surrounding vertebrae. Ten human spinal motion segments, each consisting of the T12-L1 disc, L1 vertebra, and L1-L2 disc, were imaged using quantitative computed tomography (QCT) and micro-computed tomography (µCT) and were loaded in axial compression in a stepwise fashion until failure. Custom image analysis algorithms were developed to determine average and regional bone mineral density (BMD) and intervertebral disc height from QCT and µCT images, respectively. Glycosaminoglycan (GAG) and collagen content, two known biochemical indicators of disc health, were regionally quantified using biochemical assays. Hexabrix™, an anionic image contrast agent, was employed during µCT scanning in a novel, minimally invasive approach for estimating GAG content in the disc. Statistical analyses will include validating µCT-Hexabrix™ derived GAG content with biochemical assay results, in addition to determining relationships between disc health and biomechanical characteristics in the vertebra using regression models. Preliminary results indicate that disc height in the posterior region is significantly lower than the anterior region (p = 0.00019), suggesting uneven load distribution with higher loads on the posterior side. In addition, the data suggest an inverse relationship between regional disc height and regional BMD: for discs in which a difference exists between the anterior and posterior disc heights, the aspect (anterior or posterior) with lower disc height has a higher BMD (p = 0.0019). This study suggests that regional evaluations of the heterogeneous composition and structure of the intervertebral disc can be used to ascertain the loading patterns of the adjacent vertebra, and aid in predicting failure regions.
SESSION IIb
Can You Hear Me Now?:
Hearing Research and
Visual Research
In a highly complex acoustic environment (i.e. when sounds are emitted and mixed from multiple sound sources), individuals with impaired hearing often cannot extract one source from the background cacophony, even if they wear hearing aids. This “Cocktail Party Problem” limits the ability of individuals with hearing loss to socialize in crowded settings. The project examined this problem with an emphasis on the question: will an electroencephalogram (EEG, which measures brain activity by reading voltages from the scalp) reflect how the brain groups sounds in individuals with normal hearing? This research consisted of two tasks. First, psychophysical experiments were conducted to determine the stimulus parameters (tone length and interaural time difference or ITD) that would elicit the strongest behavioral response. Second, upon discovering the appropriate stimulus parameters, an EEG experiment was designed and developed to quantify the neural correlates of perceptual organization. To complete the first task, a software program was written to achieve the following goals: to design four stimulus conditions (high frequency alone, high with low frequency interference, streaming, and noise) in which sensitivity to small changes in the ITD of a high frequency component was altered by competing sound elements; to collect subject responses from an objective 4-interval, 4-alternative, forced choice experiment; and to calculate and present the statistics from the collected data. The key findings from the first task showed that sensitivity to the high-frequency ITD depended on how the sound mixture was perceptually organized by the brain. In particular, performance was good when the high frequency was presented alone, bad when there was a low-frequency interferer, good for a “streaming” stimulus in which the low frequency interferer was perceived as part of an ongoing sequence of low tone, and bad when noise was presented before the low-frequency interferer (ruling out adaptation as a mechanism explaining the “streaming” result). For the second task, the Tucker-Davis Technologies RP2.1 system, its corresponding visual design studio, and MATLAB were used to implement precisely timed sound production, which is crucial to the analysis of EEG recordings. The stimuli created were based on those used in the psychophysical testing. The EEG experiment was designed to make use of the mismatch negativity (MMN), a neural response that is elicited by unexpected “deviant” sounds. Here, the deviant sounds were high-frequency sounds with ITDs different from those in ongoing presentations. The experiment was designed to show that deviant sounds elicited smaller MMNs in those conditions where perceptual sensitivity to changes in ITD is low. Overall, the project developed a standard procedure for recording and analyzing the neural activity linked to perceptual organization of sound. In the future, this work will be extended to testing of hearing impaired listeners. It is expected that such efforts will lead to an improved understanding of hearing loss and guide the development of the next generation of assistive listening devices.
The Analysis of the Effect of Jitter on Localization Ability of Normal Hearing Listeners with Simulated Cochlear Implants

Roman Bokhenik, Michael MacDonald, Mikhail Makalski

To improve the quality of life for the profoundly deaf, cochlear implants are used to bypass the normal hearing periphery by electrically stimulating the auditory nerve, thus restoring a measure of hearing. The most important function of a cochlear implant is to provide some level of speech recognition for the implant user. Binaural cochlear implant users are not as capable as normal hearing listeners at identifying the location of a sound source in the horizontal plane, resulting in decreased speech recognition. Central to improving the performance is the encoding and presentation of the electrical stimuli. We will report a study that determines the improvement of localization ability when a synchronous binaural jitter is introduced, focusing specifically on Interaural Time Difference detection at various frequencies. Previous models for Binaural Cochlear Implant simulations were modified to fit the specifications of the experiment, which allows normal hearing listeners to be tested as cochlear implant users. The simulation utilizes models of known physiological effects to closely represent the electrical response to impulses from Binaural Cochlear Implants. The success of this research could lead to improved localization abilities for Binaural Cochlear Implant users through modification of sound information presentation.
Hearing Aid Feedback Alarm System

