27th Annual
BME SENIOR DESIGN PROJECT CONFERENCE 2012
MAY 4th
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Raeef Istfan, Ashish Malladi, Benjamin Weinberg; Magi El Manchy, Xhorxhi Gjoka, Rahul Modi; Jae Yeon Kim, Ajinkya Nene; Katherine Black, Ryan Pope; Ian Cody MacDonald, Anne Marie Weber
Welcome from the Chair

It is my distinct pleasure to welcome our guests, our alumni, industry representatives, our faculty and our students to Boston University’s 27th Annual Biomedical Engineering Senior Design Project Conference. This conference has become an annual right of passage for all BU BME seniors, and culminates our year-long Senior Design Project Program. This program is recognized as a national model for the capstone independent design and communication experience for BME undergraduates, and helps us train the future leaders and innovators in bioengineering. Over the course of the day, our talented students will present their state-of-the-art design projects as they complete their BS degrees from one of the top Biomedical Engineering programs.

Biomedical Engineering synthesizes engineering, computation, math and physical sciences with the life sciences to advance our understanding of biology, physiology and medicine. This understanding is then exploited to develop new devices and methods to improve medical care. The BU BME BS degree program is one of the oldest such programs in the country. Our ABET-accredited BS degree program in Biomedical Engineering is designed to provide integrated training in life, physical, and engineering sciences as preparation for a variety of careers in bioengineering, applied biotechnology, and medicine. We also offer an Industrial Internship Program that places students in companies for up to a year.

Seniors must also engage their projects via a course called “Product Design and Innovation in Biomedical Engineering” coordinated by Professors Art Rosenthal and Tom Szabo, with guest lectures by members of our Industrial Advisory Board. The course teaches students concepts of design, intellectual property, patents, regulatory issues, and marketing, all in the context of their projects.

This year’s senior design project program was directed by Professor Irving Bigio. He invested much energy and organizational skills to sustain the level of excellence and impact for which this program is renowned. Professor Bigio was assisted by a team of BME faculty (Professors Mertz, Szabo, Tien, Voigt and Zaman) who read, graded and commented on all written assignments, proposal drafts, oral proposal presentations and progress reports. Their efforts helped ensure that the program continued to sustain its level of excellence. I also served as part of this team and was fortunate to enjoy the program in all of its dimensions. I also want to acknowledge the assistance of Professor Joe Bizup and Lindsey Gilbert from the BU Writing Program. Finally, a very special thank you to Christen Bailey for her sustained support and tireless efforts to coordinate all aspects of today’s program.

Our students are remarkable at rising to the challenge and I have no doubt that their presentations today will impress and entertain you. Enjoy!

Solomon R. Eisenberg, ScD
Professor and Chair, Department of Biomedical Engineering
Associate Dean, College of Engineering Undergraduate Programs
Research Centers

BioMolecular Engineering Research Center
Center for Memory and Brain
Center for Nanoscience and Nanobiotechnology
CompNet
Hearing Research Center
NeuroMuscular Research Center

Research Laboratories

Auditory Biophysics and Simulation
Auditory Neurophysiology
Auditory Neuroscience
Binaural Hearing
Biomedical Optics
Biomicroscopy
Biomimetic Materials Engineering
Biomolecular Systems
Brain and Vision
Cabodi Research Group
Cell and Tissue Mechanics
Cell Photometrics
Cellular and Subcellular Mechanics
Collins Lab
Computational Genomics
Cortical & Computational Decoding of Speech
Fields and Tissues
Frank-Kamenetskii Lab
Galagan Lab
Grinstaff Group
Han Lab
Khalil Lab
Klapperich Laboratory for Appropriate Healthcare Technologies
Laboratory for Molecular and Cellular Dynamics
Lab for Engineering Education & Development
Laboratory for Advanced Biotechnology
Matrix Mechanotransduction
Molecular Biotechnology
Natural Sounds and Neural Coding
National Emerging Infectious Disease Lab
Pulmonary Physiology and Dynamics
Respiratory Research
Respiratory & Physiological Systems Identification
Ritt Lab
Single Molecule Biophysics and Nano-Biotechnology
Smolina Group
Structural Bioinformatics
Synthetic Biology & Immune Cell Engineering
Szabo Lab
Tien Group
Vascular Interface and Microhemotfluidics
# 27th Annual Senior Design Project Conference

— Friday, May 4, 2012 —

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<td>7:15 – 8:00 AM</td>
<td>Continental Breakfast</td>
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<td>8:00 AM</td>
<td>Welcome and Opening Remarks: Prof. Irving Bigio</td>
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| 8:10 – 10:05 AM | SESSION I  
PHO 206   | We Have the Technology: Helping the Human Body                      |
|             | Session Chair: Prof. Steve Colburn                                   |
|             | Optical Walking Stick: A Vibrotactile Sensory Substitution Aid       |
|             | Mark Guirguis, Arjun Patel, Parth G. Patel                           |
|             | Investigating Electroencephalography-Based Brain-Computer Interfaces for Communication in Healthy Populations and Individuals with Motor Impairment |
|             | Xudong Chen, Anthony Rinaldi, Dante Smith                            |
|             | Design of an Experimental Environment for Investigating Hand Movement Coordination |
|             | Leslie Kim, Linda Nguyen                                             |
|             | Stochastic Resonance Knee Brace                                      |
|             | Nathaniel Hixon, Victor Radulescu                                    |
|             | Continuous Monitoring of Functional Activities and Movement Disorders in Individuals with Parkinson's Disease |
|             | Dan Chin, Aubrey Gasbarre, Alexandra Walco                           |
|             | Design of a Novel Video Game-Based Rehabilitation Tool for Velopharyngeal Dysfunction |
|             | Elias Thorp, Boris Virnik                                             |
| 10:05 – 10:25 AM | COFFEE BREAK                                                        |
SESSION IIa
PHO 206
Status Report: Diagnostic Technologies

Session Chair: Prof. Solomon Eisenberg

Visual Detection of Emerging Pathogens
Vedran Beganovic, Zachary Tochka, Anastasia Yaroslavsky

Compact Interferometric Reflectance Imaging Sensor for Biomolecular Interaction Analysis
Joseph Greenspun, Nicholas Luzod

Extraction of DNA from Blood Samples for Point-of-Care Sepsis Diagnostic Chip
Rubayath Mohsen, Alexis Rodriguez Valenti

Impedance Array for Single Cell Studies
George Chapman, Alexander Paloranta, Eric Schwarz

Quantitative High-Throughput Biomarker Discovery by Mass Spectrometry on Label-Free Arrays
Julian Anding, Herve Mathelier, Michael Shaw

Functional Imaging of the Intervertebral Disc
David Berry, Daniel Grasso, Megan Sperry

Contrast-Enhanced Computed Tomographic Imaging of Fracture Calluses
Chantal de Bakker, Keri Mroszczyk

SESSION IIb
PHO 203
Small Things: Molecules, Cells and Nanobits

Session Chair: Prof. Thomas Szabo

Tantalum Oxide-Based Nanoparticles as Contrast Agents in Biomedical Imaging
Jae Yeon Kim, Ajinkya Nene

Mesenchymal Stem Cell Matrix Remodeling
Molly Ford Dacus

Cellular Traction Force Measurement of Mesenchymal Stem Cells under Biochemical Stimulation
Dongjian Hu, Katheryn Rothenberg

Automated Design and Assembly of Reconfigurable Genetic Regulatory Networks
Aaron Berliner, Joshua Hodgson, Vanessa Yanez

A Novel Kidney Glomeruli Isolation System (KGIS)
Magi El Manchy, Xhorxhi Gjoka, Rahul Modi

Patterning of Multiple Extracellular Adhesion Molecules
Ian Cody MacDonald, Anne Marie Weber

Control of Organization and Function in a Tissue-Engineered Vascular Patch
Andrew Schiff, Angela Xie

12:25 – 1:05 PM LUNCH
1:05 – 3:00 PM  
PHO 206  
SESSION IIIa  
Just a Spoonful: Drug Delivery and Compliance

Session Chair: Prof. Catherine Klapperich

Multifunctional Targeted Colloidal Particles for Inhibition of Endothelial Cell Inflammation  
Oluwatosin Adedokun, Christopher Hernandez

Localized siRNA Delivery with Lipid-Coated Modified Polyethylminine  
Morgan Giles, Steven Mathews, Teena Varghese

In vitro Mucosal Membrane Culture Model for Drug Delivery  
Hufsa Iqbal, Angela Nocera

Design of an Algorithm Incorporating the Glycemic Index in Insulin Bolus Delivery Estimations for the Treatment of Type I Diabetes  
Julian Hart, David Nathaniel Tan

Design of a Microfluidic Device for the Preparation of pH-Sensitive Expansile Nanoparticles to Prevent Local Recurrence of Intraperitoneal Mesothelioma  
Raeef Istfan, Ashish Malladi, Benjamin Weinberg

Paper Microfluidics for HAART Drug Adherence Monitoring  
Suhina Minocha, Evelyn Orozco

1:05 – 3:00 PM  
PHO 203  
SESSION IIIb  
Connections: Interfacing to Living Systems and Tissue

Session Chair: Prof. Jason Ritt

System for Sensing, Characterizing and Displaying the Neural Signal Response of Stimulated Rat Brain Tissue in vitro  
Parth P. Patel

Neurocognitive Assessment Using the iPad Platform  
Raymond Byrne, Raphael Landaverde

Portable Proportional Myoelectric Controller  
Rachel Carande, Jessica Fraser, Benjamin Huey

Ergonomic Redesign of a Laparoscopic Clip Applier  
Katherine Black, Ryan Pope

Glenohumeral Joint Kinematics and Contact Pressures during Simulated Pitching: A Cadaveric Study  
Megan Lee, Max Lerman, Natalia Vieira

Development of LabVIEW-Based Data Acquisition System for the Evaluation of Respiratory Mechanics  
Jacob Herrmann, Frank Zong

Design of an Isolated Airway System to Establish How Long-Term Exposure to Inflammatory and Contractile Mediators Alters Airway Reactivity  
Dorothea Crowley, Sharon Wolfson

3:00 – 3:15 PM  
COFFEE BREAK
3:15 – 5:15 PM SESSION IV
PHO 206 We are the World: Global Health Technologies

Session Chair: Prof. Muhammad Zaman

Robust Dissolution System for the Detection of Counterfeit Drugs in Resource-Limited Settings
Caitlin Monahan, Dayana Rojas

Tissue Diagnostic Instrument for Global Health Applications Based on Optical Spectroscopy: Phase II
Lisa Cervia, Vincent Zuo

Robust Device for Reagent Storage in Resource-Limited Settings
Cassidy Blundell, Imaly Nanayakkara, Joseph Pirrello

System for Nucleic Acid Preparation for TB Diagnostics (SNAP-TB)
Rachel Deraney, Kaitlin Gargiulo, Chelsea Saniel

Point-of-Care Diagnostic Device for Liver Cancer and Hepatitis B in Resource-Limited Settings
Supriya Jain, Hang Su, William Tsang

Miniaturization of a System for Nucleic Acid Preparation for HIV Diagnostics (miSNAP)
Pawel Kalinowski, Rotimi Ogunbiyi

