Centers
- Biomolecular Research Center
- Center for Advanced Biotechnology
- Center for BioDynamics
- Hearing Research Center
- Neuromuscular Research Center
- Center for Advanced Genomic Technologies
- Center for Memory and Brain

Labs
- Applied BioDynamics
- Airways and Lung Tissue Dynamics
- Auditory Neurphysiology
- Auditory Neuroscience
- Binaural Hearing
- Biomedical Materials Research
- Biomedical Optics and Biophotonics
- Biomimetics Material Engineering
- Biomimetic Systems
- Biomolecular Systems
- Brain and Vision
- Cell and Tissue Mechanics
- Cellular and Subcellular Mechanics
- Cochlear Biophysics
- Computational Genomics
- Fields and Tissues
- Micro and Nano Biosystems
- Motor Unit
- Multi-Dimensional Signal Processing
- Natural Sounds and Neural Coding
- Neuronal Dynamics
- Organogenesis
- Protein Engineering (ZLAB)
- Pulmonary Physiology and Dynamics
- Respiratory and Physiological Systems Identification
- Respiratory Research
- Sensory Signal Processing
- Structural Bioinformatics
- Therapeutic Microtechnology
- Visual and Circulatory Biophysics
It is my pleasure to welcome our guests, our alumni, the biomedical industry, our faculty and our students to Boston University’s 22nd Annual Biomedical Engineering Senior Project Conference. Yes, this is the 22nd year our BME Seniors will present. These wonderfully talented people will inform you of their state-of-the-art design and research activities as the complete their bachelor’s degree from the 6th ranked BME program in the nation.

Biomedical Engineering synthesizes engineering, computation, math and physics with the life sciences to advance our understanding of biology and physiology, and then exploits these understandings to develop new devices and methods to improve medical care. Boston University’s Department of Biomedical Engineering is one of the oldest Bachelors program in the nation. Boston University has the largest Biomedical Engineering Department in the country, with 31 primary tenure-track faculty and over 70 affiliated faculty. We are one of only three departments in the country to have received a Leadership Award by the Whitaker Foundation, one of only 9 to receive a Coulter Foundation Translational Biomedical Engineering Translational Research Award, and the only program in the nation to receive both.

The Whitaker Leadership Award, received in 2001, provides for a net $32 million enhancement in Biomedical Engineering over the last five years. As the Whitaker Foundation states, “Leadership awards go to institutions that have already demonstrated national leadership in biomedical engineering and have articulated a clear and exciting vision for enhancing their leadership position.” We created a center for Nano and Micro Biosystems including Class 100 and Class 1000 bio-microfabrication facilities, a Micro and Nano Imaging facility, a Biointerface Technologies Facility, and a Biomedical Engineering Simulation and Computational Facility. All of these support a comprehensive educational and research program in Cell and Subcellular Bioengineering, Cell and Tissue Engineering, Biomaterials, Systems Biology and Genomics, Integrated Physiological Systems and Bioimaging, and Multiscale Modeling from the biomolecule to the whole organ. Our Coulter Award facilitates rapid translation of basic discovery via bioengineering to innovative technologies that impact patient care and clinical practice. The intent is catalyze collaborative projects between BME faculty and clinicians and which engage the entire commercialization network and infrastructure of the University.
The B.S. program in Biomedical Engineering is fully accredited by ABET. The undergraduate curriculum in Biomedical Engineering is designed to provide integrated training in life, physical, and engineering sciences as preparation for a variety of careers in bioengineering, applied biotechnology, and medicine. We also offer an Industrial Internship Program that can place students for up to a year.

Seniors majoring in Biomedical Engineering are required to complete a two-semester research project which includes elements of technical presentations along with actual independent design and research. At the end of the year, students present the results of their work in this exciting forum. Seniors also must engage their project via a course is called “Product Design, Development and Entrepreneurship in Biomedical Engineering” taught by our Industrial Advisory Board and the School of Management. The course teaches students concepts of design, intellectual property, patents, regulatory issues, marketing, and entrepreneurship, all in the context of their projects.

On a personal note as course director for the past 22 years I have grown so fond and proud of what our BME students and department can accomplish. Somehow, as Dean I was able to stay engaged in teaching portions of the course, although not as intimately as in the past. I want to thank the team of BME faculty that insured that the program sustain its level of excellence. Drs. Doug Cotter, John White, Steve Colburn, Chris Passaglia, Kamal Sen, Joyce Wong, Catherine Klapperich, Ed Damiano and Tim Gardner were fantastic. This has been an extraordinary experience, indeed in many ways a defining one. Good luck to you all.

Kenneth R. Lutchen,
Dean, College of Engineering

Paul Bower discusses his project on Analogue Brain-Computer interfaces using MRI at the 2006 Senior Project Conference.
Industrial Sponsored Research and Design Fellowship in Biomedical Engineering

The Industrial Sponsored Research & Design Fellowship Program is a program to help students obtain summer research positions in biomedical engineering with potential to extend to Senior Design Projects during the subsequent academic year. This program is made possible by the Donations from the Industrial Supporters of Boston University’s Biomedical Engineering Senior Project Program.

With the summer of 2007 marking the third year for this fellowship program, students will work on research projects of their choosing in one of the many on campus or local industry laboratories. Each student will be able to choose from a listing of projects and laboratories that are available. Students benefit in several ways. They are able to perform summer research that will hopefully segue into a Senior Capstone Project, they are able to refine their bioengineering skills in practical and state-of-the-art areas, learn how their academic knowledge translates to real challenges, learn to work with a scientific team consisting of a hierarchy of experience and expertise, and enhance their marketability to future employers.

The Boston University Department of Biomedical Engineering would like to acknowledge the generous support of the companies and faculty members who have made this program possible. With each company contributing a minimum of $10,000 annually plus the contributions of our faculty members, the Industrial Sponsored Research and Design Fellowship fund has collected a total $165,745 to help further the research of 17 different students.

Contributing Companies:

3M
3Wave Optics
Boston Scientific Corporation
Corning
Ethicon, a Johnson & Johnson Company
Genzyme
Guidant
Philips Medical Systems
Kenneth R. Lutchen, College of Engineering Dean / Professor – Dr. Lutchen is interested in using systems analysis and identification techniques to investigate respiratory and pulmonary mechanics as well as the relation of mechanics to ventilation distribution. He is particularly interested in the relation between lung structure and key lung properties that influence breathing and mechanical ventilation in asthmatics and emphysema patients. His work involves the use of parameter estimation sensitivity analysis, and optimal experiment design techniques for applying mathematical models to physiological data. Dr. Lutchen is also interested in signal processing associated with respiratory impedance data and heart rate variability.

John A. White, Chairman ad interim / Associate Professor – Dr. White's interests focus on the electrophysiological and pharmacological properties of ion channels and how their properties shape neuronal firing patterns and the information transmission in the mammalian brain. Electrophysiological, immunocytochemical, theoretical, and computer modeling techniques are applied. Current projects examine the molecular bases of synchronous activity associated with learning and memory, and the system-level consequences of random behavior at the molecular level.

Joyce Y. Wong, Associate Chairman, Graduate Studies / Associate Professor – Dr. Wong's research focuses on the development of biomaterials to probe how structure, material properties and composition of the cell-biomaterial interface affect fundamental cellular processes. Her current research interests include tissue engineering of small diameter blood vessels for bypass and intravascular pharmacology (e.g. stents); development of targeted nano- and micro-particle contrast agents for multi-modal (magnetic resonance, ultrasound, and optical) detection of atherosclerotic and vulnerable plaque; and engineering biomimetic systems to study restenosis and breast cancer.

Herbert F. Voigt, Associate Chairman, Undergraduate Studies / Professor – Dr. Voigt is currently engaged in experimental and theoretical studies of the neuronal circuitry in the cochlear nucleus. He uses single and multi-unit recording and analysis techniques to study the responses of neurons and neural nets to acoustic stimulation. Intracellular recording and marking techniques are used to associate physiological function to anatomical structure. Computational models are used to assist our understanding of the neural circuitry.

Irving J. Bigio, Professor – Dr. Bigio’s research focuses on medical applications of optics, lasers and spectroscopy, with an emphasis on minimally-invasive diagnostics and therapeutics. His current activities involve the development of fiber-optic probes to detect cancer using optical spectroscopy, a method that has developed the moniker “optical biopsy.” Related technology is being developed to measure certain drug concentrations in tissue with fiber-optic probes, or “optical pharmacokinetics,” in particular as an aid in the development of new chemotherapy agents. Other interests relate to monitoring the response of tumors to treatments and less invasive treatments for various pathologies, utilizing lasers and other optical technologies.

Charles R. Cantor, Professor – Dr. Cantor's research is focused on identifying biological problems that are resistant to conventional analytical approaches and then developing new methodologies or techniques for solving these problems. His laboratory has developed methods for separating large DNA molecules, for studying structural relationships in complex assemblies of proteins and nucleic acids and for sensitive detection of proteins and nucleic acids in a variety of settings. His current interests include the development of new methods for faster DNA sequencing, the development of new variations and analogs of the polymerase chain reaction, and the discovery of human genes associated with sensory perception. He is also interested in exploring the possible use of biological molecules for applications in nanoengineering and microbotics.
H. Steven Colburn, Professor – Dr. Colburn’s research involves the application of signal processing, statistical communication theory, and computational modeling to the study of hearing and hearing impairments. He is particularly interested in the measurement and modeling of binaural hearing phenomena including both psychophysical and physiological aspects. Dr. Colburn is also working in the area of simulated acoustic environments.

James J. Collins, Professor – Dr. Collins’ research is directed towards developing and implementing techniques and concepts from nonlinear dynamics and statistical physics to study and improve the function of physiological and biological systems. Specifically, his research addresses questions relating to: (1) random-walk analyses of human balance control, (2) the development of an artificial vestibular control system, (3) coupled nonlinear oscillators and locomotor central pattern generators, (4) noise-enhanced sensory function, (5) noise-shaping in networks of coupled neurons, (6) dynamical control of cardiac arrhythmias, (7) controlling cell cycle dynamics, and (8) designing and constructing genetic applets.

Edward Damiano, Associate Professor – Dr. Damiano’s research activities involve the application of biomechanics and biofluid dynamics to the study of basic physiological and pathophysiological processes at the cellular, subcellular, and extracellular-matrix levels. The focus of recent work has been on microhemofluidics in capillaries and post-capillary venules, the role of the endothelial surface layer in cardiovascular physiology, and sensory mechanotransduction in the vestibular semicircular canals. Other research activities include investigations of the interactions of leukocytes with the endothelium in capillaries and post-capillary venules, the development of a novel viscometric method to analyze non-Newtonian fluids, and the development of an automated robust control system to regulate blood glucose in Type 1 diabetes.

Charles DeLisi, Professor – Dr. DeLisi’s research includes the development and application of computational methods for determining the structure and function of large biological molecules genome organization, and information processing in cells. Areas of interest include the structural basis of voltage gating, and the docking and design of peptide hormones, neurotransmitters and antigenic peptides for drug and vaccine development. Other projects involve the use of large databases to develop expert systems and train neural networks for the problem of rapidly identifying regions of key importance in DNA and proteins.

Carlo J. DeLuca, Professor – Dr. DeLuca’s research interests are focused on the application of engineering principles to the understanding of motor control and the development of more objective patient treatment procedures. Specifically his research work involves: a) understanding how the brain and spinal cord control the individual fibers in a muscle, and groups of muscles, in healthy as well as dysfunctional individuals; b) methodologies for objectively measuring muscle fatigue during voluntary efforts; c) means for monitoring functional activities; and d) new technologies for detecting and interpreting EMG signals. He has developed various novel techniques and technologies for electromyography, some of which have been commercialized and are now used the world over. His work on motor unit control has brought forth physiological concepts such as the “common drive.”

Micah Dembo, Professor – Dr. Dembo's main research interest is the mechanical properties of living cells and cellular components. His work is mainly theoretical and computational but involves close collaboration with experimental efforts in several laboratories. He is currently involved in mechanical studies aimed at improving understanding of cell-substratum and cell-cell adhesion, cell division, cell locomotion, cell adhesion, and various passive cell deformations.
Solomon Eisenberg, Professor – Dr. Eisenberg's research is directed towards understanding the functional role played by electrically mediated interactions in connective tissues and membranes, as well as the effects and mechanisms of interactions of externally applied electric and magnetic fields. Specifically, his research addresses: electromechanical interactions in cartilage; electrically mediated transport in charged and neutral materials; computational modeling of electric field distributions in the human thorax and heart during electrical defibrillation; computational modeling of induced currents during transcranial magnetic stimulation.

Evan A. Evans, Professor – The general objectives of Dr. Evans' research are to expose the underlying physical mechanisms used by nature in design of complex biological organisms and the related physics of soft organic interfaces in liquids (polymers, membranes, etc.). The goal is to derive insights for biology, condensed matter physics, and advanced technology from the study of “nature's engineering.” Mechanical experiments at the nano and micro scales are combined with theory to examine material properties of synthetic and natural membranes, properties of biological cell structure and role of force in cell biochemical function, molecular bonding and adhesion. Material concepts extracted from these studies are applied to the design of specialized nanostructures, e.g. robust membrane capsules for chemical exchange in harsh environments and nanoconduit networks for microdevices.

Maxim Frank-Kamenetskii, Professor – Dr. Frank-Kamenetskii’s research is focused on theoretical and experimental studies of various DNA structures and their relations to DNA functioning in cell. He and his co-workers discovered a novel DNA structure, triplex H-DNA, and elaborated a comprehensive theoretical approach to treat DNA topology, i.e., knots and supercoils. His current interests include the development of new approaches to sequence-specific recognition of duplex DNA using triplex mode of binding of oligonucleotides to DNA duplex.

Timothy Gardner, Assistant Professor – Dr. Gardner’s lab is working to develop novel antibiotics, new cancer therapies, and to optimize microbes for energy production and environmental clean-up. In particular, the lab develops tools to map the genome-wide properties of gene regulatory and metabolic networks in microbes, plants and mammals. The lab applies these tools to understand the complex circuitry underlying cell physiology and mechanisms of disease. In addition, the lab uses these tools to predict the mechanism and side-effects of therapeutic drugs. Research in the Gardner lab integrates methods from diverse fields including genomics, genetics, microbiology, machine learning, bioinformatics, systems engineering and statistics.

Mark W. Grinstaff, Associate Professor – Dr. Grinstaff’s research involves the design, synthesis, and characterization of polymers for tissue engineering and drug delivery applications. His current interests include the use of novel dendritic hydrogel sealants to repair corneal lacerations and dendritic scaffolds for articular cartilage repair. Dr. Grinstaff uses an interdisciplinary research approach to understand the interactions that occur at a material-biologic interface to guide the development of designer biomaterials.

Andrew C. Jackson, Professor – Dr. Jackson’s research interests involve the application of engineering principles to the understanding of the mechanical properties of the human respiratory system. Specifically, his research efforts have been focused on computer modeling of the respiratory system, development of non-invasive tests of pulmonary function including fluid mechanics and acoustic phenomena in the airways, and identification techniques to analyze respiratory impedance data.

Simon Kasif, Professor – Dr. Kasif’s current research area is Bioinformatics, Computational Genomics and Molecular Engineering. More specifically, he has worked on analysis of microbial genomes, large scale genomic comparison and SNP detection, whole genome comparison, gene regulation, gene finding systems, and a variety of other algorithms and systems for functional genomics, structural genomics and comparative genomics. He has also studied artificial intelligence, parallel complexity and algorithms, constraint systems, computational learning theory, cognitive modeling and biologically inspired computing.
Amit Meller, Associate Professor - Dr. Meller research is directed toward the development of novel experimental techniques for the study of biomolecular interactions and dynamics, at the single molecule or at the single complex level. In particular, his research is focused on:

1. employing nanopore force spectroscopy to study RNA unfolding and re-folding kinetics,
2. DNA switches and transcription initiation kinetics,
3. RNA helicases activity,
4. mapping of transcription factors interactions with DNA,
5. ultra fast DNA sequencing,
6. development of novel optical methods for single molecule detection in biomedical applications.