Viral Doshi, Fahad Memon

Hearing aids enter feedback – oscillation mode when the signal from the speaker is picked up by the microphone and is re-amplified. The feedback oscillation typically occurs within the frequency range of 2 – 5 kHz. Most hearing aid users are hearing impaired in this frequency range and are not able to determine when their aid is in feedback mode, which leads to disturbances for normal-hearing listeners in the vicinity. The goal of this project was to design an external device which serves to notify the user when their hearing aid is in feedback mode using simple L.E.D lights. This device included a band pass filter that allowed frequencies within a narrow bandwidth to pass through. Once the signal passed through the filter, its Fast Fourier Transform (FFT) was calculated. A programming algorithm was used to code for the band-pass filter and the comparator. Through digital signal processing, the code was transferred into the external device. The algorithm compared FFT of the signal to the FFT of a stored template. If the signal was found to be at least 80% correlated with the template, the signal passed through the logic gate and lit up the L.E.D notifying the user that the aid was in feedback mode. The correlation of the two signals was determined by the magnitude of the two FFT's and the distance between the highest peaks of the two FFT's. The frequency range of the feedback differed among the available hearing aid models tested; therefore, it was determined that the user should record a template using their own hearing aid for comparison to avoid false notifications. This device was capable of determining the functional bandwidth after calculating the frequency of the feedback signal. It was able to detect feedback in different surroundings with varying ambient loudness equivalent to that found in a café or a symphony hall when kept at a distance of less than 30 cm from the aid. In the future, this type of technology can be wirelessly extended to devices such as cell phones or watches to notify users of feedback.
The Behavior of Sensitivity and Response Bias in Auditory Masked-Detection Experiments Within a Critical Band

Akash Sheth

The auditory system filters sound using psycho-acoustical means, a concept originating from an effect known as the “cocktail party effect.” In a 2005 study, the cocktail party effect was observed when modeling sensitivity in noisy environments. However, the response bias failed to fit the proposed energy detector model. In the proposed study, a similar model was proposed that was not only dependent on roving frequency within a critical band and signal level. Human subjects determined if a target sound of 1 kHz was present in noise ranging from 0.8 - 1.25 kHz. From this auditory detection experiment, the sensitivity was calculated using the sensitivity index, and the response bias was calculated using the Likelihood Ratio Test derived from Bayes’ Risk Rule by determining the criterion and calculating a z-score. For the conference it will be reported if the data acquired was similar to that of the aforementioned 2005 study, thereby validating the data acquired and allowing for further comparison between the data in the 2005 study and the data of the current study. It will also be presented at the conference if the three proposed models, the Roex model, the GammaTone model, and the Auditory Nerve Firing model correctly predicted the sensitivity and response bias trends in the data.
Visual impairment poses a potentially crippling challenge to those afflicted, with effects that threaten both personal and economic independence. Despite effort and creating electronic travel aids to help with navigation problems, these products have faced widespread problems of cost and efficacy that have hindered widespread adoption. The aim of this project was to create a robust and affordable travel aid for the visually impaired which would allow users to effectively explore their environment. This was accomplished using an analogue circuit to create precisely timed ultrasonic clicks whose echoes are collected and demodulated via analogue multiplication to serve as cues for investigation of one’s surroundings. The circuit was implemented on a printed board and a head mounted signal emitter and receiver were designed and manufactured. These were subsequently used in a series of human trials to evaluate the potential for use as a navigational tool among the blind and visually impaired. It is expected that subjects will be able to independently develop strategies such that they are able to reliably detect obstructions at a distance of several meters and navigate through spaces with minimal difficulty. Subjects are also hoped to show an ability to discriminate between objects, though likely not with the same reliability with which they could detect them, and observation of successful methods will be adapted into a set of user strategies to help with training of new users. Given subject performance it is hoped that the designed product will show promise as a potential complement to the more traditional long cane for use by the blind and visually impaired.
Otosclerosis is a disease which causes the ossicular bones of the human ear to fuse into one immovable mass. This bone rigidity, which affects approximately 10% of the Caucasian adult population, prevents sound transmission to the inner ear via air conduction, rendering air conduction hearing aids useless. Bone Anchored Hearing Aids (BAHAs) use bone conduction to stimulate the cochlea; however, they require surgery and are aesthetically unappealing. The objective of this project was to improve upon the BAHA by designing a bone conduction hearing aid, the ToothPhone, which utilizes the teeth as the initial bone conducting medium. There were three main engineering components of this project: electronic system with accompanying microphone, actuator, and mouthpiece. For the electronic system, it was desired to have flat magnitude and phase responses throughout the frequency range of 250 Hz to 8 kHz. A phase response resulting in a pure delay would also be acceptable. The voltage outputs of the microphone needed to be amplified by the electronic system to sufficient levels for actuator stimulation. The actuator was fabricated from Terfenol-D, a magnetostrictive material with high strain capabilities. When excited by a magnetic field, the actuator needed to exhibit displacement amplitudes necessary for a perceptual hearing response. Various Terfenol-D sample sizes and electromagnetic coil sizes were tested to determine the most effective combination. Finally, a mouthpiece was designed to house the actuator inside of the mouth and provide direct coupling between the actuator and the teeth of the upper jaw. An 8th order Butterworth filter was used in the electronic system to pass physiologically relevant frequencies with uniform gain. The obtained phase response, although not entirely flat, was considered to be inconsequential throughout the frequency range of interest. The gain of the system was achieved by cascading the filter with operational amplifiers. A model was developed to predict the minimum displacement amplitudes of the actuator necessary to surpass bone conduction thresholds of hearing. Displacement amplitudes of a 2.5x2.5x8mm sample accompanied with a 166 turn coil exceeded theoretical displacement values by at least one order of magnitude from 500 Hz to 8 kHz. The model was used for other sample testing as well. The details of the final actuator and mouthpiece designs will be reported, along with audiogram test results on healthy hearing human subjects: normal air conduction audiograms and bone conduction audiograms with the use of the ToothPhone.
The visual cortex within the brain is a complex network of neural pathways that allows us to visually interpret our surroundings. This network simultaneously perceives and processes thousands of visual signals into one coherent image. When a person experiences a stroke, a number of the neural pathways can be disrupted, and the visual cortex is no exception. In this study, we used psychophysical testing and functional magnetic resonance imaging (fMRI) to assess and understand the ability of both healthy subjects and four stroke patients to visually process motion in the environment, specifically focusing on visual tasks involved in self-navigation. In order to optimize clinical assessment time with the patients, we developed an algorithm that minimized the number of psychophysical tests needed to fully characterize their behavioral deficits. The statistical significance of each deficit was determined using t-test analysis comparing the patients’ performance with that of healthy subjects for each specific psychophysical test. We found visual deficits in navigation tasks relating to detection of impending collisions and relative arrival times of multiple objects. fMRI studies on healthy subjects allowed us to determine the brain regions that are significantly active during each visual-guided navigation task, while structural MRI scans allowed us to localize lesions in the patient group. Comparison between the activation in healthy subjects and lesion locations in stroke patients revealed a subset of overlapping regions in occipital, temporal, and parietal areas. In our presentation we will report the results of this comparative analysis, indicating neuro-anatomical areas that may be critical for the execution of visual-guided navigation tasks.
SESSION IIIa

