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(clockwise from top left): Ankita Shah, Aaron Colby (Session IV); Nikhil Haas, Majid Ghodousi (Session I); Lauren Ouellette, Bruce Miller (Session IIIb); Nikhil Haas, Majid Ghodousi (Session I); Daniel Bellin, Karen Chien (Session I)
Presentation Schedule

Chair’s Welcome

Visiting Companies and Laboratories

Technical Advisors

Faculty Profiles

BME Industrial Advisory Board

BME Visiting Committee

Industrial Research Fellowship Program

Project Abstracts

Centers
- Biomolecular Research Center
- Center for Advanced Biotechnology
- Center for BioDynamics
- Hearing Research Center
- Nanoscience and Nanobiotechnology
- Neuromuscular Research Center
- Center for Advanced Genomic Technology
- Center for Memory and Brain

Labs
- Auditory Neurophysiology
- Auditory Neuroscience
- Binaural Hearing
- Biomedical Materials Research
- Biomedical Optics
- Biomicroscopy
- Biomimetic Material Engineering
- Biomimetic Systems
- Biomolecular Systems
- BioRobotics
- Brain and Vision
- Cell and Tissue Mechanics
- Cellular and Subcellular Mechanics
- Cochlear Biophysics
- Computational Genomics
- Fields and Tissues
- Micro and Nano Biosystems
- Molecular Biotechnology
- Motor Unit
- Multi-Dimensional Signal Processing
- Multi-Scale Tissue Biomechanics
- Natural Sounds and Neural Coding
- Organogenesis
- Orthopaedic and Developmental Biomechanics
- Respiratory and Physiological Systems Identification
- Respiratory Research
- Steffen Lab
- Sensory Signal Processing
- Structural Bioinformatics
- The Collins Lab
- Visual Information Processing

Biomedical Engineering

44 Cummington Street, Boston, MA 02215 | 617-353-2805 | www.bu.edu/bme
# 24th Annual Senior Project Conference

Friday, May 1, 2009

## 7:15 – 8:00 AM
**Continental Breakfast**

## 8:00 AM
**Welcome and Opening Remarks:** Prof. Irving Bigio

## 8:10 – 10:15 AM
### SESSION I
**PHO 206**
**Fooling Mother Nature: Tissue Engineering and Tissue Manipulation**

**Session Chair:** Prof. Joyce Wong

- Design of Experimental and Statistical Tools for Analyzing Mechanical Regulation of Tissue Fate  
  Daniel Bellin, Karen Chien
- Articular Cartilage Deformation in an Osteochondral Plug Model  
  Mohit Butaney, Mathew Stephen
- Cavitation-Enhanced Fragmentation of Tissue Using Ultrasonic Surgical Aspirating Horns  
  Derek Yue Cao, Brian Roach
- Tissue Stretcher System for Engineered Small Diameter Blood Vessels  
  Warren Ferris, Timothy Lyford, Sean Taylor
- A Bottom-Up Approach for Engineering 3D Vascularized Tissue Constructs  
  Majid Ghodousi, Nikhil Haas
- Engineering a 3D Lung Extracellular Matrix  
  Avinash Oza, Kelsey Derricks
- Monitoring Glucose Levels with Fluorescent Sensors in Tissue-Engineered Constructs  
  Mary Balaconis, Jaclyn Lautz
- 3D Freeform Fabrication of a Hybrid Hydrogel Scaffold  
  Francis Doyle, Jr., Samuel Polio

## 10:15 – 10:30 AM
**BREAK**
### SESSION IIa

**A Picture of Life: Imaging**

**PHO 206**

**Session Chair: Prof. Tom Szabo**

**10:30 AM – 12:30 PM**

- **A New Concept in High Definition Digital X-Ray Imaging**
  Madeline Abrams, Justin Martin

- **Sensor Locator for Surface EMG Array**
  Megan Fessenden, Allie Paquette

- **Quantifying Multi-Spectral Parameters in Tissue-Mimicking Gel Phantoms that Exhibit Magnetization Transfer Phenomena: A Multi Field Study**
  Natalya Kotlyar, Katherine Schwendinger-Roy, Jaime Shaw

- **Design of an Anatomical Ultrasound Simulator**
  Kevan Desai, Michael Habib, David Scaduto

- **Driving System for a Portable Ultrasound Brain Imaging Device for Use in Forward Battlefield Areas**
  Julie Duran, Karla Mercado

- **Optical Imaging of Coral Regeneration at the Cellular Level**
  Ryan Burke, Lauren Tuthill

- **HiLo Fluorescence Endomicroscope**
  Visar Ajeti, Brett Allaire

### SESSION IIb

**NUMB3RS: Computation/Simulation/Analysis**

**PHO 205**

**Session Chair: Prof. Ed Damiano**

**10:30 AM – 12:30 PM**

- **Analysis Methods for Neurovisual Rehabilitation**
  David Ahern, Muftah Ahmed

- **Simulating Echolocation Systems Using Computational Models of Auditory Physiology**
  Andrew Dumas, Andrew Rothman

- **The Role of Temporal Fine Structure Cues in Enhancing Speech Intelligibility for Simulated Cochlear Implant Listening**
  Sruthi Ramakrishnan, Swathi Ramakrishnan

- **Asymmetries in Experimentally-Measured Inter-Aural Time and Level Sensitivity: Dependence on Spatial Origin and Type of Stimulus**
  Raymond Keffer, Akshay Navaladi

- **Implications of a Meta-Analysis of the Control Properties of Motor Units**
  Joshua Kline

- **Determination of Viscoelastic Properties of a Blood Clot via Acoustic Levitation**
  Kai Pong, Hiroo Shimoda, Hsiaoching Teng

- **The Effects of a Soy Protein Diet on the Bone Material and Structural Properties of Estrogen-Depleted Cynomolgus Monkeys**
  James Schmitz, Sonia Shah

- **DNA Sequence Analysis of Genes Linked to Schizophrenia**
  Mary Harrison, Amy Nehring

**12:30 PM – 1:15 PM**

**LUNCH**
1:15 – 3:00 PM  SESSION IIIa
PHO 206
What’s up, Doc?: Diagnostic Technologies and Microfluidic Systems

Session Chair: Prof. Chris Passaglia

Development of an Automated Microfluidics Platform for Chemical Methodology
Meredith Blakely, Anna Yanko

Pressure Control of Optical Fiber Probes Used for Detecting Cancer
John D’Agostino, Gregory Ekchian

A Thermoplastic Micro-Electro-Mechanical System (MEMS) for Microfluidic Diagnostic Platforms
Theodorus de Groot, Megan Rexius

Development of Microfluidic Device Technology for HIV Diagnostics
Peter Lombardozzi, Anoli Shah

Developing an Automated Microfluidic Device to Purify and Concentrate Bacteria from Whole Blood for SERS Bacterial Diagnosis
Michael Koan, Kenny Lin, Shauna Zane

Compact Label-Free Immunoassay Diagnostic Platform for Global Health
George Daaboul, David Rozenberg, Rahul Vedula

A Microfluidic Chip for Analysis of Mechanical Forces Generated During Cell Migration
Sean Collignon, Else Frohlich

1:15 – 3:00 PM  SESSION IIIb
PHO 205
Wired: Instrumenting Living Systems and Measurement of in vivo Conditions

Session Chair: Prof. Kamal Sen

Transmitter Board Enclosure Design for EM Tracking System
Michael Augelli, Yue Ma

Design and Integration of a Temperature Sensor into the BIS Monitoring System
Bruce Miller, Lauren Ouellette

Ambulatory Vestibular Monitoring Device
Guilherme Goretkin, Kevin Lada

Design of Real-Time System for Partitioning Volume versus Flow Dependence of Respiratory System Resistance in Asthmatics
Nathaniel Steiger, Brian Trautman

The Effects of Mechanical Forces on the Progression of Emphysema
Gopesh Sharma, Venkat Subramaniam

Understanding Contrast Adaptation in Vision
Wilson Kwan, Wan Seo

Design of an Apparatus to Assess the Visual Abilities of Rats
John Greifenberger, Nathan Lavallee

3:00 – 3:15 PM  BREAK
SESSION IV
Small Things: Nanotechnology, Molecules, Cellular Control

Session Chair: Prof. Steve Colburn

Nanotechnology in Biomedical Engineering: Nanoelectrical Biosensors
Kyum Lee, Willie Feng

Nanotechnology in Biomedical Engineering: Nanomechanical Biosensors
Nirav Bhavsar, Anand Patel

Threshold-Based Detection in Escherichia coli: Interfacing Synthetic Gene Networks
Ioana Lupascu, David Shi

Acoustically-Driven Microbubbles Mediate Cellular Uptake of Impermeable Biomolecules
Ruby Gill, Brittany Simone

Triggering Genetic Toggle Switch through Ultrasound-Induced Heating
Willis Hong, Jason Maley

Design and Characterization of a Polymer-Based Implant for Treatment of Age-Related Macular Degeneration
Rahul Ahuja, Balaji Nithianadam

Optimizing Drug Delivery Systems Using Single Molecule Imaging in Live Cells
Aaron Colby, Ankita Shah

5:00 PM Final Conference Comments: Prof. Irving Bigio, Prof. Thomas Szabo, Dean Kenneth Lutchen, BMES President Akshay Navaladi

RECEPTION IN THE ATRIUM, 2nd FLOOR, PHOTONICS CENTER
Welcome from the Chair

It is my pleasure to welcome our guests, our alumni, the biomedical industry, our faculty and our students to Boston University’s 24th Annual Biomedical Engineering Senior Design Project Conference. Our talented students will present to you their state-of-the-art design and research activities, as they complete their bachelor’s degree 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 Boston University Department of Biomedical Engineering is one of the oldest bachelor-degree programs. We are also one of the largest Biomedical Engineering Departments, with a faculty of 32 primary tenured and tenure-track professors and over 70 affiliated faculty members.

We are one of only three departments in the country to receive a Leadership Award from the Whitaker Foundation, one of only nine to receive a Coulter Foundation Translational Research Partnership Award, and the only program to have received both. Over a ten-year window these awards will represent a nearly $50 million investment in the Biomedical Engineering program at Boston University.

As a result of the Whitaker Leadership Award, we have established a center for Nano and Micro Biosystems, including Class 100 and Class 1000 bio-microfabrication facilities, a Micro and Nano Imaging facility, a Biointerface Technologies Facility, and a Biomedical Engineering Simulation and Computation Facility. All of these support a comprehensive educational and research program in Cell and Subcellular Bioengineering, Cell and Tissue Engineering, Biomaterials, Systems Biology, Synthetic Biology and Genomics, Integrated Physiological Systems, Biomedical Imaging, and Multiscale Modeling from the biomolecule to the whole organ. Our Coulter Award facilitates rapid translation of basic bioengineering discoveries to innovative technologies that impact patient care and clinical practice. The intent of the Coulter Award is to catalyze collaborative projects between BME faculty and clinicians that engage the entire commercialization network and infrastructure of the University.

The BS program in Biomedical Engineering is accredited by ABET. The undergraduate curriculum 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 for up to a year.

Seniors majoring in Biomedical Engineering are required to complete a two-semester capstone design project. At the end of the year, they present the results of their work in this exciting forum. Seniors also must engage their project 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. Dr. Bigio invested much energy and organizational skills to sustain the level of excellence and impact for which this program is renowned. Dr. Bigio was assisted by Dr. 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. Drs. Irving Bigio, Tom Szabo, Andy Jackson, Steve Colburn, Chris Passaglia, Michael Smith, Kamal Sen, David Mountain were invaluable. I also served as part of this team and was fortunate to enjoy the program in all its dimensions. Our students are remarkable at rising to the challenge and I have no doubt they will impress and entertain you scientifically today. Good luck to you all.