Modeling of Artificial Sputum for Use in Tuberculosis Diagnostics
Kali Brong, Stephanie Nelson, Shahar Torton

5:15 PM Final Conference Comments and Award Presentations:
Prof. Irving Bigio
Current & Recent Conference Attendees
27th Annual

MAY 4th

Technical Advisors
& Faculty Profiles
# 2012 Senior Design Project Technical Advisors

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<td>Jason Ritt</td>
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<td>Xu Dong Chen, Anthony Rinaldi, Dante Smith</td>
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<td>Leslie Kim, Linda Nguyen</td>
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<td>Nathaniel Hixon, Victor Radulescu</td>
<td>Leia Stirling</td>
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<td>Dan Chin, Aubrey Gasbarre, Alexandra Walco</td>
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<td>Elias Thorp, Boris Virnik</td>
<td>Cara Stepp</td>
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<td>Irina Smolina</td>
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<td>Joseph Greenspun, Nicholas Luzod</td>
<td>Selim Ünlü</td>
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<td>Julian Anding, Herve Mathelier, Michael Shaw</td>
<td>Bennett Goldberg</td>
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<td>David Berry, Daniel Grasso, Megan Sperry</td>
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<td>Jae Yeon Kim, Ajinkya Nene</td>
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<td>Molly Ford Dacus</td>
<td>Michael Smith</td>
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<td>Dongjian Hu, Katheryn Rothenberg</td>
<td>Michael Smith, Joyce Wong</td>
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<td>Aaron Berliner, Joshua Hodgson, Vanessa Yanez</td>
<td>Joel Henderson</td>
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<td>Magi El Manchy, Xhorxi Gjoka, Rahul Modi</td>
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<td><strong>Session IIb</strong></td>
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<tr>
<td>Oluwatosin Aidedokun, Christopher Hernandez</td>
<td>Mario Cabodi, Tyrone Porter</td>
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<td>Morgan Giles, Steven Mathews, Teena Varghese</td>
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<td>Parth P. Patel</td>
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<td>Raymond Byrne, Raphael Landaverde</td>
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<td>Rachel Carande, Jessica Fraser, Benjamin Huey</td>
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<td>Katherine Black, Ryan Pope</td>
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<td>Megan Lee, Max Lerman, Natalia Vieira</td>
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<td>Jacob Herrmann, Frank Zong</td>
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<td>Kenneth Lutchen</td>
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<td>Caitlin Monahan, Dayana Rojas</td>
<td>Muhammad Zaman</td>
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<td>Lisa Cerva, Vincent Zuo</td>
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Primary Faculty

IRVING BIGIO
Associate Chair of Graduate Programs for Biomedical Engineering; Professor of Biomedical Engineering, Electrical & Computer Engineering and Physics. BS, MS, PhD - 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; laser physics.

H. STEVEN COLBURN
Associate Chair of Undergraduate Programs for Biomedical Engineering; Professor of Biomedical Engineering; Director of the Hearing Research Center. BS, MS, PhD - Massachusetts Institute of Technology.
Research Interests: Measurement and modeling of binaural hearing performance; speech intelligibility in complex sound environments; the effects of hearing impairments on binaural abilities.

JAMES COLLINS
Professor of Biomedical Engineering; University Professor; William F. Warren Distinguished Professor; Investigator, Howard Hughes Medical Institute. BA - College of the Holy Cross; PhD - University of Oxford.
Research Interests: Synthetic biology; systems biology; antibiotics.

EDWARD DAMIANO
Associate Professor of Biomedical Engineering. BS, PhD - Rensselaer Polytechnic Institute; MS - Washington University.
Research Interests: Integrated cellular and extracellular biomechanics; biofluid dynamics; microchemofluidics; non-Newtonian rheology; closed-loop blood-glucose regulation.

CHARLES DELISI
Dean Emeritus; Metcalf Professor of Science and Engineering; Professor of Biomedical Engineering and Physics. BA - City College of New York; PhD - New York University.
Research Interests: Developing and applying computational/ mathematical methods and high throughput experimental methods to analyze changes in gene and protein expression profiles of cells in response to various endogenous and exogenous signals.

CARLO DE LUCA
Professor of Biomedical Engineering and Electrical & Computer Engineering; Research Professor of Neurology; Director of the NeuroMuscular Research Center. BA - University of British Columbia; MS - University of New Brunswick; PhD - Queens University.
Research Interests: Motor control of normal and abnormal muscles; innovative technology for monitoring and analyzing surface EMG signals.

MICAH DEMBO
Professor of Biomedical Engineering. BS - Allegheny College; PhD - Cornell University.
Research Interests: Statistical mechanics in biological systems; cell information processing and signal transduction; thermodynamics and mechanics of cell adhesion; biophysics of cell deformation; active motility.

SOLOMON EISENBERG
Associate Dean for Undergraduate Programs; Chair and Professor of Biomedical Engineering; Professor of Electrical & Computer Engineering. BS, MS, ScD – Massachusetts Institute of Technology.
Research Interests: Electrically-mediated phenomena in tissues and biopolymers; cartilage biomechanics; computational modeling of electric field distributions in the human thorax and heart during defibrillation.
EVAN EVANS
Professor of Biomedical Engineering.
BS, MS - Rensselaer Polytechnic Institute; PhD - University of California, San Diego.
Research Interests: Nano-microscale mechanics; ultrasensitive force probes and extreme resolution optical techniques; material properties of cellular structure; role of structural forces in cell biochemistry.

MAXIM FRANK-KAMENETSKII
Professor of Biomedical Engineering.
MS, PhD - Moscow Physical Technical Institute; ScD (IVth degree) - Institute of Chemical Physics, USSR Academy of Sciences.
Research Interests: DNA structures; DNA topology; DNA functioning; PNA (peptide nucleic acid).

JAMES GALAGAN
Associate Professor of Biomedical Engineering; Associate Director of Systems Biology; Associate Director of Microbial Genome Analysis. BS – University of California, Davis; PhD – Massachusetts Institute of Technology.
Research Interests: Developing efficient and accurate methodologies for the analysis of genomic data, with a particular focus on infectious diseases; computational biology; genomics; microbiology.

MARK GRINSTAFF
Professor of Biomedical Engineering and Chemistry. BA - Occidental College; PhD - University of Illinois, Urbana-Champaign.
Research Interests: Biomaterials; tissue engineering; drug delivery; macromolecular chemistry and engineering; self-assembly; nanodevices.

XUE HAN
Assistant Professor of Biomedical Engineering. BS - Beijing University; PhD – University of Wisconsin, Madison.
Research Interests: Neurotechnology; optical neural modulation; optogenetics; neural prosthetics; neural network dynamics; brain rhythms; neurological and psychiatric diseases; cognition.

ANDREW JACKSON
Professor of Biomedical Engineering.
BS, MS - University of Nevada; PhD - University of Mississippi Medical School.
Research Interests: Respiratory physiology; respiratory mechanics; role of airway closure in asthma.

SIMON KASIF
Professor of Biomedical Engineering.
BS - Tel Aviv University; MS, PhD - University of Maryland.
Research Interests: Computational biology; computational functional and comparative genomics; biotechnology; algorithm design; bioinformatics; computer-aided biology.

AHMAD KHALIL
Assistant Professor of Biomedical Engineering. BS – Stanford University; MS, PhD – Massachusetts Institute of Technology.
Research Interests: Synthetic biology; systems biology; programmable microfluids; transcription regulation; mechanobiology; single-cell analysis; single-molecule biophysics.
Catherine Klapperich
Associate Professor of Biomedical Engineering and Mechanical Engineering. MS – Harvard University; PhD – University of California, Berkeley. Research Interests: Nanomechanics of hydrated biomaterials; gene expression in cells at the cell-biomaterial surface; microfluidic device design.

Kenneth Lutchen
Dean; Professor of Biomedical Engineering. BS - University of Virginia; MS, PhD - Case Western Reserve University. 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.

Amit Meller
Associate Professor of Biomedical Engineering. BS – Tel Aviv University; MS, PhD – Weizmann Institute of Science. Research Interests: Employing nanopore force spectroscopy to study RNA unfolding and re-folding kinetics; DNA switches and transcription initiation kinetics; RNA helicases activity; mapping of transcription factors interactions with DNA; ultra-fast DNA sequencing.

Jerome Mertz
Professor of Biomedical Engineering and Physics. BA - Princeton University; PhD - Université Paris VI and University of California, Santa Barbara. Research Interests: Development and application of new optical microscopy techniques to biological imaging.

David Mountain
Professor of Biomedical Engineering; Research Professor of Otolaryngology. BS – Massachusetts Institute of Technology; MS, PhD - University of Wisconsin. Research Interests: Auditory information processing; sensory biophysics; computer simulation; biomedical electronics; biomedical signal processing; environmental engineering.

Jason Ritt
Assistant Professor of Biomedical Engineering. BS – Oberlin Conservatory; MA, PhD - Boston University. Research Interests: Neuroscience of sensorimotor behaviors; biological active sensing; functional role of embodiment in neural computation; brain-machine interfaces; neural prosthetics.

Kamal Sen
Director of Graduate Admissions for Biomedical Engineering; Associate Professor of Biomedical Engineering. BA - Bates College; MA, PhD - Brandeis University. Research Interests: Neural coding of natural sounds; hierarchical auditory processing; neural discrimination; population coding of natural sounds; learning in single neurons and auditory networks.

Barbara Shinn-Cunningham
Professor of Biomedical Engineering and Cognitive & Neural Systems. BS – Brown University; MS, PhD – Massachusetts Institute of Technology. Research Interests: Auditory attention; spatial hearing; neuro-electric imaging; neural coding; plasticity and learning in auditory tasks.
CASSANDRA SMITH
Professor of Biomedical Engineering, Biology and Pharmacology. BA, MS - West Virginia University Medical School; PhD - Texas A&M University. **Research Interests:** Molecular biotechnology; genomics; schizophrenia; breast cancer twin studies.

MICHAEL SMITH
Assistant Professor of Biomedical Engineering. BS - University of Memphis; MS, PhD – University of Virginia. **Research Interests:** Mechanotransduction via the extracellular matrix; fibronectin structural biology; engineered cell culture platforms for regulating cell behavior in vitro.

DIMITRIJE STAMENOVIC
Associate Professor of Biomedical Engineering. Dipl. Ing - University of Belgrade; MS, PhD - University of Minnesota. **Research Interests:** Respiratory mechanics; cellular mechanics; rheology of soft tissues and cells; mechanics of foam-like structures.

BELA SUKI
Professor; Biomedical Engineering. MS, PhD - Jozsef Attila University. **Research Interests:** Mechanical properties of living tissues; the ensemble behavior of complex biological systems; nonlinearities in biological systems.

JOE TIEN
Associate Professor of Biomedical Engineering. BS – University of California, Irvine; MA, PhD – Harvard University. **Research Interests:** Vascularization of biomaterials; quantitative physiology of engineered tissues; biomaterials for microsurgical applications; lymphatics and interstitial transport.