Seeing is Believing: Imaging Technologies and Imaging Agents
Localized, Dynamic Measurements of Intracapillary Blood Pressure in Live Mice During Intravital Microscopy

Felita Agus, Lawrence Yu

Clinical and experimental evidence implicates elevated intracapillary blood pressures in renal glomeruli as an important trigger of glomerular damage. It is not known how the resulting changes in the mechanical environment in the glomerulus lead to glomerular damage, or how to prevent this damage from occurring. Therefore, it is desired to study and characterize the relationship between intracapillary blood pressure and glomerular tissue behavior. As the glomerulus is an extremely complex microscopic tissue structure, which is difficult to faithfully model in vitro, intravital microscopy is being developed as an approach for studying this relationship in the intact glomerulus. A method for measuring intracapillary glomerular pressures is needed to fully exploit this approach. We developed an injectable pressure transducer composed of microbubbles, small enough to flow freely through murine capillaries. Fluorescence resonance energy transfer technology (FRET) was used to provide a readout of pressure external to the microbubbles. FRET modulates the emitted wavelength of two fluorophores depending on their proximity. For this application, two appropriately chosen fluorophores were randomly embedded in the walls of the microbubbles. The emitted wavelength of the fluorophores changed as a result of FRET, depending upon how much the microbubbles were compressed by changing external pressure. The transducer was designed so that two-photon epifluorescence illumination could be used to excite the fluorophores in the microbubbles, as they traveled through the glomerular capillaries in an intravital preparation. To develop, validate, and calibrate the transducer a pressure chamber was created in which the static pressure could be varied and measured. We hope to obtain measurements quantifying the varied fluorescence emission spectra of the microbubbles in response to the externally applied pressure. A model of the bubble response to static pressure will then be derived to calibrate the sensitivity of the transducer over the typical pressure range found in vivo from micropuncture measurements. This transducer may be useful for many applications where dynamic pressure data is desired inside small or spatially-varying environments which are amenable to epifluorescence imaging.
Microscopy is an indispensable tool for biological research and medical diagnostics. While high resolution, diffraction-limited images can be acquired with light microscopy, the high pixel density cameras needed to record these images are often expensive. In addition, growing interest in macroscopy requires the camera pixel resolution to be much greater than that of commercially available cameras. We have designed an imaging system capable of producing high-resolution images using signal-processing techniques and an inexpensive, low-resolution camera. This system employs a technique called dithering to acquire multiple images that are shifted a small distance, smaller than the pixel size of the camera. These low-resolution images are numerically up-sampled to produce an image of higher pixel density. Finally, a de-convolution filter is applied to the up-sampled image to remove blurring and other artifacts. The results have shown that it is possible to obtain higher pixel-resolution images through dithering and multi-frame restoration. Our device has the potential to reduce the cost of high-resolution image acquisition in microscopy and be useful in applications of macroscopy.
Micro-Engineered Multispectral MRI Contrast Agent