Solomon Eisenberg
Associate Dean of Undergraduate Programs
Chairman, Biomedical Engineering
24th Annual Senior Design Project Conference

VISITING COMPANIES AND LABORATORIES
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### Visiting Companies and Laboratories

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24th Annual Senior Design Project Conference

TECHNICAL ADVISORS AND FACULTY PROFILES
## 2009 Senior Design Project Technical Advisors

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<th>Technical Advisor</th>
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<td><strong>Session I</strong></td>
<td>Daniel Bellin/Karen Chien</td>
<td>Elise Morgan</td>
<td>Orthopaedic &amp; Develop. Biomechanics (BU-ME)</td>
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<td>Joyce Wong</td>
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<td>Majid Ghodousi/Nikhil Haas</td>
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<td>Avinash Ozai/Kelsey Derrick</td>
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<td>Madeline Abrams/Justin Martin</td>
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<td>Megan Fessenden/Allie Paquette</td>
<td>Serge Roy</td>
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<td>Hernan Jara</td>
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<td>Joshua Kline</td>
<td>Carlo De Luca</td>
<td>BU Neuromuscular Research Center</td>
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<td></td>
<td>Kai Peng/Hiroo Shimoda/Hsiaoching Teng</td>
<td>R. Glynn Holt</td>
<td>Holt Laboratory (BU-ME)</td>
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<td></td>
<td>James Schmitz/Sonia Shah</td>
<td>Roberto Fajardo</td>
<td>Orthopaedic Biomechanics Laboratory</td>
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<td></td>
<td>Mary Harrison/Amy Nehring</td>
<td>Cassandra Smith</td>
<td>Molecular Biotechnology Lab (BU-BME)</td>
</tr>
<tr>
<td><strong>Session IIIA</strong></td>
<td>Meredith Blakely/Anna Yanko</td>
<td>Aaron Beeler</td>
<td>BU Center for Chemical Methodology</td>
</tr>
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<td></td>
<td>John D'Agostino/Gregory Ekchian</td>
<td>Irving Bigio</td>
<td>Biomedical Optics Lab (BU-BME)</td>
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<td></td>
<td>Theodorus de Groot/Megan Rexius</td>
<td>Catherine Klapperich</td>
<td>Microdevices &amp; Microenvironments Lab (BU-ME)</td>
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<td>Peter Lombardozzi/Anoli Shah</td>
<td>Ulkan Demirci</td>
<td>BMM Labs</td>
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<td>Michael Koon/Kenny Lin/Shauna Zane</td>
<td>Alexi Sauer-Budge</td>
<td>Fraunhofer USA</td>
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<td>George Daaboul/David Rozenberg/Rahul Vedula</td>
<td>Selim Unlü</td>
<td>Biological Sensing &amp; Imaging Lab (BU-ECE)</td>
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<td></td>
<td>Sean Collignon/Else Frohlich</td>
<td>Xin Zhang</td>
<td>Microsystems Technology Lab (BU-ME)</td>
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<tr>
<td><strong>Session IIIIB</strong></td>
<td>Michael Augelli/Yue Ma</td>
<td>Samuel Akins</td>
<td>GE Healthcare, Surgery-Navigation</td>
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<td></td>
<td>Bruce Miller/Lauren Ouellette</td>
<td>Chuck Vadala</td>
<td>Aspect Medical Systems Inc.</td>
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<td>Guillerme Goretkin/Kevin Lada</td>
<td>Steven Rauch</td>
<td>Massachusetts Eye and Ear Infirmary</td>
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<td>Nathaniel Steiger/Brian Trautman</td>
<td>Kenneth Lutchen</td>
<td>Resp.&amp;Physio. Systems Identification (BU-BME)</td>
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<td></td>
<td>Gopesh Sharma/Venkata Subramaniam</td>
<td>Bela Suki</td>
<td>Cell &amp; Tissue Mechanics Lab (BU-BME)</td>
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<td>Wilson Kwan/Wan Seo</td>
<td>Christopher Passaglia</td>
<td>Visual Information Processing Lab (BU-BME)</td>
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<td></td>
<td>John Greifenberger/Nathan Lavellee</td>
<td>Christopher Passaglia</td>
<td>Visual Information Processing Lab (BU-BME)</td>
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<tr>
<td><strong>Session IV</strong></td>
<td>Kyum Lee/Willie Feng</td>
<td>Shyam Erramilli, Raj Mohanty</td>
<td>BU Physics</td>
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<td></td>
<td>Nirav Bhavsar/Anand Patel</td>
<td>Shyam Erramilli, Raj Mohanty</td>
<td>BU Physics</td>
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<td>Ioana Lupascu/David Shi</td>
<td>James Collins</td>
<td>Collins Lab (BU-BME)</td>
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<td>Ruby Gill/Brittany Simone</td>
<td>Tyrone Porter, James Collins</td>
<td>Medical Acoustics Lab (BU-ME)</td>
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<td>Willis Hong/Jason Maley</td>
<td>Stephen Redenti</td>
<td>Schepens Eye Research Institute</td>
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<td>Rahul Ahuja/Balaji Nithianadam</td>
<td>Mark Grinstaff, Amit Meller</td>
<td>Grinstaff Lab/Single Molecule Biophysics and Nano-Biotechnology Lab (BU-BME)</td>
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<td>Aaron Colby/Ankita Shah</td>
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</table>
Boston University
Department of Biomedical Engineering
Faculty Profiles

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
Ph.B., Chemistry, Columbia Univ, Ph.D., Biophysical Chemistry, Univ of California, Berkeley

**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

**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

**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

**CARLO J. DE LUCA**
Professor, Biomedical Engineering & Neurology, Research Professor Electrical and Computer Engineering; Director, NMRC; B.A., U of British Columbia, M.Sc., 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., Biophysics, 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

**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
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: Electricity 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 Associate 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

AMIT MELLER
Associate Professor, Biomedical Engineering;
Ph.D., Physics, Weizmann Institute of Science,
Rehovot Israel, Msc, Pysics Weizmann
Institute of Science, Rehovot Israel B.S., Tel
Aviv University

Research Interests: Nanopore force spectroscopy of RNA
folding kinetics, DNA switches and transcription initiation
kinetics, RNA helicase activity, transcription factor/DNA
interaction ultra fast DNA sequencing optical methods for single
molecule detection

EVAN EVANS
Professor, Biomedical Engineering
B.S., M.S., Engineering Physics, Rensselaer
Polytechnic Institute, Ph.D., Engineering
Science, University of CA at San Diego

Research Interests: Nano-microscale
biomechanics; ultrasensitive force probes and
extreme resolution optical techniques; material properties
of cellular structure; role of structural forces in cell biochemistry

TIM GARDNER
Assistant Professor, Biomedical Engineering
Ph.D., Biomedical Engineering, Boston
University; B.S., Mechanical Engineering,
Princeton University LOA Amyris Biotech.

Research Interests: Gene circuit mapping,
modeling and engineering; bacterial stress
response and virulence regulatory circuits; metabolic network
mapping/modeling; microbial energy production; microarray
expression analysis; drug mechanism of action

ANDREW C. JACKSON
Professor, Biomedical Engineering
B.S., M.S., Mechanical Engineering,
University of Nevada, Ph.D., Biophysics and
Physiology, University of Mississippi
Medical School

Research Interests: Respiratory physiology;
respiratory mechanics, role of airway closure in asthma

KENNETH R. LUTCHEN
Dean, College of Engineering, Professor,
Biomedical Engineering, B.S., Engineering
Science, University of Virginia, M.S., Ph.D.,
Biomedical Engineering, Case Western

Research Interests: Airway and lung tissue
mechanics and ventilation; Computational
modeling of structure-function relations in the lung;
Mechanical ventilation; Integrated biomechanics of the lung;
linear and nonlinear systems identification

JEROME MERTZ
Professor, Biomedical Engineering &
Physics Ph.D., Physics, Université Paris VI
& University of California, Santa Barbara,
B.A., Physics Princeton University

Research Interests: Development and
application of new optical microscopy techniques to biological
imaging
DAVID C. MOUNTAIN  
Professor, Biomedical Engineering & Otolaryngology  
B.S., Electrical Engineering, Massachusetts Institute of Technology, M.S., Ph.D., Electrical Engineering, University of Wisconsin

Research Interests: Auditory information processing; sensory biophysics; computer simulation; biomedical electronics; biomedical signal processing; environmental engineering

CHRIS PASSAGLIA  
Assistant Professor, Biomedical Engineering  
Ph.D., Biomedical Engineering and Neuroscience, Syracuse University; B.S., Biomedical Engineering, University of Iowa

Research Interests: Visual information processing and transmission; retinal physiology in normal and diseased states; computational models of neural coding, visual prostheses

KAMAL SEN  
Associate Professor, Biomedical Engineering  
B.A., Physics, Bates College, M.A., Ph.D., Physics, Brandeis University

Research Interests: Electrophysiological recording of neural responses in auditory processing, theoretical methods to characterize neuronal encoding, computational models of natural sound processing

CASSANDRA L. SMITH  
Professor, Biomedical Engineering; Biology, & Pharmacology, B.A., Biology & M.S., Medical Microbiology, West Virginia University Medical School, Ph.D., Genetics, Texas A&M University

Research Interests: Molecular Biotechnology and Genomics

MICHAEL L SMITH  
Assistant Professor, Biomedical Engineering  
B.S. Mechanical Engineering University of Memphis, M.S. & Ph.D., Biomedical Engineering, University of Virginia

Research Interests: Cellular mechanotransduction through the extracellular matrix; fibronectin structural biology; and microfabricated surfaces for engineering cell function

TEMPLE F. SMITH  
Professor, Biomedical Engineering; Director, BioMolecular Engineering Research Center; B.S., Physics, Purdue Univ, Ph.D., Nuclear Physics, University of Colorado

Research Interests: The syntactic and semantic structure of the genetic information in biomolecular sequences, structures, and their evolution

DIMITRIJE STAMENOVIĆ  
Associate Professor, Biomedical Engineering  
Dipl. Ing., Mechanical/Aeronautical Engineering, University of Belgrade (Yugoslavia), M.S., Ph.D., Mechanics, University of Minnesota

Research Interests: Respiratory mechanics; cell mechanics; rheology of soft tissues; mechanics of foam-like structures

BÉLA SUKI  
Professor, Biomedical Engineering M.S., Physics, and Ph.D., Biomechanics, Jozsef Attila University, Szeged (Hungary)

Research Interests: Mechanical properties of living tissues; modeling the dynamic and nonlinear behavior of complex biological systems; pulmonary physiology

JOE TIEN  
Associate Professor, Biomedical Engineering  
B.S., Physics, B.S., Mathematics, University of California, Irvine, A.M., Ph.D., Physics, Harvard University

Research Interests: Microvascular tissue engineering; microvascular physiology; hydrogels

LUCIA M. VAINA  
Professor, Biomedical Engineering & Neurology,  
MS, U. Timisoara and Urbino; PhD Mathematical Logic, Sorbonne, Doctorat d'Etat ès Sciences & Médecine (Neurologie), Human & Computational Vision, Institut National Politechnique de Toulouse

Research Interests: Computational visual neuroscience; biological and computational learning; functional and structural neuroimaging
SANDOR VAJDA
Professor, Biomedical Engineering, MSc, Electrical Eng, Gubkin Institute (Former USSR), MSc, Applied Mathematics, Éötvös Lorand Univ (Hungary), PhD, Chemistry, Hungarian Academy of Science

**Research Interests:** Scientific computing applied to problems in engineering, biochemistry, and biology, with focus on molecular mechanics, protein structure determination, protein-ligand interactions, docking, and drug design

HERBERT F. VOIGT
Professor, Biomedical Engineering; Associate Research Professor, Otolaryngology, School of Medicine, Ph.D., Biomedical Engineering, Johns Hopkins University B.E. (E.E.), City College of New York

**Research Interests:** Auditory neurophysiology; neural circuitry; neural modeling

JOYCE WONG
Associate Professor, Associate Chair for Graduate Programs Biomedical Engineering SB, Materials Science and Engineering, MIT, Ph.D., Materials Science and Engineering, Program in Polymer Science and Technology, MIT

**Research Interests:** Biomaterials, tailoring cell-material interfaces for drug delivery and tissue engineering applications; direct, quantitative measurement of biological interactions

**Affiliated Faculty**

PIERRE DUPONT
Professor, Biomedical Engineering and Mechanical Engineering BS, MS, PhD, Mechanical Engineering Renssealer Polytechnic Institute

**Research Interests:** Robot kinematics, dynamics and control. Medical applications of robotics. Image guidance of minimally invasive surgery

THOMAS A. EINHORN
Professor and Chairman, Orthopedic Surgery, Professor Biomedical Engineering MD, Cornell University Medical College

**Research Interests:** Hip and knee replacement and reconstructive surgery, treatment of metabolic disease, orthopaedic trauma surgery, the biology of skeletal repair and regeneration

SHAYAMSUNDER ERRAMILLI
Professor Biomedical Engineering and Physics. BS, University of Pune; MS Indian Institute of Technology; PhD, University of Illinois

**Research Interests:** High-resolution infrared microscopy for studying

BENNETT GOLDBERG
Professor, Biomedical Engineering and Physics MS, PhD, Physics, Brown University; BA, Harvard University

**Research Interests:** Experimental condensed-matter physics and polymer physics
STEPHEN GROSSBERG  
Wang Professor of Cognitive and Neural Systems; Professor of Biomedical Engineering, Math & Psychology, Chair, Dept of Cognitive and Neural Systems  
Ph.D., Mathematics, Rockefeller University  
Research Interests: Vision, audition, language, learning and memory, reward and motivation, cognition, development, sensory-motor control, mental disorders

JAMES A. HAMILTON  
Professor Biomedical Engineering and Physiology and Biophysics, Research Professor of Medicine  
Research Interests: novel approaches to biomedical problems by integrating physical-chemical and physiological/biochemical approaches complemented with molecular modeling, molecular biology and other cell biology methods

ALLYN E. HUBBARD  
Professor, Biomedical Engineering & Electrical and Computer Engineering  B.S., M.S., Ph.D., Electrical Engineering, University of Wisconsin  
Research Interests: Auditory physiology; experiments and modeling; neurocomputing; VLSI in biomedical applications; biosensors