Jerome Mertz, Associate Professor – Dr. Mertz’s research is in the development and applications of novel optical microscopy techniques for biological imaging. Most of these techniques are based on nonlinear optics with femtosecond lasers. Specific research topics include the application of two-photon excited fluorescence (TPEF) microscopy to deep imaging in brain tissue and visualization of endogenous fluorescence for clinical applications. Other topics include the application of second-harmonic generation (SHG) microscopy to cell membrane potential imaging and the photocontrol of chromophore orientation dynamics in biological membranes. Finally, alternative contrast mechanisms are being investigated including interferometric mechanisms based on optical coherence tomography (OCT) and nonlinear detection (Auto-confocal microscopy).

David C. Mountain, Professor – Dr. Mountain’s research centers around the experimental and theoretical study of electromechanical processes in the cochlea. Dr. Mountain is also interested in bioacoustic signal processing; sensory biophysics; measurement of evoked potentials and otoacoustic emissions; biomedical electronics.

Christopher Passaglia, Assistant Professor – Dr. Passaglia's research is aimed at elucidating how visual neurons process information. His work involves quantitatively analyzing the response characteristics of neurons early along the visual pathway and incorporating experimental findings into mathematical information transmission in normal and diseased states.

Kamal Sen, Assistant Professor – Dr. Sen’s research investigates the model system of the songbird to answer questions regarding how neurons in the brain encode complex natural sounds, neural substrates of selectivity for and discrimination of different categories of natural sounds, and whether these substrates are innate or shaped by learning.

Cassandra L. Smith, Professor – Dr. Smith’s research brings novel approaches and tools from the interface of genomics, genetics and biomolecular technology to complex disease studies. Current research interests include understanding how genomic DNA instability contributes to multifactorial diseases like schizophrenia that are linked to both genetic and environmental factors. Some of these studies use monzygotic (aka identical) twins, discordant for schizophrenia to understand how the well twin avoided disease. The goal of this research is to prevent and/or minimize schizophrenia. Other research takes a combinatorial chemistry approach to isolate aptamers (DNA mimics of antibodies) for use as cancer tumor targeting reagents. The goal of this research is to develop effective targeted therapies for cancer treatment and detection while minimizing damage to bystander cells.

Temple Smith, Professor – Dr. Smith is director of Biomolecular Engineering Research Center. The center has two major research objectives: to develop statistical computer approaches to detect syntactic and semantic patterns in DNA, RNA, and protein sequences and structures; and to use computer pattern analysis of those sequence patterns to understand regulation of gene expression, protein structure, and molecular evolution.

Dimitrije Stamenović, Associate Professor – Dr. Stamenović’s research centers around theoretical and experimental studies of mechanics of living tissues. His current interests are in microstructural analysis of cells, cartilage and lungs with the goal of relating their mechanical properties to the underlying structural design and distending stresses. Dr. Stamenović is also interested in mechanical properties of gas-liquid foams and microstructural determinants of foam elasticity.
Béla Suki, Associate Professor – Dr. Suki's research interests focus both on experimental and theoretical investigation of soft tissue biomechanics from fiber to organ level with special emphasis on the mechanical properties of the lungs. His current works involve dynamics of the stress-strain relationship of tissue strips, and statistical mechanical and micromechanical modeling of avalanche phenomena in airway opening. Other interests include nonlinear system identification and signal processing applied to biomedical systems and signals.

Joe Tien, Assistant Professor – Dr. Tien's main interests are tissue engineering; self-assembly and self-organization; and programmable cellular microenvironments. Dr. Tien and his group focus on the fabrication of artificial tissues through control of the cellular microenvironment, including branched networks such as vasculature and the pulmonary tree, and spatially complex aggregates such as liver acini. Members of the group design substrates that direct cellular interactions at the microscale and elicit a desired behavior and develop new technologies in-house as needed, to fabricate organized cell cultures. The group also uses these tools to examine how spatial and temporal variations in microenvironment affect the behavior of cells. Current work focuses on how the location and timing of cell-cell and cell-matrix interactions coordinately regulate cell behavior.

Lucia M. Vaina, Professor – Dr. Vaina's main areas of current interest involve: (1) models of visual motion analysis in the human brain, based on computational, psychophysical, structural, and functional-neuroanatomical methods; (2) functional plasticity-learning and neurorecovery, functional neuroimaging and neuronal network models; and (3) functional MRI of the human visual system.

Sandor Vajda, Professor – Dr. Vajda's research centers on scientific computing; computational chemistry; combinational optimization; molecular biology, protein and peptide structure determination; protein engineering; drug and vaccine design. His goal is to develop a methodology that will permit a predictive understanding of ligand recognition by protein receptors. Such understanding is the key to rational drug and vaccine design strategies, and requires the solution of several challenging problems. He is currently studying the following problems: (1) evaluation of binding free energy in protein-ligand complexes; (2) development of efficient docking algorithms that will find structures for the complex at or near the global free energy minimum; (3) predicting the ensembles of conformations adopted by short linear peptides in solution; (4) design of amino acid mutations to induce certain changes in the affinity and specificity of a binding site.

Zhiping Weng, Assistant Professor – Dr. Weng's research focuses on computational approaches to the determination of protein structure and function and the engineering of novel proteins with desired properties. Her research interests include genome sequence analysis, classification of protein families, homology modeling, structure alignment, sequence and structure pattern recognition, the development of target energy functions and search algorithms for receptor-ligand interaction, and the design of novel sequences for stronger and more specific binding.
Thomas Einhorn, Professor – Professor Einhorn’s interests include research on the repair and regeneration of bone and cartilage, reconstructive surgery of the hip and knee, and the treatment of metabolic bone disease.

Bennet Goldberg, Professor - Dr. Goldberg’s research focus includes low and room-temperature near-field scanning optical microscopy and spectroscopy in semiconductors and biological systems. Ultra-high spatial resolution combined with time-resolved spectroscopy provide new ways of examining mesoscopic systems. Magneto-optics and magneto-transport of two and one-dimensional electron systems are used to examine spin-textures in interacting electrons.

Shayamsunder Erramilli, Professor - Dr. Erramilli’s research interests include: Development of Infrared and Raman microscopy for imaging biological samples, using intrinsic contrast mechanisms; Applications of Scanning Near-field Infrared Microscopy for imaging single living cells, with a view to understanding the contribution of membrane lipids to the physics of cell motion; Application of high resolution vibrational microscopy for screening pathological tissue; Specifically seeking to correlate vibrational microscopy data with synchrotron x-ray scattering data; Development of vibrational infrared pump-probe 2-D spectroscopy for the study of biomolecules; Development of novel infrared fibers (silver halide) and Quantum Cascade Laser sources for biomedical applications. [Collaboration with Prof Irving Bigio]; Development of Quantum Raman Microscopy using entangles photons.

Stephan Grossberg, Professor – Dr. Grossberg’s work concerns modeling how the brain controls behavior, and how to develop new technologies that more closely emulate properties of biological intelligence, especially how individuals can successfully adapt in real time to changing environmental conditions. Recent research projects include work on neural models of vision; audition; variable-rate speech perception; learning; memory; categorization and recognition; recall; reward and punishment; adaptive sensory-motor control; cortical development; and neural substrates in areas such as visual cortex, parietal cortex, inferotemporal cortex, prefrontal cortex, basal ganglia, cerebellum, reticular formation, spinal cord, and superior colliculus. Technological applications to machine vision, adaptive pattern recognition, and robotic systems are also being made.

James A. Hamilton, Professor - Dr. Hamilton is a Professor of Biophysics and Physiology and Director of the Cardiovascular Magnetic Resonance Spectroscopy and Imaging Laboratory at the Boston University School of Medicine. Dr. Hamilton’s research program has two main components; fatty acid transport (structural and cell biology) and MR imaging of atherosclerosis and ectopic fat. His programs are interdisciplinary with strong translational components in obesity, diabetes, cardiovascular disease, and inherited lipid disorder.

Allyn Hubbard, Associate Professor – Dr. Hubbard's research is comprised of two major areas that partially overlap each other. The first is auditory science, which includes both experiments and models involving the mammalian, peripheral auditory system. The second research area involves building integrated circuit chips that are targeted at biomedical applications. One chip currently under development is to implement the traveling-wave amplifier model of the cochlea. Another chip creates a micro-electrophoresis chamber, which has embedded sensors that can detect DNA or other large molecules. A major focus is currently the fabrication of neural-net chips that mimic the biological vision system.
W. Clement Karl, Associate Professor – Dr. Karl's research is concerned with the development and use of statistically-based techniques for the extraction of information from images and multidimensional fields. One aspect of his work concerns the development of multiresolution methods for the processing and estimation of signals and images. For example, multiresolution approaches are being developed and used for tomographic image formation and MRI segmentation. Another aspect of his research concerns the estimation of fundamentally geometric quantities or, more generally, the role that geometry or shape may play in estimation problems. An example of this work is the estimation of cardiac vessel shape in angiograms. He is in charge of the Multi-Dimensional Signal Processing Laboratory.

Catherine Klapperich – Assistant Professor - Dr. Klapperich’s research centers on the molecular interactions that take place at the cell-biomaterial interface. She is specifically interested in the integration of cells or cell components into synthetic device environments in microscale and nanoscale systems. Her experiments focus on the integration of molecular level data from genomic and proteomic analyses into iterative materials design. Applications include microfluidic device design and polymer based tissue engineering.

Nancy Kopell, Professor – Dr. Kopell's major current interest is dynamics of the nervous system, especially rhythmic behavior in networks of neurons. Some of the specific projects on which she has worked include work on the biophysical substrate of network coherence, creation and modulation of cell assemblies, and synchronization across distances. A long-range goal is to understand how the dynamical properties of local networks help to filter and transform the patterned input from other parts of the nervous system, to provide clues to the function of dynamics in the nervous system. She continues to be interested in Central Patten Generators, networks of neurons that govern rhythmic motor behavior. Another ongoing interest of hers is also in geometric theory of singularly perturbed systems.

Elise F. Morgan, Assistant Professor – Dr. Morgan’s research focuses on relationships between structure and mechanical function of musculoskeletal tissues at multiple length scales. She uses both experimental and computational methods to explore how the deformation and failure behaviors of tissues, primarily bone and cartilage, depend on the tissue microstructure; and conversely, how the differentiation and adaptation of tissues and cells are modulated by their local mechanical environment. Dr. Morgan is also interested in the mechanics of general multi-scale media and damage mechanics.

S. Hamid Nawab, Professor – Dr. Nawab’s research interests include Computational signal processing and its application to electromyographic signals, auditory signals, and patient activity signals from wearable sensors. His current work focuses on the exploration of novel algorithms, architectures and design environments for the processing and understanding of biosignals. This includes projects in auditory scene analysis, decomposition of indwelling and surface EMG signals, and wearable sensors for patient monitoring.

Matthew A. Nugent, Professor - Dr. Nugent is a Professor of Biochemistry and Ophthalmology at the Boston University School of Medicine. Dr. Nugent’s research program combines traditional biological and biochemical approaches with those of biomedical engineering. In this regard, a considerable amount of the research in his lab involves the development and use of quantitative mathematical models of dynamic cellular processes, as well as concepts related to tissue engineering and controlled drug delivery technology.

Tyrone Porter, Assistant Professor - Dr. Porter is interested in development of targeted ultrasound contrast agents for image enhancement (molecular imaging), perfusion imaging, and image-guided drug delivery. His interests also cover ultrasound-enhanced transport of drugs and genes across cell membranes and ultrasound-enhanced drug activity, and tissue response to acousto-mechanical forces. In addition, his work includes use of ultrasound with polymers, such as the ultrasound-induced release of therapeutics from polymeric biomaterials and modification of polymer structure and/or function due to energy deposition from ultrasound.
Daniel Segré, Assistant Professor - Dr. Segré is interested in the evolutionary dynamics of biological networks, in particular in the interplay between response to genetic and environmental perturbations, genomic-level functional organization, and optimal adaptation. His lab’s goals include developing constraint-based models to study the regulatory and evolutionary dynamics of metabolic networks across different organisms, cell types, and interacting cell populations.

Barbara Shinn-Cunningham, Associate Professor – Dr. Shinn-Cunningham’s research interests include psychoacoustics, localization of sound sources and binaural hearing. She works with models of auditory perception, auditory plasticity and learning.

H. Eugene Stanley, Professor - Dr. Stanley's current research includes work on the physical mechanisms in liquid water. This surrounds a liquid-liquid phase transition hypothesis that arose from molecular dynamics studies on the structure and equation of state of supercooled bulk water. Other research includes the application of statistical physics to understanding and preventing diseases related to protein misfolding, such as Alzheimer's disease. This includes using statistical and condensed matter physics to study the early stages of aggregation of the amyloid beta-protein that eventually makes up the toxic fibrils and plaques found in the brains of Alzheimer patients. His lab is refining protein-folding models designed to identify the areas of the amyloid protein that are involved in the misfolding process, and to predict forms that the proteins are likely to take in the human brain.

Malvin C. Teich, Professor – Dr. Teich’s research interests center on the statistical behavior and signal processing of biological signals. He is studying how acoustical and optical stimuli are encoded into fractal sequences of action potentials at various locations in the auditory and visual systems, and how the fractal nature of the electrocardiogram can be used to distinguish normal and diseased patients. He is investigating the neurobiological origins of such behavior. He is also studying a new class of neural-based psychophysical models that consider the ascending pathways of sensory systems as amplifying neural networks. He is also developing a quantum-optical microscope that should be useful for high-resolution fluorescence studies in the neurosciences.

Joe Z. Tsien, Professor – Dr. Tsien’s research is aimed at understanding the organization principles underlying the neural network encoding and processing of learning and memory. The lab's strategy is to take an integrated approach that combines molecular genetics, physiology, computational mathematics, and behavioral techniques. With the latest capacity to measure simultaneously ensemble activities of over 200 hundreds of individual neurons in the brain of freely behaving mice, researchers in the lab are studying the molecular and network mechanisms of learning behaviors. Current projects include: 1) The molecular and ensemble analysis of short-term memory; 2) The molecular and ensemble analysis of consolidation and storage of long-term memory; 3) The molecular and neural analysis of memory retrieval; 4) Methods for enhancing or erasing memories; 5) Monitoring and decoding neural networks; 6) Computational analysis of neural population dynamics and memory codes; 7) Brain-Machine-Interface conversions.

Martin Steffen, Assistant Professor – Dr. Steffen’s research focuses on developing the tools of systems biology for mammalian cells. Currently we are emphasizing the technique of mass spectrometry. Using mass spec, one can currently identify a few thousand proteins in a single experiment, as well as many important post-translational modifications.
M. Selim Ünlü, Professor – Dr. Ünlü has broad research interests including applications of nano-optics, optoelectronic devices and spectroscopic techniques to various biological and biomedical problems. One of the recent activities involves development of biosensors based on optical waveguides and resonators. The evanescent field of a planar waveguide can be used to probe small changes in the index of refraction of objects in a well on the surface of the waveguide. Resonant optical systems enable high fidelity operation for exquisite sensitivity, as well as high density arrays for massively parallel operation. Such platforms can be ultimately used for pathogen detection and biomolecular analysis. Our research group has developed a new interferometric technique in fluorescent imaging called spectral self-interference fluorescence microscopy which yields nm-scale axial height determination. The goal of this research effort is to study sub-cellular processes as well as nanoscale biological structures such as trans-membrane proteins and surface bound nucleotides.

Matt Wachowiak, Assistant Professor - Dr. Wachowiak’s research interests include odor coding, olfactory information processing, imaging, temporal dynamics of neural activity, relationship between sampling behavior and neural coding. His current work focuses on how odor information is encoded and processed by the brain, and how odor coding and neural activity is shaped by an animal's sampling behavior. Fluorescence-based imaging methods are used to monitor activity from defined populations of neurons in response to olfactory stimulation in preparations that include brain slices, intact anesthetized animals, and awake behaving animals. His lab is particularly interested in the temporal dynamics of activity across populations of neurons in the olfactory pathway, how these dynamics encode stimulus information, and how this code is shaped by sampling behavior.

Research

Natalia Broude, Research Associate Professor – Dr. Broude’s research has been focused on chemistry of nucleic acids, isolation, sequencing and expression studies of a family of human genes coding for Na, K-ATPase. Her current interests include the development of new approaches to genome-wide targeted genomic differential display, genomic methylation profiling.

Marc Herant, Research Assistant Professor – Dr. Herant's main research interests are in developing a better understanding of cell shape and motion through the construction of theoretical models. Areas of current effort include the mechanics of phagocytosis and the dynamics of the lamellipodium.