Amr Aly, Maggie Cox, Rachel Horenstein

Currently, Magnetic Resonance Imaging (MRI) contrast agents are only capable of altering the brightness of an image, thus ignoring additional information that potentially could be extracted from a MRI scan. A microengineered, multi-spectral contrast agent particle was microfabricated using iron and iron oxide. The particle design utilizes a magnetic double disk geometry separated by a non-magnetic polyimide spacer. By varying the geometrical properties (disk thickness, radius, and disk-to-disk separation), the water diffusing through the particle has a resonance frequency alteration. This change produces a unique spectral shift and the particles can be distinguished in order to give information about the temperature, pH, or presence of enzymes at any location in the body. The fabrication process consisted of three major procedures: patterning of the photoresist using photolithography (Suss Micro Tec Photolithography), thin film deposition of iron or iron oxide using electron beam/sputtering (Edwards Auto 360 E-Beam Evaporator), and spin coating of a polyimide layer. Photolithography patterns were designed using a Computer Aided Design (CAD) software program (AutoCAD) and printed on chromium masks using a mask writer (Heidelberg Instruments DWL 66 Laser Writer). Silicon wafers were coated with photoresist and patterned using these masks. Following photolithography, a thin film of iron/iron oxide was deposited on the wafers and the desired pattern was etched using a lift-off process. A polyimide layer was spin coated onto the wafers followed by the deposition and lift off of a second magnetic thin film. O₂-plasma was used to etch the polyimide layer into the desired geometrical profile. All particles had a disk thickness of 200-nm, but the radius of the magnetic disk was varied in order to fabricate two different sized particles. Larger particles had a radius of 5-μm and smaller particles had a radius of 2.5-μm. A magnetometer (SQUID) and X-Ray Diffraction were used to analyze the material properties of iron/iron oxide. Finite Element Analysis was done on a model of the particle using the COMSOL software to produce the resulting magnetic field that the particle will experience when placed in the MRI scanner. The particles will be validated in an 11.7 Tesla (T) magnetic field to quantify their improvement on regular contrast agents.
Image-able Thermometer for Magnetic Resonance Imaging

Brian Chan, Nicholas Labriola, Matthew Lawrence

Monitoring patient temperature during Magnetic Resonance Imaging (MRI) is a crucial aspect of maintaining patient safety and comfort during scanning. Patient safety during MRI is becoming a major concern of many physicians; since the increasing strengths of MRI machines can cause an increase in patients’ body temperature. Current techniques for monitoring patient temperature, such as fluoroptic thermometry, proton resonance frequency, and PARACEST agents are insufficient. The objectives of this project were to design a non-invasive thermometer which could be placed on the surface of a patient’s skin and respond to changes in patient temperature during MRI. The device needed to be designed such that it was image-able during MRI scanning without interfering with the scan. SolidWorks was utilized to create a prototype of the device in order to determine the device’s ideal dimensions. Polycarbonate, polyethylene and a Mylar film were the materials used to create the body of the device since they do not cause any interference with the MRI images. Additionally, another portion of the device was created out of a softer material, Polydimethylsiloxane, in order to allow for the device to sit comfortably and securely upon the patient’s forehead. Mylar film was the material chosen for direct contact with the patient to allow for temperature conduction through the device to react with the expandable material within, ethanol. As the ethanol was heated, its expansion though the channel was correlated to changes in temperature and appeared brightly in the MRI images. The accuracy and response time of the device in respect to changes in temperature were analyzed and compared to results of current techniques. The device was shown to be image-able in the MRI, however, the accuracy and response time can be improved through further testing of materials. This device provides an inexpensive, accurate, and non-invasive solution for efficient monitoring of patient temperature during MRI scans.
Skeletal muscle and bone wasting are major healthcare problems, and one possible future therapy for muscle-and bone-associated wasting diseases involves stem cell treatment. Adult stem cell lineage commitment is influenced by both intrinsic cellular states and extrinsic microenvironmental cues. One potential way to cure wasting diseases is by combining stem cell treatment with anabolic agents to actively rebuild lost bone masses or muscle tissues. In this project, we evaluate the capacity for small compound libraries to influence cellular commitment using a simple and efficient colorimetric assay that measures muscle stem cell conversion between myogenic and osteogenic programs in vitro. A high-throughput system was used to test FDA approved compound libraries for compounds that mediated lineage commitment towards the osteogenic phenotype in bone morphogenic protein 2 (BMP-2) induced C2C12 mouse-muscle-derived stem cells. A colorimetric assay utilizing alkaline phosphatase to stain for bone cell activity was used to screen compounds. Two compounds were isolated from a library of five hundred compounds and showed significant enhancement of up to four times greater commitment towards the osteogenic phenotype compared to control conditions. Osteogenic phenotype was classified as alkaline phosphatase positive cells. With these two compounds, we systematically measured the influence of initial cell density, compound concentration, and time dependence on lineage commitment. In our presentation we will report the results of these measurements. The results of this study show that select compounds can promote specific lineage commitment and provide environment cues to skew stem cells towards a certain phenotype. The results of this study could apply to promoting lineage commitment for downstream use in regenerative medicine.
Diffusion Tensor Magnetic Resonance Imaging (DTI) is a non-invasive tool that enables visualization of fiber tracts in the white matter of the human brain. Internal microstructures such as neural axons generate anisotropic water diffusion, which produces the necessary signal used to collect a minimum of seven diffusion weighted images (DWI) to produce a single DT image. Imaging sequences and algorithms that are currently used to process and display DTI data may be inaccurate. Fidelity of acquired data to actual diffusion behavior can be validated using physical phantoms. The objective of this study is to design and develop fiber phantoms that exhibit orientation-dependent diffusion properties for validation of DTI experiment results. The phantoms, which were made with either polyester or Dyneema fibers, consisted of parallel and twisted fiber orientations. Diffusion weighted PROPELLOR and diffusion weighted multi-shot echo planar imaging (EPI) sequences were used to acquire DTI data, which were subsequently processed by an algorithm developed by Philips Medical Systems to perform tractography. Fractional anisotropy (FA) values, used to quantify the preferred direction of water diffusion, were obtained to assess the diffusion properties of the fiber phantoms. Tractography of Dyneema phantoms rendered more, and significantly longer, fibers than polyester phantoms in both the parallel and twisted fiber orientations. The acquired DWI and DTI images show that the PROPELLOR sequence images, when compared to the EPI images, exhibit smaller geometric distortions and higher FA values, respectively. DTI results suggest that Dyneema fibers arranged in simple orientations are suitable for use as a phantom to test pulse sequences and tractography algorithms. Furthermore, for simple fiber configurations, PROPELLOR sequences are more sensitive to diffusion anisotropy than EPI sequences.
SESSION IIIb