W. CLEMENT KARL  
Professor, Biomedical Engineering & Electrical and Computer Engineering  S.B., S.M., Ph.D., Electrical Engineering and Computing Science, Massachusetts Institute of Technology  
Research Interests: Multiresolution statistical signal and image processing; geometric estimation

CATHERINE KLAPPERICH  
Assistant Professor, Biomedical Engineering, PhD, Mechanical Engineering, UC, Berkeley; S.M., Engineering Sciences, Harvard University  
Research Interests: Disposable Diagnostics, Nanomechanics of hydrated biomaterials, biocompatibility at the cell-biomaterial interface, tissue engineering scaffold and microfluidic device design

NANCY KOPELL  
Professor, Biomedical Engineering & Mathematics and Statistics  
PhD University of California, Berkeley, 1967  
Research Interests: Dynamics of the nervous system especially rhythmic behavior of networks of neurons, how dynamical properties of local networks help to filter and transform the patterned input from other parts of the nervous system

ELISE F. MORGAN  
Assistant Professor, Biomedical Engineering & Aerospace and Mechanical Engineering  
MS PhD Mechanical Engineering, UC, Berkeley; B.S. Mechanical Engineering, Stanford University  
Research Interests: Mechanical behavior of biological materials; mechanical stimulation of tissue differentiation; micromechanics of multiscale media; damage mechanics

HAMID NAWAB  
Professor of Biomedical Engineering, Professor of Electrical and Computer Engineering, PhD, SM, SB, Electrical Engineering, MIT  
Research Interests: Computational signal processing, analysis of brain signals, analysis of patient activity signals, analysis of auditory signals
MATTHEW NUGENT
Professor of Biomedical Engineering, Professor of Biochemistry, Departments of Biochemistry and Ophthalmology BUSM BA & PhD, Biochemistry Brandies University

Research Interests: response of tissues to injury and disease, design and use of polymer-based controlled drug delivery systems, tissue engineering, and the development of computational models of dynamic biological processes

TYRONE PORTER
Assistant Professor, Biomedical Engineering, & Aerospace and Mechanical Engineering BS Electrical Engineering, Prairie View A&M Univ., PhD Bioengineering, Washington University

Research Interests: New ultrasound technologies and novel chemical formulations for assessing tissue perfusion, targeted contrast enhancements of diseases in ultrasound images, improving uptake and activity of drugs while reducing adverse side effects

DANIEL SEGRÉ
Assistant Professor, Biomedical Engineeringg, Bioinformatics, Biology PhD, Life Sciences, Weizmann Institute of Science M.Sc., Physics, University of Trieste

Research Interests: Evolutionary dynamics of biological networks, in particular the interplay between response to genetic and environmental perturbations, genomic-level functional organization, and optimal adaptation

EUGENE STANLEY
Professor, Biomedical Engineering, Physics, Physiology, BUSM, University Professor BA Wesleyan University, PhD Harvard University, 1967

Research Interests: Application of statistical physics to understanding and preventing diseases related to protein misfolding; to better understand economic questions (Econophysics), physical mechanisms in liquid water; and threat networks and threatened networks

MARTIN STEFFEN
Assistant Professor, Biomedical Engineering & Genetics and Genomics, BA Chemistry, Dartmouth College; MD/PhD Chemistry, Stanford University

Research Interests: Tools of systems biology for mammalian cells, technique of mass spectrometry, identifying post-translational modifications, characterizing proteomic differences

MALVIN CARL TEICH
Professor, Biomedical Engineering, Electrical and Computer Engineering; & Physics; SB, Physics, MIT, MS, Electrical Engineering, Stanford University, PhD, Electrical Engineering, Cornell University

Research Interests: Wavelet analysis of fractal biological signals; neural coding; auditory and visual psychophysics; quantum imaging

SELIM UNLU
Professor, Electrical and Computer Engineering, Professor, Associate Biomedical Engineering Dean of Graduates PhD, Electrical Engineering, University of Illinois, Urbana-Champaign

Research Interests: Optical characterization and nanophotonics, solid-state and biological phenomena at the nanoscale
MATTHEW WACHOWIAK  
Assistant Professor, Biomedical Engineering and Biology BS Zoology, Duke University, PhD Neuroscience, University of Florida  
**Research Interests:** Olfactory coding and synaptic processing, imaging, neurophysiology

KATHERINE ZHANG  
Assistant Professor, M.S. and Ph.D., Mechanical Engineering, University of Colorado at Boulder, B.Eng. and B.Eco, Engineering Mechanics, Tsinghua University, China  
**Research Interests:** Mechanical behavior of soft biological tissue, Cardiovascular mechanics, Multi-scale modeling of biological composites, Micro- and nano-mechanics of thin film devices

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Research Faculty

NATALIA BROUDE  
Research Associate Professor, Biomedical Engineering BS, MS Organic Chemistry, Moscow State University; PhD, Organic Chemistry, DSci Molecular Biology, Inst of Bioorganic Chemistry  
**Research Interests:** Functional genomics, structure/function relationships in nucleic acids, development of advanced methods for genomic studies

DANIEL EHRLICH  
Research Professor, Biomedical Engineering B.S. Physics, Ph.D. Optical Engineering, University of Rochester, 1977  
**Research Interests:** Optics, lithography, biosensors and biomolecular assays, with a current emphasis on microfluidic instruments for high-content, high-throughput cell-based assays and deep-UV imaging

MARIO CABODI  
Research Assistant Professor, Biomedical Engineering Ph. D. Cornell University, 2003, M. Sc. Imperial College of Science and Technology, London, UK  
**Research Interests:** Microfluidic devices; tissue engineering, and biomaterials

THOMAS L. SZABO  
Research Professor, Biomedical Engineering; PhD, Physics, University of Bath, UK; MS, Electrical Engineering, University of Rochester; BS, Electrical Engineering, University of Virginia School of Medicine  
**Research Interests:** Medical imaging, diagnostic ultrasound, tissue characterization, transduction, biomedical signal processing, wave propagation, nonlinear acoustics
Boston University's Biomedical Engineering
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Senior Vice President & Head of Drug and Biomaterial Research & Development
Genzyme Corporation

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Director, Biology & Preclinical Development
Pulmatrix, Inc.
Class of 1990

Art Coury, Ph.D.
Former Vice President of Materials Research
Genzyme Corporation

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Co-Founder, President & CEO
3Wave Optics, LLC

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Solace Therapeutics

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Johnson & Johnson COSAT
Class of 1989

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Boston Scientific CRM

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Medtronic, Inc.

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Professor, BU School of Management
Director, Entrepreneurship & Management Institute

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3M Health Care Business
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Senior Vice President & Head of Drug and Biomaterial Research & Development
Genzyme Corporation

Art Coury, Ph.D.
Former Vice President of Materials Research
Genzyme Corporation

Steve Girouard, Ph.D.
Senior Director, Emerging Technologies
Johnson & Johnson COSAT
Class of 1989

Warren Grill, Ph.D.
Professor
Duke University
Class of 1989

Sheila Hemeon-Heyer, JD, RAC
Vice President, Global Regulatory Affairs
Boston Scientific Corporation
Class of 1981

Pat Loughlin, Ph.D.
Professor
University of Pittsburgh
Class of 1985

David Meaney, Ph.D.
Professor and Chair
University of Pennsylvania

Kristina Ropella, Ph.D.
Professor and Chair
Marquette University

Art Rosenthal, Ph.D.
Coulter Translational Partnership Project Director
Adjunct Professor, Biomedical Engineering
The Industrial Research Fellowship Program is a program to help students obtain summer research positions in biomedical engineering with potential to extend to Senior Design Projects during the subsequent academic year. This program is made possible by the Donations from the Industrial Supporters of Boston University’s Biomedical Engineering Senior Design Project Program.

With the summer of 2009 marking the fifth year for this fellowship program, students will work on research projects of their choosing in one of the many on campus or local industry laboratories. Each student will be able to choose from a listing of projects and laboratories that are available. Students benefit in several ways. They are able to perform summer research that will hopefully segue into a Senior Capstone Project, they are able to refine their bioengineering skills in practical and state-of-the-art areas, learn how their academic knowledge translates to real challenges, learn to work with a scientific team consisting of a hierarchy of experience and expertise, and enhance their marketability to future employers.

The Boston University Department of Biomedical Engineering would like to acknowledge the generous support of the companies and faculty members who have made this program possible. With each company contributing a minimum of $10,000 annually plus the contributions of our faculty members, the Industrial Sponsored Research and Design Fellowship fund has collected a total $165,745 to help further student research.

Contributing Companies:

3Wave Optics
Boston Scientific Corporation
Corning
Ethicon, a Johnson & Johnson Company
Genzyme
Guidant
Philips Medical Systems
SESSION I
Fooling Mother Nature: Tissue Engineering and Tissue Manipulation
Osteoarthritis is a disease characterized by damage to cartilage in joints. No treatment has been developed for regenerating cartilage in patients with osteoarthritis. However, mechanobiological research has identified mechanical stimulation as a potential means of promoting cartilage formation. This project has developed experimental and statistical tools for investigating how mechanical loading of healing bone fractures can regulate the types of skeletal tissues produced during the healing process. Specifically, these tools enable determination and correlation of local strains and local tissue formation in healing rat femurs that are mechanically stimulated with cyclic bending motion. Strain distributions are measured using a novel optics-based technique. Tissue type distributions are determined using histology. Statistical analyses are then used to compare strain distributions with tissue type distributions. Results from these analyses ultimately describe whether cartilage is more likely to form in tissue regions experiencing low, medium, or high strains during bending. In this project, methods were designed for hydrating specimens during strain measurements without producing large water droplets and interfering with measurement quality. Techniques were designed to control the orientation of specimens throughout histological processing. These techniques enable morphological alignment of the sectioned planes to the plane where strains are measured. Image registration methods were designed to determine regional mapping between strain and tissue type distributions, ensuring that statistical comparisons made are anatomically accurate. The utility of all experimental tools was validated using biological samples, and analytical tools were validated using data from strain and histology experiments. In the future, the experimental methods developed in this project can be applied to a range of in vivo experiments to determine how mechanical stimulation affects tissue fates.
Articular cartilage is an anisotropic, inhomogeneous material that lines the end of long bones in synovial joints. The composition and organization of the extracellular matrix components vary along the depth and surface of the tissue. Our aim in this work is to establish the feasibility of using Contrast Enhanced computed tomography (CECT) to obtain 3D deformations in articular cartilage. This will help establish the mechanical behavior of articular cartilage. Osteochondral plugs excised from bovine knee joints were immersed in an anionic, iodinated contrast agent (Hexabrix™) and secured in a custom built, microCT compatible, micro-compression device. The plugs were subjected to a step displacement of 20% in unconfined mode and imaged using microCT. A 3D volumetric deformation was determined using the Maximum Likelihood Estimate (MLE) method that was developed in MATLAB. The variation of glycosaminoglycan (GAG) content along the depth of the tissue before and after compression was analyzed by the mapping the changes in CT attenuation. The micro-compression device allowed for application of controlled compressive deformation (resolution, 5 μm) and imaging using microCT. The MLE technique was able to compute the 3D deformation of the cartilage after being exposed to an anionic, tri-iodinated, contrast agent and imaged by microCT. The CT attenuation analysis before and after compression showed the increase in the volume fraction of GAG content with compression of the cartilage. In this study we have designed and built a custom micro-compression device that is microCT compatible and allows application of controlled compressive deformations to articular cartilage. We have established the feasibility of using contrast enhanced CT along with the Maximum Likelihood Estimate (MLE) to compute volumetric deformation in articular cartilage. This project provides us with the initial results to determine 3D deformations in cartilage using CECT to better understand the deformation behavior of articular cartilage and improve our understanding of structure-property relationships in normal and diseased tissue, as might occur during osteoarthritis.
Cavitation-Enhanced Fragmentation of Tissue Using Ultrasonic Surgical Aspirating Horns