Damir B. Khismatullin, Research Assistant Professor - Dr. Khismatullin's current research activities are focused on the biomechanics of leukocytes (white blood cells) and other living cells and biomedical applications of gas microbubbles (ultrasound imaging, drug delivery, shock-wave lithotripsy). The main objective of this research is to integrate computational modeling, in vitro and in vivo experiments to improve understanding the dynamics of living cells and microbubbles under both physiological and pathophysiological conditions. He is also interested in bio-fluid mechanics (blood flow, mucus transport in the lung airways), nonlinear dynamics of multiphase and non-Newtonian fluids (bubbly liquids, emulsions, and polymer solutions), and shape oscillations of liquid drops.

Thomas L. Szabo, Research Professor – Professor Szabo’s research goals are overcoming present limitations in imaging the body using ultrasound and other imaging modalities and finding new ways of extracting diagnostically useful information about tissue structure, health and function noninvasively. His work involves the following: multi-modal and 3D digital imaging and beam forming, signal processing, ultrasound-induced bioeffects, simulation and measurement of mechanical tissue properties, and scanning acoustic microscopy.
SCHEDULE and TECHNICAL ADVISORS
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:15 – 7:45 AM</td>
<td>Continental Breakfast</td>
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<tr>
<td>7:45 AM</td>
<td>Opening Remarks: Dr. Kenneth R. Lutchen</td>
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<tr>
<td>8:00 – 9:55 AM</td>
<td>SESSION I</td>
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<td>PHO 206</td>
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<td>Patient Monitoring and Bioinstrumentation</td>
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<td><strong>Session Chairs:</strong> Ken Lutchen, Chris Passaglia</td>
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<td></td>
<td>Use of single-frequency transfer impedance to study the effect of deep breaths in bronchoconstricted healthy asthmatic subjects</td>
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<td><em>Julissa Pina &amp; Craig Fritch</em></td>
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<td>Investigation of Skin Prepping Mechanisms to Improve Ionic Conductivity on an EEG Electrode</td>
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<td><em>Graham Houtchens</em></td>
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<td>The Assessment of Trapped Gas Volumes in Bronchoconstricted Asthmatics and Non-Asthmatics</td>
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<td><em>Patrick Raleigh</em></td>
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<td>Analysis of Microvascular Hemodynamics using Micro-particle Image Velocimetry</td>
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<td><em>Amy Trongnetrpunya</em></td>
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<td>9:55 – 10:20 AM</td>
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</table>
10:20 – 12:00 PM  SESSION IIA
PHO 206  Nano- and Micro-Biotechnology

Session Chair: Joyce Wong
Ed Damiano

Microfluidic Production of Gas Filled Monodisperse Polymer Microbubbles to be Used as Ultrasound Contrast Agents
Jason Nami

Antineoplastic Drug Delivery Through the Use of Polymer Nanoparticles
Joseph Walpole

Development of a Molecular Component Editor for Predicting Small Molecule Interactions
Linh Phan

Developing Purely Electronic Recognition Method for DNA-Transcription Factors Interactions Using Nanopores
Andrew Chow

Delivery of Genetic Material to the Cellular Surface via a Novel Nanofibrous Material
Rakesh Patel

Low-Cost High Efficiency Microarray
Tiancheng Wang

Microchip Based Macromolecule Analysis
James Schrode

Characterizing and Mutating the mer Promoter to Build a Bacterial Mercury Sensor
Disha Shah

10:20 – 12:00 PM  SESSION IIB
PHO 205  Neuroscience, Neuroengineering and Auditory Science

Session Chair: John White

NeuroMuscular Adaptations During Bed Rest
Robert Li

Noise-enhanced Gait Stability
Andrew Galica

The Effect of Context on the Perception of a Virtual Auditory Object
Michael DeFuria

The Effect of Signal Modulation on Divided Attention
Desiree Balderrama

Designing Software to Identify Bird Species Via Bird Song Identification
Tristan Carrier

The Effects of Spatial Location on Temporal and Spectral Grouping of Sound Complexes
Stephen Babcock

Optimization of Synaptosomal Dopamine Release Experimentation by Suprafusion Machine Streamlining and Cell Viability Assessment
Trevor Arneberg

Investigating the Relationship Between the Behavioral and Neural Response of Songbirds to Complex Stimuli
Julie Young

12:00 – 12:50 PM  LUNCH
<table>
<thead>
<tr>
<th>12:50 – 2:45 PM</th>
<th>SESSION IIIA</th>
<th>Biomechanics and Biomaterials</th>
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<tr>
<td>PHO 206</td>
<td>Session Chair: Ed Damiano Joyce Wong</td>
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<td>Engineering an <em>In Vitro</em> Model of Localized Microvascular Inflammation Matt Prosen</td>
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<td>Defining the Relationship between Bone Density, Bone Geometry, and Bone Strength Anderson Mach</td>
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<td>The Use of Finite Element Analysis to Assess the Effects of Osteoporosis Drug Treatment on Bone Strength Neil Patel</td>
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<td>3-D Visualization of Spine Fracture Andrew Baker</td>
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<td>Non-invasive assessment of femoral geometry Christina Piron</td>
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<td>Instrumentation to Measure Fluid Mechanics in Compliant-Walled Tubes Jordan Biswurm &amp; Kathryn D’Agnes</td>
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<td>Determining the isolated and combined effects of airway size, thickness, and stimulation on healthy and asthmatic single airway and whole lung function Nimesh Patel</td>
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<td>An <em>In-Situ</em> Study of Deep Inspirations during Bronchoprovocation in Excised Lung Lobes Danny Miranda</td>
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<td>Exploring a Link Between A20 Expression and Vascular Wall Biomechanics Roy Arjoon</td>
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<td>The Effects of Cyclic Strain on Vascular Smooth Muscle Cell Carolyn Yee</td>
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<th>12:50 – 2:45 PM</th>
<th>SESSION IIIB</th>
<th>Imaging and Modeling</th>
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<tr>
<td>PHO 205</td>
<td>Session Chair: Kamal Sen</td>
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<td>Feature Extraction of Neuronal Population Activity Measured with Two-Photon Microscopy Natalie Brill</td>
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<td>Exploring the Neural Effects of Transcranial Direct Current Stimulation via Diffusion Tensor Imaging and other Blood Flow Imaging Techniques Arup Chakrabarti</td>
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<td>Time Course Measurements of Liver &amp; Kidney Hemangiomas in Tsc2 Mice Models Henry Cheng</td>
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<td>Time Course Measurements of Lung Tumors in a Drug Trial of a Transgenic Mouse Model Hieu Ngo</td>
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<td>Quantitative MRI of the Pediatric Brain in Comparison with the Adult Brain Ashley Martin</td>
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<td>Characterization and Measurements of the third ventricle in Hydrocephalic Mice Thuan Ngo</td>
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<td>True Dual Contrast Agents for Cellular MRI Matthew Marzelli</td>
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<td>Modeling the Dynamic Behavior of the Circadian Clock in <em>Limulus polyphemus</em> Raphael Mattamal</td>
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<td>Limitation of Personalized Airway Trees for Probing Image Based Structure-Function Relations in the Lung Noah Levit</td>
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<tr>
<th>2:45 – 3:15 PM</th>
<th>BREAK</th>
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</table>
Angiopoietin-1 Proteomic Profiling: Genetic Engineering and Receptor Targeting in Cardiac Myocytes
Emily Parodi

Tumor targeting with Anti-CEA aptamers
Akash Patel

Cataloguing human kinase substrates to build a representative kinase substrate library for the quick establishment of kinase enzyme assays
Kristifor Sunderic

Quantifying Promoter Activity During Stringent Response to infer influence of (p)ppGpp on crp and arcA promoters
Justina Tam

An Analysis of Chromosomal Fragility in Schizophrenic Subjects
Stephen Gallagher

Sirt1 Signaling in the PI3K/AKT Pathway
Johanna Jacob

Modification of a genetic toggle switch in Escherichia coli to allow multiple transcription factor input networked using Boolean logic
Peter Voyvodic

Optimization of Power Generation in Microbial Fuel Cells through Insertional Mutations of Shewanella oneidensis MR-1
Stephen Schneider

Closing Remarks

Final Conference Comments: Dr. Kenneth R. Lutchen

RECEPTION IN THE ATRIUM, 2nd FLOOR, PHOTONICS CENTER
## 2007 Senior Project Technical Advisors

<table>
<thead>
<tr>
<th>Session I</th>
<th>Student</th>
<th>Technical Advisor</th>
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<tbody>
<tr>
<td></td>
<td>Julissa Piña / Craig Fritch</td>
<td>Andrew Jackson</td>
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<td>Graham Houtchens</td>
<td>Rafael Cordero</td>
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<td>Daniel Mang</td>
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<td>Xiaoyan Chen</td>
<td>Ousama A’amar</td>
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<td>Olga Starobinets</td>
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<td>Monica Ortiz</td>
<td>Robin Cleveland</td>
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<td>Vitaly Dobromyslin</td>
<td>Kevin Kwaku</td>
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<td>Session II A</td>
<td>Jason Nami</td>
<td>Wynter Duncanson</td>
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<td>Joseph Walpole</td>
<td>Yolonda Colson</td>
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<td>James Schrode</td>
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<td>Disha Shah</td>
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<td>Robert Li</td>
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<td>Andrew Galica</td>
<td>Attila Priplata</td>
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<td>Desiree Balderrama</td>
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<td>Matt Prosen</td>
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<td>Natalie Brill</td>
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<td>Arup Chakrabarti</td>
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<td>Henry Cheng</td>
<td>Yanping Sun</td>
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<td>Hernan Jara</td>
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<td>Matthew Marzelli</td>
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<td>Raphael Mattamal</td>
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<td>Session IV</td>
<td>Emily Parodi</td>
<td>Maria Rupnick</td>
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<td>Akash Patel</td>
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<td>Stephen Schneider</td>
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VISITING COMPANIES and LABORATORIES
| 1. | 3M Health Care | St. Paul, MN |
| 2. | 3Wave Optics, LLC | Boston, MA |
| 3. | Abiomed | Danvers, MA |
| 4. | Advanced Medical Ventures | Redwood City, CA |
| 5. | Albert Einstein College of Medicine | New York, NY |
| 6. | Arrow International | Reading, PA |
| 7. | Artech Associates and Venture Advisors | Boston, MA |
| 8. | Aspect Medical Systems | Norwood, MA |
| 9. | Astra Zeneca | Waltham, MA |
| 10. | BD Medical | Waltham, MA |
| 11. | Beth Israel Deaconess Medical Center | Boston, MA |
| 12. | BioTrove, Inc. | Woburn, MA |
| 13. | Boston Scientific Corporation | Boston, MA |
| 14. | Boston University School of Management | Boston, MA |
| 15. | Brigham & Women's Hospital | Boston, MA |
| 16. | Children's Hospital Boston | Boston, MA |
| 17. | Columbia University Medical Center | New York, NY |
| 18. | ConMed Electrosurgery | Centennial, CO |
| 19. | Cordis Corporation | Warren, NJ |
| 20. | Corning Incorporated | Acton, MA |
| 21. | Cynosure, Inc. | Westford, MA |
| 22. | DEKA Research | Manchester, NH |
| 23. | Draeger Medical Systems, Inc. | Andover, MA |
| 24. | Essex Orthopaedics | Andover, MA |
| 25. | Ethicon, Inc. | Somerville, NJ |
| 26. | GE Global Research | Niskayuna, NY |
| 27. | Genzyme Corporation | Cambridge, MA |
| 28. | Harvard Medical School | Boston, MA |
| 29. | Hebrew Senior Life | Boston, MA |
| 30. | Iandiorio & Tesca | Waltham, MA |
| 31. | InfoSciTex | Waltham, MA |
| 32. | Instrumentation Laboratory, Inc. | Lexington, MA |
| 33. | Massachusetts General Hospital | Boston, MA |
| 34. | Medtronic, Inc. | Minneapolis, MN |
| 35. | Merck & Co., Inc. | Boston, MA |
| 36. | Merrimack Pharmaceuticals | Cambridge, MA |
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37. Miranda Laboratories  Bedford, MA
38. MIT Lincoln Laboratory  Cambridge, MA
39. MITRE Corporation  Bedford, MA
40. National Instruments  Woburn, MA
41. Navimedix  Cambridge, MA
42. Neurometrix, Inc.  Waltham, MA
43. Neuroptix Corporation  Acton, MA
44. Oakwood Medical Investors  Cleveland, OH
45. OmniSonic Medical Technologies, Inc.  Wilmington, MA
46. Parexel International  Waltham, MA
47. Perceptive Informatics  Waltham, MA
48. Philips Medical Systems  Andover, MA
49. Pulmatrix, Inc.  Cambridge, MA
50. Raytheon  Waltham, MA
51. Respironics  Brighton, MA
52. SOLX, Inc.  Boston, MA
53. Transform Pharmaceuticals, Johnson & Johnson  Lexington, MA
54. Tufts - New England Medical Center  Boston, MA
55. Tyco Healthcare  Mansfield, MA
56. US Air Force Biomedical Sciences Corps  Burlington, MA
57. Whitehead Institute for Biomedical Research  Cambridge, MA
58. Wyeth  Cambridge, MA
59. Wyle Labs / NASA  Houston, TX
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Artech Associates and Venture Advisors
Advent International

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Life Sciences
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Class of 1990

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Vice President, Biomaterials Research
Genzyme Corporation

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3Wave Optics, LLC

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Kendall Division / Tyco Healthcare
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Women’s Health & Urology
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Oakwood Medical Investors, LLC
Class of 1989

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Monitoring, Cardiac & Monitoring Systems
Philips Medical Systems

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Chief Scientific Officer
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Bruce H. KenKnight
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Boston Scientific CRM

Peter Russo
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Director, Entrepreneurship and Management
Institute.

Gregg A. Vandesteeeg, Ph.D.
Vice President, Research and Development
3M Health Care
<table>
<thead>
<tr>
<th>Company/Laboratory</th>
<th>Representatives/Visitors Directory</th>
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</table>
| 3M Corporate Technology & Health Care Markets | Gregg A. Vandesteeg  
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| Aspect Medical Systems | Rafael Cordero  
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| Elizabeth Afanasewicz | Product Development Engineer  
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| Kevin Kwaku | Electrophysiologist |
| Christiane Ferran | Associate Professor of Surgery and Medicine |
| Gottfried Shlaug | Assistant Professor of Neurology |
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| Colin Brenan | Chief Technology Officer  
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| Bruce KenKnight | VP of Research & Business Development |
| Weenna Bucay-Couto | Research Scientist II  
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Seung-Schik Yoo
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Director, International Relations

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Merrimack Pharmaceuticals

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Hebrew Senior Life

Attila Priplata
Research Fellow

Miranda Laboratories

Henry Miranda
Sole Proprietor

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Andrew Watchorn

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Mr. Walt Olson PhD,
VP, CRM Research

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Heather Rasich, Class of 2006
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OmniSonic Medical Technologies, Inc.

Maximillian Fiore
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Wilmington, MA 01887

Merck & Co., Inc.

Julie Gorenstein
Staff Biologist
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Boston, MA 02115
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Parexel International
*Andrea DeIulio*
Imaging Research Supervisor
200 West Street
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PROJECT ABSTRACTS
SESSION I:
Patient Monitoring and Bioinstrumentation
Use of single-frequency transfer impedance to study the effect of deep breaths in bronchoconstricted healthy and asthmatic subjects

Craig Fritch
Julissa Pina

In the United States, approximately 20 million people suffer from asthma, a disease that accounts for almost 2 million trips to the emergency room and 5,000 deaths per year. Bronchoconstriction, a result of asthma, cause the airways to narrow reducing the amount of air entering the lungs. In order to reverse the affects of bronchoconstriction, a person takes deep breaths decreasing the airway resistance (R_{aw}) and increasing the airflow into the lungs. However, asthmatics are unable to maximally dilate their airways completely reversing the affects of constriction. The current method uses multiple-frequency oscillations to determine the total respiratory system resistance (R_{rs}), providing accurate yet noisy data. The intention of our research was to improve the methods used to investigate respiratory mechanics by validating the use of single-frequency transfer impedance (Z_{tr}) measurements for applications involving asthmatic lung-function measurements. Z_{tr} measurements were acquired at baseline, and before and after a deep breath (DB) during induced obstruction at an 8 Hz forcing function. By implementing a recursive least-squares (RLS) algorithm, Z_{tr} data was fit to the equation, P_{tr} = R_{rs} \dot{V}_{osc} + E_L \dot{V}_{osc}, where P_{tr} is the pulmonary pressure, \dot{V}_{osc} is the flow through the airway opening, E_L is the lung elasticity, and \dot{V}_{osc} is the oscillating volume. R_{rs} \approx R_{aw} + R_{ti}, but at 8 Hz R_{rs} \approx R_{aw}. The equation was able to accurately estimate the changes in R_{aw} by employing a forgetting factor, which updates the parameter estimates after each new data point. Our work shows that single-frequency measurements can sufficiently characterize and track asthmatic lung function and offer a greater signal-to-noise ratio than multiple-frequency data.
Investigation of Alternate Prepping Mechanisms to Improve Ionic Conductivity on an EEG Electrode

Graham Houtchens
Aspect Medical Systems, Inc.