LUCIA VAINA
Professor of Biomedical Engineering; Research Professor of Neurology. MS, University of Timisoara and Urbino; PhD – Universite Paris I (Pantheon-Sorbonne); Doctorat d’Etat es Sciences and Medecine (Neurologie) – Institut National Polytechnique de Toulouse. **Research Interests:** Computational visual neuroscience; neuronal mechanisms underlying spatial representation; visual motion perception; perception and action.

SANDOR VAJDA
Professor of Biomedical Engineering; Director of the Biomolecular Engineering Research Center. MS - Gubkin Institute; MS - Éötvös Lorand University; PhD - Hungarian Academy of Science. **Research Interests:** Scientific, primarily optimization, computational chemistry and biology (including protein and peptide structure determination); protein engineering; drug design.

HERBERT VOIGT
Professor of Biomedical Engineering; Associate Research Professor of Otolaryngology. BA – City College of New York; PhD - Johns Hopkins University. **Research Interests:** Auditory neurophysiology; neural circuitry; neural modeling.
JOYCE WONG
Associate Professor of Biomedical Engineering. BS, PhD – Program in Polymer Science and Technology, Massachusetts Institute of Technology.
Research Interests: Biomaterials; tailoring cell-material interfaces for drug delivery and tissue engineering applications; direct, quantitative measurement of biological interactions.

WILSON WONG
Assistant Professor of Biomedical Engineering. BS - University of California Berkley, PhD – University of California Los Angeles.
Research Interests: Systems biology of cancer; cell adhesion and migration in 3D environments; cellular mechanics; applications of biomedical engineering in the developing world.

MUHAMMAD ZAMAN
Assistant Professor of Biomedical Engineering. PhD - University of Chicago.
Research Interests: Systems biology of cancer; cell adhesion and migration in 3D environments; cellular mechanics; applications of biomedical engineering in the developing world.

CHARLES CANTOR
Professor Emeritus of Biomedical Engineering and Pharmacology. BA - Columbia University; PhD - University of California, Berkeley. LOA, CSO Sequenom
Research Interests: Human genome analysis; molecular genetics; new biophysical tools and methodologies; genetic engineering.

TEMPLE SMITH
Professor Emeritus of Biomedical Engineering. BS - Purdue University; PhD - University of Colorado. Research Interests: Syntactic and semantic structure of the genetic information in biomolecular sequences, structures and their evolution.
NATALIA BROUDE
Research Professor of Biomedical Engineering. BS, MS – Moscow State University; PhD, DSci – Institute of Bioorganic Chemistry, Moscow.
Research Interests: Functional genomics; genome-wide methods for genome studies; bacterial internal organization.

MARIO CABODI
Research Assistant Professor of Biomedical Engineering. MS – Imperial College of Science and Technology; PhD – Cornell University.
Research Interests: Micro and nanofabrication applied to biomedical engineering problems.

DANIEL EHRLICH
Research Professor of Biomedical Engineering. BS, PhD – University of Rochester.
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.

ODED GHITZA
Research Professor of Biomedical Engineering. BS, MS, PhD – Tel Aviv University.
Research Interests: Decoding speech using neuronal oscillations; hierarchical neuronal oscillators and the basis of cortical computation; analysis of MEG signals recorded while performing a speech perception task; predicting consonant confusions in noise; modeling damaged cochleae using speech-governed methodologies.

DYMTRO KOZAKOV
Research Assistant Professor of Biomedical Engineering. MS – Moscow Institute of Physics and Technology; PhD – Boston University.
Research Interests: Macromolecular recognition; networks of signaling protein-protein interactions; druggability of genomes; protein design.

ARTHUR ROSENTHAL
Professor of Practice in Translational Research in Biomedical Engineering; Director for the Coulter Translational Partnership Program. BS – University of Connecticut; PhD – University of Massachusetts.
Research Interests: Design, development, marketing and entrepreneurship in biomedical engineering.

IRINA SMOLINA
Research Assistant Professor of Biomedical Engineering. BS, MS – Moscow Institute of Physics and Technology; PhD – Institute of Bioorganic Chemistry, Russian Academy of Science.
Research Interests: Exploring the possible use of biological and synthetic DNA analogs for applications in bioengineering, molecular imaging and single-molecule analysis.

THOMAS SZABO
Research Professor of Biomedical Engineering; Research Professor of Mechanical Engineering. BS – University of Virginia; MS – University of Rochester; PhD – University of Bath.
Research Interests: Medical imaging; diagnostic ultrasound; tissue characterization; transduction; biomedical signal processing; wave propagation; nonlinear acoustics.
CHRISTOPHER CONNOR
Assistant Professor of Biomedical Engineering; Assistant Professor of and Director of Research for the Department of Anesthesiology. BA, M.Eng – Cambridge University; PhD – Massachusetts Institute of Technology; MD – Harvard University. 
Research Interests: Applying the principles of minimally-invasive medical engineering, physiology and information technology to clinical issues in anesthesiology.

DOUGLAS DENSMORE
Assistant Professor of Biomedical Engineering and Electrical & Computer Engineering. PhD – University of California, Berkeley. 
Research Interests: High-level languages for synthetic biology; data exchange standards for biological parts and devices; system-level design of embedded systems; computer architecture; design for test.

THOMAS EINHORN
Professor of Biomedical Engineering; Chairman and Professor of Orthopaedic Surgery. MD – Cornell University Medical College. 
Research Interests: Hip and knee replacement and reconstructive surgery; treatment of metabolic disease; stem cell surgery for avascular necrosis of the hip and knee; nonunion fractures.

SHYAMSUNDER ERRAMILLI
Professor of Biomedical Engineering and Physics. BS – University of Pune; MS – Indian Institute of Technology; PhD – University of Illinois. 
Research Interests: Biological physics.

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SESSION I

We Have the Technology: Helping the Human Body
Optical Walking Stick: A Vibrotactile Sensory Substitution Aid

Mark Guirguis, Arjun Patel, Parth G. Patel

There are few electronic ambulation aids that are commercially available for blind persons, and the aids which are available are often cumbersome, expensive, and unreliable. Traditional devices, such as the walking stick and guide dogs, have several limitations and do not take full advantage of today’s technology. The goal of this project is to employ the concept of sensory substitution to create an effective, modular, and cost effective electronic ambulation aid for the visually impaired. We have designed a system that utilizes inexpensive sensors to obtain optical information about the user’s environment, which is conveyed to the user through unique tactile signals transmitted via a vibro-tactile actuator placed on the tip of the user’s index finger. Whereas most other aids use algorithms to transmit limited information from sensors to users, the device developed here provides users with a rich set of information and lets users interpret the data. The device designed and tested in this study demonstrates the possibility of developing a functional and inexpensive travel aid by exploiting the concept of sensory substitution and the dynamic nature of the human brain. This version of the device successfully applies sensory substitution to transmit visual data through tactile signals, and experiments have shown that users are successfully able to locate objects using the device. Future versions of this device will incorporate a wider array of unique tactile signals to convey more visual information to users, and make improvements to system hardware and software components.
Locked-in Syndrome (LIS) is a neurological condition characterized by the loss of most or all motor control while retaining cognitive functions. As a consequence, locked-in individuals are unable to interact physically with their environment and have limited or no means to communicate. Brain Computer Interfaces (BCIs) offer a method for locked-in patients to communicate with others and to manipulate their surroundings. By collecting electro-encephalogram (EEG) data and converting the recorded brain activity into usable computer commands, a paralyzed individual can navigate computer menus, or control a computer cursor. Applications for BCIs include a grid shaped word and phrase selector, a TV remote, or a mobile robotic platform. Our approach was to design a custom and economic EEG acquisition cap, complementary decoder software, and software applications for a locked-in individual who has retained the ability to blink. The method of control for our BCI will be to induce steady-state visually evoked-potentials (SSVEP) with a four-choice flashing stimuli presented on a computer screen in front of the user. We have created custom electrodes to acquire EEG data from the visual cortex, and microcontroller firmware to transmit recorded data to a computer. We also have two applications to use with the BCI, one being a menu of phrases, another being an infrared transceiver and program to control a television. Finally we have a diagnostic program which graphically displays changes in output from the user and EEG cap in response to varying SSVEP stimuli.
Often stroke causes dysfunction of upper extremities, especially the hands, limiting functionality and execution of daily activities. Current quantifying methods are limited to one-dimensional analysis of hand and finger movement data which measures the time it takes to complete a task. The aim of this project is to design a computer program that will determine stroke patient hand deficits using fourteen sensor data collection gloves as input for the program which was implemented in Matlab. The sensors collected flexion data of each of the major joints of the hands, which are the metacarpophalangeal joint (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP). By observing and researching current stroke rehabilitation techniques, hand grips were selected to reflect interactions with everyday objects which are consistent with current research. Once a variety of hand positions were selected, a group of normal subjects were tested using both words and images as stimuli. By applying linear regression and multivariate analysis of variances between groups (MANOVA), the hand positions selected were tested to determine consistency between normal subjects and differentiable hand positions in terms of the data collected. Certain hand oriented tasks were eliminated due to large variability in normal subject data. Additionally, some tasks were determined to have large overlap in the data collected making the hand positions redundant for the purposes of this program. After applying the program to test two stroke patients, hand positions were eliminated or added based on further observations of stroke patient hand kinematics. Future testing is necessary to ensure that the program can be applied to patients who suffer from varying hand deficits. Additionally, the differences in the hand kinematics detected will be used to generate two-dimensional visual feedback for use during rehabilitation. To understand the long-term hand deficits suffered by stroke patients, this program will be implemented in a future brain imaging study to relate the difference in brain activity and the difference in the hand movement data.
Stochastic Resonance Knee Brace