Derek Cao, Brian Roach

Integra NeuroSciences’ Cavitron Ultrasonic Surgical Aspirator (CUSA) EXcel™ is the undisputed market leader in ultrasonic tissue ablation and has been involved in more than 65,000 surgeries per year with a history in surgery of over 25 years. Though renowned for its precision in cutting soft tissues such as brain tumors and liver, the system’s efficiency in cutting hard tissues such as bone and efficacy in fragmenting tenacious viscoelastic and fibrous tissue can be improved to enable expanded applications. Cavitation might be exploited to improve efficacy by utilizing the energetic collapse of bubbles to assist in fragmenting tissue. Specifically, there are four major steps to this project: 1) the detection of cavitation in liquid; 2) the detection of cavitation in tissue; 3) a removal rate study examining the effects of cavitation on cutting efficacy; and 4) the design and implementation of a cavitation-enhancing device into the current CUSA EXcel™ model. Validation experiments confirmed that the system has different cavitation thresholds with 23 kHz and 36 kHz driving frequencies in both distilled water and saline. The frequency spectra obtained during these experiments using 500 kHz and 1 MHz ultrasonic transducers verified the presence of a cavitation signature (broadband noise). Similar cavitation signatures were observed when the same detection method was applied in fresh bovine liver and beef steak, suggesting the occurrence of cavitation in tissue. In addition, the removal rate studies have shown up to a 60% increase in tissue removal using cavitation-assisted cutting methods. These results have facilitated a method to quantify cavitation in tissue. Moreover, the senior project has also shown the feasibility and practicality of implementing a mechanism to enhance tissue fragmentation using cavitation-assisted cutting methods, with the potential to improve the outcome of future surgeries and the capability of enabling new medical applications.
Researchers in the field of cardiovascular healthcare have produced cell sheets with anisotropic fiber alignment patterns. With controllable fiber alignment, these cell sheets may contribute to the design of suitable replacements for blood vessels. Because the fiber alignment of a tissue sample varies as the sample is stretched, a device that generates fiber alignment maps correlated with the stretching force would be helpful in the engineering process of tissues with defined structure. A piezoelectric cylinder is used to sense the force applied to the sample during a stretching experiment. Simultaneously, a high-speed CCD camera collects images through a focusable optical train. The images and the applied force data are sent to a computer, where alignment maps are generated by software based on the work of Tower et al. (2001). The process is initiated by a user-operated graphical user interface (GUI). The data are post-processed, and then the alignment maps and corresponding force measurements are displayed in the GUI. The tissue sample is suspended in an easily accessible well, designed to minimize friction during the stretching process. The well also keeps the sample in a saline solution, simulating the natural environment of a blood vessel. An additional advantage of this device over similar systems is its cost. Standard optical elements were used instead of a more expensive, custom zoom lens system. In place of a delicate and expensive sensor device, a robust and inexpensive piezoelectric cylinder was used to measure the stretching force. These selected components cost an order of magnitude less than their alternatives. The ability to generate high-resolution fiber alignment maps correlated with stretching force measurements gives the device potential for use in research beyond the development of tissues for treating cardiovascular disease.
A Bottom-Up Approach for Engineering 3D Vascularized Tissue Constructs

Majid Ghodousi, Nikhil Haas

The generation of three-dimensional vascular networks is one of the major challenges of tissue engineering today. While certain organ-specific tissue networks can be derived in vitro using stem cells and a scaffold, the viability of these tissues is limited since they lack an intrinsic vascular network to supply nutrients to (and remove waste from) their cells. In order to push the synthesis of complex organs toward clinical application, a method of generating 3D vasculature must first be developed. Here we describe the directed assembly of cell-laden poly(ethylene glycol) (PEG) hydrogels that closely mimic blood vessels as a novel approach toward overcoming this challenge. Due to their hydrophilic nature, PEG hydrogels bind to one another in a hydrophobic environment. By exploiting this interaction, tubular hydrogel building blocks formed using photolithography were assembled in mineral oil into larger, vascular constructs. Linear arrays of hydrogels were assembled and the final direction, size, and shape of the bifurcating network were controlled by the design of the photolithographic mask. The dimensions of the hydrogel units, viscosity of the oil, speed of the assembly process, and distance between consecutive hydrogels were systematically adjusted and their effects on the assembly of the hydrogels were examined. For each of the mentioned parameters, there was an optimal value that provided consistent results and allowed for the greatest number of hydrogels to assemble. By implementing these optimized values into our fabrication process, fully assembled constructs were consistently achieved. Constructs were made stable using a secondary crosslinking procedure and were perfused with fluorescent beads. To facilitate the perfusion process, assembled constructs were encapsulated in an additional hydrogel layer. Prior to assembly, human umbilical vein endothelial cells (HUVEC) were encapsulated within the hydrogel units. The construct was then surrounded with an additional hydrogel layer containing smooth muscle cells (SMC), simulating the cellular structure of blood vessels. A lumen with a 500µm diameter was branched into consecutively smaller channels, reaching 100µm, with the limiting factor for lumen’s size being the resolution of photolithography. While several cylindrical-based designs were tested, the approach described in this report can be made available to many different designs, leaving room for the development of larger and more complex vascular networks using this method.
Chronic obstructive pulmonary diseases such as emphysema are the fourth leading cause of death in the United States. Emphysema results from the gradual degradation of lung tissue, leading to loss in the ability of the lung to efficiently deliver oxygen. Proteases released by inflammatory cells influence the breakdown of proteins (collagen and elastin) that provide mechanical support within the extracellular matrix (ECM), resulting in increased stress on the remaining matrix. In an effort to engineer a functional ECM replacement, we focused on comparing the biochemical and mechanical responses of neonatal lung fibroblast Gelfoam constructs to various frequencies of cyclic stretching. All studies were completed with and without ascorbate (vitamin C) treatment to modify extracellular matrix composition. The structural importance of collagen and elastin in the ECM led us to complete gene analysis of type 1 collagen and elastin in Gelfoam constructs with and without cyclic stretching at two different frequencies. A 235% increase in elastin mRNA levels and a 927% increase in relative protein content was observed with ascorbate treatment compared to controls unstretched Gelfoam constructs. Stretching caused no significant changes in mRNA levels, but trends indicated potential differences. The mechanical stretching caused no significant loss of sample as the Young’s Modulus, which was calculated with the initial dimensions of the sample, remained constant with time. The ascorbate treated Gelfoams showed an increasing trend in stiffness. The resulting data provided critical clues to methods that could be used to selectively modify the biochemical properties or stiffness of the ECM. Data from this study and future studies, including those where Gelfoam matrices are treated with growth factors and chemicals and subjected to controlled mechanical stimulation, might allow for the in vitro production of biochemically and mechanically functional pulmonary ECM that could be used therapeutically for the treatment of lung disease.
Monitoring Glucose Levels with Fluorescent Sensors in Tissue-Engineered Constructs

Mary Balaconis, Jaclyn Lautz

Sustaining proper nutrients within a multi-layered tissue construct has been a major challenge in vascular tissue engineering. Glucose nanosensors being developed for diabetic care could serve as a monitoring system for ensuring that all layers of these constructs are receiving a sufficient amount of glucose. The overall goal of this project was to monitor glucose levels within stacked cell sheets using fluorescent nanosensors. The two main sub-aims were to design robust fluorescent sensors capable of measuring glucose at physiological levels and to develop thermoresponsive substrates to allow cell sheet attachment and proliferation at temperatures above 32°C and cell sheet detachment below 32°C. For the first main sub-aim, we, along with researchers at the Charles Stark Draper Laboratory, have designed minimally-invasive fluorescent glucose sensors based on a competitive binding scheme between a boronic acid derivative, fluorophore, and glucose. These sensors have proven functional at physiological glucose levels with a dynamic range between 1 mM and 340 mM and a dissociation constant of 31.5 mM. The cell sheet substrate has been successfully grafted with the thermoresponsive polymer, N-isopropylacrylamide (NIPAAm), by photo-polymerization. Also, the amount of PNIPAAm grafted on the PDMS has proven to have a direct relationship to UV exposure time and photoinitiator concentrations. Cell attachment and proliferation on the modified substrates at incubator temperatures (37°C) has been proven successful. The detachment of cell sheets from the substrates at 25°C has also shown promising results for completely detaching and rapidly stacking cell sheets. The successful development of the glucose nanosensors and the progress of the thermoresponsive substrate have provided a foundation for future work involving glucose monitoring within tissue constructs.
3D Freeform Fabrication of a Hybrid Hydrogel Scaffold

Samuel Polio, Francis Doyle, Jr.

The field of tissue engineering is growing at a rapid pace and requires the tools to create three dimensional (3D) environments in which cells and their behavior can be studied. A 3D scaffold is more relevant than a traditional Petri dish for use in studying cell interactions as it more closely resembles *in vivo* conditions. In addition to the cells being present in a 3D environment, the tissues they help compose *in vivo* are inhomogeneous: they integrate many different types of cells and scaffold components. To construct a physiologically relevant scaffold in three dimensions, various microelectromechanical fabrication technologies have been applied to construct 3D scaffolds, but these lack flexibility in designing scaffolds as compared with 3D rapid prototyping techniques. Freeform fabrication technology offers the ability to fabricate scaffolds in a high throughput manner with user defined specifications using 3D or multilayered 2D input. In this work, we report the design and creation of both hybrid and composite hydrogel scaffolds using a multi-channeled, 3D tissue printer. The first design displayed the potential utility of drug delivery through the use of growth factors. It was demonstrated that the components of the fibrin hydrogel used to contain the growth factor could be changed to enhance the drug releasing capabilities of the hydrogel as shown by the changes of morphology of the mouse neural stem cells used for experimentation. The second scaffold, though not fully printed, showed the ability to create a composite construct of human umbilical vein endothelial cell coated, dextran beads for the study of vascularization of tissue engineered scaffolds. Together, these scaffold designs demonstrate the ability to design and fabricate complex hybridized hydrogel structures with cells using 3D freeform fabrication techniques. The techniques developed will serve as a basis for future experiments in creating 3D tissues composed of multiple cell types and scaffold materials *in vitro*. With further development, these methods could become powerful tools for the tissue engineering community as 3D freeform fabricated composite scaffolds could be used in a wide range of experiments to study cell interactions, proliferation, migration, or morphology within a user-designed scaffold.
24th Annual Senior Design Project Conference

SESSION IIa

A Picture of Life: Imaging
A New Concept in High Definition Digital X-Ray Imaging

Madeline Abrams, Justin Martin

Current x-ray technology provides healthcare professionals with a limited resolution image of the area of interest. Current system limitations require invasive diagnosis that delays treatment of disease, may be painful to the patient, and also may expose them to unnecessary risk. We report a real-time x-ray imaging device with resolution as low as 1µm. A fiber optic layer embedded with scintillating particles will convert x-rays into visible light that can be easily read by a charged coupled device. The particles absorb the x-rays and emit visible light, which is guided down the fiber cables via total internal reflection. At the exit, a standard CCD collects and produces the image. Each fiber with be ~1µm in diameter. Each fiber is a distinct pixel creating vast improvements in image resolution, while the CCD allows real time imaging for immediate diagnosis. Scintillating particles are synthesized with an aerosol deposition torch at a much lower cost than conventional methods. Various materials were analyzed to determine the ideal scintillator based on x-ray absorption, visible light emission, particle size, and scattering efficiency. The scintillating bundle layer provides a needed adaptation to modern x-ray imaging that will lead to increased resolution and real-time imaging while dramatically reducing production cost.
Sensor Locator for Surface EMG Array

Megan Fessenden, Allie Paquette

Surface electromyography (sEMG) is a technique for measuring electrical signals from skeletal muscles. This technique has potential for a variety of research and clinical applications in assessing neuromuscular function. However, there is no standard protocol for consistent placement of the sensor on a given muscle during sEMG testing. The absence of such a standard method results in inconsistent sEMG data across different studies. In an effort to solve this problem, a study was designed to find ideal locations for sEMG sensor placement and to investigate the anatomical factors that influence the results at different sites. Statistical modeling was used to determine potential relationships between sEMG motor unit decomposition results for each site and the physiological characteristics of each site. Ideal sensor placement zones were located on the four muscles tested, and the skinfold thickness of the tissue was found to be the most influential anatomical factor on sEMG signal quality and decomposition results. Based on this study, the identified sensor placement zones and a protocol for locating these zones on different muscles will provide guidance for researchers and clinicians for placing the sensor when performing sEMG.
Quantifying Multi-Spectral Parameters in Tissue-Mimicking Gel Phantoms That Exhibit Magnetization Transfer Phenomena: A Multi-Field Study

Jaime Shaw, Natalya Kotlyar, Kate Schwendinger-Roy

Quantitative Magnetic Resonance Imaging (qMRI) is a process in which images are obtained with tissue specific pixel values corresponding to measurable quantities. There is great need for qMRI techniques with full multi-spectral quantitative MRI capabilities. The overall objective of this study was to design a calibration phantom to mimic qMRI parameters of healthy brain tissue and to design a Mathcad algorithm to generate magnetization transfer (MT) parameter values. We report a study in which quantitative parameter (T1, T2, proton density (PD), diffusion (D), and MT) measurements were obtained from an agarose and sucrose phantom to determine the optimal solutions to mimic white matter, grey matter, and cerebrospinal fluid (CSF) of a healthy human brain. A scalable phantom was designed and scanned at 1.5 and 11.7 T. It was determined that the sucrose solutions demonstrated PD, D, T1, and T2 values in the range of biologic tissue and the agarose solutions demonstrated MT phenomena. The MT parameter values determined from the Mathcad algorithm were analyzed as a function of agarose concentration. The resulting protocol and quantitative model can be extended to the development of a standard qMRI calibration phantom.
Design of an Anatomical Ultrasound Simulator