The ability to acquire quality biopotentials from surface electrodes is largely dependent on the skin impedance of the subject, with high impedances causing increases in noise and impedance mismatches with the instrumentation. Aspect Medical Systems has developed an electrode system which contains a set of flexible tines embedded in the electrodes which effectively brush aside the outer layer of skin to lower skin impedance. However, in some cases the patient can sense the prepping action of the tines when the electrodes are pressed against the forehead. The goal of this project was to develop and test different skin prepping mechanisms which can be built into sensors in the same manner as Aspect’s current impedance lowering mechanism but have alternative structures that may be more cost effective to produce and reduce the prepping sensation to patients. The first approach was to investigate a method which used different geometries of rigid tines to effectively alter the configuration of the outer layer of skin to create ionic channels for signal conduction. This task was accomplished by creating samples of varying tine geometry and comparing skin impedance measurements through electrodes using these tines to electrodes with the current technology on four subjects using paired t-testing. Three geometries were investigated, with two of the geometries being constructed with machined samples and the third geometry being constructed by a novel fixture. Results showed that for various geometries the tines were effective, with one of the geometries outperforming the currently available product. Additionally, subjects reported less prepping sensation with all of the geometries.

The second approach was to continue with a set of flexible tines like the current product, but to use a material which contained a different density of tines. Again, these samples were tested on subjects and skin impedance recordings were taken and compared to skin impedance readings on the same subjects wearing sensors constructed with the currently available technology. The new material proved to work as effectively as the currently available product and subjects reported less prepping sensation with the new material. The different approaches resulted in two new mechanisms being developed that are effective at lowering skin impedance while minimizing sensation to the patient, and are promising alternatives to the current technology for future sensor products.
Assessment of Trapped Gas Volumes in Bronchoconstricted Asthmatics and Non-Asthmatics

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Asthma is a complex disease that has been not fully yet characterized. Many individuals and laboratories have devoted immense time and resources to characterize and identify changes of measurable quantities in or from the lung such as input impedance ($Z_i$), transfer impedance ($Z_{tr}$), standard pulmonary function tests (PFTs) and the degradation of ventilation heterogeneity. The goal of this project was to quantify and assess the correlation of trapped gas volumes to bronchoconstricted asthmatics and non-asthmatics while monitoring airway resistance ($R_{aw}$). This was done by obtaining trapped gas measurements using the multi breath nitrogen washout (MBNW) technique and $Z_{tr}$ measurements. The $Z_{tr}$ forcing function was an amplified pseudo-random noise containing frequency components 2-64 Hz in 2 Hz increments. The MBNW and $Z_{tr}$ measurements were performed on subjects underline baseline conditions and after maximal bronchoconstriction. At baseline conditions, the non-asthmatics (NA) had a forced vital capacity (FVC) % predicted value of 106±0 SD and, and the asthmatic subject had a % predicted FVC of 98±0 SD. Neither the asthmatics nor the non-asthmatics displayed evidence of gas trapping at baseline. At post challenge, the non-asthmatics $R_{aw}$ reduced less than compared to the asthmatic group. In addition to $R_{aw}$ differences, the relative difference between the trapped gas volumes released from the peripheral airways after a deep breath was significant. These are qualitative descriptions of the data due multiple, un-controllable error. However, further research using this experiment in the following months will provide a more conclusive insight to the statistical significance between the two groups.
Analysis of Microvascular Hemodynamics
using Micro-particle Image Velocimetry

Amy Trongnetrpnunya

Microcirculatory disorders, or disorders afflicting the capillaries, arterioles, or venules, such as hypertension, sickle cell anemia, and diabetes disturbs blood flow in microcirculation and greatly impacts public health. However, before discovering the means to treat, prevent, or lessen the effects of microcirculatory diseases, we must first understand the two most important parameters that determine the forces or mechanisms involved in the microvascular hemodynamics in an individual microvessel – vessel diameter and discharge hematocrit. Currently, there exists no accurate or simple method for predicting discharge hematocrit in a microvessel in vivo, so we sought to develop a method to obtain a comprehensive look-up table of hematocrit distributions for various correlating viscosities and shear-rates. A flow chamber was designed such that while the tube is perfused with hemodiluted blood obtained from cardiac punctures from male mice, micro-particle image velocimetry was used to extract the viscosity, shear stress, and shear rate distributions of the flow. Confocal microscopy was then used to obtain radial distributions of red blood cells along the diameter of the tube using a 2ms line scan placed across the diameter of the 48μm polyethylene capillary tube. This approach removes any possibilities of distorting the hematocrit distribution. The hematocrit distribution was extracted directly from the confocal microscopy images and could be correlated to corresponding viscosity, shear rate, and shear stress distributions, which serves as a proof of the method needed for future studies in order to construct a comprehensive look-up table of hematocrit distributions for various viscosities and shear rates.
Effects of Vibrotactile Feedback of Foot Pressure on Gait and Balance Function

Daniel Wai Heng Mang
NeuroMuscular Research Center

There is considerable evidence that vibrotactile feedback in the lower limbs and foot-sole cutaneous mechanoreceptors contribute to the control of upright balance. A wearable prosthetic balance device has been previously created to use vibrotactile feedback, as a result of changes in ground reaction force (GRF) and center of pressure (COP) under the feet, to address the problems of balance disorders. Measurements of GRF and COP are clinically useful indicators of a subject's stability. In this project, we refined the balance device in order to make the device more user-friendly and transparent for patient use. COP and GRF characteristics of walking up and down a flight of stairs and a ramp were analyzed and catalogued. A tactor firing sequences for the insole device was created to increase mediolateral (ML) vibrotactile feedback while walking up and down a flight of stairs. The foot device was redesigned to allow for greater (ML) sensitive and better ergonomics. Two new algorithms were created to address the limitations of the device. A "smart" algorithm, based on the different COP and GRF characteristics allowed the device to differentiate between various gait tasks. In addition, an auto-calibration algorithm eliminated an initial calibration phase where the user was required to stand still for five seconds. The wearable prosthetic balance device became more user-friendly and transparent to the patient by incorporating the two new algorithms and modifications.
Design and Construction of a Vertical Polar Nephelometer

Xiaoyan Chen

Biophotonics Laboratory, Boston University

Studies have shown that enhanced apoptosis is desirable in chemotherapy of a tumor. However, current methods of detecting apoptosis in vivo are too slow to be clinically useful. By looking at the light scattering from cells as a function of angle, a nephelometer can, in theory, rapidly measure the size, shape and refractive index of particles responsible for scattering. Therefore, the nephelometer could potentially detect the change in shape and size of organelles in cells undergoing apoptosis in vitro. However, the nephelometer with a horizontal setup currently in use did not appear to distinguish between normal and apoptotic populations of cells, even though its operation was first verified using solutions of polystyrene spheres. Polystyrene spheres are homogeneous spherical particles whose scattering intensity, according to Mie theory, depends on their size, refractive index relative to the surrounding medium, illuminating wavelength, and the polarization of the beam. The horizontal setup requires that the measured cells be suspended in growth medium and placed in a test tube. Most cells lines are adherent and grow on culture plates. Taking measurements of these cells in suspension disrupts them from their native state and may change their architecture. A vertical version of the nephelometer that allows optical measurements to be performed on cell culture plates instead of cell suspensions was fully developed. In addition, a new dc motor with a built-in high resolution optical encoder was used instead of the optical wedge and reference beam in the horizontal setup to obtain more accurate determination of collection angle. Polystyrene spheres of 2.9, 4.5, 7 and 9.6 μm were used to validate the system. The phase function of 2.9 μm matched very well with Mie theory with a correlation coefficient of 0.9048. However, the spheres with other sizes did not match well with the theoretical data, possibly due to index mismatch of the medium with air or the noise in the detection system itself. Cells treated with apoptosis-induced agents and normal cells were both tested using the vertical nephelometer at one and half hour, four hours and six hours. There was a continuously increase in the difference between treated and untreated cells’ phase function as time increases. Apoptotic cell condensation and fragmentation begin around 4 hours after treatment and is wide spread at 8 hours. Therefore, the increase in difference with time may be due to the change in nuclear morphology. These data suggest that the vertical nephelometer is able to detect apoptosis rapidly in vitro. In the future, based on the study of apoptosis in vitro using the vertical nephelometer, a new device that could detect apoptosis rapidly in vivo may be implemented and guide physicians to the most efficient method of chemotherapy in a very short time.
Drug Eluting Ureteral Stents
Olga Starobinets
Boston Scientific, Department of Urology

Loss of urinary function, caused by kidney stones or tumors lodged within the ureter produces an accumulation of toxic waste materials, which can severely damage the kidney. Ureteral stents are tube-like polymeric devices, which are typically inserted into the ureter to relieve obstruction and facilitate urinary drainage. Depending on the pathology of the disorder, a ureteral stent might be inserted into a patient for any period of time ranging from several weeks to several months. Unfortunately, 80% of patients implanted with ureteral stents report feeling pain and discomfort. The objective of the project was to design, manufacture, and test a drug eluting ureteral stent capable of delivering a pain alleviating drug straight into urothelium.

To achieve drug delivery at a controlled, predictable rate, drug particles were integrated into the polymeric matrix of the ureteral stent coating. Due to a localized nature of the proposed drug delivery, it was resolved that for optimal patient comfort 10% of drug's oral dose or 0.04 mg should be eluted daily. The project investigated possible techniques of incorporating drug particles into polymeric structures. Drug loading methods such as imbibing, coating, and co-extrusion were assessed. A number of biocompatible synthetic polymeric compounds such as polyurethanes and silicones were tested to optimize drug loading profiles. Once designed and manufactured kinetic drug release experiments were carried out to establish daily drug release rates for the sample stents. The stent with release properties closest to the targeted values was subjected to the flow-through studies. Flow-through experiments were designed to closely imitate conditions in the human body. The optimal stent was fabricated via co-extrusion; it had an outer wall thickness of 0.00577 inches and contained 38.89 mg of drug. Conducted kinetic drug release and flow-through experiments indicated that the stent maintained constant release rates comparable to the target value of 0.04 mg/day throughout the incubation period. In the future, animal studies involving porcine subjects will be conducted. The drug levels in urinary tract tissues and the effects of the drug on stone passage will be determined. The overall goal of the project was to eliminate pain and discomfort often associated with ureteral stenting by introducing a pain alleviating drug into the composition of a ureteral stent.
Analysis of Principal Contributing Factors to the Decreased Success of Extracorporeal Shock Wave Lithotripsy with Ureteral Kidney Stones

Monica E. Ortiz
Physical Acoustics Laboratory, Boston University

Kidney stones affect nearly 3 million people every year. These stones are painful to pass naturally and frequently cause damage to tissue of the renal system. The most successful treatment to pulverize stones is extracorporeal shock wave lithotripsy (ESWL). ESWL is a non-invasive technique which employs focused shock waves to disintegrate stones. While ESWL is successful for most kidney stones, it fails when stones dislodge from the kidney and move into the ureter. To remedy the problem in these cases, more invasive and uncomfortable procedures must be employed. The two principal hypotheses for the decreased success of ESWL with ureteral stones are decreased cavitation activity and an increase in the shock wave rise time. An agar-based tissue phantom which accurately describes the acoustic properties of ureteral tissue was used in conjunction with a ureter stone model. Phantoms to test the effect of shock wave attenuation were tested for thicknesses of 0-cm to 4-cm in 0.5-cm increments. A PVDF hydrophone was used to visualize the incident shock waves for each phantom. From these waveforms, the rise time and peak positive pressure for 20 waveforms was measured for each. Lithotripsy treatment included 400, 20-kV shock waves administered through degassed water having a conductance of 660 mS/cm ± 60. Under these conditions, eight stones were tested for each phantom. A similar procedure followed to test the effect of cavitation on fragmentation. Phantoms with well depths of 0-cm to 3.5-cm in 0.5-cm increments were tested with eight stones under the same lithotripsy conditions. The percent fragmentation by mass for increasing phantom thickness showed a significant (p = 0.05) decrease when compared to the control (phantom thickness of 0-cm). When plotted against the rise time data, a linear fit with a correlation coefficient of 0.201 was obtained. Conversely, the fragmentation for the cavitation phantoms significantly decreased initially at a well depth of 0.5-cm, increasing after this to a fragmentation of 26%. Fragmentation patterns were studied for each phantom type. Attenuation phantom samples showed a wide range of fragment size and cavitation phantom samples showed a similar pattern to a well depth of 1.5-cm, but for deeper wells showed a more uniform pattern. In conclusion, our data shows that attenuation of the shock wave increases with tissue depth, translating into decreased fragmentation for ureteral stones.
Vitaly Dobromyslin

Quantitative Studies of T-wave Memory Accumulation and Resolution in the Isolated Rabbit Heart

Cardiac Electrophysiology Research Laboratory
Beth Israel Deaconess Medical Center

The electrocardiogram (ECG) can often be misinterpreted resulting in erroneous cardiac diagnoses. One example is differentiating between oxygen starving (ischemic) cardiac tissue, as can occur with heart attacks, and a non life-threatening phenomena called the T-wave memory (TWM). TWM refers to a change in electrocardiographic direction of the T-wave (TW) following a period of abnormal electrical activation as can occur from bundle branch blocks or commonly from periods of ventricular pacing. Series of experiments were performed on the isolated, perfused hearts of New Zealand White rabbits where the goal was to test whether TWM could be induced by applying electrical potential to the surface of the heart (i.e. pacing). The evolution and resolution of TWM following pacing at the left lateral ventricle was investigated. Three channel (i.e. x-, y-, and z-channel) orthogonal ECG signals were acquired from the surface of the beating heart with several custom manufactured sets of electrodes and, later, a commercially available circular mapping catheter equipped with electrodes. The acquired data were digitized, filtered, and eventually displayed using the program Chart. Electronic calipers feature in Chart was used to sample the amplitude of the T- and QRS-complexes. These measurements were fed into custom Matlab software which displayed T-waves (TW) and QRS complexes as 3-D vectors intersecting a computer generated model of the heart surface. The program also calculated two-dimensional projections of three-dimensional repolarization (TW) and depolarization (QRS) vectors onto frontal, transverse and sagital planes. Results indicate that significant degree of memory can be induced in cardiac tissue during left ventricular (LV) pacing of 2-minute minimum duration. Neither long nor short duration (\(<\) 2min) atrial pacing induced any detectable amount of TWM. The custom software was effective in allowing user clearly see changes in TW and QRS vectors.
SESSION IIA:
Nano- and Micro-Biotechnology
MICROFLUIDIC PRODUCTION OF GAS FILLED MONODISPERSE POLYMER MICROBUBBLES TO BE USED AS ULTRASOUND CONTRAST AGENTS