Nathaniel Hixon, Victor Radulescu

Decreased proprioception in the knee can lead to instability, re-injury, or complication of degenerative diseases such as osteoarthritis. Injury, disease, and aging are causes of decreases in knee proprioception. Although knee bracing and elastic bandaging are methods currently used to compensate for proprioceptive losses, these methods do not significantly improve proprioception during dynamic or weight bearing tasks. Our approach to this problem was to use stochastic resonance to enhance proprioception by mechanically stimulating the mechanoreceptors in the knee joint with a sub-threshold level of noise. Stochastic resonance (SR) is the phenomenon where the application of a specific level of noise can enhance signal recognition and detection in biological systems. We achieved this by embedding piezoelectric mechanical actuators in a knee brace to deliver targeted SR stimulation to the mechanoreceptors in the patellar and quadriceps tendons. An electronic control box comprising of a programmed Arduino microcontroller was designed to generate the noise and to control the amplitude and presence of SR stimulation. As part of a pilot study, a subject with an ACL injury performed joint position sense (JPS), standing balance, and dynamic squat tasks with SR stimulation (test condition) and without SR stimulation (control condition) while wearing the device. These conditions were analyzed in a motion capture laboratory equipped with AMTI OR-6 force plates and Vicon cameras and were used to measure changes in knee angle and load distribution. It was found that the introduction of stochastic resonance stimulation increased power generation during a squat and improved the accuracy of JPS of the injured leg.
Parkinson’s disease (PD) impacts patients’ quality of life and daily activities by decreasing motor functions due to neurodegeneration. The primary concern with PD is how patients’ gait and postural stability are compromised, leading to falls that are particularly hazardous for the elderly. Physical therapy in conjunction with external rhythmic stimulus, or sensory cueing, has been shown to improve patients’ compromised abilities. In this senior design project, sensory cueing in the form of a rhythmic auditory stimulus (RAS) has been implemented into functional activity monitors (FAMs), which are small wireless devices including an iPod application and sensors consisting of a gyroscope calibrated by an accelerometer that records movements. The objective was to improve the FAM’s accuracy, real-time feedback delay, and measure additional functional activities that will enhance patients’ rehabilitation. Algorithms were developed to filter and analyze FAM data transmitted to the iPod Touch. Accuracy of the FAM’s sensors and the transmission delay were compared to the Motorola PDA used in previous research. The purpose of comparing these results was to check the accuracy of the algorithms for real-time feedback during instrumentation manipulations at different amplitudes and movement frequencies. Additional algorithms were designed to detect an excessive forward lean of the trunk, a disordered stride frequency, and exercise duration in human subject testing. To evaluate forward lean, five subjects completed one trial walking at varying inclines and the FAM successfully emitted auditory feedback for the set thresholds of 14 and 20 degrees. For step frequency, one subject walked at varying frequencies while the FAM emitted auditory feedback for the set thresholds of 0.8 and 1.2 Hz. For exercise duration, five subjects completed three trials of varying walking speeds. At the end of one minute, an auditory cue was given and subjects successfully ended their exercise. Results show that the iPod Touch is comparable to the Motorola PDA and provides feedback with a delay ranging from 0.2-1.0 seconds, increasing as angular velocity reached 20 and 30 degrees per second. For all experimental procedures, the FAM provided accurate feedback for the established thresholds. The FAM can be further adapted for other rehabilitation needs, such as assisting stroke victims in regaining their endurance. The application is an invaluable tool for physical therapists and expands the FAM’s functionalities. It is hypothesized that the benefits provided by the FAM during physical therapy will help improve patients’ overall quality of life. These capabilities can provide a greater understanding of functional activity deficiencies in the human body.
Design of a Novel Video Game-Based Rehabilitation Tool for Velopharyngeal Dysfunction

Elias Thorp, Boris Virnik

The velopharyngeal port is the small opening in the back of the throat that connects the nasal cavity to the pharynx. Proper function of the velum, which opens and closes this port, is essential for the production of intelligible speech. Impairment of this function results in speech that is highly nasalized and often unintelligible. This study focuses on designing a sensor to assess velopharyngeal function objectively while being minimally invasive and appropriate for at-home use. The sensor was designed using a wide band accelerometer and a standard headset with microphone. This device was used to develop a control signal comprised of the measured nasal acceleration and acoustic output. In two different experiments, speech data were collected from healthy young adults producing vowels in both nasalized and non-nasalized contexts using the developed sensor. For the first experiment (N = 6), three data normalization strategies were explored to develop a control signal capable of reliable sensitivity and specificity of nasalization in a variety of vowel contexts. A second experiment (N = 8) was used to compare the consistency of the designed sensor and control signal to the industry gold standard. The normalization strategy showed high discriminability of nasalization and reduced effects of intra-speaker variability when compared to the standard methods of velopharyngeal assessment. Utilizing the developed control signal, a videogame system was developed to be used in conjunction with the sensor to provide visual feedback about velopharyngeal function and promote rehabilitation. In a small pilot study, videogame enjoyability and sensor usability were measured in both children and adults. Results suggest that the simple game is easy to play while being enjoyable for a wide range of participants. This sensor coupled with the videogame-based rehabilitation tool provides high discriminability between nasalized and non-nasalized vowels and appropriate visual feedback to promote rehabilitation.
SESSION IIa

Status Report:
Diagnostic Technologies
Visual Detection of Emerging Pathogens

Vedran Beganovic, Zachary Tochka, Anastasia Yaroslavsky

Infectious disease is a leading cause of death in developing countries, largely due to a limited access to resources and a lack of appropriate diagnostic tools. Traditional diagnostic methods rely on culture amplification of the bacterial pathogen, a time and labor consuming process, while new technologies like real-time PCR tend to be expensive and not readily available to health care facilities with limited funding. We report a new method for the detection of bacterial pathogens that employs a combination of Peptide Nucleic-Acid (PNA) technology, Rolling Circle Amplification (RCA), and a DNA enzyme (DNAzyme) sensor system. This method can distinguish between DNA sequences based on a single nucleotide mismatch, has a low limit of detection, and does not require any elaborate diagnostic equipment. The developed protocol was successfully used to detect a short (less than 30 base-pair) sequence of \textit{E. coli} DNA under non-denaturing and isothermal conditions. The results presented here indicate that this detection protocol has the potential to improve clinical diagnosis of bacterial pathogens in resource-limited settings.
Compact Interferometric Reflectance Imaging Sensor for Biomolecular Interaction Analysis

Joseph Greenspun, Nicholas Luzod

Microarrays are commonly utilized in biosensing applications to measure phenomena such as gene expression and protein binding interactions. Despite the ubiquity of microarrays, there exists no standard method to quickly determine spot morphology. Poor spot morphology can lead to misleading data in diagnostic binding experiments and invalid test results. Current fluorescent techniques have high sensitivity but fail to produce quantitative measurements. A device, the Interferometric Reflectance Imaging Sensor (IRIS), was previously reported by Daaboul, et al. which is capable of determining height across a layered silicon substrate by measuring optical interference. This height measurement directly correlates to the accumulation of biomass. A device has been designed which retains the same capabilities of IRIS while reducing its size, cost, and experimentation time. Our system images the output of a handheld projector onto the surface of a microarray and uses a photodetector to acquire reflectance data for three narrowband illumination spectra. The data is reconstructed into images and analyzed to determine surface topography. A dilution experiment was conducted using Immunoglobulin G (IgG), and measured using both IRIS and the developed device. The results showed comparable sensitivity between devices. Work is currently progressing toward the creation of a standalone embedded system capable of automated data collection and processing for remote applications.
Extraction of DNA from Blood Samples for Point-of-Care Sepsis Diagnostic Chip

Rubayath Mohsen, Alexis Rodriguez Valenti

Sepsis is a life threatening medical condition caused by the presence of pathogenic organisms in the bloodstream. Detecting bacterial infections in the blood to provide immediate diagnosis and treatment is essential to saving lives. Currently, diagnoses are determined through blood culture, which may take up to three days to confirm and identify the presence of pathogenic organisms in the bloodstream. This delay results in the use of broad-spectrum antibiotics preventing a point-of-care diagnosis. We report a study in which DNA is extracted from E. coli infused blood to quantify the amount of bacteria present. Porous polymer monoliths were created using High Internal Phase Emulsion (HIPE) to extract DNA from the lysed blood samples. DNA extraction rates were examined and optimal conditions were determined. These results can be applied to a patient-safe method to reduce the overuse of antibiotics and reduce the mortality rate due to sepsis.
Impedance Array for Single Cell Studies

George Chapman, Alexander Paloranta, Eric Schwarz

Cell impedance sensing provides a specific platform for noninvasive studies of environmental effects on cell viability, such as a cell’s reaction to certain chemicals. Current methods of cell impedance sensing rely on detecting the impedance across an entire cell culture, which is ineffective at determining changes occurring within cells. We proposed a device that improves on the current methods of cell impedance sensing by isolating single cells and performing single cell impedance sensing. The device isolates cells by using electrodes to induce dielectrophoresis. Dielectrophoresis (DEP) induces a directed force upon a dielectric particle placed in a non-uniform electric field, and is a proven method capable of a high degree of specificity that does not affect cell viability. The generated electric field from the DEP-inducing electrodes was simulated using COMSOL Multiphysics, and electrode geometry was optimized so that the gradient of the electric field created a cell-trapping region. The scope of our project included designing a device for isolating cardiomyocytes, and a separate device for isolating cardiac side population cells. Each device will be capable of measuring the impedance across each isolated cell. The devices were fabricated using physical vapor deposition and photolithography techniques. In our first iteration of the devices, we only included the DEP-inducing electrodes to favor the inclusion of many variations of each design. From these devices, we determined the optimal electrode design for cell isolation to include in the second iteration of the devices, where the impedance-sensing electrodes will be included; second generation devices will be designed in future studies. Electrical impedance was tested using a low throughput design as proof of principle, and shows the electrical impedance testing of single cells is possible. Based on these findings, second iteration devices can be fabricated and promise successful measurements of single cell electric impedance readings.
Quantified High-Throughput Biomarker Discovery by Mass Spectrometry on Label-Free Arrays

Julian Anding, Herve Mathelier, Michael Shaw

A biomarker is the generic term given to molecules, primarily proteins, that have enabled clinicians to better diagnose disease, develop specialized treatment regimens, monitor treatment response, and provide more accurate prognosis. Despite a decade of intensive search, there are few validated biomarkers available, given the tens of thousands of proteins that change state in response to human disease. Thus, there is a great need for novel biomarkers especially those related to chronic disease, such as heart disease and cancer. A promising new technology has recently been developed that couples protein assays with mass spectrometry to enable biomarker discovery. The protein assays are measured using Interferometric Reflectance Imaging Sensor (IRIS), which optically detects height changes indicative of protein binding activity. The captured protein is then identified and characterized using Matrix Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS). Combining the technology platforms, referred to as IRIS-MALDI, aims to be a high-throughput and less costly technique for biomarker discovery and allows for simultaneous development of the validation assay. However, the technology has had limited success due to high batch-to-batch variability in starting surface heights of the chips for assaying proteins. The objective of this project is to improve the technology by redesigning the chip and performing proof-of-principle experiments using the known biomarker, Prostate Specific Antigen (PSA). Several modifications to the chip manufacturing process were made, including adding quality control, incorporating more favorable antibody immobilization conditions and creating a superhydrophobic chip surface for better confinement of analyte and matrix. The results from several batches of chips produced indicate low spot-to-spot chip surface variation. A PSA titration assay performed on a modified chip was also conducted and likewise indicated low variation in the antibody and PSA accumulation heights. MALDI-TOF MS confirmed the presence of PSA at the higher concentrations. Feasibility experiments for an on-chip digestion were conducted and demonstrated the ability of MALDI-TOF MS to accurately detect samples on the scale of tens of femtomoles. The redesigned chip improves the efficiency of IRIS-MALDI and augmented protocols show the potential to increase the amount of relevant information produced concerning novel biomarkers.
Loss of glycosaminoglycan (GAG) content in the nucleus pulposus of the intervertebral disc (IVD) has been identified as a precursor to osteoarthritis. Currently, there is no clinically available, minimally invasive, diagnostic technique to predict biochemical degeneration of the IVD. In this study, a non-destructive, diagnostic technique for assessing IVD degeneration was developed and tested ex vivo, as a first step towards developing a clinically feasible method. This technique used a new, cationic, iodinated contrast agent in conjunction with computed tomography (CT) imaging. The objective of the study was to determine whether contrast-enhanced CT (CECT) imaging of the IVD could predict spatial variations in GAG concentration and mechanical properties within the disc tissues. Various methods of delivery of the contrast agent were explored to optimize transport of contrast agent into the GAG-rich areas of the IVD (7 discs, ages 41-85 years): 1) immersion following complete dissection of the disc from the adjacent vertebrae; 2) immersion following partial dissection of the disc from the adjacent vertebrae; 3) direct injection; and 4) direct injection with mechanical convection, simulating walking. Following CECT imaging, GAG content was assessed using a biochemical assay. For a separate set of discs (n=3, ages 42-85 years), multiple cylindrical samples of tissue were harvested for each disc (n=44 total) and underwent CECT imaging and biochemical analysis. Half of these samples underwent creep testing prior to CECT imaging. Delivery methods 1 and 2 were found to be too slow, while method 4 produced the fastest distribution of the contrast agent throughout the disc and the best predictions of GAG content (R²=0.72, p<.0001). Tissue samples from the healthy IVDs showed a trend between CECT attenuation and GAG content (R²=0.10, p=.06). The cylindrical samples from the nucleus pulposus and annulus fibrosus showed a trend between CT attenuation and aggregate modulus (p=0.1, R²=0.26) and a correlation between CT attenuation and permeability (p=0.03, R²=0.37). The investigation of optimal delivery methods and efficacy of the contrast agent that was carried out in this study provides a basis for further development of this CECT technique for ex vivo, and possibly in vivo, use for understanding IVD degeneration.
Contrast-Enhanced Computed Tomographic Imaging of Fracture Calluses