Kevan Desai, Michael Habib, David Scaduto

Ultrasound imaging is a safe and effective imaging modality, but one that is difficult for the practitioner to master. Current ultrasound training systems are expensive and do not present the clinician with consistent patient anatomy. The objective of this project is to develop a low-cost, anatomically correct ultrasound simulator. Images rendered from W.P. Segars’ XCAT cardio-thoracic mathematical model were mapped to a patient model mannequin, providing consistent patient model physiology. Using a combination of open-source applications and MATLAB libraries, these images were transformed to resemble ultrasound images. A corresponding mock transducer was developed using an inexpensive optical sensor to provide realistic, user-driven input to the simulator. An imaging rendering and instructional software interface was developed as a front end to the simulation system. These components were combined to produce a crude working prototype of the training system. A coordinate tracking transducer is used to scan the patient mannequin, and corresponding ultrasound-like images are rendered in the software interface. The basic ultrasound imaging experience is recreated using this approach. The finished prototype provides a foundation for future comprehensive training systems. These systems will be inexpensive and realistic, and will render ultrasound training available to populations in which ultrasound has hitherto been economically impracticable.
Driving System for a Portable Ultrasound Brain Imaging Device for Use in Forward Battlefield Areas

Julie Duran, Karla Mercado

In the frontline battlefield areas, soldiers have a high risk of cranial penetration by foreign bodies, such as metal, wood, and glass. Medical imaging is necessary to detect the presence of these foreign bodies to determine whether evacuation is necessary for further medical attention. A portable trancranial ultrasound device is appropriate for such cases. The overall objective of this project was to design and construct a low-cost, portable multi-channel ultrasound pulser-receiver that would excite the ultrasound transducers and receive the signals. The system improves upon a previously-constructed single-channel pulser-receiver device. In this system, the pulse generator was connected to a multiplexing system to allow for selective excitation among six transducers positioned around the skull for comprehensive brain imaging. The multiplexing system was comprised of six PCB relays that connected the pulse generator to the transducers. A rotary dial was used to selectively direct power to a single PCB relay. A high voltage DC power supply was constructed to produce a variable transducer excitation voltage between ±60 - 170V to overcome the high attenuation inherent in the skull. To test the system, three 1 MHz transducers were coupled to an in vitro human calvarium to investigate a range of transducer incident angles as well as the minimum detectable scatterer size using a stainless steel sphere. Ranging the incident transducer angle between 0 - 45° allowed the optimum angle for longitudinal to shear mode conversion to be identified, using a technique that increases the ultrasound energy transmitted through the skull bone. It was found that positioning the transmitting transducer at an incident angle less than 30° produced high pressure amplitudes for longitudinal propagation. High pressure amplitudes for shear propagation were observed at an incident angle of 40°. The greatest pressure amplitude was observed between 15 and 20°. Our results also show that the minimum scatterer radius our system can detect through skull bone is 1.25mm. The optimal angles for detection of the 1.25 mm radius target were 70° and 280°. These results were compared to MATLAB simulations of incidence angle transmission amplitude and angle-dependent scattering patterns to optimize system performance for comprehensive brain imaging.
Optical Imaging of Coral Regeneration at the Cellular Level

Lauren Tuthill, Ryan Burke

Insights into the process of coral regeneration will help marine scientists to build models to predict how coral reefs are affected by stresses to the system. With such models, resource managers can develop better management strategies and hopefully keep the ecosystem from the verge of collapse. This project develops a method for studying lesion regeneration of the stony coral *Pocillopora damicornis*. Lesioned samples were allowed to heal for either four or twelve days after the initial lesion was made. Standard histological procedures were used to obtain thin sections of the lesioned areas of coral. These sections were stained with a hematoxylin and eosin stain for examination with a light microscope, while unstained sections were examined with an epifluorescent microscope. Concentrations of zooxanthellae and autofluorescent cells were determined from regions of interest and were compared spatially and temporally. Initial results suggest that concentrations of zooxanthellae are greater in the polyps surrounding a lesion than in the coenosarc or in the tissue of a control sample. However, there seems to be no correlation between the zooxanthellae and the autofluorescent cells. The results of this study may be used to explain organismal observations of the regeneration process.
HiLo Fluorescence Endomicroscope

Visar Ajeti, Brett Allaire

Performing minimally-invasive 3-D imaging of cells and tissues is important to the biomedical community. Confocal microscopy is one such technique that offers optically-sectioned images with out-of-focus background rejection. However, confocal microscopes tend to be very expensive, difficult to implement and offer low temporal resolution. Recently, it has been shown that wide-field microscopy can be used as an alternative to realize optically-sectioned images by modifying the illumination pattern. The significance of this project arises from the demand to improve upon existing wide-field microscopy imaging techniques in order to gather optically-sectioned images of high resolution at a faster rate. The objective of this project was to design and construct a fluorescence endomicroscope utilizing a new technique called HiLo imaging, developed in the Mertz Laboratory, to perform real-time 3-D cellular imaging in vivo. This technique requires structured and uniform illumination to provide two images that are processed and yield a confocal-like, optically-sectioned image, with out-of-focus background rejection and little or no motion-induced artifacts. Our project was to build and test various methods to rapidly switch between structured and uniform illumination as well as integrate image acquisition in the process. We were able to achieve significant improvements in image acquisition rate compared to previous endomicroscopes in our laboratory, reducing the effects of motion artifacts in processed images. In addition, this was the first time the HiLo processing algorithm was combined with the image acquisition program to create integrated image acquisition and processing software. Although we were able to successfully integrate the two components, hardware and software limitations hindered our efforts to image samples at video rate. Future work on this project will concentrate on improving the software aspect of our project, such as reducing processing time of the HiLo algorithm.
SESSION IIb

NUMB3RS:
Computation/
Simulation/Analysis
Lesions in the human brain caused by stroke can lead to neurovisual behavioral deficits that have effects on daily activities such as reading or driving a car. Although studies using both imaging and qualitative clinical scales to link behavior and neurological functionality exist, neurovisual impairment in complex visual motion perception has been rarely addressed using imaging and quantitative behavioral evaluation methods in conjunction. This project utilized functional magnetic resonance imaging (fMRI) on normal subjects to determine the neural substrate of higher level visual motion tasks which underlie tasks from everyday living (e.g. navigation and recognition of object motion). We augmented the psychophysical test battery already existing in the Brain and Vision Research Laboratory with additional tests (Biological Motion, 3D Structure from Motion). These psychophysical tests are tests that quantitatively measure behavior. We studied normal subjects’ neural activation while they performed these tests in fMRI. We then studied stroke patients with lesions in the visually responsive cortex with the same psychophysical tasks as used by normal subjects in fMRI. The lesion sites and neurobehavioral deficits experienced by patients were correlated to determine the association between neuropathology and visual behavior. We then retrained these patients' behavioral deficits using psychophysical tests that addressed the behavior to which the patients were impaired. Success of neurovisual retraining was varied, with some patients improving significantly (p < 0.05) in the neurovisual tasks on which they were impaired while other patients did not. These results indicated that neurovisual rehabilitation may be possible, but a more comprehensive exploration over a larger scale must be undertaken before any definitive conclusions can be reached. Overall, the purpose of this study was to determine whether a correlation between patient behavior, lesion location, and cortical region activated by fMRI can be made. When such a relationship is made, this correlation will have important clinical value for diagnosis and prognosis of higher level visual deficits on complex visual tasks involved in activities of daily living.
Simulating Echolocation Using Computational Models of Auditory Physiology
Andrew Dumas, Andrew Rothman

Many species of bats and dolphins rely on their echolocation abilities instead of their vision to navigate and capture prey. The acoustic and neural processing mechanisms of these echolocating species serve as a model for the improvement of aids for the visually impaired. Ultimately, the goal is to develop an aid that rivals the echolocation ability of these animals. An initial step in attaining this goal is to model the bat sonar system by bringing together biophysical models of auditory physiology with modules designed to mimic processing performed by the brain. To this end, the EarLab desktop modeling environment was used to simulate the auditory nerve (AN) responses of a bat, using parameters extrapolated from a behavioral audiogram of the Big Brown Bat (Eptesicus fuscus). Echoes were recorded using a biosonar device initially created as a prototype aid for the visually impaired. An “echo-response library” was populated with AN responses to echoes of commonly encountered objects (e.g. chair, table, etc.). A classifier module was developed to identify the objects using a spectrogram correlation algorithm that compares an unknown input echo with the pre-compiled library of template responses. After comparing the response to an unknown echo with all the templates in the library, the classifier predicted which object the input echo represented. Two additional modules were developed in MATLAB to independently extract target range and localization information in the horizontal plane from the AN responses. Results from the classifier have shown that objects yielding the most complex echoes due to multiple glints are more easily identified. Conversely, objects with smooth planar surfaces are easily confused due to their tendency to reflect sound waves strongly: either directly back to or away from the microphones. Accuracy of range estimates computed from the AN responses of echoes decreases with the signal-to-noise ratio, as either range or signal noise increases. Additionally, the acoustics of the biosonar device have been problematic in estimating azimuth from interaural level differences (ILD). Due to the electronics used and lack of a head shadow resulting from the microphone placement, the level differences between microphones have been unreliable and inconsistent with expectations. Through further refinement of both the biosonar prototype and software used in this investigation, we expect future improvements in speed and accuracy. Hardware implementation of the software algorithms along with the use of an embedded digital signal-processing unit may be able to deliver closer to real-time performance, enhancing the practicality of using such a device as a mobility aid.
The Role of Temporal Fine Structure Cues in Enhancing Speech Intelligibility for Simulated Cochlear Implant Listening

Sruthi Ramakrishnan, Swathi Ramakrishnan

Speech recognition has been shown to degrade strongly in noisy environments for normal-hearing individuals and cochlear implant (CI) users. When the interfering background noise fluctuates over time, normal-hearing individuals are able to “listen in the dips” of the masker and identify target speech. However, CI users, who suffer from profound hearing loss, are unable to benefit from this ability to extract information from a speech signal in the presence of steady or fluctuating background noise.\(^1\) The main objective of this project is to explore whether changes in regularity and synchrony of the temporal fine structure (TFS) of a speech signal provide any dip-listening benefit in allowing CI users to identify speech. To achieve this, a noise-vocoded speech signal and a novel pulse-train-vocoded signal, simulating the use of sparse temporal cues in CI speech, were generated. Regularity was studied by altering the time interval between the pulses within a frequency band of a signal and synchrony was examined by temporally jittering the pulses across frequency channels. CI simulation experiments, designed in MATLAB, were performed on normal hearing individuals, presenting them with various noise and pulse-train-vocoded carriers in the presence and absence of steady and modulated noise and pulse-train maskers. The results show that the asynchronous pulse-train carrier, comprised of irregular and temporally jittered pulses at 2.5ms, enabled high speech intelligibility when presented with steady and modulated maskers. Additionally, subjects gained the greatest dip-listening benefit when presented with this speech carrier in masking noise. Such results suggest that when speech is processed in this form it is easier to understand and subjects have a greater advantage in recognizing the speech when the masker is modulated. The results suggest that the difficulty that CI users have in “listening in the dips” of noise is due, in part, to a lack of difference in TFS between the target and masker. Therefore, this work illustrates that for CI coding strategies to be effective, TFS of the signal is critical.
Asymmetries in Experimentally Measured Inter-Aural Time and Level Sensitivity: Dependence on Spatial Origin and Type of Stimulus

Akshay Navaladi, Raymond Keffer

Aging is often accompanied by loss of hearing ability, a problem that is fairly easily addressed by the use of hearing aids that amplify auditory stimuli reaching the hearing aid user’s ears before playing them to him/her. However, despite the popularity of their products, hearing aid manufacturers have failed to address the issue of asymmetries inherent in the human auditory system with regard to the spatial origin and type of stimulus. In other words, they have failed to address our predisposition to hear sounds coming from certain directions better than other directions, and our predisposition to hear certain types of sounds better than others. Previous experiments concerning the detection of these differences have only studied differences between tonal and narrowband noise stimuli, ensuing in insufficient results. In this study, we measured both time and level JNDs on five human subjects, for three different locations of the reference stimulus (left, midline and right) using a 4 Interval 2 Alternative Forced Choice paradigm and for two types of stimuli (tonal and broadband noise). We found that the time JND measured in the midline case was at least 37µs smaller than that measured with the reference stimulus shifted to the left or right of the subject by ± 600µs. Likewise, we found that the level JND measured in the midline case was at least 0.2dB smaller than that measured with the reference stimulus shifted to the left or right by ± 24dB. Finally, we found that the time JND measured using noise was at least 4µs smaller compared to that measured using tones, while no such trend was observed in the level JND case. These data suggest that humans can detect shifts in spatial location of sound sources in front of them much better than they can towards the sides, and that small changes in spatial location of noise are more easily perceived than those in tone. The knowledge gained from this study can be used to design hearing aids that can better compensate for the age related loss of hearing ability to the sides compared to the front, and with regard to tones compared to noise, thus providing enhanced hearing capabilities to hearing aid users.
Implications of a Meta-Analysis of the Control Properties of Motor Units