Jason Nami
Cellular and Subcellular Mechanics Laboratory

Ultrasound is a safe, cheap, portable, and noninvasive imaging modality that is used clinically for diagnosis. Using sequences of ultrasonic waves that are sent into the patient, reflected waves are generated due to interaction with tissue, organ and fluid interfaces, and these waves are then detected and reconstructed into images. The limitation, however, is that tissue with similar acoustic properties are unable to generate a significant number of reflected waves to reconstruct a good image. To aid in the imaging process, microbubbles can be used to act as ultrasound contrast agents. The hollow nature of the microbubbles combined with the resonating capability of the microbubbles enables them to act as a point source of reflected sound waves that can be used to increase the contrast of reconstructed images. To generate microbubbles, a double emulsion process is used where immiscible solutions interact to generate droplets of one solution in another. A polymer solution of polylactic-glycolic acid was used to form the shell material of the double emulsions. Previous work in with ultrasound contrast agents has generated polymer microbubbles, but these particles are heterogeneous in size. The goal for this project was to thus generate a working bench top protocol to design polymer microbubbles, and then to adapt and modify this protocol and place it on a microfluidic device. This new microenvironment was then used to generate double emulsions that are monodisperse. The advantage of this is that reflected waves generated from a population of monodisperse particles all have the same resonating frequency, and thus these waves can be summed in intensity when reconstructing an image. Initial ultrasonic testing was performed on the particles generated on the bench top, and this showed that the polymer microbubbles were robust enough to maintain a signal intensity that was 80% of the original signal over a period of twenty minutes. The design of the microfluidic device used to generate polymer double emulsions was a double T-junction, where each emulsion step occurred at one of the T-junctions. A drip method was used where each emulsion droplet was formed by dripping one solution into a second faster flowing solution. The immiscibility of the two solutions prevented mixing. The final result was that using microfluidic technology, monodisperse polymer microspheres were generated at controlled regular intervals.
ANTINEOPLASTIC DRUG DELIVERY
THROUGH THE USE OF POLYMER NANOPARTICLES

Joseph Walpole

Developed at:
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Grinstaff Lab, Boston University

Non-small cell lung cancer (NSCLC) is the leading cause of death attributed to cancer in the United States, claiming approximately 167,000 lives each year. This grim prognosis for patients presenting with late-stage NSCLC has prompted many to both develop new and improved current standards of thoracic oncological care. In particular, occult micrometastatic nodal disease as a result of NSCLC presents a serious morbidity that is typically treated by combining lymph node dissection with systemic chemotherapy regiments. However, removal of all sentinel lymph nodes (those draining the primary tumor site) remains difficult and inefficient as the complex lymphatic network of the thoracic cavity is highly variable and poorly characterized. This investigation sought to provide targeted delivery of antineoplastic drugs to potential sites of secondary tumor foci (i.e. sentinel lymph nodes) through the use of a novel polymer-based drug delivery platform. Nanoparticles formed from a novel methyl-methacrylate polymer were generated and determined to be of sufficiently small diameter (<100 nm) so as to facilitate lymphatic migration. Incorporation of the antineoplastic drug Paclitaxel into the nanoparticles (1% weight/weight) was also accomplished. Innate cytotoxicity of the polymer and drug delivery efficacy were evaluated through in vitro cell proliferation assays. Results demonstrate that Paclitaxel-loaded, but not unloaded, nanoparticles effectively suppress tumor cell proliferation and establishment of small tumor burdens (akin to micrometastatic nodal disease) in an in vivo heterotopic tumor model. Ultimately, our nanoparticle polymer-based drug delivery platform has the potential to provide clinical oncologists with a safe and effective therapy for improving the care and prognosis of patients with micrometastatic disease as is common in NSCLC.
Linh Phan
Development of a Molecular Component Editor for Predicting Small Molecule Interactions

The structural characteristics were defined to create a representation of a molecule based on the atom type. This was necessary for the simulated reactions for testing interactions between proteins and proteins or small molecules. These characteristics consisted of atom bonds, bond angles, bond orders, hybridizations, and aromatic rings. The information was obtained from X-ray crystallography experiments, which has a limited resolution (approximately 2.0 Å) and can result in some missing heavy atoms due to shielding. Previous approaches to the analysis of the structural information were too specific and did not account for a molecule’s tendency to bend and rotate. Therefore, a program was written in the C language to recalculate the atom bonds, bond angles, bond orders and hybridizations and find aromatic rings based on the atom types and spatial locations. These calculations were specific to molecules that contain only carbon, hydrogen, nitrogen, oxygen, and sulfur atoms. The atom bonds were determined by calculating the distance between all atoms and then filtering them so that only atoms within two angstroms of each other were recorded. By comparing the calculated bond length to a list of typical bond lengths based on atom type, the bond order was identified. The distances were used to calculate the unit vector in relation to the current atom. Then the angles between bonds were calculated. Based on the characteristic angles specific to each atom type and the calculated angles between bonds, the hybridizations of the atoms were identified. Planes, defined using three points, were used to find aromatic rings of sp² hybridized atoms. The aromatic rings contained atoms on the same plane within a set distance. The characteristic angles and bond lengths verified the aromatic rings. Finally, the number of expected atom bonds was compared to the number of calculated atom bonds using the sum of the bond orders to locate the missing atoms. After determining the structural characteristics of the molecule, the molecule could be used to predict protein and small molecule interactions. The program reduced the amount of time spent on calculations and was sufficient for most compounds.
Developing a Purely Electronic Recognition Method for DNA-Transcription Factors Interactions Using Nanopores

Project Member: Andrew Chow
Single Molecule Biophysics & Nano-biotechnology Lab at Boston University

Scientists have been focusing on developing a broad view of gene activation via transcription factors and on the complex interactions of single and multiple transcription factors (TF) on DNA. Current experimental tools permit only the genome-wide probing of a single TF (at a time) and with fairly poor resolution (~500 bps). In addition, these technologies are both labor intensive and expensive to perform. We propose to use nanotechnology, specifically nanopores, to establish a novel and cheap data collection and observation technique for DNA and protein-DNA interactions, and in particular TFs. The focus of the method will be to recognize DNA and TF-DNA using the nanopore. Then we will characterize the kinetics of each molecule by determining binding and affinity rates between the protein and its respective double stranded DNA (dsDNA) binding sequence with respect to current blockage levels and translocation times. The TF known as Sp1, and its human genome binding sequence, will be used in the proof of concept. Data analysis on the nanopore experiment will verify the presence of DNA and TF-DNA complexes and provide numerical information on binding and affinity rates of the TF to the human genome. In addition, time logs from the data acquisition will provide insight on the time frame required to perform the nanopore experiment. Although, the nanopore process is not meant to eliminate current methods, it will provide an electronic method of analysis which will be able to verify and present numerical data. In addition, the nanopore method has the ability examine TF-TF-DNA interactions, including binding and affinity rates. If successful, the use of nanopores, as a new technique, will eliminate costly amplification processes, and have the capability to examine multiple bindings of protein.
Delivery of Genetic Material to the Cellular Surface via a Novel Nanofibrous Material

Rakesh Patel

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Beth Israel Deaconess Medical Center & Harvard Medical School

Unregulated cellular growth within the body can have catastrophic consequences as evidenced in cardiovascular diseases such as atherosclerosis and restenosis post vascular angioplasty. Proliferation of neointimal smooth muscle cells is central to lesions of atherosclerosis, a disease characterized by the narrowing of the vascular lumen and hardening of the arteries, and restenosis post balloon angioplasty as depicted by an obliterative vasculopathy of the artery following its initial repermeabilization. Vascular restenosis is particularly problematic upon implantation of medical devices such as stents and vascular grafts. Previous studies by Ferran et al have unraveled potent anti-inflammatory and antiproliferative functions of the 7-Zinc finger protein A20 in neointimal smooth muscle cells (SMC), making it an ideal gene therapy candidate that could be locally applied at the site of injury to prevent and or cure lesions of neointimal hyperplasia. Our aim was to investigate the possibility of incorporating adenoviral particles to biodegradable nanomaterials that could be applied at the site of vascular injury to achieve expression of “protective” transgenes. Our data demonstrates that we could successfully incorporate the control β-galactosidase adenovirus into our designed nanomaterial. Further, the rAd. βgal incorporated in the nanomaterial remained fully functional and was able to transduce cells in vitro, in a manner similar to what is achieved when using the usual infection medium. This data represents a strong proof of principle for the future application of this technology to either coat stents or other implantable devices which will allow the local delivery of “protective” molecules to the vessel wall.
Low-Cost High Efficiency Microarray

Tiancheng Wang

In the biomedical field, a gene microarray, an instrument capable of accurate and efficient measurement of mRNA expression levels in cells, has shown an enormous potential in the scientific industries because it can analyze thousands of genes at once. Until recently, microarray has depended on glass as substrate. Historically, glass is the most widely used substrate for DNA microarray. Glass substrate’s high UV light transmittance rate is critical for the UV light deprotection process of DNA synthesis; however, glass’s high affinity for DNA creates high background noise. The purpose of this study was to investigate the possibility of improving DNA microarray’s signal to noise ratio using Zeonor 750R substrate, a plastic material which was manufactured to the dimension of 1” by 3” and thickness of 1.00±0.01mm. The surface of the Zeonor slide was then oxidized by plasma treatment and spin coated with 40% polyethylene glycol (PEG) solution, which resulted in a reactive surface for oligonucleotide coupling. DNA was consequently synthesized on Zeonor and glass substrates using microarray fabricator. The effectiveness of the Zeonor substrate was analyzed using hybridization. Fluorescent labeled target molecules were hybridized with cognate probe sequences on the microarray, causing each spot to glow with an intensity proportional to the level of hybridization. Based on the fluorescent intensity, the signal to noise ratio of Zeenor was obtained and compared to glass substrate using an Axon scanner. The consequential data were evaluated using Matlab. The results were inconclusive to validate the hypothesis that Zeonor will improve microarray’s signal to noise ratio based on the fact that plastic has lower affinity for DNA. Using the methodology developed in this study, we can gain a better understanding of the functional properties of Zeonor substrate with the ultimate goal of creating a low cost high efficiency microarray substrate.
Microchip Based Macromolecule Analysis

J. Neal Schrade

In the analysis of macromolecules, such as DNA segments, the process of electrophoresis requires the labeling of the sample analytes for measurement and analysis. This step requires additional time and resources to allow for macromolecule detection. The purpose of this project is to develop a semiconductor-based detector that will be able to indicate the presence of macromolecules in solution. Development of this process uses the innate electrical charge of macromolecules, identical to that used by electrophoresis, in order to separate the sample constituents. This electrical charge can be used to generate a signal in the gate of a transistor. Using internal amplification on the semiconductor device, the amplified signal can then provide a proportional response to the proximity of the charge to detect macromolecules. Development of this type of detection eliminates the need of sample labelling by providing direct indication. Sample analysis could then be performed by measuring the relative velocity of the macromolecules from multiple detectors. This signal output will allow for automation of the measurement process by providing an output usable by computer interface. The development of this macromolecule detection system will simplify the process of electrophoresis, allowing for a reduction in time and cost by eliminating the need to label as well as automating the measurement process.
Characterizing and Mutating the *mer* Promoter to Build a Bacterial Mercury Sensor

Disha Shah

Boston University
Advanced Biodynamics Laboratory

Approximately 100 tons of mercury waste is produced in the United States annually. Consequently, a prominent area of current research focuses on cheap and efficient detection and sequestration techniques of mercury from the air, soil, and liquid bodies. While there are several detection methods currently in place, the sample preparation for these methods is laborious, and expensive. Therefore, a promising alternative is to exploit the naturally occurring mercury detection mechanisms available in bacteria to engineer a bacterial sensor that can detect, and sequester mercury from its environment. The objective of this study was to first characterize the natural *mer* promoter from *Pseudomonas Aeruginosa* and then to test the impact of mutations in the promoter sequence on the strength of the promoter. The natural promoter was characterized by cloning it to a plasmid with a reporter gene (GFP) and testing GFP fluorescence via flow cytometry. It was found that the natural *mer* promoter is leaky and fluoresces without mercury inducement. The mutant promoter was constructed by randomizing the spacer sequence and found to have higher GFP fluorescence levels than the natural promoter, indicating a stronger promoter. Additionally, when the natural promoter was tested in the presence of a chelator-EDTA, GFP fluorescence decreased. This is indicative of the fact that the natural promoter may be being activated by a different ion in the cell culture.
SESSION IIB:

Neuroscience,

Neuroengineering,

and

Auditory Science
NeuroMuscular Adaptations During Bed Rest
Robert Li
NeuroMuscular Research Center

The objective of this study was to investigate the neuromuscular adaptations that influence muscle force production following bed-rest. The project studied the data of healthy adult men of ages 30-55 who underwent 28 days of strict bed-rest followed by 14 days of standardized weight-bearing physical activity. The bed-rest subjects in this study were assigned to 2 groups: a) a Non-Exercise group without resistive exercise; and b) an Exercise group, receiving resistive exercises 6 days a week. Electromyographic signals were collected from the First Dorsal Interosseous (FDI) and Vastus Medialis (VM) muscles during isometric contractions at 50% of the subject’s maximum voluntary contraction (MVC) force. Analysis of the data collected from these subjects led to novel discoveries regarding the effects of bed-rest on motor unit firing behavior: 1) among subjects of the Non-Exercise group, there was significant decrease in the amount of common fluctuations among mean firing rates of motor units post-bed-rest compared to pre-bed-rest; 2) the progressive decrease observed in the firing rates of concurrently active motor units during constant-force contractions was not as rapid following bed-rest in the FDI muscles of both the Non-Exercise and Exercise groups; 3) there was a decrease in the average firing rates of motor units following bed-rest in both muscles of all subjects; and 4) there was a significant decrease in the MVC force in the FDI and VM muscles for subjects in the Non-Exercise group, but not for subjects in the exercise group. These results indicate that bed-rest induces significant changes to the control properties of motor units, and that resistive exercise can serve as a countermeasure for these adaptations.
Noise-Enhanced Gait Stability

Andrew Galica

Somatosensory function decreases with age, resulting in diminished motor performance and gait stability. Subsensory mechanical vibrations applied to the soles of the feet have enhanced sensorimotor function in stationary studies. The goal of this study was to determine whether input noise to the soles of the feet can reduce gait variability, an indication of falling likelihood, in a population of elderly recurring fallers. Data from healthy young subjects was added for comparison purposes. For each six minute trial, subjects walked in a pair of vibrating sandals at a comfortable pace around an elliptical track during which noise stimulation was applied for half of the trial. Gait cycle data was captured using force sensing resistors that are wired to a foot-switch circuit and placed under the heel and ball of the foot on the sandal. Data analysis was performed by determining heel strike and toe lift off events. Normalizing the stride, stance, and swing time intervals for each half of each trial, the standard deviations were calculated. In 6 elderly recurring fallers and 12 young subjects, the application of noise reduced the variability associated with all gait intervals. Two-way repeated measures ANOVAs were applied to determine the main effects of stimulation (control vs. noise) and population (elderly fallers vs. young) on gait variability as well as to investigate whether an interaction exists between stimulation and age. The main effects of stimulation described a significant difference for stride (p<0.005), stance (p<0.040), and swing (p<0.020) intervals. The interaction between stimulation and elderly fallers displayed significance in the stride (p<0.022) and swing (p<0.035) intervals. As a result, vibrating insoles could potentially decrease fall risk in elderly recurring fallers by reducing the variability associated with their gait.
The Effect of Context on the Perception of a Virtual Auditory Object

Michael DeFuria

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The development of a virtual reality environment that contains 3-D visual, motion, and tactile experiences has increased dramatically in recent years. A realistic, 3-D virtual sound has been a goal of recent auditory research. The virtual sounds must contain the same spatial cues found in a natural sound. The goal of this project was to determine the effect of specific parameters on a subject’s ability to determine the distance of a virtual auditory object. Psychoacoustic experiments were created to quantify the effects of visual cues and paired distance sound presentation on a subject’s ability to judge the distance of a virtual sound source. The virtual sound sources were created using measured head related transfer functions as filters to play a noise, creating a virtual sound that contained the spatial information of the real stimulus. Psychoacoustic control experiments were used to assess a listener’s ability to accurately estimate the distance of a virtual sound source. Although the paired distance experiments showed a substantial amount of individual variability, the results did not systematically affect virtual sound source distance perception. The visual environment influence experiment had similar results. However, the addition of visual cues to the environment at the physical sound source locations increased the listener’s ability to identify the correct origin of the sound. This result was found consistently across all subjects.
The Influence of Signal Degradation on Divided Listening