NUMB3RS:
Computation, Simulation, Analysis, Sequencing
3D Avatar for the Representation of Physiological Data

Aneesh Acharya, Maisam Dadgar

Representing a vast array of physiological data on a proper display is valuable in determining the effectiveness of full body simulations in the military. Current products do not sufficiently analyze or display the data acquired from the large number and different types of sensors needed. Taking input from a pre-existing suit embedded with physiological sensors including EOGs, EMGs, EKGs, pressure sensors, accelerometers, and stretch sensors, a new graphical user interface (GUI) has been developed to provide an accurate representation with a single, unified expression of streaming data in real time. A combination of various tools, including Microsoft Visual Studio, was used to design the GUI in C++, a ubiquitous and royalty-free programming language. The 3D avatar was designed using Blender, an open source 3D content creation software package. The created GUI gives the user easy access to all of the incoming raw data, which is visually represented on multiple graphs. In addition, the 3D avatar is used to represent the raw data in an intuitive, innovative manner, supplemented with popup displays for more detailed information on each body segment. Data is loaded through the main GUI and then distributed to the dependent objects, such as the charts and 3D avatar. This allows for one chief component to control and coordinate the entire GUI so everything remains synchronized. The new GUI enables the user to quantitatively measure the differences between real life and simulated responses. The software can be effectively used in conjunction with the suit to accurately record, monitor, and analyze physiological data from a trainee pilot, patient, or any other human subject.
Personalized Genomic Medicine: Length Variation in Short Tandem Repeats

Evan Appleton, Prabhat Dhar

Single-nucleotide polymorphisms (SNPs) have been moderately explored and credited with deleterious effects upon coding regions in the human genome. Repeat-length polymorphisms (RLPs) have not yet been studied in great detail for deleterious effects in proteins. We have suspicion that RLPs might affect proteins associated with cancer and other diseases. In prior repeat-length analysis we discovered that genome-wide repeat patterns were seen only in relatively large genomes, suggesting that major trends would not be visible in exclusively coding regions. Therefore, we examined specific genes that have been associated with diseases in an effort to identify and locate specific RLPs between the human reference genome and the diseased genome. This was done by retrieving information about specific RLPs that were documented in previous studies as having potential relation to certain diseases such as cancer. In abnormal genes with RLPs, the protein sequence of both the human reference gene and the abnormal gene were determined and secondary structure predictions were made using publicly available online software. For cases in which it was found that a specific RLP significantly impacts the secondary structure of a given protein for disease, the 3-D location of the translated RLP was visualized using online software resources. Cases in which the RLP did not appear to impact secondary structure we documented and examined for larger-scale trends. Given the results of this analysis, we intend to speculate about the impacts of specific RLPs upon tertiary and quaternary protein structure.
The incredible molecular heterogeneity of cancer is one of the main obstacles that have prevented the success of treatments targeted at the general cancer population. The novel field of personalized genomics is being developed to solve this problem by individualizing patient treatment. Each patient’s tumor has unique mRNA and protein expression profiles and is optimally treated using a specific cocktail of drugs. The chief objective of this project was to design a method to determine the drugs best suited to target each patient’s cancer using a computational predictive model. The model was trained and tested using data from 59 publically available cancer cell lines, known as NCI-60 cell lines. Two sets of data were obtained from each NCI-60 cell line: one set containing mRNA expression profiles for over 13,000 genes, and the second set with the response of each cell line to 118 known cancer drugs. MATLAB was used to perform correlations on the data to identify gene-drug pairs with strong correlation values. It was decided that only drugs with high response values in multiple cell lines would be analyzed, as these drugs had the highest probability of successfully producing reliable biomarkers. The classifiers to predict drug response based on gene expression profiles of cell lines were produced using the program WEKA (Waikato Environment for Knowledge Analysis). Classifiers used by the system include Simple Logistic, Bayesian Logistic Regression, and Logistic Model Decision Tree. It is expected that a set of drugs will be identified and analyzed to determine both effectiveness in preventing cell growth and clinical applicability based on current trends in cancer treatment. Future experimental validation of this technique would involve testing the responsiveness of patient tumor cells when treated with the chosen drugs. Eventual clinical use of this technique would involve using a patient’s tumor expression data to predict the personalized set of drugs necessary to most effectively combat the patient’s cancer.
DNA Sequence Analysis of Genes Associated with Schizophrenia