Chantal de Bakker, Keri Mroszczyk

X-ray computed tomography (CT) is a reliable imaging tool used to non-invasively evaluate complications in the healing of bone fractures, but standard CT only allows for the visualization of mineralized tissue, limiting its application to the later stages of fracture repair. Recently, CT imaging in the presence of a cationic contrast agent has been developed as a method for visualization of the non-mineralized, cartilaginous soft callus, which forms during the early stages of fracture healing and is essential to the healing process. However, the ability of contrast-enhanced CT (CECT) to track the healing process has not yet been assessed. This project aimed to further develop the CECT method for ex-vivo monitoring of fracture repair by evaluating the effects of incubation time and callus composition on visualization of the soft callus. Fracture calluses in the femora of C57BL/6J mice were scanned both before and after they were exposed to the contrast agent. The resulting images were registered, and the pre-incubation image was subtracted from the post-incubation image to create a 3-D map of the locations of contrast agent. The thresholds on the subtracted images that were required to consistently label cartilage tissue were determined through a custom analysis of the histograms of image intensity. To establish an optimal incubation time such that cartilage could be quantified accurately, the calluses were exposed to the contrast agent for times ranging from 1 to 14 hours. The extent of diffusion of the contrast agent was determined by calculating both the area and mean intensity of tissue classified as cartilage at each incubation time. These values were fitted to an exponential curve, which approached equilibrium values after approximately eight hours of incubation. Fracture calluses harvested at 7, 14, and 21 days post-fracture were then analyzed using an incubation time of eight hours to quantify cartilage within the heterogeneous and temporally evolving callus and to compare the morphology of the soft callus among different stages of healing. The total volume and the average intensity of cartilage tissue were calculated for each specimen and compared among the three days. Differences were observed in both the total volume and mean intensity of cartilage tissue, which may demonstrate that the CECT method is able to distinguish among the tissue compositions present at different points in the healing process. Overall, the results of this study constitute substantial progress towards establishing CECT imaging as a non-destructive means of assessing fracture healing, which will ultimately facilitate both experimental studies of the healing process and pre-clinical trials that require monitoring of the fracture site.
SESSION IIb
Small Things: Molecules, Cells and Nanobits
The implementation of contrast agents in Computed Tomography (CT) has served to revolutionize the field of biomedical imaging by creating enhanced images of physiological structures through non-invasive techniques. Iodinated compounds, the primary contrast agents used in CT scans, are limited by their poor sensitivity, short blood circulation time, and lack of specificity to detect certain pathogen bodies. We report a study in which a novel contrast agent was developed that should effectively overcome the aforementioned limitations. Initially, this task involved the design of non-iodine based X-Ray attenuating nanoparticles. Preliminary research revealed that PEGylated tantalum oxide (TaOx-PEG) nanoparticles to be a potentially superior alternative to iodine as the primary compound of a CT contrast agent. The TaOx based nanoparticles were rapidly produced using a simple micro-emulsion technique. During the synthesis procedure it was determined that minimizing the concentration of ethanol present in the micro-emulsion directly decreased particle size. Thus, the concentration of ethanol was altered to produce particles of varying sizes. Scanning electron microscopy, transmission electron microscopy, dynamic light scattering, and microCT devices were utilized to assess the size and X-Ray attenuation of these particles. The optimized particles were mass-produced and will be further analyzed in vivo in rat subjects to determine the particle blood circulation time and specificity to liver fibrosis. So far, this investigation has yielded several significant results. First, scanning electron microscopy has revealed that Tantalum oxide nanoparticles of varying sizes, 20-60 nm, have been successfully synthesized using the micro-emulsion technique. Second, size characterization experiments have proved that the size of the particles can be directly controlled through the addition of ethanol. Third, analysis of the optimized nanoparticles, using a microCT device, has indicated the particle X-Ray attenuation to have maxed out the current CT X-ray attenuation of 3071 HU – a value directly related to the significantly large concentration of TaOx nanoparticles. Fourth, it has been determined that lyophilization of the particles was an effective technique to increase the concentration of the particles. These key findings have demonstrated the feasibility of using TaOx-PEG as the next generation CT contrast agents, with their extended circulation time, superior X-ray sensitivity, and improved specificity compared with current iodinated contrast agents.
Mesenchymal Stem Cell Matrix Remodeling

Molly Ford Dacus

Fibronectin (Fn) in its fibrillar form is present in the extracellular matrix (ECM) during dynamic physiological processes where matrix remodeling occurs, e.g., stem cell differentiation and wound healing. Fn is a unique ECM structure since it is extremely extensible, is actively stretched by living cells, and has been shown to have dramatically altered mechanical and biochemical properties as it is stretched. These changes in mechanical and biochemical properties are important since they may actively regulate cell behavior. This project developed a fluorescence optical microscopy-based tool to measure how FRET changes can be used as an indication of the presence of Fn in its relaxed and stretched states. FRET is used for measuring distances at the nanometer scale under the principle that FRET occurs only when donor and acceptor fluorophores that label a protein are within 10nm apart. Because FRET efficiency decreases as donor and acceptor fluorophores move further apart, the mechanical strain state of Fn can be inferred by the relative decrease in FRET efficiency as a labeled Fn fiber is stretched. This project also developed a mathematical model to predict optimal fluorophore labeling ratios so that the FRET data is mechanically sensitive to Fn in its relaxed and stretched states. The ability to experimentally detect and measure the mechanical strain state of Fn during matrix assembly and remodeling in real time is essential for understanding the physical interactions between cells and their ECM and can lead to exciting future developments aimed at understanding the function of Fn fibril growth and stretch in complex physiological processes that require matrix remodeling.
Currently, there is still limited understanding about how cells interact with their environment. This information is key to understanding basic cell processes such as migration and division, generating tissue-mimicking devices, studying development, and examining the mechanical differences between healthy and diseased cells. It is known that cells exert traction forces (CTFs) on their environment through protein complexes that act as attachment points, but these forces have only been quantified for a limited number of cell types. Biochemical stimulation is often a major factor influencing complex cellular processes, and quantifying the traction forces during these processes could lead to a better understanding of the influence of biochemical cues on cellular behavior. This project is designed to create a system for exploring the CTFs of mesenchymal stem cells (MSCs) under biochemical stimulation geared toward differentiation. Bone marrow derived MSCs are being used widely as a cell source for tissue engineering and regenerative medicine due to their ability to differentiate into various lineages. We adopted a well-studied method of differentiating MSCs into smooth muscle cells (SMCs) using biochemical stimulation with a combination of transforming growth factor beta 1 (TGF-β1) and ascorbic acid (AA) treatment. Because of the contractile nature of SMCs, we hypothesize that CTF measurements can be used as an indicator for exploring different stages of MSC differentiation. We utilized an existing technique to measure CTFs in this project. Briefly, fluorescently labeled fibronectin (Fn) dots were microcontact printed onto polyacrylamide (PAA) gels to serve as focal adhesion points for MSCs. The CTFs were calculated using the displacement of the dots as well as known mechanical properties of the PAA gel. It was verified that the use of a PAA gel with a pattern of Fn dots as the platform to quantify CTFs during complex processes such as cell differentiation is feasible. Mesenchymal stem cells without biochemical stimulation, MSCs with biochemical stimulation, and SMCs were cultured on the patterned PAA gel. The cells survived on the substrates, attaching to areas with the Fn pattern, and the pattern remained clear throughout the duration of the culture period. The images that were taken throughout this time period can be used for traction force calculations. Using this method, more information about the changes in traction forces of MSCs under various types of biochemical stimulation can be obtained, which can potentially lead to a better understanding of interactions between cells and their surroundings.
Automated Design and Assembly of Reconfigurable Genetic Regulatory Networks

Aaron Berliner, Joshua Hodgson, Vanessa Yanez

Once upon a genome, in a cell far away, there existed three kingdoms of genetic regulatory networks (GRN). One was reconfigured through the flipping of genetic segments by invertase interactions; another was edited through Multiplex Automation Genetic Engineering (MAGE); the last was formed through the swapping of genetic segments by modular cloning techniques. With the aim of synthetic biology to precisely design and implement functionality into living organisms, the need for dynamic and robust genetic engineering tools has grown. Here we describe three separate designs for such tools and their application to the study of genetic regulatory networks. First, a genetic device was designed to be configurable into any promoter-gene test combination under control of special recombinases called invertases. Fluorescent protein constructs with each invertase recognition site (rox and lox) were built using the BioBricks™ assembly method to characterize the invertases (Cre and Dre). A second approach towards designing a GRN was done based on MAGE. A bio-automation heuristic was designed and implemented as an optimization strategy for MAGE, which selects an optimal set of insertion, deletion, and substitution operations required to transform one genome into another. This optimization strategy was articulated as a software artifact called “Enchantress” and was tested for both local and full genome transformations. The creation of Enchantress marks the introduction of software to guide selective genome transformation with a direct output to an automation process. The third approach presented here for generating a GRN was based on the “swapping” of genetic segments at specific overlapping 4-bp sequences using the MoClo assembly method. A software package utilizing modular cloning has been developed in which a genetic circuit can be designed and read by the software, outputting different ways in which the desired circuit can be built given the resources within the lab. Although the invertase flipping, MAGE editing, and modular cloning differ in their methods, their end goal is shared; each provides a new method for the synthetic biology community to build into the biological world.
A Novel Kidney Glomeruli Isolation System (KGIS)