Desiree Balderrama
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This project investigated the ability of listeners to divide attention between two simultaneous talkers, S1 and S2. In the divided attention task subjects reported keywords from S1 and S2 in a particular order, which is indicated by a keyword. Previous studies have shown that changing the listening conditions for divided listening affects S1 and S2 differently. Two experiments examined the effect of signal distortion on two dichotically presented simultaneous talkers. In a control selective attention task, subjects were required report S1 and ignore S2. In the divided attention task, the subjects reported S1 followed by S2. In Experiment 1, a noise masker of varying levels was played along with S1 and S2. Performance for selective attention was significantly higher than performance in the divided case. Also, S1 performance was uniformly higher than S2 for all noise levels. In Experiment 2, signals with varying amounts of the original speech frequency information (vocoded speech) were used as S1 and S2. Similar to Experiment 1, selective attention produced significantly higher performance than divided attention. Also, S1 performance was higher than S2 performance, but not by as much as in Experiment 1. The cost difference between S1 and S2 was higher for the noise experiment than the vocoded speech experiment. In both experiments, the kind of errors made in the divided listening task support the idea that the ability to report the second message, S2, is affected by acoustical degradation due either to additive noise or reduced spectral representation (vocoded speech).
An Algorithm To Identify Bird Species From Their Vocalizations

Tristan Carrier

Identifying bird species for novice bird watchers can be a difficult task because they must rely on books and audio playback devices. Song birds produce unique audio signals where each bird's song contains unique amplitude and frequency information within a song. The differences between these songs can provide enough information to identify a species based solely on their vocalizations. An algorithm that identifies these differing characteristics of a bird song and uses the information to identify a bird's species has been developed. Song samples of common birds found in the United States acquired from the Cornell Lab of Ornithology are used to produce a library of bird songs. Bird songs acquired from a CD produced by the Peterson's Field Guide system are compared against the library using normalized cross correlations. The algorithm separates each song from the Peterson's Field Guide into smaller components where each component can be compared to the smaller components of the songs in the algorithm's library. The normalized cross correlation coefficients are calculated and used to visually and computationally distinguish between different songs. Using the maximum correlation coefficient values, the algorithm is able to correctly match the input song to the correct species in the algorithm in 5 of 6 species.
The Effects of Spatial Location on Temporal and Spectral Grouping of Sound Complexes

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The perceptual organization of a sound mixture containing two simultaneous sources depends on which source is focused on by the listener. Implementing new experimental methods confirms the role of spatial cues in how a listener segregates sound sources when their attention is directed at one particular source. Two sources, each consisting of a sequence of tone complexes, along with a complex (the “target”) that could logically belong to either source, were presented to subjects. Spatial properties of each source were varied. Subjects indicated the perceived strength of the two sources in different experimental blocks by adjusting the intensity of the target in a single-source “match” stimulus. Perceived intensity values were recorded in dB directly from the subject’s “matching” response. Having a quantification of how much target energy is perceived in each source makes this an extremely useful and unique experiment in the field of psychoacoustics. In conclusion, the quantified “matching” assay was validated, and unlike in previous related work, the target was perceived to “trade” between the two sources.
Optimization of Synaptosomal Dopamine Release Experimentation by Suprafusion Machine
Streamlining and Cell Viability Assessment

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Parkinson’s disease affects more than 6 million people worldwide. The disease is quite debilitating due to the large number of motor and non-motor symptoms. These symptoms are a result of the degeneration of dopaminergic neurons of the striatum region of the brain. Treatments to increase the activity of existing striatal dopamine neurons may provide possible therapies for symptoms of this disease. One way of studying dopaminergic activity in the striatum is through observation of dopamine release from isolated nerve terminals (synaptosomes). Synaptosomes, which are prepared from rat brains, can then be experimented on to improve dopamine release. These experiments are only accurate as long as the synaptosomes are functioning as close to in vivo as possible; therefore, it is important to be able to assess the metabolic activity of the synaptosomal preparation over time. The goal of this project is to create a way to automate an instrument and assess the cellular preparations of this experiment. Synaptosomal viability can be measured spectrophotometrically through the formation of formazan from MTT (3-(4,5-Dimethylthiazol-2-y1)-2,5-diphenyltetrazolium bromide), a reaction catalyzed by the activity of succinate dehydrogenase. This activity, which is present in the citric acid cycle of cellular respiration, is an indicator of the metabolic activity of the synaptosomes and portrays a more accurate idea of synaptosomal quality. Currently, we are characterizing the optimal parameters for the execution of this assay. To study synaptosomal dopamine release, synaptosomes are placed in a 6-chambered Brandel Suprafusion apparatus and perfused with artificial cerebrospinal fluid. Drugs can be introduced into the perfusion medium and resulting dopamine release is assessed. The current protocol requires human intervention to manually maneuver the reagent probes and to reverse the flow of the peristaltic pump during switching from bulk buffer to drug solutions. This leads to problems such as unstable baseline neurotransmitter release, reducing the amount of quality data in each experiment. These problems can be addressed by the implementation of electrically controlled micro fluidic valves from The Lee Company to allow the switching of the reagents perfused over the neurons to be less invasive.
Investigating the Relationship between the Behavioral and Neural Response of Songbirds to Complex Stimuli

Julie Jie Ling Young
Natural Sounds and Neural Coding Laboratory

Abstract

Learning the underlying neural mechanisms of the human auditory system is vital to the development and enhancement of auditory prosthetics. Zebra finches present an ideal model for the study of auditory physiology. Like humans, zebra finches learn vocal communication during their youth by mimicking the vocalizations of their parents. Furthermore, humans and songbirds have developed complex circuitry that maintains perception, production, and auditory learning. However, the relationship between behavioral and neural responses of the primary auditory area of the zebra finch to complex natural sounds is poorly understood. The overall objective of this project was to develop a behavioral learning paradigm and to assess the relationship between the male zebra finch’s behavioral ability to recognize complex acoustic stimuli and the neural responses to the same stimulation. The behavioral learning paradigm consisted of four training phases that began with the bird performing at a 50% correct song discrimination and concluded with the bird performing at 88% correct for song discrimination. In recordings from awake songbirds we found auditory neurons in field L that contain sufficient information for perfect classification.
SESSION IIIA:

Biomechanics and Biomaterials
Engineering an In Vitro Model of Microvascular Inflammation

Matt Prosen
The Tien Group

An in vitro model of inflammation can be used to provide a convenient, inexpensive, and non-invasive method for testing pharmaceuticals in their early developmental stages. Though a structurally stable in vitro microvessel model has been created by Chrobak et al., it is unable to localize inflammatory agents in the region surrounding the microvessel. The purpose of this project was to improve upon this model by creating and characterizing a mechanism for the spatial localization of inflammatory agents in the abluminal space surrounding the microvessel. This was accomplished by first modifying the previous microvascular model to accommodate a localization channel that bisected the main channel. The localization of inflammatory agents was then characterized by tracking the diffusion and convection of various volumes of the fluorescent marker fluorescein through the localization channel using fluorescence microscopy. The intensity of fluorescent light at various points along the microvessel and the intensity contrast ratio between points were then calculated from the resulting images. This data was used to determine which volume condition of fluorescein created the highest spatial localization around the microvessel. Diffusion alone was shown to produce only $8.18\% \pm 2.37\%$ of the light intensity of the 100 µl convection trial after 65 minutes, and did not produce a peak contrast ratio over the time period tested. 88% of the convective trials produced a maximum increase in contrast ratio and minimum full-width-half-maximum values 5 to 15 minutes after the addition of fluorescein. In conclusion, diffusion alone did not produce spatial localization of fluorescent markers in the model. Therefore, a convective component is needed to increase the concentration contrast of an inflammatory agent in the model. Furthermore, the optimal time interval to perform a permeability assay in future in vitro microvascular studies was determined to be 5 to 15 minutes after the addition of an inflammatory agent. The determination of which volume condition best spatially localized an inflammatory agent was inconclusive.
Design of a Mechanical Testing System to Simulate Hip Fractures

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Osteoporosis is a skeletal disorder characterized by decreased bone strength resulting in a greater risk of fracture. The reduction of bone strength is caused by age-related decline in bone mass and deterioration of microarchitecture. Fractures at the hip are a major health concern due to the financial burden, increased mortality, and disability associated with them. Although bone mineral density is the most important indicator of bone strength, measures of bone density have not clearly or consistently distinguished between elderly hip fracture subjects and non-fractured controls. More than 90% of hip fractures are caused by a fall, suggesting that falling, rather than osteoporosis may be the dominant risk factor for hip fracture. The objective of this study is to design a mechanical testing system to simulate a fall to the side with impact to the greater trochanter to evaluate failure load, stiffness, and energy absorbed to failure. This mechanical testing system will be used in future studies to evaluate various non-invasive imaging assessments of hip fractures.
The Use of Finite Element Analysis to Assess the Effects of Osteoporosis Drug Treatment on Bone Strength

Neil Patel
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Beth Israel Deaconess Medical Center and Harvard Medical School

Osteoporosis is a degenerative bone disease that is characterized by an increase in bone resorption rate leading to decreased bone mass. Although treatment methods exist, their effects on bone mechanics are not well understood. Understanding these effects can help gain insight into the optimal use of drugs treatments. The overall goal of this study was to develop a method for evaluating effects of osteoporosis therapies on bone strength in small animal models using μCT-based finite element analysis. To accomplish this objective we first tested the technique using aluminum foams and then applied it to a study in which ovariectomized rats were treated with an osteoporosis therapy. Twelve isotropic FE models of aluminum foam samples of different volume were scanned using a μCT scanner. μCT data of each sample was converted to finite element models using a voxel-to-element conversion technique. Finite element analysis was used to apply uniaxial compression in the cranio-caudal direction on each model to simulate experimental mechanical testing. Stiffness values obtained from the FEA method were compared to mechanical testing data of the aluminum samples. A strong correlation for stiffness was found (R² = .72). Upon verification of the procedure, a similar protocol was applied to vertebral body samples from four test groups: (1) SHAM, (2) osteoporotic with no zoledronate treatment, (3) osteoporotic with early zoledronate treatment, (4) osteoporotic with late zoledronate treatment. Vertebral body stiffness values were weakly correlated to stiffness values obtained using mechanical testing (R² = .38). Based on this finding, there is a necessity for refinement in the protocol for it to be applicable to biological specimens with varying structure and material properties.
3-D Visualization of Spine Fracture
Andrew Baker
Orthopaedic and Developmental Biomechanics Laboratory

Spine fractures, often the result of the bone disorder osteoporosis, present a significant health and financial burden. Frequently occurring in the absence of trauma, spine fractures progress gradually often without symptom. Current methods of fracture risk assessment correlate bone density to strength, but do not consider the trabecular structure of the vertebra providing little insight to the failure process. The identification of failure patterns is necessary to gain better understanding of the genesis and propagation of fracture throughout the vertebra. This project combined axial compression testing and high resolution \( \mu \)CT scanning to enable 3-D visualization of the failure process during incremental loading of a sample of human vertebra. Displacement vectors were determined via digital image analysis. Using these displacement values, 3-D strain distributions were calculated for multiple loading conditions. Maximum local strains within a whole bone volume ranged from -0.50 to 4.4 when loaded to 17.0\% global strain. Strains were also shown to increase traveling medially into the vertebral body. Further work is needed to analyze a larger number of vertebral samples to draw more generalized conclusions of the failure process. Additionally, more complex loading conditions during testing are needed to more accurately recreate \textit{in vivo} fracture progression.
Non-invasive assessment of femoral geometry

Christina Piron

Although low bone mineral density (BMD) is among the strongest risk factors for fracture, a number of clinical studies have demonstrated the limitations of BMD in assessing fracture risk. These observations have highlighted the need for new methods that assess other factors related to total bone strength including bone size, shape and microarchitecture. This study will evaluate the ability of certain non-invasive imaging modalities (both 2D and 3D) to measure the geometrical properties of the human proximal femur. To achieve this goal, 30 formalin-preserved proximal cadaver femurs free of metastases from men and women aged >65 were obtained. Ten geometrical parameters of the neck and shaft regions, including cortical thickness, of the femur were analyzed by radiogrammetry and dual-energy X-ray absorptiometry based hip structural analysis (HSA) both of which are capable of 2D imaging. Averages and standard deviations were calculated for each parameter for each method. The relationship between the results of radiogrammetry and HSA were assessed with bivariate regression and correlation tests. Micro-computed tomography (μCT), which is capable of 3D imaging, of the neck and shaft regions was used to analyze neck and shaft cortical thickness. The average and standard deviations of these results were calculated. The cortical thickness results from μCT were compared to the corresponding results of radiogrammetry and HSA with a paired t-test and correlation analyses. All shaft measurements made by HSA had moderately high correlation (r > 0.7) to the corresponding radiograph measurements. All directly measured neck parameters, except for neck cortical thickness (r = 0.136), also had moderately high correlation (r > 0.6) between the two imaging methods. Shaft cortical thickness results analyzed by both radiogrammetry and HSA differed significantly (p < 0.0001) from the corresponding μCT cortical results. Of the 2D imaging modalities, only HSA had a high correlation to the 3D imaging method of μCT (r = 0.843). In conclusion, the high correlation may allow for the manipulation of HSA measurements to allow for the accurate measurement of femoral geometry. This result is ideal because HSA provides a non-invasive method of analyzing bone geometry which could be used clinically without exposing patients to unnecessary radiation.
In compliant walled tubes the flow of fluid in the tube cannot exceed the propagation velocity. This concept is known as flow limitation. During a forced vital capacity expiration maneuver in a human lung it has been observed that flow limitation occurs. During a partial forced expiration (initiated at a volume less than total lung capacity) the expiratory flow can briefly exceed the flow limited velocity. The reason for these hyper-critical flows is unknown but is thought to be related to the frequency. It has been speculated that the higher frequency content during the initial part of the forced expiration maneuver will cause hyper-critical flows. The main objective of this project is to design and fabricate a device that can measure the pressure, flow and frequency dependent behavior of compliant tubes, including instrumentation and software development. The device is designed to measure pressure and flow at the inlet and outlet of a compliant tube and to measure the flow resulting from tube oscillations. A prototype device was built and pressure and flow transducers were selected. Software was written to acquire 4 channels of analog data (2 pressure channels and 2 flow channels) as well as to analyze and graph the data. Two experiments, measuring resistance and wave propagation, were designed to test the effectiveness and quality of the device and data acquisition software.
Determining the isolated and combined effects of airway size, thickness, and stimulation on healthy and asthmatic single airway and whole lung function.