Jason DeBoer, Heather Macken

Schizophrenia is a neuropsychiatric disease involving altered states of consciousness that affects about 1% of the population and typically becomes symptomatic during the second or third decades of life. While it is known that schizophrenia is linked to certain environmental and genetic factors, there has not been a single set of factors that are associated with all cases of schizophrenia, nor has a factor been identified that specifically leads to development of the disease. There are repetitive DNA sequences that account for genomic instability and have a predisposition to mutation. This project designed a method to test the composition, frequency, and distribution of the repeat sequences in genes associated with schizophrenia compared to repeat sequences in a control set of genes. Repeat sequences were found using the Tandem Repeat Finder program. Statistical analysis was performed, leading to the conclusion that genes associated with schizophrenia had repeat sequence length distributions that were significantly different from distributions in the control genes. We also aim to demonstrate that the repeat sequences of the genes associated with schizophrenia and the control genes have significantly different base compositions by examining the G, C, A, and T content of the repeat sequences.
An In Silico Operon Model of *M. tuberculosis* Utilizing RNA-Seq Evidence

Dmitri Boulanov, Nicholas Kaiser

*Mycobacterium tuberculosis* (MTB) is a bacterium responsible for over nine million new tuberculosis infections around the world each year, primarily in underdeveloped countries. Development of effective therapeutics and diagnostics requires additional insight into the regulatory network and pathogenic mechanisms utilized by MTB to infect its host. The creation of an accurate operon map and functional genome annotation are the first steps towards this goal. We report the design of an in silico operon model of MTB, developed in Java to utilize the CONRAD gene prediction engine. This multi-state machine learning model relies on semi-Markov chain conditional random fields (CRF) to predict operon structure on a gene pair basis across the MTB genome by incorporating evidence from a broad array of available data sources. Unpublished RNA-Seq transcriptome data, intergenic distance, gene expression correlation, and DNA strand orientation comprise a set of four characteristics used to identify operons. Filtered RNA-Seq data provided the team with a high resolution map of transcribed regions, allowing for the development of quantifiable MTB operon structure characteristics. The addition of this transcriptome evidence enabled the model to predict operons more exactly than the best previous annotation. The high predictive performance achieved by the combination of this machine learning approach with RNA-Seq data presents the opportunity for a complete functional annotation of the MTB genome.
SESSION IV

What’s up, Doc?: Diagnostic Instrumentation and Microfluidic Systems
Development of a Multiplexed, Label-Free Hepatitis Assay for Clinical Diagnostics