Joshua Kline

It has been well documented that during muscle contraction, motor unit firing rates and recruitment patterns vary as a function of force. Independent studies of individual muscles have further revealed that these properties vary across muscles. This project aims to unify the results in the literature, and explore the relationship between motor unit output and motoneuron feedback mechanisms throughout the human musculature. A meta-analysis was performed on data compiled from peer-reviewed journal publications. Outcomes of a weighted regression analysis demonstrate a correlation between the amount of proprioceptive feedback from muscle spindles, and the observed firing rates and recruitment patterns of motor units. That is, muscles with more spindles have lower motor unit firing rates and recruit their motor units over a larger force range than muscles with fewer spindles. A model was designed to quantify motor unit output as a function of muscle spindles and contraction force. Results of the model indicate that during voluntary isometric contraction, muscle spindles decrease the net excitation received by motoneurons of the homonymous muscle. This decrease is more pronounced at higher force levels. It is implicated that spindles, possibly in conjunction with Golgi tendon organs, are in part responsible for the observed motor unit behavior. The constructed model provides an explanation for the potential sources of variation of motor unit control properties reported in the literature. This study is useful in contributing to a more complete model of the human motoneuron pool.
The viscoelastic properties of blood clots have been studied in the interest of developing new medical device technology to treat cardiac patients. The main objective of this project was to develop a consistent method of measuring and determining the viscoelastic properties of a blood. This task involved designing a non-contact method of acoustic levitation and imaging processing, a reproducible blood clot sample, and a liquid chamber for a contact method of measurement. Both the acoustic levitator and liquid chamber use a range of ultrasonic stimuli to mechanically vibrate the blood clot while a digital camera records the physical deformations of the clot. Imaging processing data from these developed methods of measurement were to be analyzed with analytical models that will extract the storage and loss moduli of the blood clot. Key results included the standardization of the procedure for manufacturing blood clots with consistent size and spherical shape. Clots were made from a mold template with multiple spherical wells for efficient production. The mold template could create blood clots with a 65% success rate; it produced clots with an accuracy of ±0.2 mm from the desired diameter size. The problem of evaporation of the clots during their production was solved by using baby oil to coat them. The liquid chamber measurement system produced a qualitative analysis of the blood clot’s non-modal deformations due to ultrasonic stimuli. This system was used to measure the baseline amplitude values of the host fluids oscillations and compare it to the blood clot’s deformations using a time-based comparison. The acoustic levitation method allowed measurements of the deformation and location change of the clot. A thin oil coating of the levitated clot sample was showed to be effective in decreasing the evaporation rate of the levitated clot in air. Additionally, the deformation and location change of a clot in response to various frequencies showed the thin oil coating did not affect the measurement of the viscoelastic properties. The results of the liquid and air levitation measurement systems proved that they are viable and efficient methods of measuring the viscoelastic properties of blood clots.
The Effects of a Soy Protein Diet on the Bone Material and Structural Properties of Estrogen-Depleted Cynomolgus Monkeys

James Schmitz, Sonia Shah

Postmenopausal bone loss is a common concern among women as they age. Estrogen depletion during menopause leads to bone loss with minimal new bone deposition. Several treatments including bisphosphonates and parathyroid hormone are currently used to combat this bone loss. Soy isoflavones have been found to have structural similarity to estrogens and bind to estrogen receptors, raising the question of their potential effects on estrogen mediated pathways. The consumption of isoflavones in high concentrations may reduce menopausal symptoms, osteoporosis, and other health problems. The objective of this study was to determine the effects of a soy diet on estrogen-depletion related bone loss for skeletally mature female Cynomolgus monkeys. Seventy-four Cynomolgus monkeys (age 10 years) were randomly assigned to two diet groups: soy (n= 34) or control diets (n=35). After 32 months of these respective diets, individuals were ovariectomized (OVX), and further divided to create four groups consisting of pre- and postmenopause diet combinations: control-soy (n=18), control-control (n=18), soy-control (n=17), and soy-soy (n=16). Monkeys were sacrificed 32 months later, and vertebrae and femora were harvested. Micro-computed tomography (μ-CT) was used to assess trabecular and cortical bone structure of the fifth-lumbar vertebral bodies (L-5). Peripheral quantitative computed tomography (pQCT) was used to assess bone structure and density of all femora. In addition, a four-point bending mechanical test was developed to assess the material properties of the monkey femora. This protocol was validated by testing six cylindrical wood dowel samples with a diameter of 4.76 mm. The average elastic modulus calculated was 8.77 GPa (SD=0.927) and the actual elastic modulus of the wood is 10.2 GPa. The percent error for the four-point bending protocol was -14.04%. After validation, eight femoral specimens were tested to failure and load displacement curves were measured. Elastic moduli, maximum force, stress at yield and strain at yield were calculated. Results generally indicated that soy has a very slight effect on bone quality. μ-CT and pQCT results indicated no structural changes for soy fed individuals. However, μ-CT analysis suggested that a post-OVX soy diet increased L-5 cortical bone mineral density 2.7% (p=0.02). In the distal femur, pQCT analysis indicated total bone mineral density increased 5.8% (p=0.04) and subcortical density increased 1.6% (p=0.04), but no differences existed in the midshaft. Four-point bending tests resulted in no significant differences across any diet group in Young’s modulus, maximum force, strain at yield or stress at yield. This study shows that soy has no effect on bone structure, but a slight effect on cortical bone tissue density in metaphyseal-like regions.
DNA Sequence Analysis of Genes Linked to Schizophrenia

Mary Harrison, Amy Nehring

Schizophrenia is a complex disease linked to multiple genetic and environmental factors. In 2003, Professor Cassandra Smith and colleagues reported that schizophrenia and other neuropsychiatric diseases are linked to genomic instability. Today, an increasing number of studies support this conclusion. No single or small number of genes has been linked to schizophrenia. Instead, over 100 genes have been linked to schizophrenia in different families. Easier to study neuropsychiatric single gene diseases, such as Fragile X disease and Huntington’s disease, are also linked to genomic instability at specific tri-nucleotide repeating sequences. The goal of this research is to examine the contribution of DNA sequence composition to genomic instability in schizophrenia. A preliminary study examined the sequences of ten genes positively linked to schizophrenia (BDNF, COMT, DAOA, DISC1, DRD1, MTHFR, NOTCH4, RELN, and TPH1). These genes and their associated promoters were analyzed separately. Specifically, these sequences were examined for the presence of repeating sequences that would be prone to mutation, shared transcription factor binding sites not only for co-regulation but also as sites for genetic and epigenetic variability, and co-localization with fragile sites that are regions of the genome known to be unstable. Preliminary results suggest a possible correlation between genes linked to schizophrenia and susceptibility to mutation and alternative splicing. This project included enhancements to The Schizophrenia Gene Analysis Database (SchizoGAD) Project (http://schizogad.bu.edu), which strives to provide the research community with a useful tool to advance schizophrenia research. SchizoGAD, a free online public database, allows researchers to access known information about the genetic basis of schizophrenia, draw comprehensive conclusions that span data derived from multiple studies, and determine new areas to research.
SESSION IIIa

What’s up, Doc?: Diagnostic Technologies and Microfluidic Systems
Inherent properties of microfluidics allow for the facility of transportation, mixing, and separation of reagents with a broad range of reaction conditions such as reagent and reaction concentrations, temperature, and time. These abilities are innate to microfluidics because of the surface area and mass transfer which combined offer a small scale approach to performing relatively pure reactions in high yields with a precise control over the reaction conditions. In order to further explore these intrinsic capabilities of reagents, the center for Chemical Methodology and Library Development at Boston University (CMLD-BU) has developed an automated microfluidics platform. The platform uses the technique of pulse flow, which is the injection of reaction plugs into a continuous stream of solvent. The disadvantage of this technique is the axial dispersion which arises at the liquid/liquid interface, between the reaction pulses and the carrier solvent. This dispersion hinders the ability to obtain pure reactions and allows for cross-contamination between individual reaction plugs, which in turn decreases the high-throughput ability of the system. In order to overcome these limitations, the system was modified to allow for steady state gas-liquid segmentation, which is uniform segmentation of gas and reaction pulses. This was done through the addition of a new high-pressure syringe pump, a back pressure regulator, a mass flow controller, and a gas-liquid separator. The creation of a steady state gas-liquid segmentation was achieved at higher than desired flow rates and minimized the dispersion which was accruing through the system, but did not increase the high throughput ability of the system.
Pressure Control of Optical Fiber Probes Used for Detecting Cancer

John D'Agostino, Gregory Ekchian

Optical Biopsy techniques are capable of extracting physiological information from optical reflectance measurements providing the ability to detect disease in vivo. These reflectance measurements are obtained by directly placing a fiber optic probe on the surface of a tissue sample. At this time, the effects of a probe’s pressure on the physiological properties of the tissue have yet to be fully understood. A study was conducted during which localized probe pressure was applied to live tissue in situ. To ensure constant probe pressure throughout the study, a closed-loop feedback pressure application system was developed and implemented. Throughout the duration of constant pressure application, the tissue sample was illuminated with white light while reflectance spectra were collected three times per second. The reflectance spectra were analyzed using a previously developed analytical reflectance model to determine how the pressure of the probe affects blood volume fraction, oxygen saturation, blood vessel radius, and reduced scattering coefficient of the tissue. Changes in these parameters were tracked as a function of time, before, during and after the application of pressure.
A Thermoplastic Micro-Electrical-Mechanical System (MEMS) for Microfluidic Diagnostic Platforms

Theodorus de Groot, Megan Rexius

Fully integrated microfluidic diagnostic platforms, invaluable devices for the detection of genetic and infectious disease, have largely been manufactured from glass or various elastomers. These materials are high-cost, non-durable, and non-disposable and have subsequently kept powerful microfluidic diagnostic technology from being available at the point of care. A thermoplastic substrate combined with commercially-available fluorinated ethylene-propylene (FEP) Teflon film was used to fabricate a microfluidic device with on-chip microvalves, micropumps, and micromixers. The FEP film was bonded between two thermoplastic layers possessing channel patterns, and it served as the deflecting membrane which controlled fluid flow. The bonding strength at the plastic-Teflon boundary was determined using a pressurized blister test. Using this method, the bonding improvement as a result of different surface modification treatments was established. The designed on-chip microcomponents were operated by a software controlled pneumatic array capable of the actuation of vacuum and air. The software program was developed in LabVIEW to have a user-friendly interface, and control of fluid by the functioning of the microcomponents was demonstrated. The components were capable of maneuvering and mixing precise volumes of fluid, and were shown to have high performance over extended use. On-chip biological assays can be incorporated into the developed Micro-Electrical-Mechanical System (MEMS). The microcomponents were fabricated from materials suitable for integration with point-of-care microfluidic diagnostic applications for which the characteristics of low cost, durability, and disposability are ideal.
HIV AIDS poses a serious infectious disease threat to public health. HIV disease staging and monitoring to determine the initiation and dosage of antiretroviral treatment (ART) requires accurate CD4$^+$ cell count and HIV viral load (i.e. number of HIV viruses per ml of blood). Practical immunoassay based microfluidic devices have been developed for CD4$^+$ cell counting in resource limited settings. However, these immunoassay based microfluidic devices degrade over time as they are exposed to high temperature and moisture conditions. As a result, until proper methods have been devised for preserving the functionality of these CD4$^+$ cell counters, they cannot be introduced in the market for use in resource limited settings. Point of care testing (POCT) to monitor HIV viral load using microfluidic devices has not yet been implemented owing to the challenges related with capturing and enumerating the HIV viruses from blood samples. In this project we aim to further develop POCT techniques for HIV diagnosis. First, we propose to freeze dry the microfluidic CD4$^+$ cell counter to prevent the degradation of the immobilized anti-body and thereby enhance the shelf life of the immunoassay based microfluidic chip. The CD4$^+$ cell capturing efficiency of the freeze dried chips was compared with that of the regular chips. The study showed that the cell capturing efficiency and specificity of the microfluidic channels remained intact after the freeze drying process. Next, we propose to develop a microfluidic that passively filters serum from whole blood samples. This device utilizes a commercially available micro filter to passively extract 4µl of serum from a 10µl whole blood sample. This serum separation device can be used to separate HIV virus containing serum from whole blood of infected patients and can therefore be integrated with an immunoassay based microfluidic device that can capture HIV viruses.
Developing an Automated Device to Purify and Concentrate Bacteria from Whole Blood for SERS Bacterial Diagnosis