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Respiratory and Physiological Systems Identification Laboratory

Asthma is a respiratory disease characterized by airway hyper-reactivity (AHR) and airway hypersensitivity (AHS) to airway smooth muscle (ASM) stimulation. The structural features of airways responsible for asthma are largely unknown. It is especially difficult to understand the role of airway structural features in asthma because they cannot be manipulated in vivo. The overall objective of this project was to use advanced modeling methods to explore how specific structural airway parameters control single airway and whole lung function in asthma. First, we designed a computational algorithm that simulates airway constriction as function of baseline airway diameter, ASM stimulant dose and wall thickening. Then we applied the algorithm to simulate single airway constriction in asthma. Finally, we applied the algorithm to an entire airway tree to simulate whole lung degradation in asthma. The most significant feature of the algorithm is its incorporation of an airway bi-stability, a theoretical phenomenon in which an airway can constrict from an open state to a near-closed state with a minimal increase in ASM tension. At the single airway level, the current study was designed to allow dose of a bronchoconstrictive agent to be the input and airway constriction to be the output. The algorithm allows for manipulation of several important airway parameters: wall layer thickening, baseline airway diameter, and applied ASM stimulant dose. Using the algorithm, constriction of airways was simulated for various values of these parameters to determine their effects on single airway reactivity and sensitivity. We compared reactivity and sensitivity for cases of homogeneous wall thickening and cases of isolated thickening of individual airway wall layers. By coupling the constriction model to an impedance algorithm, we then determined how the key airway parameters and location govern whole lung resistance and elastance. We simulated airway constriction for lung models with homogeneous wall thickening, with wall thickening localized to a specific region, and with the stimulant dose applied heterogeneously. We found that increased maximum ASM tension associated with ASM thickening in peripheral airways (and not central airways) is primarily responsible for AHR and AHS at small stimulant doses. At larger stimulant doses, central airway wall thickening also contributes to AHR and AHS in asthma. We also found that increasing the amount of heterogeneity of airway constriction in an asthmatic lung increases lung resistance and the frequency dependence of lung resistance. In summary, we have developed a computational model in which the constriction response to an input stimulant dose can be explicitly determined at the single airway and whole lung levels. The model allows us to explore how specific single airway and airway tree structural features modulate the role of AHR and AHS in asthma. This study, therefore, represents a significant advancement in 3-D structural modeling of the lung.
An In-Situ Study of Deep Inspirations During Bronchoprovocation in Excised Lung Lobes

Daniel Miranda
Respiratory and Physiology Systems Identification Lab

Asthma is a pulmonary disorder that is characterized by airway hyper-reactivity, which results in airway constriction that affects the body’s ability to sustain acceptable levels of ventilation. It has been shown that deep inspirations work well to dilate airways in healthy lungs but not in asthmatic lungs. Also, lack of dynamic stretching of isolated airway smooth muscle or of airways in-vivo could lead to stronger airway smooth muscle capable of amplifying constriction. Generally, the airways within the lung are tethered to the parenchyma, which produce a distending force on the airway. The distending forces that are produced from the parenchyma are not well understood, yet may be a factor in asthma. This project involved the design and application of an experimental system to track airway caliber during static and dynamic conditions with deep inspirations. Using a method proposed by Jensen et al., 8 Hz pressure oscillations at the airway opening allowed tracking of airway resistance as a surrogate of diameter [10]. The experimental system consisted of a scaled Plexiglas box, piston pump, and LabView control and acquisition software that allowed different breathing conditions to be applied to a lung lobe. With that system, two protocols were designed. Protocol 1 looked at static airway pressure relations before and after airway smooth muscle provocation without dynamic breathing. Protocol 2 examined the same effects with continuous dynamic oscillations. The goal of protocol 2 was to see if dynamic breathing mitigated the impact of methacholine. The results show that under in-situ conditions, airways are expanding and being recruited isotropically with the lung. It was observed that the bronchodilatory effect of deep inspirations result from overall airway recruitment opposed to overall airway dilation, meaning that isotropic expansion between airways and lung parenchyma is a possible consequence of airway recruitment overshadowing airway dilation. Furthermore, the presence of dynamic oscillations was shown to have no statistical effect on a deep inspirations ability to recruit and dilate airways both before and after airway smooth muscle stimulation. However, data suggests that dynamic oscillations have a greater effect on protecting against the degree of airway de-recruitment following deep inspirations. Overall, the observed degree of airway and alveolar de-recruitment in response to methacholine provide strong evidence that the decreased lung function seen in asthmatic subjects is not a primary consequence of airway and parenchymal decoupling.
Exploring a Link Between A20 Expression and Vascular Wall Biomechanics

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Biomimetic Materials Engineering Laboratory

Vascular disease is an extremely prevalent disease with a complex pathophysiology. As vascular disease develops, increasing inflammation at the vascular wall results in the migration and proliferation of vascular smooth muscle cells (SMC) from the medial layer of the vessel to form an intimal layer. This migration and proliferation of SMCs forms atherosclerotic lesions, or intimal hyperplasias that obstruct the lumen and alter blood flow. In this project, we examined the relationship between vascular biomechanics and the expression of the atheroprotective protein A20. A20 is a potent and broad inhibitor of the transcription factor NF-κB, which plays a key role in a major inflammatory pathway activated during arterial occlusion. We used an acute injury model of vascular disease, which develops primarily because of damage inflicted on the endothelium. Rat carotid arteries that underwent balloon angioplasty were used as the experimental group of vessels. Atomic force microscopy was used to quantify the stiffness of the control and experimental groups of vessels. The mean stiffness was found to be significantly greater in the experimental group compared to the control group. Hydrogel substrates with stiffnesses representative of those found with the AFM were subsequently used to model the mechanics of the healthy and injured vessels. Bovine SMCs were cultured on 31 kPa and 84 kPa hydrogels and stimulated with cytokines to induce an inflammatory response from the cells. We found that IkBα expression was significantly higher on the 84 kPa hydrogel. These results indicate that SMCs cultured on stiffer substrates undergo a stronger and more sustained inflammatory response via activation of the transcription factor NF-κB. The observed over expression of IkBα on stiffer substrates may imply that the expression of A20 was hindered, hence impeding atheroprotective responses of the cell. Our results provide evidence for the first time that a relationship may exist between vascular biomechanics and A20 expression.
Vascular Smooth Muscle Cell Response to Multi-Frequency Cyclic Strain

Carolyn Yee
Cellular and Subcellular Mechanics Laboratory

Coronary Artery Bypass Grafting (CABG) is the most common surgical procedure performed in the US. The problem with CABG is that an autologous vessel is not always available, leading to the use of synthetic grafts, such as Dacron and Teflon. However, both Dacron and Teflon fail when used as small caliber vascular grafts (arteries less than 6mm in diameter). It is known that the orientation of cells change in response to an applied cyclic strain and this correlates to a vessel’s strength. The ability to control cell orientation would be useful for vascular tissue engineering. Therefore, the goal of this project is to access the effects of multi-frequency cyclic strain on vascular smooth muscle cells (VSMC). VSMC are being studied because they are the most abundant cells found in arteries. The aim is to see if cells align in a particular for various frequencies and whether there is a response to threshold frequency.

VSMC were seeded onto polydimethylsiloxane (PDMS) substrates. A cyclic strain apparatus was utilized to subject the PDMS substrata to a 10% cyclic strain at either a static stretch of 0Hz (defined as one cycle every 20 min) or 1Hz for a period of 24 hours. Control samples were not subjected to strain. After 24 hours the cells were imaged and assessed for orientation. A cell was considered aligned if oriented parallel (0°) or perpendicular (90°) relative to the applied strain. Threshold was considered reached if 50% or more of the cells move to either orientation.
SESSION IIIb: Imaging and Modeling
Feature Extraction of Neuronal Population Activity Measured with Two-Photon Microscopy

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There are few techniques that can capture neural activity with high temporal and spatial resolution. In addition to relaying multidimensional data, the recording technique must also display neural activity from a network of cells. A newly established technique analyzes the transient characteristics of epilepsy by simultaneously measuring the calcium dynamics of multiple neurons from a brain slice. The goal of the project was to create software to derive dynamical networks from the calcium imaging recordings. Synchrony among neurons in the network were determined by comparing the calcium signals of all possible pairs of cells in the network using the cross correlation function. The software developed displays neural network diagrams where dots in the network represent the spatial locations of the neurons and lines connecting them show the degree of synchrony between them. The analysis recorded more correlated pairs in the network during seizure like events than in the non-seizure data. The correlation structure calculated the correlations between neural activities for durations of 2 seconds to show patterns evolving throughout time. A model was used to quantify the activity of the neurons in the measured network based on the connection strengths between the cells. The model was used to assess if the strength of neural synchrony alone can portray seizure like behavior. The time dependent neural networks provided insight into seizure network dynamics.
Exploring the Neural Effects of Transcranial Direct Current Stimulation via Diffusion Tensor Imaging and Other Blood Flow Imaging Techniques

Arup Chakrabarti

Neuroimaging Laboratory at Beth Israel Deaconess Medical Center and Harvard Medical School

Transcranial Direct Current Stimulation (tDCS), a portable, safe, non-invasive, brain stimulation technique, is capable of modulating cortical excitability by applying small magnitude direct current to the brain. Despite the recent upsurge in the use of tDCS, there has been very little research done to examine the neural effects of the stimulation. TDCS is increasingly being used in clinical applications to help those with neurological and psychiatric disorders as well as in research applications to see how tDCS can influence behavior and what the associated neural underlyings of these behavioral effects are. The main challenge in investigating the neural effects from tDCS is to find a physiological brain imaging technique that is sensitive enough to detect brain tissue effects of direct current stimulation. Traditional MR imaging techniques have not been able to detect changes in response to tDCS. With the advent of Diffusion Tensor Imaging (DTI), an MRI technique, the possibility of examining subtle changes in the brain became possible. DTI works by examining water diffusion in the brain, which is directly linked to cortical activity, and calculating tensors that show the strength and direction of diffusion. The overall goal of this project was to examine and quantify the brain tissue effects of tDCS using DTI and to determine and model current attenuators of tDCS. Subjects underwent 20 minute sessions of tDCS, while DTI scans were taken before and after stimulation. The DTI data was used to examine changes in Fractional Anisotropy, the directionality of diffusion (FA), and Mean Diffusivity (MD) in the brain. Subtracting the scans obtained before from after the tDCS stimulation results in brain regions showing a change in fractional anisotropy (FA). These brain regions were also used in conjunction with Fiber Tracking (FT). FT uses the tensor values to calculate and visually show the change in both the strength and direction of diffusion as a result of tDCS. The results show that tDCS does have an impact on water diffusion in the brain, and that DTI was a valid method to investigate the brain tissue effects of tDCS. TDCS was able to increase the strength of diffusion along white matters tracts. Our studies have provided preliminary data, methods, and a framework to investigate tDCS-induced brain tissue effects.
Tuberous Sclerosis (TS) complex is a rare, hereditary disease that forms abnormal tuber-like growths called hamartomaceous lesions, which can be distributed at multiple sites throughout the body. This autosomal-dominant disorder in humans is caused by mutations on either of two genes—Tsc1 or Tsc2—that regulate cellular growth. The occurrence of TS is 1 in 6,000, and an estimated 1 to 2 million people are affected globally with no effective medical therapy at hand. Despite surgical treatment, chemo, radiation, hormonal, and targeted therapy techniques, TS patients still have a poor prognosis and high rate of development of kidney cysts and liver hemangiomas. Failure of traditional therapies have led to the assessment of treatment efficacy, utilizing mice models of tumorigenic cancer to precisely determine changes in TS tumor volume over the period of the disease course. The goal of this project was to quantitatively analyze the development of kidney cysts and liver hemangiomas in Tuberous Sclerosis mice over a time course measurement through non-invasive Magnetic Resonance Imaging. More specifically, the project will gear towards (1) developing a baseline growth trend for TS using MRI and (2) testing the combination therapy of IFN-γ (Interferon Gamma) and Rapamycin on both organs. Starting from nine and a half month of age, the mice were scanned once a month to determine the amount of lesions in the kidney and the liver. A baseline curve for TS tumor growth in the kidney was not determined because of the unpredictability of the growth of TS cells. Instead, the tumor volume and tumor counts for the kidney was compared to the before and after treatment for each treated subject. The TS tumor growth trend was affected by anti-angiogenic drugs. The combination therapy of IFN-γ and Rapamycin showed a 43 to 67%, a two fold decrease in the average number of tumors compared to untreated mice. There were not many scans collected for the liver because Tsc2+/− develop mostly kidney lesions. From the available MRI scans, the liver tumor volume of treated subjects were seen to have decreased over the period of the disease course but it cannot be concluded that Rapamycin was effective in inhibiting the tumor or lesions from growing on the liver cells. More analysis will be necessary to prove the anti-angiogenic drug to be effective. Ideally, this project will further TS curative research by testing the effects of anti-angiogenic therapeutics. In time, research such as this will hopefully lead to a less debilitating and more successful kidney and liver treatment method.
Time Course Measurements of Lung Tumors in a Drug Trial of a Transgenic Mouse Model

Small Animal MRI Lab at Brigham and Women’s Hospital

Lung cancer is currently the leading cause of cancer deaths. Though there are different types of treatment available for lung cancer (Surgery, Chemotherapy, and Radiation), none of these patients drastically increase survival rates in patients, with a 5-year survival rate of about 15%. Several different types of novel treatments are being developed to help increase the survival rate of lung cancer patients. Anti-angiogenic drugs, or drugs that prevention of blood vessels that feed tumors, are one of the novel treatments being studied. Another subset of drugs being studied is molecular targeted treatments. These types of treatments affect certain pathways and inhibit their expression. Epidermal growth factor receptors (EGFR) which have been shown to be present in lung cancer patients, is one of the main targets for this new type of therapy. To test the efficacy of these novel treatments, a transgenic mouse model has been created mimic a human reaction to these novel treatments. The mice are then given the treatment and imaged using magnetic resonance imaging (MRI). From the volume measurements made, it was possible to determine that for all subjects treated with CI-1040 expressed tumor shrinkage of about 20% when compared to original tumor volume. Erbitux was shown not to shrink tumors in 82% of cases, but when compared to untreated control subjects, it was shown that the tumor growth rate of Erbitux treated subjects was 66% lower. This indicates a positive outlook for molecular targeted treatments as an alternative to conventional therapies.
Quantitative MRI of the Pediatric Brain in Comparison with the Adult Brain

Ashley Martin

There have been very few studies done on the development and maturation of brain tissues of the normal pediatric brain. This limited knowledge in pediatric brain maturation is due to the sensitive and slightly controversial nature (concept) of experiments performed involving pediatrics. Although there is a lack of brain research done in pediatrics, a variety of studies have researched the maturation of the adult brain using Quantitative MRI (Q-MRI) techniques. The senior research project was designed to investigate the entire progression of human brain aging by combing pediatric and adult populations. The project used Q-MRI techniques to process and analyze MR images. The subjects were scanned on a 1.5T Phillips MRI scanner and image data was obtained using a Mixed-Turbo Spin Echo (Mixed-TSE) pulse sequence. This pulse sequence enabled the acquisition of a variety of tissue relaxation parameters necessary for image processing and analysis. A high-level programming environment (MathCAD 2000i) was used for image processing, brain segmentation, and spectral analysis. Several MathCAD algorithms were used to generate $T_1$, $T_2$, and secular-$T_2$ weighted maps of the whole brain. A separate algorithm was used to segment these quantitative maps into sections that approximate the frontal, parietotemporal, occipital, and cerebellar lobes of the brain. A final algorithm produced a multi-subject spectrum for each $T_1$, $T_2$, and secular-$T_2$ tissue relaxation spectra. These multi-subject spectra provided tissue maturation distributions for the whole-head intracranial matter, frontal, parietotemporal, occipital, and cerebellar segments of the brain. These spectral distributions show a distinctive difference between the tissue development and maturation in pediatrics in comparison to adults. The pediatric T1 spectra show that the brain is primarily composed of GM tissue or GM-like tissue for a brief time after birth. The GM tissue shows a decrease in T1 relaxation values as a function of increasing subject age. WM tissue is not seen just after birth, but begins to appear by 2 years of age. The WM tissue shows a decrease in T1 values for pediatrics and then a subtle increase in T1 values as a function of increasing age in adults. The generation of normative spectra for $T_1$, $T_2$, and secular-$T_2$ relaxation values as a function of age provides a standard of comparison for future studies in normal as well as diseased subject brain tissue development. These baseline spectra may provide useful information for physicians in assessing whether a patient’s progression of brain tissue development differs from the normative tissue development curves. If the diseased tissue maturation characteristics are known, this could lead to earlier diagnosis and treatment of a specific disease in a patient. These findings could also provide information for future development of techniques to impede or possibly prevent the onset of the disease.
THUAN NGO