Leslie Baggesen, Chelsea Pereira

Hepatitis B Virus (HBV) affects more than 350 million people worldwide, with approximately 15-40% of patients developing cirrhosis, hepatocellular carcinoma, or liver failure in latter stages of infection. Early detection of HBV is vital to developing proper treatment regimens for infected patients to prevent such complications. HBV infection is confirmed when hepatitis antibodies and antigens are detected in the blood at specific levels. The objective of the project was to develop a multiplexed, label-free hepatitis assay for use in the diagnosis of hepatitis infection. Laser-based spectral reflectance imaging biosensor (SRIB) technology was utilized to quantify the amount of hepatitis bound to a substrate surface in initial experiments. A protocol was developed to bind relevant antibodies (Ab) and antigens (Ag) to the surface of silicon chips and to measure the amount of binding activity on these chips. The chips are initially coated with a novel polymeric surface coating, which allows biological molecules to specifically and strongly bind to the surface. Ag and Ab of interest are then spotted on the surface of the substrate using the BioRad BioOdyssey Calligrapher MiniArrayer. Previous experiments showed that detectable levels of binding occurred when substrates were incubated in solutions containing phosphate buffered saline (PBS) and HBV surface Ag or Ab. A subsequent series of end-point incubation experiments were completed by submerging the substrates in a variety of solutions containing infected fetal bovine serum. The amount of each specific Ag and Ab in the serum was quantified by the SRIB; this value is directly related to the stage of infection of the patient. After incubation in 25% bovine fetal serum in PBS with HBV surface Ab and Ag, the mean percent increase in optical height was 41.5% for spotted antigens, and 32.3% for spotted antibodies. A flow cell was utilized to complete a titration and multiplexed experiment in which the substrate was exposed to varying concentrations of multiple hepatitis Ab and Ag in solution. Data from the titration was collected using an LED-based SRIB system. Such an HBV assay has the potential to impact the management of this disease in a clinical setting by enabling physicians and patients to actively monitor the status of infection and efficacy of treatments.
Researchers at Draper Laboratory have developed fluorescent based glucose nanosensors that create a relationship between emission intensity and glucose concentration. Research conducted in vivo with mice specimen has required a more advanced method of sensor injection than commercially available due to targeted tissue depth and volume of injection. The objective of this project was to design a hand-held device capable of injecting nanosensors into the epidermis layer of a mouse. A prototype was designed to dispense 5 µL of nanosensors at a depth of 150 microns into tissue. A stepper motor driven screw was used as a syringe pump to dispense fluid from the sensor reservoir. A second stepper motor controlled the needle tip insertion and retraction. To effectively administer sensors to the epidermis skin layers specialized glass-pulled needles were fabricated. The small needle tip size and tapered shape made the glass needles optimal for shallow injections. The electronic components were controlled using a microcontroller, stepper motor drivers, and a 12V power supply. The final prototype design can be operated using only one hand; actuating each injection process with the control buttons mounted near the thumb. Quantitative research has shown that a 5µL sensor injection will generate an effective area for accurate fluorescence emission readings.
Family name and first name

Design of a Portable Optical Reader for Measuring Fluorescence Signal from Nanoparticle Sensors for \textit{in vivo} Glucose Monitoring

Andrew Keiser, Kevin Yu

Blood glucose monitoring with finger-prick glucometers often carries the risk of infection and cause discomfort, whereas non-invasive optical methods based on the absorption, scattering, or reflection properties of glucose minimize the pain of glucose monitoring. However, the common problems associated with optical methods include signal interference and variability in human tissue composition especially between skin types. The objective of the project was to design a portable optical glucose monitor that reads fluorescence from glucose-sensitive nanoparticles in the skin and is insensitive to skin type, inexpensive, and pain-free. Our approach to noninvasively monitor glucose concentration was a ratiometric measurement between fluorescent glucose-sensitive nanoparticles and a reference fluorophore both embedded in the epidermis. Excitation of both fluorophores was accomplished by using light emitting diodes, and fluorescence detection was accomplished by using high performance optical filters and silicon avalanche photodiodes. The design of the portable device also includes a USB connection to a computer for monitoring and recording results. We hope to demonstrate that injection of glucose-sensitive nanoparticles in mice will cause fluorescence signal to decrease with increasing glucose concentration; thereby, validating the ratiometric measurement approach. The device can be used to monitor glucose concentration non-invasively, and the design of the device allows for interchangeable optical components to accommodate for the fluorescence measurement of other biological analytes.
A Dielectrophoresis-based Microfluidic Delivery System for Single Cell Trapping

Aleksander Jonca, Matthew Lee, Jeremy Levesque

Researchers of pharmaceutical products and stem cells have always expressed interest in the response of individual cells to external stimuli. Sensing technology has been developed to monitor these cellular responses; however, there is no current platform to assist this technology by trapping single cells in a designated location. We present a novel method of trapping individual cells in a medium using negative dielectrophoresis (nDEP). A lab on a chip system has been fabricated to accept a high throughput of medium containing E. Coli cells which are injected at a steady flow rate. These cells are then trapped at specific sites where sensing can be done on single cells while in a natural microenvironment. Use of photolithography during fabrication enabled the etching of electrodes and channels to perform nDEP upon a glass slide. We aim to show that the completed product is able to isolate single cells. We also hope that continued testing will show the dependence of trapping on the flow rate of the medium as well as the applied voltage to the electrodes. Finally, we hope that analysis of the results indicates that this method of cell trapping is viable to assist and complement cell signal sensing technology.
Optical Characterization of Mechanical Properties of Ultrasound-Stimulated Biological Cells

Max Jativa, Doris Ling

Current cancer diagnostic methods consist of inaccurate biopsies of visible tumors, or time consuming blood tests. The abnormal levels of biochemical agents that result from genetic mutations cause alterations in the cytoskeletal integrity. The objective of this study is to determine whether or not malignant cells display unique mechanical properties that can be measured with optical scattering. Healthy and apoptotic cancer cells were acoustically stimulated to study differences in their physical properties by analyzing their frequency responses. Our experiment consisted of acoustic stimulation of single cells and characterization of the resulting mechanical perturbations using optical scattering. The experimental setup passes live cells in a laminar flow into a water medium where they are excited mechanically by a single ultrasound pulse centered at about 15 MHz. A HeNe laser directed at the site of acoustic excitation causes the passing cells to scatter light. Data collected will be analyzed to determine correlations between the differences observed between the frequency responses of apoptotic and healthy cell lines. Our study will determine if significant property changes can be measured using optical characterization of the responses to ultrasound pulses of cancer cells with stable cellular structure and cancer cells undergoing cytoskeletal breakdown.
Origami Microfluidics: A Novel Rapid-Prototyping Technique