Magi El Manchy, Xhorxhi Gjoka, Rahul Modi

When analyzing kidney disease pathogenesis, the biomechanical environment with respect to the behavioral response of glomeruli (induced stress) plays an integral role in the development of localized sclerosis. However, the current sieving technique implemented for glomerular isolation and capture from kidney tissue dates back nearly 50 years; producing a misleading, impure, and low-yield fraction of damaged samples. The objective of this proposal is to improve upon this crude technique by designing and implementing a microfluidic device that will maximize efficiency and minimize trauma when isolating glomeruli from kidney tissue. Three computer-aided designs (made on SolidWorks) serve as high-resolution transparency masks for photolithography and laser-etching. Two lateral displacement microfluidic devices with different filtration geometries and one balloon-tunnel microfluidic device will be tested. With the successful separation of glomeruli and confinement of tubules, we hope to achieve ≥ 80% total sample yield and ≥ 95% glomeruli purity within two hours of isolation time. Our novel kidney glomeruli isolation system (KGIS) will therefore allow for glomerular isolation according to morphologic appearance and the assessment of their biomechanical properties. Thus, this device will help develop fundamental new insight and facilitate renal pathology studies.
Cells constantly explore, bind, and pull on the environment around them, and quantifying the forces exerted by the cell on its surroundings is essential for understanding cellular processes such as migration and differentiation. This project aims to design a novel system to simultaneously measure the cell traction forces (CTFs) on multiple spatially distinct ligands on soft, physiologically relevant, hydrogels. The extracellular matrix (ECM) is made up of many different interconnected molecules, so the incorporation of multiple cell adhesion molecules provides a more complex and accurate ECM mimetic than single molecule systems. The system is a dual-patterned hydrogel consisting of fibronectin (Fn) and gelatin, and permits new insight into the investigation of extracellular matrix-cell interaction. The dual-pattern was created by successively patterning arrays of Fn and gelatin dots using polydimethylsiloxane (PDMS) stamps. The system was confirmed with a proof of principle bovine serum albumin (BSA)-Fn dual-pattern. A gelatin-Fn dual pattern was created on a glass coverslip, but subsequent transfers to gels were unsuccessful. The dual patterning procedure has been verified and experimental use will investigate cross talk between multiple ligands. By measuring the displacement of dots adjacent to the dots bound and displaced by cells, a Matlab algorithm will be designed to account for inaccurate data output by the current program. Data has been collected from previous single ligand experiments to enable future programing to reduce the calculation error. The creation of a successful algorithm to account for adjacent dot displacement will increase the accuracy of not only this project’s data but of CTFs found using micropatterning methods.
Control of Organization and Function in a Tissue-Engineered Vascular Patch

Andrew Schiff, Angela Xie

Nearly 1% of children in the United States are born with congenital heart defects. Current vascular grafts composed of synthetic materials or decellularized tissue lack growth potential in vivo and therefore, often require multiple surgeries in pediatric patients. An autologous tissue-engineered vascular patch (TEVP) has the potential to grow with the child, but current technologies have so far been unable to achieve clinically desirable burst pressure and tensile strength for a human arterial model. The long-term objective of this project is to develop a TEVP with defined 3D structure and the mechanical strength necessary for surgical implantation and sustained viability in vivo. Specific focus here was on the design of a bioreactor to mechanically condition tissues by effectively mimicking the physical environment provided to blood vessels in vivo. To recapitulate native vessel architecture, protein microcontact printing or topographically patterned substrates were used to culture human mesenchymal stem cells into confluent aligned sheets. Patterned cell sheets were harvested intact from thermo-responsive or enzymatically degradable polymer substrates. We explored various techniques to stack cell sheets into 3D configurations to create multi-layer tissues with defined cellular organization. For the design of the bioreactor, a peristaltic pump and syringe pump were used to provide the system with steady basal and regular pulsatile flow, respectively. A LabVIEW program was written to acquire data from high-precision measurement systems to monitor flow and pressure profiles of the circulating fluid. A parallel-plate bioreactor chamber was designed to provide uniform laminar flow and physiological shear stresses to the engineered tissue, and chamber design specifications were verified by COMSOL modeling. Implementation of a media reservoir into the flow loop promoted gas and nutrient exchange and maintenance of the desired pH and oxygen levels for tissue formation. The designed bioreactor allows for the dynamic culture of tissues under mechanical conditions similar to those seen in vivo, and provides regulation of flow, pressure, gas and nutrient transport, and pH. Bioreactor conditioning of TEVPs is ongoing and will provide insight into the effects of flow on the structure and resulting mechanical properties of vascular tissue constructs.
SESSION IIIa

Just a Spoonful: Drug Delivery and Compliance
Atherosclerosis, the hardening and narrowing of arterial walls, is often caused by an inflammatory response due to an accumulation of cell-modified low-density lipoproteins (LDL) in the endothelial wall which stimulates plaque formation. Small interfering RNA (siRNA) has been found to successfully knock down the expression of vascular adhesion molecule-1 (VCAM-1), which is involved in the production of plaque. We report a study in which an in-vitro model is designed for the detection of atherosclerotic plaque and targeted delivery of VCAM-1-siRNA to inflamed endothelial cells using immunofunctionalized microbubbles. Microbubbles were coupled to an anti-VCAM-1 antibody by a polyethylene glycol-biotin-streptavidin bridge. Our data shows that VCAM-1 expression was significantly upregulated by incubating endothelial cells with lipopolysaccharides. Adhesion of VCAM-1-targeted ultrasound contrast agents onto LPS-inflamed endothelial cells increased with the surface antibody densities. The project will provide an efficient method both the detection and targeted delivery of siRNA to atherosclerotic sites in clinical settings.
Localized siRNA Delivery with Lipid-Coated Modified Polyethyleneimine

Morgan Giles, Steven Mathews, Teena Varghese

Atherosclerosis is the accumulation of plaque in blood vessels that leads to heart attacks and strokes. By targeting the gene responsible for accumulation, vascular cell adhesion molecule-1 (VCAM-1), complications arising from atherosclerosis can potentially be mitigated. Small-interfering RNA (siRNA) can selectively silence VCAM-1, but requires packaging in vivo for protection and delivery. Polyethyleneimine (PEI) is a cationic polymer proven to complex and deliver siRNA, but also suffers from cytotoxicity and low circulation time. Liposomes, a more biocompatible delivery vehicle, are limited by their poor control of drug release. By combining PEI with lipids, we created a lipid-polymer hybrid nanoparticle to deliver siRNA and inhibit VCAM-1 expression; the nanoparticle will be composed of a PEI core inside a pH-sensitive lipid shell. This hybrid approach attempts to maximize the efficacy of siRNA delivery by integrating biocompatibility, prolonged circulation time, and transfection efficiency into one vehicle. To decrease adverse effects resulting from high cationic charge densities, PEI was modified through acetylation and succinylation. All versions of PEI showed negligible cytotoxic effects at treatment concentrations. Modified PEI was complexed with siRNA at a 4.01 N/P charge ratio between the nitrogens of the PEI and the phosphates of the siRNA to form a polyplex (PPX) of optimal size and zeta potential. This PPX was loaded into a pH-sensitive liposome to improve stability. The lipid-coated polyplexes (LCPs) were characterized with respect to size, shape and zeta potential and compared to unloaded liposomes and uncoated PPXs. The resulting vehicle is meant to optimize siRNA transfection and silence expression of VCAM-1 in endothelial cells, in an attempt to reduce the adverse effects caused by atherosclerosis.
In vitro Mucosal Membrane Culture Model for Drug Delivery

Hufsa Iqbal, Angela Nocera

Most beneficial drugs required for treatment of neurodegenerative disorders cannot reach affected areas of the brain due to the impermeability of the blood-brain barrier (BBB). Endoscopic skull base surgery has provided a method of replacement of the BBB tissue with highly permeable nasal mucosal tissue. Though originally intended as a method of reconstructing the skull base following transnasal brain surgery, recent insights suggest that this substitution can be used as a platform for drug delivery directly to the brain while bypassing the BBB. The objective of the project was to develop an in vitro mucosal membrane model that mimics the tissue in vivo and to characterize the presence and function of mucosal permeability glycoprotein (P-gp), an ATP dependent efflux pump, which plays a key role in drug absorption and transport. Through the use of fluorescent immunohistochemistry and enzyme linked immunosorbent assays, the membranous expression of P-gp was determined in the presence of different combinations of P-gp irritants and inhibitors. P-gp function was subsequently determined by quantifying the transport kinetics of both intrinsic and extrinsic P-gp substrates (intracellular cytokines and Rhodamine 123, respectively) in the setting of two different P-gp inhibitors. Our results suggest that an in vitro model of direct transnasal central nervous system (CNS) drug delivery may be cultivated from primary human sinonasal epithelial cells. Furthermore, we have demonstrated that in both normal and inflamed mucosa, P-gp is present. We have seen that P-gp transport properties are proportional to its degree of expression on the different types of mucosa. This in vitro culture will become a platform for testing of various drug-carrying polymers to determine which will most efficiently cross the mucosal membrane based on our modifications. With continued progress, mucosal tissue can eventually be implemented as a specialized pathway for high molecular weight drugs to access the CNS.
Design of an Algorithm Incorporating the Glycemic Index in Insulin Bolus Delivery Estimations for the Treatment of Type I Diabetes

Julian Hart, David Nathaniel Tan

Type I diabetes is a disease characterized by the inability to regulate blood glucose. Although insulin pump therapy has been successful in preventing the most extreme effects of the disease, hypoglycemic and hyperglycemic episodes still occur due to variability in carbohydrate digestion rates. This study aims to account for this variability by employing the glycemic index (GI). The GI compares the rise of blood glucose after two hours for a specific food relative to pure glucose. Unlike conventional insulin treatment, which delivers a set amount of insulin per unit carbohydrate in a single dose, we propose a novel treatment using two doses. This treatment still administers the same net amount of insulin, but splits the dosage based on the glycemic index. This novel therapy was tested on streptozotocin-induced diabetic swine. The first insulin dosage was administered at the moment the pig was given either a high or low GI meal. The second dose was then administered 30 minutes later. The blood glucose responses for conventional and modified treatments were then compared, quantifying hypoglycemic and hyperglycemic episodes by intensity and duration. The results show a significant difference between the glycemic response to high and low GI food for conventional treatment. The difference was less pronounced in the modified treatment. Comparing the two treatments, there was a general decrease in hypoglycemic episodes with the two-dose model for low GI food, but no significant difference in high GI food. The difference in hyperglycemic episodes in both cases was insignificant. Despite a limited number of trials, the evidence supports the efficacy of the new treatment. Efforts to further improve the insulin dosage algorithm are expected to yield more definitive results.
Mesothelioma is an exceedingly aggressive form of cancer, which 2500 Americans are diagnosed with every year. Current options that are available for the treatment of mesothelioma are poor; even with complete surgical resection, the locoregional recurrence rate is higher than 80%. A novel treatment for mesothelioma is chemotherapeutic drug delivery using pH-sensitive expansile nanoparticles (eNPs). Unfortunately, the current production method, a miniemulsion suspension polymerization, does not consistently provide large quantities of nanoparticles with narrow size distributions. Studies have shown that nanoparticles are most effective at diameters of 100 nm, a size that is large enough to avoid clearance via the filtration mechanisms of the body, such as the kidneys, but small enough to avoid most immunological responses. Prior to human trials, a reliable and consistent method of nanoparticle production must be established. To meet this need, we propose the design and construction of an automated microfluidic device that utilizes microscale channels and fluid flows to manufacture eNPs. Six microfluidic chip designs have been fabricated out of polydimethylsiloxane using soft lithography techniques. Poly(lactic-co-glycolic acid) non-expansible nanoparticles have been synthesized and characterized using several fluid compositions and flow conditions. Currently, eNPs are being synthesized using the devices and the fluid parameters are being optimized to produce particles with a mean diameter of 100 nm and a polydispersity < 1.3.
In 2009, the World Health Organization (WHO) determined that 33.3 million people were infected with the human immunodeficiency virus (HIV). The majority of the population infected with HIV/AIDS live in developing countries, where there is little help or education. The current method of treating HIV positive patients uses Highly Active Antiretroviral Therapy (HAART). However, for this treatment to be effective, the patient must adhere to a strict schedule. We propose to develop a detection method to directly monitor the adherence of the patient to the prescribed antiretroviral therapy. We focus on detecting azidothymidine (AZT), one of the drugs used in the treatment plan that is cleared in the urine of the patient. Because antibodies that detect azidothymidine are expensive, we propose "Click" Chemistry as a detection mechanism. The particular mechanism used here is the Azide Alkyne Huisgen cycloaddition. This mechanism relies on the interaction between the azide terminal in one reagent and an alkyne group in the second reagent and is done in the presence of a Copper I catalyst. The chemical compound for AZT contains the azide group needed for this reaction to proceed. By altering the chemicals and their concentrations in the alkyne reagent, the presence of AZT diluted in urine has been detected on gel blot paper and Whatman filter paper. The aims of this project are to identify potential reagents with alkyne groups that react with the AZT molecules present in the urine, and provide a color change readout that can be displayed on paper. A successful result will indicate a visible and distinct change in color of the reagent when exposed to AZT diluted in urine.
SESSION IIIb