Michael Koan, Kenny Lin, Shauna Zane

The increasing prevalence of antibiotic resistant bacteria such as multi-resistant *staph. Aureus* (MRSA) and multi-drug resistant tuberculosis necessitate a rapid, accurate, and inexpensive diagnostic modality to identify infectious bacterial strains and to enable targeted drug therapies. Cell-culturing, the current standard diagnostic technique, is inadequate because it is time-intensive and requires trained technicians in specialized laboratories. Surface-Enhanced Raman Spectroscopy (SERS) is a novel technique that promises direct, fast, and accurate identification of bacteria in solution based on each strain’s characteristic spectrum. However, SERS requires a pure sample of bacteria. The objective of this project was to develop an automated centrifuge-based device to prepare a 10 mL sample of whole blood for SERS imaging by purifying and concentrating any bacteria present in the blood. Experiments were performed using *E. coli* bacteria and a protocol was developed to extract bacteria from whole blood. Centrifugation was chosen as the driving force behind the device because it separates blood components based on density and provides a mechanism of fluid propulsion. Major design tasks included the identification of a selective lysis solution, the optimization of centrifugation steps, and the development of an insert that fits inside existing swinging-bucket centrifuges. The optimal procedure was determined to be centrifugation of 5 mL blood with 5 mL of 0.8% Na₂CO₃ with 0.05% TritonX-100 lysis solution for 5 minutes at 3,220 rcf (relative centrifugal force) followed by a wash step to further remove blood contaminants. Bacteria recovery has been demonstrated to be over 50% and is sufficient to obtain a viable chemical signature from SERS that positively identifies *E. coli*. This work demonstrates the application of SERS to bacteria identification and proposes a protocol to automate the SERS sample preparation process.
The need for improved infectious disease diagnostics, especially in developing nations, has recently received much attention from global health organizations. The laser-based Spectral Reflectance Imaging Biosensor (SRIB) has proven to be a powerful, high-throughput, label-free immunoassay platform for detecting biomolecular binding interactions on reflective, layered silicon substrates. However, the SRIB is not practical for global health and field applications because it is large, expensive, and lacks portability. An inexpensive and compact LED-based optical biosensor is presented that uses interferometry, which was proven to be an effective tool for biological detection by the SRIB. Four surface-mount LEDs with wavelengths in the visible range and narrow spectral bandwidths are used to illuminate an oxide functionalized silicon substrate. The reflectance signature of the sample is captured for each wavelength of light by a CCD camera. The recorded data is then processed using Fresnel reflectivity coefficients, and the topology of the wafer is determined by calculating the effective oxide thickness on the surface. An increase in calculated thickness indicates binding of target molecules to the specific probes spotted on the wafer. An integrated software platform with a simple, easy-to-use graphical user interface was developed that allows for the dynamic detection of these interactions in a high-throughput, microarray format. The system can also be used with higher magnifications for increased spatial resolution and single sub-wavelength object detection. At low magnification, we have shown an RMS noise floor of 3pm, which corresponds to a sensitivity limit for mass accumulation on the surface of 3pg/mm². This sensitivity is comparable to the SRIB, but with a much more economical design and much smaller footprint. Also, the high magnification capability of the system allows for the resolution of single 100nm polystyrene beads at low density, a scenario analogous to single virus detection. The long-term impact of these results is the future development of a commercial optical immunoassay technology that will address the need for high-throughput disease diagnostics for research and clinical applications around the world.
A Microfluidic Chip for Analysis of Mechanical Forces Generated During Cell Migration

Sean Collignon, Else Frohlich

Cell migration is a microscopic *in vivo* process where cells crawl to partake in crucial physiological functions relating to embryonic development, wound healing, and tissue development. Abnormalities of cell migration result in pathologies such as tumor metastasis, angiogenesis, chronic inflammation, and various immune response dysfunctions. The mechanism behind cellular migration and the role of intracellular proteins in the instigation of cell directionality remain poorly understood without effective biomedical devices available. The development of microfluidic biochip technologies enables detection, sample preparation, and treatment on a single chip. We have designed and fabricated a novel microfluidic chip for guiding and quantifying vascular smooth muscle cell (VSMC) migrations. The chip features micropillar arrays imbedded in a multichannel microfluidic chip, where cell migration may be guided by utilizing the characteristics of laminar flow. Non-blending layers of fluid injected through the multi-channel device simulated a wounded edge across a monolayer of cells by limiting flow of trypsin, a serine protease, to half of the main channel, promoting cell migration in a desired direction. Control over cell directionality allows for the measurement and analysis of mechanical forces generated during cell migration in relation to migratory responses from intracellular protein inhibition. The micro-fluidic chip template was designed and manufactured using photolithography techniques. Polydimethylsiloxane (PDMS) served as the bulk material of the two compromising chip layers (channels and pillars), which were subsequently aligned and adhered to form the device. It was confirmed through both computer simulation and experimentation that the optimized arrangement of the chip design effectively held laminar flows of trypsin and cell media. Thus, this microfluidic device allows the user to simultaneously acquire force data during cell migration and observe migratory patterns to ultimately gain a better understanding of the underlying mechanisms of cell migration and directionality.
SESSION IIIb
Wired: Instrumenting Living Systems and Measurement of in vivo Conditions
Transmitter Board Enclosure Design for EM Tracking System

Michael Augelli, Yue Ma

An electromagnetic surgical navigation system utilizes electromagnetic fields to locate surgical tools that are used in minimally invasive image-guided surgery. The electromagnetic tracking system consists of a printed circuit board (PCB) used as a transmitter and a microsensor used as a receiver. The main shortcoming of an EM tracking system is that any metallic object in the vicinity interferes with the system’s accuracy. In the operating room, eliminating the presence of metals is not possible. To reduce the threat of metallic interference, the frequency of the current applied to the transmitter must be reduced. However, this decrease in frequency results in a decrease in signal strength and tracking range. To compensate for the decreased frequencies, the power applied to the PCB must be increased to maintain the same tracking range. This increase in power will result in an increase in temperature on the surface of the PCB. To limit the temperature of any patient- or surgeon-contact surfaces, a PCB enclosure is necessary. However, the additional weight of this enclosure will cause the entire device to deflect, negatively impacting the tracking accuracy. To prevent the PCB from deflecting as well as regulate the temperature of patient- and surgeon-contact surfaces, the design of the enclosure has been optimized using mathematical models that utilize the basic principles of heat transfer and beam mechanics. The prototype has been constructed out of polyetherimide (PEI) and has been tested to determine the enclosure’s effects on accuracy, heat dissipation, and structural performance. Studies have revealed that the enclosure does not impact tracking accuracy. Thermal and deflection studies have been conducted to act as a verification of the mathematical model. In the future, the prototype will be used in clinical studies to evaluate the effects of metallic interference on the tracking accuracy within a specific range. The model will be used by GE as a design tool for future product designs that will be integrated into the surgical navigation system.
Perioperative temperature monitoring is necessary because the effects of hypothermia are costly, both for the patient’s health and for the hospital, but the monitoring is often avoided due to the invasiveness and inconvenience of current temperature measurement techniques. With more consistent monitoring, more patients may be helped not to become hypothermic perioperatively, which will decrease costly complications in surgery and increase patient satisfaction. This project incorporated temperature sensing into Aspect Medical System’s widely used electroencephalogram monitoring system to allow for an accurate, easily monitored core temperature reading. The temperature sensing was added to the system by incorporating a thermistor into a modified Quatro sensor; the thermistor is located over the temple electrode near the temporal artery. This location was chosen because the temporal artery is fed by the carotid artery which is fed by the aorta, and thus is a good approximation of core temperature. To test the sensor prototypes, the forehead temperatures of human subjects were compared to their oral temperatures, which was considered core temperature. An algorithm was developed to convert the thermistor resistance measurements into temperature, using the characteristic curves of the thermistor. With the algorithm, the prototype measurements were within 1.0°C of the forehead temperature and within 2.5°C of the oral temperature.
Ambulatory Vestibular Monitoring Device

Guilherme Goretkin, Kevin Lada

Millions of patients experience some form of balance disorder. It is clinically useful to test the patient’s vestibular system which is closely tied to his sense of balance. Currently, the standard of testing vestibular function is by using special, custom-made equipment in a vestibular laboratory to measure eye movements through the vestibulo-ocular reflex (VOR). However, symptoms may be intermittent and not present while the patient is in the vestibular laboratory. We have created a small wearable device that collects and stores biological signals from the VOR and electrocardiogram (EKG). Four channels of VOR and one channel of EKG data are collected and converted to 24-bit resolution at 200 samples per second, and will be stored in an internal microSD card. It has been shown that the VOR recordings in the ambulatory setting have repeatability and signal clarity comparable to measurements taken with laboratory-based equipment. Our prototype is designed to accommodate further bio inputs using accelerometers, rate sensors, and sound input and output. This finalized device will open a new field of ambulatory vestibular monitoring that will someday provide clinically and diagnostically useful information about the human vestibulo-ocular reflexes, as well as how other physiological systems may affect balance.
Design of a Real-Time System for Partitioning Volume versus Flow Dependence of Respiratory System Resistance in Asthmatics

Nathaniel Steiger, Brian Trautman

Current methods for diagnosing asthma are often tedious for the patient and are highly dependent on patient cooperation, motivating the need for a method that can easily assess asthma severity. The forced oscillation technique (FOT) is an effort independent and noninvasive method that can probe overall mechanical lung function, including respiratory system resistance ($R_{rs}$). Variations in $R_{rs}$ during breathing reflect the distention of airway caliber. Recent studies confirm that patients have stiffer airways, and that this stiffness may reflect airway conditions associated with hyper-responsiveness. We developed a simple computational model that works in tandem with a unique data acquisition system to quantify how $R_{rs}$ varies with lung volumes and flows of breathing. A pilot study was performed on 10 healthy and 6 asthmatic subjects during various breathing maneuvers that encompassed a wide range of volumes and flows. The model parameters were estimated using a linear regression. We first evaluated volume dependent differences in healthy and asthmatic subjects by fitting a simple model with distinct parameters to inspiration data only. These results showed that while there was no statistically significant difference, there was a tendency for the volume dependent parameters in asthmatics to be less than healthy subjects, indicating stiffer airways. Next, we compared the fluctuations in resistance between healthy and asthmatic subjects and used a second order quadratic flow dependent model to examine the origins of the fluctuations. We found that a large portion of variability was due to non-physiological flow effects without any relevance to fluctuations in airway caliber. In conclusion, we designed a versatile system for producing reliable resistance data in real time in healthy versus asthmatic subjects and a simple modeling approach for quantifying volume versus flow effects and variability. In asymptomatic asthmatics there was no dramatic difference in parameters associated with volume or flow differences, although there was slight evidence of stiffer airways. It may be that substantial differences are evident in moderate asthmatics at baseline compared to healthy subjects. We believe the system may provide an alternative approach to distinguish asthma severity.
Emphysema is one type of chronic obstructive pulmonary disease (COPD) usually associated with cigarette smoking. The mechanism and progressive nature of emphysema is not well understood which is why there is no cure. One approach to understanding the progressive nature of emphysema is to study the properties of the lungs following mechanically induced breakdown of the alveoli in both emphysematous and normal mice. To test this, normal C57bl/6 mice were treated with porcine pancreatic elastase (PPE), a compound used to mimic the effects of emphysema, and used on either day 14 or 21 after treatment. Normal mice underwent constant volume ventilation (CV, 8 ml/kg) with 2 intermittent deep inspirations (2DI at 30 cmH$_2$O) every minute. PPE treated mice were divided into 5 groups: 2 week PPE treated mice receiving 2DI per minute (CV2DIE 2WK), 3 week PPE treated mice with 2DI per minute (CV2DIE 3WK), 2 week PPE treated mice with 4DI per minute (CV4DIE 2WK), CV with no DI (CVE), and PPE treated mice with no ventilation (No-Vent E). Respiratory mechanics were monitored and measured continuously. After ventilation, the lungs were resected – the left lobe of the lung was stretched until failure in order to determine the failure stress of the lung tissue, and the right lobe was fixed in formalin for imaging of the parenchymal structure using confocal microscopy. Ventilation of normal mice showed that the respiratory elastance remained constant. However, compared to the normal mice group, the CV2DIE 2WK group’s elastance decreased by 22% (p<0.001), CV2DIE 3WK dropped 32% (p<0.001), and CV4DIE 2WK decreased 29%, which was different from that during CV2DIE 2WK (p<0.01). Using confocal microscopy, average airspace diameters (D) were obtained and showed dependency on both treatment and ventilation. The average diameter of the airspaces were 35 ± 4.3 µm for normal lungs, 67 ± 16.7 µm for PPE treated lungs, and 105 ± 28.2 µm for lungs that were both PPE treated and underwent CVDI. The ventilated lungs also showed higher irregularity in diameter and shape as well as thickened alveolar walls. These results demonstrate that increasing mechanical forces leads to an accelerated lung function decline as a result of airspace enlargement following rupture of the alveolar walls. Moreover, our results may have clinical implications: inappropriate mechanical ventilation may lead to worsening of COPD and accelerate the progression of emphysema.
Understanding Contrast Adaptation in Vision