Andrew Fisher, Charles Jahnke

The development of microfluidic systems has miniaturized chemical procedures for biomedical applications and spurred the innovation of microfluidic point-of-care devices. Current biomedical applications have expanded to include both two and three-dimensional microfluidic chips, the complexity of which resulted in an increased time and cost of device fabrication. Standard prototype methods utilize physical molds and high-temperature presses, but advances in the field have begun the development of a rapid-prototyping technique called xurography. Xurography—razor writing—utilizes computer-aided design and off-the-shelf cutter-plotters to define microstructures in layers of plastic films, which are then stacked, aligned and pressed into functional three-dimensional chips. In an effort to further expedite the prototype process we introduce a novel method of construction modifying typical CAD design and utilizing material properties of the film to precisely fold the film into layers. The folded layers are pressed into microfluidic chips, thus eliminating the time and cost associated with alignment of standard prototyping. Optimization of the cutter-plotter—including force, speed and razor orientation—varied with material and material-thickness, requiring initial setup tests and time for new materials. Using 44 and 100-μm Cyclo Olefin Polymer (COP) film, two-dimensional point alignment tests demonstrated deviations of 300 μm (±200 μm) and 90 μm (±20 μm), respectively. Channel alignment tests, aimed at mimicking practical use, were one-dimensional and did not exceed point test deviations. Deviations of this scale were acceptable in most microfluidic prototypes and with further optimization of film requirements, may compare to current custom molded patterns. An enzyme-linked immunosorbent assay (ELISA) test established a baseline and proof-of-concept for functional microfluidic chips using the origami method. The optimized procedure developed in this study facilitates accurate and rapid fabrication of inexpensive microfluidic devices.
Pneumonia is a devastating acute respiratory infection that kills 1.8 million children worldwide each year, with the majority of these deaths taking place in the developing world. Vital point-of-care diagnostics, which could improve these health outcomes, are generally absent from these remote regions because of infrastructural and environmental difficulties. A robust, solar-powered pulse oximeter can overcome the challenges that render conventional devices insufficient. We investigated the requirements for introducing a viable, affordable device in resource poor settings. Through our contacts at the Boston University School of Public Health, we identified rural Zambia as a suitable target for design considerations and possible field-testing. In addition, we reverse engineered several industry standard pulse oximeters to determine if power consumption could be lowered by altering the electrical configuration. Financial and resource barriers for the target users were vital in all decision making. The final prototype is powered by cell phone batteries, which are readily available and affordable in Zambia. The battery is charged in a solar unit that is worn by community health workers in the field. We estimate a final device manufactured from the materials we have selected will be able to serve a community health worker for over a year of frequent use without failure. The ease of use of the prototype was tested on a variety of subjects and a thorough instructional manual was developed to ensure user competency. The last step is to use pulse oximetry data to direct patient triage such as inpatient versus outpatient care. Successful implementation of this technology will allow community health workers to identify patients with acute respiratory disease at a higher rate and allocate medical resources accordingly.
Portable, No-power, Nucleic Acid Extraction Device

Francis Jareczek, Mark Mazzochette, Sean Moser

The prevalence of communicable infectious disease in Third World countries is partially due to a dearth of accurate, rapid diagnostic testing. Available technologies for such testing are lacking due to space and power requirements, high costs, and device complexity. We report the design of a portable, no-power, nucleic acid (NA) extraction device to isolate and purify NAs from human samples for downstream amplification and diagnostic tests. Hollow plastic straws containing silica-impregnated porous polymer monoliths (PPMs) were used with an air pressure distributing fixture for the rapid extraction of NAs. We modified PPM parameters to determine the optimum materials composition for efficient DNA extraction. We measured extraction efficiency for both DNA and RNA by comparing the total NA quantity flowed through the straw to the amount extracted from the input solution. DNA and RNA-containing straws were stored for varying time durations to evaluate extracted NA quality and lifespan. Polymerase chain reaction was used to estimate post-storage NA quantities. A polymer-based reagent was designed and used to improve in-straw RNA storage. Extraction efficiency was approximately 15-20% for DNA and 25% for RNA. DNA stored up to two months at varying temperatures was minimally degraded. Negligible unstabilized stored RNA (1-5%) remained in the straws after only one week at elevated temperatures. When stabilized with the polymer-based reagent, RNA degradation was reduced. With improvements in efficiency, this portable, no-power device will provide rapid, cost-effective NA extraction for downstream amplification and diagnostic tests, eventually improving patient treatment in low-resource settings.