Connections: Interfacing to Living Systems and Tissue
The standard method to detect rat neural signals, such as action potentials, is to use a single glass microelectrode to record from single neurons. The size of the rat brain limits simultaneous recordings with multiple glass microelectrodes. The current method also requires additional bulky instrumentation such as amplifiers. In this study, neural recordings were obtained and amplified from the tissue of a rat brain in vitro utilizing a multi-input neural sensory (MINS) chip to detect evoked local field potentials. The chip was initially tested with simulated field potentials from a waveform generator. The project applied techniques, such as current source density analysis of neural signals recorded with the chip, to analyze the 2-dimensional neural circuit of the rat hippocampus. Fourier analysis was used to determine if the chip detected frequencies of field potentials in the same ranges as those detected from standard glass microelectrodes. The key findings from the experiment showed that the MINS chip was able to detect simulated sinusoidal waveforms that exhibited local field potential frequencies. The chip recorded stimulus during neural tissue recordings. The device, with improvements, is a viable advancement for multiple and simultaneous extracellular recordings of rat brain slices in vitro.
Neurocognitive Assessment Using the iPad Platform

Raymond Byrne, Raphael Landaverde

For many neurological patients, deficits in vision and perception are a major impediment to their activities in daily life. Assessing these perceptual and cognitive deficits, however, has proven difficult largely due to a lack of portable instrumentation for on-the-spot assessments. This project aims to help solve this problem by creating a novel iPad application for performing a variety of these diagnostics. This application is designed for performing psychophysical examinations spanning a variety of test types and protocols, all presented within a descriptive user interface for easy testing. By leveraging the advantages of the iPad platform, the application is able to quickly register new patients, perform relevant diagnostics, and store data for easy digital delivery of results via e-mail, all from a portable device. To support these user-level features, a testing framework underlies the software, facilitating the efficient implementation of future psychophysical examinations within the application. This underlying framework ensures that this application can be easily supported and updated to become more comprehensive over time. The application leverages a combination of native iOS techniques and third party technologies, including openGL and cocos2d for graphics development, with the goal of creating the most intuitive and portable set of psychophysical diagnostic tools for clinicians and patients. By taking advantage of the many features of the iPad, this application can be readily applied in both clinical and non-clinical settings for easy, on-the-spot assessment of various perceptual and cognitive deficits.
Robotic exoskeletons have been used in research facilities to aid in neurological rehabilitation. Exoskeleton rehabilitation is most effective when proportional myoelectric control is used to activate the artificial pneumatic muscles. Unfortunately, current control methods require the user to be tethered to a desktop computer and therefore exoskeletons cannot be used outside of research laboratories or special facilities. Since this setup is not portable, it does not provide the consistent therapy needed for effective rehabilitation. It is our goal to bring such robotic technology closer to becoming an effective and widespread rehabilitation option by making the technology more portable. The exoskeleton uses proportional pressure controllers (PPCs) to actuate the artificial muscles. The strength of the output from the PPCs is determined by proportional myoelectric control: as muscle activity increases, the output increases. The goal of this project was to engineer a portable controller that could input an electromyogram (EMG) signal and process it into the desired output signal. We created a controller that uses left and right soleus muscle activity, obtained from surface EMG sensors, as the signal inputs and uses analog and digital signal processing to create a control signal. The inputs are amplified and brought into the range of 0-5V before being input into a digital microcontroller. The microcontroller filters the signal and detects its envelope, forming the control signal. The control signal is then subject to adjustable, user-controlled thresholds and gains. The signals are then outputted from the microcontroller to a digital-to-analog converter and amplified to create a 0-10V signal used to drive the PPCs. The signal is effectively proportional to the EMG signal of the soleus muscle. The engineered portable controller has successfully been tested with the PPCs to actuate a hip exoskeleton. When paired with portable pressure controllers, this portable system is easier to use and just as effective in rehabilitation as a fixed laboratory setup. Through the use of portable proportional myoelectric controllers, robotic exoskeletons can be used outside of a designated laboratory setting.
Ergonomic Redesign of a Laparoscopic Clip Applier

Katherine Black, Ryan Pope

Minimally invasive laparoscopic surgeries have revolutionized surgical medicine through reduced recovery times and improved patient outcomes. Despite continual advancement in techniques and instruments, surgeons report higher levels of discomfort and strain in their hands, wrists and arms after performing laparoscopic procedures. Laparoscopic clip appliers require large activation forces compared to other common instruments and make a logical choice for ergonomic redesign. Using ergonomic standards for surgical instruments, an existing laparoscopic clip applier made by Applied Medical was studied and then redesigned to improve its ergonomics. The handle has been reoriented from a pistol grip to an in-line format to reduce wrist strain, and the trigger has been relocated to more efficiently use finger strength. The internal mechanisms have also been improved to boost the overall mechanical advantage of the device, reducing activation force. Design verification testing was conducted to determine if the new device has equivalent clip closure and retention as the predicate device. Through the new design and hand orientation, trigger closure force was roughly halved, which will reduce hand strain over long procedures and make the device easier to use. This was accomplished while maintaining statistically comparable clip closure. We have concluded that the new design meets both ergonomic and functional specifications and is ready to be developed further for injection mold design and production. With millions of procedures performed in the United States each year, improved laparoscopic instrument ergonomics will reduce strain and discomfort for surgeons; allowing them to work more effectively with lower operating room time and procedure costs.
Glenohumeral Joint Kinematics and Contact Pressures during Simulated Pitching: A Cadaveric Study

Megan Lee, Max Lerman, Natalia Vieira

The glenohumeral (GH) joint has the greatest range of motion in the body and is highly susceptible to injury, especially during overhead motions such as pitching. Many athletes do not restore the full functionality of their shoulders after current methods rehabilitation. Kinematics and contact pressure are valuable tools to evaluate shoulder injuries and repairs with respect to their normal states. Previous phases of this study have successfully mapped the translation and rotation of the humeral head against the glenoid. The objective of this project was to correlate the contact pressure with the motion of the glenohumeral joint during simulated pitching. This phase of the study surgically integrated an array of pressure transducers into the shoulder to understand how the humeral head contacts the glenoid face at specific pitching phases. The transducers produced repeatable results and the implementation protocol preserved the integrity of the kinematic data previously validated. Furthermore, the motions of the instrumented and intact GH joints were not statistically different. Thus, these relevant correlations have been translated into a meaningful presentation for clinical use.
Clinicians require accurate and instantaneous measurements of the mechanical status of the respiratory system for decision support on ventilator management strategies in critically ill patients. However, there are a variety of diseases that alter the mechanical structure and function of the respiratory system in ways that are difficult to detect with conventional pulmonary function tests. Respiratory impedance provides insight to the pathological status of the respiratory system, and is sensitive to changes in both structure and function, as well as heterogeneity in mechanical parameters. Respiratory impedance is not widely used as a diagnostic reference, in part due to the lack of measurement systems designed specifically for clinical implementation. In this project, we designed a LabVIEW software interface to acquire and store physiologic pressure and flow waveforms, perform spectral analysis, and visualize respiratory impedance spectra. The software is capable of time- and frequency-domain modeling of respiratory mechanics in real-time during data acquisition. The software has been validated by characterizing the voltage-current frequency response of RC series circuits. The software was then used to control a pneumatic pressure oscillator to characterize the frequency-dependent properties of a mechanical test lung model, the inertance of gas oscillating in a long plastic tube, and the gas compression compliance of a rigid container; the software has also been used to apply time-domain models to spontaneous breathing patterns of healthy humans. The software we have developed is a viable and practical tool for real-time assessment of lung mechanics. User-friendly interface and visual representation of physiologic parameters can help bridge the gap between academic use and clinical implementation of frequency domain respiratory analysis.
Asthma is a chronic condition characterized by airway hyperresponsiveness (AHR), in which airway smooth muscle (ASM) shortens excessively in response to an agonist causing exaggerated airway narrowing and closure. Increases in the amount of ASM, and in the force generation capability of the ASM, as well as structural remodeling of non-muscle elements within the airway wall have been hypothesized as possible causes of AHR. In addition, the dynamic forces associated with breathing might modulate the contractile capability of the ASM. Few studies have shown how a normal airway can undergo these structural changes and progress into a clinically defined asthmatic airway. It is thought that long term exposure to inflammatory mediators and smooth muscle contractile agonists will remodel the airway wall so as to facilitate AHR. For this project, a complete experimental system was designed, prototyped, and constructed for the purpose of conducting experiments that will lead to a better understanding of the specific pathways controlling and contributing to airway remodeling and AHR. The first objective of this project was the design and development of the experimental system and its components. This system followed specific functional specifications enabling bovine airways to remain viable over a period of 10 hours, while undergoing continuous transmural pressure fluctuations resembling tidal breathing. A tissue bath and pressure control and delivery system were designed and built. The bath allowed for multiple bovine airways to undergo testing, while maintaining a sterile environment and ultrasound compatibility for real-time measurement of luminal radius and wall thickness. The second objective was the design and implementation of experimental protocols. Preliminary experiments tested the responsiveness of bovine airways over four hours and provided evidence that a system allowing for the testing of bovine airways over a longer period of time is necessary to cause significant structural changes. Later experiments conducted in the new system established that airway viability was maintained for 10 hours under both static and dynamic transmural pressure conditions. The effect of a chronic low dose of acetylcholine on airway reactivity was also assessed under static and dynamic pressure conditions. These studies concluded that airway viability and reactivity were the same for both static and dynamic pressure conditions. Finally, the experiments established that 10 hours is not a sufficient amount of time to cause structural modifications within the airway wall that result in functional changes.
SESSION IV