Wilson Kwan, Wan Seo

Currently, the origin of visual contrast adaptation is not clear and its mechanism is not well understood. It is our hypothesis that contrast adaptation may be a by-product of an existing visual adaptive mechanism called luminance adaptation. Due to the simplicity of its visual system and its similarities with the human optic nerve fiber, we report a study in which neural responses were obtained from the latest eye model of *Limulus Polyphemus* (Horseshoe crab) proposed by Passaglia et al. and from a single optic nerve fiber of the animal, upon exposure to a newly designed Pseudo random binary sequence stimulus with varying contrast. To eliminate luminance adaptation effect, the designed stimulus could modulate contrast at constant luminance (or mean intensity of stimulus). Spike analysis was then performed using a LN (“linear-nonlinear”) model that was implemented into MATLAB to study the temporal processing between the stimulus and the neural response as well as their instantaneous relationship which describes contrast gain control of the eye. As a result, the response predicted by the eye model showed an increase in contrast gain upon exposure to a contrast decrease: the retinal sensitivity, characterized by the amplitude of the linear filter, increased from 0.58 to 0.64 when contrast decreased from 100% to 30%. The physiological data showed a similar result with amplitude of 0.53 in response to the same 100% contrast stimulus. It was concluded that contrast gain could be modulated at constant luminance for the current eye model. Since the model only contains luminance adaptation component, it is strongly suggested that contrast adaptation is a by-product of luminance adaptation.
Design of Apparatus to Assess the Visual Abilities of Rats

John Greifenberger, Nathan Lavallee

During the later stages of glaucoma, a patient’s field of vision is drastically restricted; however, the effects of the disease on visual acuity (temporal and spatial frequency) are not fully understood. To study visual pathologies, animal models are often used to enable laboratory testing. Rats are a commonly used subject for this purpose. To effectively perform these studies, it is necessary to have both a baseline of standard rat vision and an efficient, reliable testing technique. Previously used techniques have not accounted for the free mobility of the subject’s head, which impairs the accuracy of temporal acuity results. These techniques have also relied on significant researcher interaction per trial. For our project, we designed a testing apparatus and method that uses a behaviorally motivated task to assess the visual abilities of both healthy and visually impaired rats. The non-invasive, fully automated design detects the presence of the subject’s head in a motion-inhibiting cone at a specified distance from a display monitor. The designed system is able to output a spatial frequency stimulus ranging from 0.1 to 0.6 cycles per degree or a temporal frequency stimulus of 1, 4, 9, 16, 25, or 36 Hertz. If the rat responds correctly to the displayed stimulus, the system automatically delivers a reward and records the result. In future experiments, this apparatus will be used to acquire visual acuity data from healthy and glaucoma-induced rats.
SESSION IV

Small Things: Nanotechnology, Molecules, Cellular Control
Detection of biological markers is important in pharmacology and medicine. Nanotechnology has significantly enhanced the sensitivity of detection through the use of nanoscale structures as sensing platforms. We present a study in which silicon nanowires were used as a conductance channel between the source and the drain of a field effect transistor (FET) to detect biomarkers via conductance change caused by biomolecular binding on the surface of the nanowires. Arrays of multiple 200nm wide nanowires were fabricated through complementary metal-oxide-semiconductor (CMOS) compatible top-down methods including electron beam lithography. In addition, a microfluidic flow cell was designed and integrated with the device to provide a continuous flow of solution over the nanowire arrays. The surfaces of the nanowires were functionalized according to the target biomarker. Our primary biomarker of interest was CA15.3, which is an antigen associated with breast cancer. Serum samples with varying concentrations of CA15.3 were passed through the device via a flow cell while a bias voltage was applied. Conductance differences due to a change in concentration of CA15.3 were not definitively observed. However, nanowires functionalized by biotinamidocaproyl-labeled bovine serum confirmed our device’s ability to detect changes in conductance when tested for antibiotin. The surface functionalization of the device for CA15.3 antibodies needs to be improved before it can be a viable real-time, label-free, and highly sensitive FET-based sensor.
Early identification of metastatic breast cancer would lead to significant improvements in the treatment of breast cancer patients. Currently an ELISA test is used to measure relevant concentrations of the breast cancer tumor marker CA15.3, a strong indicator for metastatic breast cancer. However, this test is considered slow and not very accurate. The objective of this project was to design and develop a nanomechanical cantilever-based biosensor that can detect the cancer antigen 15.3 (CA 15.3) biomarker. The nanomechanical approach would be quicker than the standard ELISA technique while showing similar, or better, levels of sensitivity. The task required three main processes: fabrication of the devices, functionalization of the devices, and testing analysis. The nanomechanical cantilevers were fabricated using aluminum nitride (AlN) wafers which provide piezoelectric properties upon chemical binding events. The wafers were fabricated using a standard nanofabrication technique in a three-cycle process to produce a final chip with free-standing cantilevers with a molybdenum ground electrode and a gold top electrode. The device was then functionalized using a thiol surface modification technique using CA 15.3 antibodies. The final device was tested using an electric circuit with an LCR meter and LabView software. The capacitance of the device was measured with and without the antigen. The average capacitance with no antigens present in solution was 39.65pF while the average capacitance with 1100 U/mL of CA 15.3 antigen was 30.61pF. The average capacitance with 2200 U/mL of antigen was 29.11pF. This decreasing trend shows the antibody-antigen binding event caused a significant change in the piezoelectric properties of our cantilevers. A Student’s t-test results in a p-value of 6.53×10^{-7} showing that the values of blank solution versus antigen solution are statistically significant. The data collected shows that the nanomechanical cantilever-based biosensor has the potential to be a viable method for detecting CA 15.3 or possibly other biological particles. With further design provisions and extensive testing, this method may provide an alternative to the standard ELISA technique for cancer antigen 15.3 detection by providing a quicker turnaround and slightly better sensitivity.
Threshold-Based Detection in *Escherichia coli*: Interfacing Synthetic Gene Networks

David Shi, Ioana Lupascu

A genetic counter with a digital output could have many applications in biotechnology. Developed in *E. coli*, the counter behaves as a four-state cellular memory unit and could be used as a controller to study and direct cellular processes. While the capacity to design and control biology holds considerable promise for the future, foundational technologies must first be developed so that engineered biological systems behave as desired. The counter, for instance, exhibits undesirable output 'leakiness': a weak output signal is generated before it has counted to its maximum. Here we report a synthetic genetic device designed to filter the output signal of the genetic counter. Exploiting features of the genetic toggle—a bistable gene-regulatory network—this filtration system would pass gene expression signals that exceed a certain threshold (superthreshold), effectively endowing the counter with digital output behavior and making it more practical as a cellular controller. The genetic three-counter—originally designed to express Green Fluorescent Protein—was reconstructed to output TetR protein, enabling the network to be interfaced with the toggle switch. The toggle plasmid pTSMa was also modified to depend on LacI and TetR protein inputs, resulting in a system with predictable, temperature-independent behavior. The two completed plasmid constructs were then co-transformed into *E. coli* strain JM2.300 to study the integrated network’s response to various chemical inputs. Experiments showed that the counter’s output was sufficient to induce switching in the LacI/TetR toggle. However, superthreshold TetR expression signals were generated by the counter when induced with either two or three pulses of arabinose. To elicit filtering behavior from the system, two input pulses of arabinose must generate a subthreshold output from the counter while three input pulses must generate a superthreshold output. To achieve this, we are currently fine-tuning the counter’s protein expression level and the filter’s switching threshold.
Acoustic cavitation has been known to create pores on the cell membrane through which therapeutic drugs or other macromolecules could be delivered to the cell’s cytoplasm. It has been shown that both types of cavitation (stable and inertial) cause cell permeabilization; however, there has been no quantification of the material delivered or identification of appropriate cavitation parameters for different molecule delivery. Here we intended to determine which type of cavitation yields higher molecule delivery as well as whether there is a correlation between type of cavitation activity and size of molecule delivered. It is known that cavitation can be lethal to cells and therefore we also attempted to identify the appropriate cavitation parameters such that cell viability remained above 80%. By constructing a novel exposure system for murine endothelial cells, we were able to conduct cavitation experiments where the cells were exposed to lipid-shelled microbubbles and 20kDa (representative of small molecules) dextran-FITC molecules. The amount of fluorescent molecule delivered and the viability of the cells were both quantified using flow cytometry coupled with hemacytometry. Our data suggests that microstreaming due to stably oscillating bubbles is the primary driving force behind sonoporation, rather than the shearing forces caused by inertially collapsing bubbles. In general, we found that stable cavitation was also less damaging to the cells, making it a better option for future therapeutic applications to treat cardiovascular diseases. These conclusions will be useful in directing further cavitation studies pertaining to cavitation’s potential for drug delivery.
Triggering Genetic Toggle Switch through Ultrasound-Induced Heating

Jason Maley, Willis Hong

As researchers and clinicians in the field of genetic engineering work to translate discoveries in gene therapy from the laboratory to the hospital, they face the tremendous challenges of delivering and activating the desired therapy in a controlled manner, and safely targeting the areas of interest within the patient without adverse systemic responses. One novel approach to targeted genetic therapy may be to control a temperature sensitive genetic toggle switch by heating the precise area of interest in a patient and locally activating gene expression. The reported study developed a model to test the feasibility of controlling a genetic toggle switch, and therefore gene expression, within tissue using high-intensity focused ultrasound as a means of targeted heating. An ultrasound phantom was created to hold and maintain cells and respond to ultrasound targeting by mimicking the heating that tissue would experience under similar conditions. A genetic toggle switch that could be flipped between two states to turn green fluorescent protein (GFP) production on or off was then employed within *E.Coli*. The “on” state was activated after 7-12 hours of a chemical incubation, resulting in GFP production as a reporter. Significant flipping of the toggle switch to “off” state was then achieved after only 35 minutes of ultrasound-induced heating. This study shows that focused ultrasound-induced heating is a practical, non-invasive, and targeted means of controlling toggle switch gene expression within physiologically relevant time and temperature parameters. The results now serve as a foundation for future work that will further study ultrasound activation of the toggle switch for the controlled production of clinically relevant proteins. From cancer to cystic fibrosis, mutated genes and protein deficiencies account for the presence a multitude of dangerous and currently incurable diseases. By controlling expression of any desired gene at the exact site of a patient’s ailment, ultrasound-induced activation of a genetic toggle switch may offer a safe and effective means of treating these diseases.
Design and Characterization of a Polymer-Based Implant for Treatment of Age-Related Macular Degeneration

Rahul Ahuja, Balaji Nithianandam

Wet Age-related Macular Degeneration is an ocular disease that stems from the leakage of newly formed capillaries behind the retina. The leakage damages Retinal Pigment Epithelial (RPE) cells and consequently photoreceptor cells leading to loss of central vision. Biodegradable polymers have previously been shown to be safe vehicles for transplantation of replacement cells and delivery of drugs into the eye. The goal of this project was to design a Poly (ε-Caprolactone) (PCL) scaffold for the delivery of functional RPE cells and the protein, Pigment Epithelial Derived Factor (PEDF), to prevent the formation and leakage of new blood vessels in the sub-retinal space. Different transplant release models were evaluated with varying concentrations of PEDF to determine the most desirable release model for the final transplant. High molecular weight PCL crosslinked with a peptide hydrogel infused with PEDF provided the desired release and was chosen. In addition, type IV collagen was successfully crosslinked with PCL to improve the biocompatibility of the transplant. In vitro testing was performed with mouse RPE cells which were successfully adhered onto the transplant. The transplant was then tested in photoreceptor and endothelial cell cultures in separate experiments to test the neuroprotective characteristics of RPE cells and antiangiogenic properties of the released PEDF. Due to the presence of PEDF, endothelial cell proliferation was reduced by over 47%. This confirmed the protein's ability to maintain function after being incorporated into a polymer. Moreover it was established that survival rate of photoreceptors increased by more than 30% in the presence of the transplant in vitro, compared to samples of plain PCL in photoreceptor tissue culture. Therefore, it was concluded that PCL may be an effective biopolymer for the delivery of PEDF and RPE cells and can be used for the treatment of wet Age-related Macular Degeneration.
Polymers and polymeric derivatives have proven to be highly effective in providing localized and controlled drug delivery to tumor cells. Nanoparticles, which are expansive hydrogel encapsulants, increase drug efficacy by delivering directly to the resection site and thereby reducing the side effects of systemic chemotherapy. A critical component of this delivery system is determining the release profile to ensure constant, steady delivery of the drug. Current techniques of determining the release kinetics utilize \textit{in vitro} methods such as High Performance Liquid Chromatography (HPLC) or fluorescence microscopy. However, these methods fail to predict the impact of biological interactions on the release profile. We detail a novel assay that can be used to advance researchers’ understanding of the release kinetics of localized drug delivery systems by activating fluorescent pathways within live cells. A small molecule, anhydrotetracycline (aTc) is loaded into the particles. When taken up by the cell, it activates an mRNA transcriptional response indicated by the onset of a fluorescent signal. Quantification of the fluorescence allows determination of the amount of aTc metabolized by the cell and thus an accurate assessment of the effective release kinetics of the nanoparticles. Results showed that insufficient quantities of aTc were loaded into the system to trigger cell mechanisms. However, further tests were conducted to ensure the proper function of the nanoparticles themselves; and results showed proper functioning.