We are the World: Global Health Technologies
Currently, 10% of pharmaceutical drugs on the world market are classified as counterfeit or substandard, while this prevalence increases to 30% in developing countries. The problem is exacerbated in these areas by high rates of infectious diseases and corresponding large amounts of medication required for treatment. The purpose of this project is to improve an already existing system for the detection of these types of medications by enhancing functionality and portability. The current apparatus transports two solutions—the dissolved drug and a fluorescing probe targeted for the drug’s active ingredient—through a microfluidic channel. After thorough mixing, the emission intensity is measured to determine the concentration of active ingredient by comparison to a standard curve of known concentrations and fluorescence intensities. Different microfluidic channel designs were tested to determine which achieved the fastest flow rate while providing the most thorough mixing. To make the system appropriate for resource limited settings, the dissolution, pump, and detection components were altered. The dissolution system was first changed from an elevated motor-driven mechanism to a system using a homemade magnetic stir-plate. A peristaltic pump was also fabricated to greatly reduce the cost and size of the system. The detection system is in transition from a commercial fluorescent microscope to using an LED and plastic color filter with data capture on a cell-phone camera. Finally, all components were integrated into a lightweight, plastic container. This system provides a compact, inexpensive, robust, and portable way to detect counterfeit or substandard drugs at a cost of less than $2 per test.
In developing countries there is a need for early diagnosis of cancer non-invasively with a time-efficient and low-cost device that can work with minimal infrastructure. The Generation I Global Device developed by last year’s senior project group in the Biomedical Optics lab is a portable, battery-operated diagnostic instrument. It utilizes the principle of Elastic Scattering Spectroscopy (ESS) to detect anomalies present in malignant and dysplastic cells. It operates at four different wavelengths by sequentially triggering four high-powered LEDs. Although the device offers a reasonable level of performance for its cost, further improvements were needed in the design to improve its efficiency and reduce the cost. Our goal was to design an improved Generation II device by eliminating some of the more expensive components, optimizing the optical coupling with the use of laser diodes, and developing an Android application to make the device user-friendly for global applications. In addition, the Generation II device incorporates six laser diodes at wavelengths of 405nm, 445nm, 532nm, 635nm, 650nm, and 808nm, which provide greater signal strength compared to the LEDs and improve diagnostic accuracy by providing more spectrum sampling points. A fiber-optic probe was designed to deliver the light from each of the laser diodes to the tissue through a bundle of six interconnecting optical fibers, and to collect the backscattered light from the tissue to the photodiode through a single fiber-optic. The microcontroller is programmed to pulse the laser diodes sequentially for calibration or measurement by pressing the calibrate or measure switches, respectively. The system displays the ratio of backscattered light from the tissue sample to the calibration reference on a color LCD display. The device offers Bluetooth connectivity and can be paired with an Android phone to facilitate more complex data analysis. The Generation II system produces readings with improved consistency when the discrete wavelengths ratios are compared to the full spectrum of the ESS system. The Generation II device has been proven to provide accurate measurements and is ready to be deployed for global health use.
Robust Device for Reagent Storage in Resource-Limited Settings

Cassidy Blundell, Imaly Nanayakkara, Joseph Pirrello

Infectious disease is a significant problem in developing nations, where access to medical care for diagnosis and treatment is not always available. Point-of-care (POC) diagnostic technologies are being developed to enable accurate and inexpensive detection of disease in these resource-limited areas. However, POC devices are limited by the need to refrigerate or freeze diagnostic materials, which is not an option in rural areas lacking modern infrastructure. In this project, we offer a paper-based dry reagent storage system that will maintain reagent viability over the course of two weeks, withstand high temperatures, and can be integrated into existing microfluidic devices. Reagents, such as proteins, are dried onto laboratory filter paper, a ubiquitous and inexpensive substrate and stored for a given period of time. Following storage, protein is reconstituted into a buffer solution, to create a resuspended antibody solution, for diagnostic use. Reconstitution yield is quantified using either dot-blot assays or fluorescence-activated cell sorting (FACS) flow cytometry. FITC-conjugated anti-integrin beta-1 is the protein used in testing. The filter paper substrate has been incorporated into a PDMS-based microfluidic device, allowing for ease of use. Untreated filter paper has a low reconstitution yield of protein stored for one week, indicating a large percentage of the original protein degrades. Chemical treatment of the paper has led to an improved yield, using filter paper that has been modified by a coating of 60% glycerol. This robust platform will increase availability of disease diagnosis, allowing patients to obtain the medical care they require.
System for Nucleic Acid Preparation for TB Diagnostics (SNAP-TB)

Rachel Deraney, Kaitlin Gargiulo, Chelsea Saniel

Tuberculosis (TB) is a contagious disease caused by *Mycobacterium tuberculosis* that infects approximately one-third of the world. Other than culture identification, the detection of bacterial DNA from a sputum sample is one definitive method to diagnose tuberculosis. In resource-limited areas, the detection of bacterial DNA continues to be a problem due to a lack of proper lab equipment and the difficulty of storing and transporting samples. Currently, the gold standard for diagnosing TB is culture techniques using blood or sputum samples. The problem with these techniques is that the sample must be processed within 30 hours of collection, which is often difficult in rural areas of developing countries. In this study, sputum lysis chemistry was developed for *Mycobacterium smegmatis*, a BL1 model organism for *Mycobacterium tuberculosis*. The sputum lysis chemistry was then integrated with a porous polymer monolith (PPM) that optimized the extraction of genomic nucleic acids from synthetic sputum inoculated with known concentrations of bacteria. Moreover, modifications to the current System for Nucleic Acid Preparation (SNAP) apparatus were made to better suit it for tuberculosis diagnosis (SNAP-TB). The SNAP-TB system is designed to be powered by a bicycle pump that can process up to six sputum samples at one time and incorporates both the sputum lysis chemistry and PPMs. Ultimately, SNAP-TB could be an accurate and efficient point-of-care tuberculosis diagnostic technique with further optimizations of the lysis buffer and PPM formulations. The system uses disposable components for self-contained testing without the need for electricity in developing countries and could potentially limit the spread of this contagious disease.
Liver cancer is a major health problem that affects millions of people worldwide. The most common risk factor for liver cancer is chronic infection with the hepatitis B virus (HBV). Currently, one reliable method is direct biopsy, which is invasive, expensive, and rarely used in resource-limited settings. Effective and accurate methods for clinical diagnosis of cancer and hepatitis B are urgently needed for developing countries. In this project, a biosensor was designed to detect specific biological analytes by converting biological entities into electrical signals. The biosensor used in the project has six layers. Starting from the bottom, there is a layer of silicon (Si) wafer, a thin layer of copper (Cu), a layer of piezoelectric micro-cantilever sensor (PEMS) made of zinc oxide (ZnO), another thin layer of copper, a layer of difunctional thiol, and a layer of antigen/antibody for disease detection. The Cu layer was deposited on top of the Si wafer using thin film deposition because ZnO does not bind directly with Si. The ZnO layer was sputtered onto the Cu layer and this serves as the biosensor. The biomarkers attach to the antigens/antibodies, and the resonant frequency of the PEMS changes. The change in resonant frequency over the concentration threshold indicates the presence of liver cancer or hepatitis B. The PEMS is expected to detect hepatitis B surface antibodies (HbsAg) and alpha-fetoprotein (AFP). Di-functional thiols were used to link the biomarker binding sites to the Cu layer through self-assembled monolayer (SAM). The Cu layer was sputtered on top of the ZnO layer to ensure thiol binding as thiol does not directly bind to the oxide layer. The Fourier transform infrared spectroscopy (FTIR) was performed to confirm that copper has a better binding affinity for thiol than aluminum. ZnO was chosen over other common piezoelectric material because its low cost reduces the cost of fabrication and hence makes the device affordable. However, more study on surface chemistry and electrical circuits is needed in order to improve the efficiency and conductivity of the device.
Miniaturization of a System for Nucleic Acid Preparation for HIV Diagnostics (miSNAP)

Pawel Kalinowski, Rotimi Ogunbiyi

The System for Nucleic Acid Purification (SNAP) is a point of care molecular diagnostic device that successfully isolates and extracts viral RNA from whole blood samples containing HIV virions. This technology combats the problem facing resource limited settings; expensive, electric powered centrifuges and cold chains to prevent the degradation of samples. The current SNAP device is very intricate and has low extraction efficiency of RNA. Incorporating microfluidic compartments allows for greater sensitivity and specificity of eluted RNA. This purpose of this study is to design and manufacture a microfluidic SNAP devices that perform the same processes as the original using less raw materials (blood, BoomD, alcohols, etc.) BoomD is a guanidine thiocyanate (GuSCN)-based lysis buffer. Color confirmation results demonstrate that mixing is attainable using a system where the fluid travels up and down the three-layered PDMS microfluidic device. In addition, the porous polymer monolith mix (PPM), which sifts out and captures the glycogen-RNA precipitate, is successfully stored on chip through the use of UV initiation. For testing purposes, the whole blood is spiked with viral RNA. The output, eluted RNA, is amplified and analyzed using polymerase chain reaction (PCR.) By incorporating microfluidics we were able to make an integrated device that successfully performs viral RNA extractions.
Modeling of Artificial Sputum for Use in Tuberculosis Diagnostics

Kali Brong, Stephanie Nelson, Shahar Torton

Development of a robust tuberculosis diagnostic is urgently needed to help impede spread of the disease in low-income developing regions. The critical role of sputum in tuberculosis diagnosis presents the relatively unexplored research area of sputum modeling and digestion. A phantom sputum sample has the potential to accelerate and optimize development of a microfluidic device for tuberculosis diagnosis. The current research aims to improve on existing models for artificial sputum by creating a sample with rheology that mimics that of real sputum. Sputum sample design began by studying the bulk rheology of pure, inorganic materials commonly used in artificial sputum samples. The AR 2000 rheometer was used to test the materials and establish a methodology that gives consistent and precise results. A Matlab program that graphs each of the trials and allows for easy and quick comparison of the materials’ viscous and elastic properties has been created. The program has been used to compare the rheology of materials with that of real sputum samples. A solution of 20% (w/v) porcine gastric mucin with 12.5% (w/v) gelatin in water demonstrated the most similar rheological properties to real sputum samples. The aforementioned mucin and gelatin combination has been chosen as an ideal generic starting point for the artificial sample. Due to real sputum heterogeneity and variability between samples, additional constituents such as DNA, albumin and nonpathogenic bacteria can be incorporated into the artificial sample. Addition of DNA and albumin to the sample has been studied and found to have no significant effect on the bulk rheology of the sample. However, including the components in the sample is important to ensure that the design of a digestion procedure is applicable to real sputum. The proposed sample can be used in future research to optimize the microfluidic device for tuberculosis diagnosis.