Characterization and Measurement of the 3rd Ventricle in Hydrocephalic Mice

Small Animal MRI Laboratory, Brigham and Women's Hospital

Hydrocephalus is a chronic condition that is characterized by abnormalities in the flow or resorption of cerebrospinal fluid (CSF), or ventricle blockage, resulting ventricular dilation within the brain. There is an estimated incidence of 1 in 1500 births within the United States. This study proposes the use of T-2 weighted Magnetic Resonance Imaging (MRI) to examine the volume of the ventricular space in hydrocephalic and non-hydrocephalic mice to create a model of hydrocephalus for study. The model was created using a transgene of Heparin Binding Epidermal Growth Factor (HB-EGF) over expression. Using these acquired images, baselines of severity of hydrocephalus were created, and the animals were categorically separated. A wide range of variability in ventricle volumes was observed over time between all of the animals. From the study, it is shown that 55.56% of the animals in the study with the growth factor over expression exhibited hydrocephalus. The growth factor also appears to have gender specificity in the implication of hydrocephalus, with 60% of male and 40% of female subjects expressing hydrocephalus. This suggests that there is a sex-linked genetic characteristic or hormonal process relating to the onset of hydrocephalus.
Cell replacement therapies require the ability to monitor implanted therapeutic tissues throughout their regenerative time course, \textit{in vivo}. Cellular MRI has emerged as a prime candidate to achieve this, but is currently limited by both contrast agent effectiveness and the ability to achieve microscopic resolution with a high signal-to-noise ratio (SNR). Gadolinium-chelates (Gd-DTPA; Magnevist) and superparamagnetic particles of iron oxide (SPION; Feridex) are two commonly used MR contrast agents that exhibit inherently different relaxation properties. Assuming minimal mutual interaction between these two agents, we were motivated to investigate the creation of dual contrast properties by mixing the two in aqueous solution and intracellularly administering them to NIH3T3 fibroblasts. Using the Inner Volume 3-Dimensional Fast Spin Echo scan sequence (IV-3DFSE), we aimed to achieve enhanced contrast of these magnetically labeled cells at cellular resolution with a high SNR. Concentration-dependent relaxivity coefficients were first obtained from each contrast agent, independently, in saline solution in a 3 Tesla magnetic field. These coefficients were then used to predict both the $R_1$ and $R_2$ relaxation rates of a dual contrast agent using a linear model combining the effects of both contrast media. The predicted relaxation rates were experimentally confirmed from 25 dual contrast solutions (combinations of Feridex-concentration ranging from 0 to 1 $\mu$g/mL and Magnevist-concentration ranging from 0 to 0.20 mM, post-mixing). Intracellular administration of Feridex and Magnevist was achieved separately via the use of transfection agents and was verified by live/dead cell viability testing. Additionally, IV-3DFSE imaging successfully visualized contrast enhanced cells at cellular resolution with a good SNR. In this study, we have shown that the combination of Feridex and Magnevist in an aqueous solution exhibits unique and predictable relaxivity properties that are unattainable via the individual use of either agent. By verifying the ability to intracellularly administer each contrast agent via both MR imaging and cell viability testing, while achieving cellular resolution and a high SNR, we have provided a basis for the further development of a true dual contrast agent for cellular MRI. The method may be applied in future applications to create ‘user-tunable’ contrast conditions for the visualization of magnetically labeled cells in the context of cell replacement therapy.
Modeling the Dynamic Behavior of the Circadian Clock in *Limulus polyphemus*
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Visual Information Processing Laboratory

Despite the extensive research into the daily circadian rhythms of the common horseshoe crab, *Limulus polyphemus*, there is still no comprehensive mathematical model that accurately and adequately describes the response of the circadian clock in the visual system to light stimuli applied at different phases throughout its 24-hour circadian cycle. By measuring the electroretinogram (ERG) voltage emitted by the visual system in response to external light stimuli, as well as the time, duration, and intensity of a light stimulus introduced to the test subject’s eye, phase plane portraits relating the ERG voltage amplitude and light intensity can then be calculated. By constructing phase plane portraits of circadian rhythms recovering from being interrupted at different phases of the circadian cycle, a phase response curve of the dynamic response of the circadian clock in the visual system can then be made. From the phase response curves, comprehensive mathematical models describing the nonlinear behavior of the visual system when exposed to light entrainment can then be derived. Two models have been developed to relate the ERG voltage emitted by the visual system in response to external light and the intensity of the external light itself. The first mathematical model is derived from a differential model by Tyson that was initially proposed to model circadian rhythms affecting the dimerization and proteolysis of two proteins, PER and TIM, in *Drosophila melanogaster*. The second mathematical model is derived from a Van der Pol oscillator model by Pittendrigh that was initially proposed to model circadian rhythms affecting photoperiodism in insects such as *Drosophila melanogaster* and *Sarcophaga argyrostoma*. The final result of the project, the Adapted Van der Pol Oscillator Model, is capable of accurately predicting the baseline ERG voltage waveform of the visual system in different lighting conditions, the phase portraits of the visual system’s circadian oscillator under light stimulation along any phase of the circadian cycle, and the phase-response curve of the dynamic response of the visual system’s circadian clock.
Asthma is a lung disease of increasing prevalence. Asthmatics experience marked decreases in ventilation efficiency caused by allergic reactions of the airways. Hyperpolarized (HP) $^3$He MRI facilitates the visualization of ventilation dysfunction but is not able to derive information on an airway-by-airway basis. Three-dimensional models provide a powerful medium for non-invasive study of lung disease. This project interfaces anatomically explicit 3D airway tree models with imaging and mechanical data to reveal the structural manifestations of asthma on a personalized basis. The approach used is a previously established computational paradigm called Image Functional Modeling (IFM). This project has evaluated potential limitations and advancements of IFM in the context of clinical applications. We assessed the possibility that ventilation loss is largely caused by closures that are confined to very small airways. This involved the design and application of software to relate the location of airway closures to the extent of ventilation degradation in a 3D model. This capability also allowed us to address the issue of non-perfect spatial mapping of airways in models. A second challenge was to establish the degree to which IFM depends on whether 3D models are personalized or not. 3D lung models of enhanced patient specificity were synthesized using methodology established by Miluntinovic et al. Rendering of HP $^3$He MRI scans and cryosection images of a frozen cadaver (VHD, US National Library of Medicine) provided information to tailor models to the lung shapes and sizes of individual healthy and asthmatic patients. Studies were performed to evaluate the sensitivity of model structural features to the parameters guiding their creation. Patient specific models were shown to be robust and to uniquely reflect variations in the thoracic cavities of different patients. Consistent distortions of peripheral airway distributions in patient specific models have indicated that geometrical improvements are necessary. Simulations of lung resistance and lung elastance (i.e. $R_L$ and $E_L$) with patient specific airway tree models were shown to be consistent with but clearly distinct from generic model equivalents. Patient specific and generic models were used to locate the airways responsible for post-bronchoprovocation terminal lung unit ventilation defects based on the conducting pathways. Predictions suggest that the majority of adverse airway remodeling caused by asthma occurs in the lung periphery but airways of all sizes can potentially be afflicted. The IFM approach is rapidly moving in the direction of enabling clinicians to personalize asthma therapies by precisely targeting hyper-reactive airways for drug delivery.
SESSION IV: Biotechnology and Systems Biology
Heart disease is the leading cause in morbidity and mortality in developed countries and the incidence continues to rise. Cardiac insults that compromise cardiac function trigger a remodeling process characterized by the loss of cardiac myocytes which, in turn, leads to further loss of function. Current research is focused on discovering cardioprotective agents that will counteract this loss. Angiopoietin-1 is a secreted protein that promotes cardiac survival, which has been attributed solely to its angiogenic effect acting on the blood vessel endothelium. However, it has been recently established that angiopoietin-1 promotes cardiac myocyte survival directly via integrin binding. The goal of this project was to identify the integrin subunits that serve as receptors for angiopoietin-1 on cardiac myocytes, and to describe the binding characteristics of each angiopoietin-1/integrin subunit interaction. Using fluorescent immunocytochemistry, cardiac myocytes were probed for the following integrin subunits: $\alpha_v$, $\alpha_5$, $\alpha_6$, and $\beta_1$. Recombinant angiopoietin-1 was produced by transiently transfecting HEK-293 cells. The recombinant angiopoietin-1 was biotinylated, and incubated with cardiac myocytes to confirm colocalization of angiopoietin-1 with integrin receptors. Angiopoietin-1 colocalized $\alpha_v$, $\alpha_5$, $\alpha_6$, and $\beta_1$, identifying these integrin subunits as novel receptors for angiopoietin-1 that trigger the signaling cascade promoting cardiac myocyte survival. Colocalization between integrin subunits was compared by determining each angiopoietin-1:integrin subunit pair’s colocalization coefficient via ImageJ. ImageJ analysis of the colocalized and non-colocalized integrin cluster sizes revealed a shift in frequency towards increased cluster size for colocalized integrin clusters. This cluster shift supports the hypothesis that angiopoietin-1 promotes integrin clustering, and as a result, increased cardiac myocyte survival via the amplified signaling pathways activated through integrin clustering. These findings will assist in evaluating the therapeutic potential of angiopoietin-1 in preserving cardiac function following injury.
Cancer is a major public health problem in the United States and other developed countries. Cancer is a disease characterized by uncontrolled division of cells and their ability to spread throughout the body by metastasis. Many current cancer treatments have serious side affects such as damage to surrounding healthy tissue. With the advances in tumor pathology have led to the development of targeted therapies. Aptamers, single stranded oligonucleotides affinities and specificities comparable to those of antibodies. Of great interest is the use of these aptamers to target carcinoembryonic antigen (CEA). CEA is a 180 kDa glycoprotein over-expressed on many different cancers, especially cancers of the breast and the gastrointestinal tract. To investigate the binding affinity and specificity between these aptamers and CEA, fluorescent polarization (FP) assays were performed in vitro and the affinities were analyzed by applying a non-linear least squares regression to calculate the dissociation constant, $K_D$, which is a measure of binding. In this study, an aptamer has been described that binds to CEA with $K_D$ determined to be 135 nM. Potential applications of this research include the development of these therapeutic molecules for use as improved cancer treatments and diagnostics.
Cataloguing kinase substrates to build a representative kinase substrate library to enable the quick establishment of kinase enzyme assays

Kristifor Sunderic

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ABSTRACT

Protein kinases are enzymes that mediate most of the signal transduction in the body and many aspects of cell life, reacting to changes from outside the cell and communicating them to the cell interior. The key role of protein kinases in many cellular signaling pathways and in several diseases such as cancer, metabolic disorders, and inflammation has generated great interest in kinase enzymes as therapeutic targets (1). Because kinases have become popular drug targets, vendors are making assays more available. But this information is scattered, redundant, and lacking annotations. There is no indication whether the peptides used in these assays are natural or artificially engineered, or what protein they originate from. Because multiple kinases can phosphorylate a single substrate, and a single kinase can phosphorylate multiple substrates, organizing these substrates into a data structure and finding a minimal, representative set of kinase substrates that gives maximal coverage would establish fast and efficient kinase assays for use by enzymologists. A complete, detailed, and well-defined database of human protein kinase substrates will facilitate drug development by enabling the quick establishment of kinase enzyme assays, therefore improving the speed and efficiency of kinase drug discovery projects. Data from existing kinase assay profiles are compiled including the kinase used and the peptide sequences it showed affinity for. The data is standardized to eliminate redundancy, and the sequences will be matched to parental proteins using the Sequence Retrieval System (SRS). We identify a representative list of kinase substrates involved in crucial cell signal transduction pathways. The kinase substrates, along with all pertinent data, are organized in an Access database and made available to discovery scientists who will benefit from the information.
Quantifying Promoter Activity During Stringent Response to Infer the Influence of Guanosine Tetraphosphate and Guanosine Pentaphosphate on crp and arcA promoters
Senior Project Student: Justina Tam

Bacteria are able to use a variety of adaptive responses such as stringent response, that allow them to adapt to adverse environmental conditions. Stringent response is a bacterial response to conditions of starvation, leading to the accumulation of GDP and GTP derivatives, called (p)ppGpp. These derivatives are one of the key regulators of the changes seen in stringent response. Stringent response has been shown to be involved in the development of improved antibiotic resistance. Thus, understanding the mechanism of action of key regulators of stringent response, such as (p)ppGpp, can lead to the development of better ways to control unwanted bacterial growth. This project uncovers the mechanism of action of (p)ppGpp on two promoters which have been found to be up-regulated during stringent response. Specifically, this project aims to determine whether (p)ppGpp directly or indirectly regulates these promoters through measurements of promoter activity on various strains of Escherichia coli (E. coli), constructed with P1 transduction and transformation during serine hydroxamate-induced stringent response.

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An Analysis of the Induction of Chromosomal Fragility from Nicotine Treatments

Stephen D Gallagher
Molecular Biology Research Laboratory

Although cigarette smoking has been associated with many deleterious effects, the effect of nicotine, the major alkaloid of cigarette smoke, has not been fully characterized. While smoking is associated with a higher frequency of cancer, the role of nicotine itself is unclear. Results from other studies on the genotoxicity of nicotine have been contradictory. Several studies have established a correlation between nicotine dose treatments and inhibition of apoptosis, programmed cell death via fragmentation of DNA. The inhibition of apoptosis promotes tumorigenesis via removal of growth limiting controls. This paper explores the genotoxicity of nicotine in vitro on two colorectal adenocarcinoma cell lines and two non-cancerous schizophrenic cell lines. The genotoxicity was quantified through single cell gel electrophoresis. The relative percentage of DNA moving away from the nuclear region (quantified from the intensity of fluorescence) was considered the percent of DNA damage within a given cell. Nicotine dose treatments demonstrated an increase in the number of cells expressing damage. Of the cells expressing damage, nicotine dose treatments increased the percentage of DNA damage. When treated both with hydrogen peroxide, a known apoptosis inducer, and nicotine, two cell lines exhibited a decrease in percentage of DNA damaged. Using the area of damaged DNA versus the area of the nuclear region, another quantification of damage, a similar result was obtained. Quantification of damage from the area eliminates the possibility of the intensity data being skewed by the inner filter effect. The results demonstrate nicotine alone induces DNA damage. When treated with hydrogen peroxide the results suggest the cells began to undergo apoptosis while nicotine dose treatments inhibited apoptosis.
Sirt1 Signaling in the PI3K/AKT Pathway

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Sirt1 is a nicotinamide adenine dinucleotide (NAD)-dependent histone deacetylase protein that plays a key role in cell survival, metabolism and programmed cell death. Phosphoinositide 3-kinases and Protein Kinase B compose one of the central cancer causing pathways in cells and are often referred to as the PI3K/AKT pathway. Sirt1 has been shown to regulate several proteins in the PI3K/AKT pathway; however, there is little information on regulation of Sirt1. Recent research on mammalian mouse cells showed that PI3K inhibition prevented Sirt1 from entering the nucleus of cells where it is normally found. Another study showed that a Sirt1 homologue in yeast cells, Sir3, was phosphorylated by Protein Kinase C in the MAPK pathway which shows similar properties to the PI3K/AKT pathway. Due to the association between Sirt1 and the PI3K/AKT pathway, the overall objective of this project was to determine if the PI3K/AKT pathway was regulating Sirt1 in prostate cancer cells. Kinase phosphorylation of Sirt1 was tested through phosphatase digestion using western immunoblot and alkaline phosphatase CALF Intestinal (CIP) enzyme along with its inhibitor. The enzyme works by dephosphorylation of serine, threonine and tyrosine residues in proteins. Sirt1 phosphorylation was also tested using Immunoprecipitation to isolate all forms of Sirt1 protein from prostate cancer cells. A phosphoserine antibody that detected any site of phosphorylation on the protein was used to detect modifications to the Sirt1 protein. An immunostaining localization assay tested several types of inhibitors that targeted kinases in the PI3K/AKT pathway. Sirt1 delocalized from the nucleus to the cytoplasm in prostate cancer cells due to PI3K inhibition. Sirt1 was shown to have possible phosphorylation potential; however, the phosphorylation assays did not yield conclusive results. The combination of these results suggests that Sirt1 is regulated in the PI3K/AKT pathway somewhere downstream of PI3K, but upstream of AKT.
Modification of a genetic toggle switch in *Escherichia coli* to allow multiple transcription factor inputs networked using Boolean logic

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The rapidly emerging field of synthetic biology is concerned with using engineering approaches to modify the genetic and biomedical pathways in existing organisms. The genetic “circuits” designed are often created as analogous components to elements of electrical engineering, such as toggle switches and oscillators; however, currently there lacks a genetic component designed for Boolean circuitry. The goal of this project was to conduct an extensive mathematical analysis on a modification of an existing toggle switch such that it required two separate stimuli to be turned ‘on’, effectively wiring its input as a Boolean AND gate. The toggle switch chosen turned ‘on’ when incubated with IPTG and turned ‘off’ when incubated at 42°C, but would be modified by adding an fnr binding site such that the toggle would only turn on if aerobically incubated with IPTG. The approach consisted of phase plane plots, bifurcation diagrams and stability diagrams in order to analytically verify that the addition of an fnr binding site would effectively wire the toggle’s input as a Boolean AND gate, expanding the possibilities of synthetic biology in fields such as oncological detection.
Optimization of Power Generation in Microbial Fuel Cells through Insertional Mutations of *Shewanella oneidensis* MR-1

Stephen J. Schneider  
The Gardner Laboratory

Microbial fuel cells (MFCs) currently have no practical applications and despite advancements in physical fuel cell design to increase efficiency, there is still a need for a fundamental understanding of dissimilatory metal reducing bacteria (DMRB) before their metabolic capabilities can be harnessed for water and waste management systems, bioremediation, or clean energy production. This insight may be provided through the investigation of *Shewanella oneidensis* MR-1, a type of Gram-negative DMRB with the ability to anaerobically respire a multitude of electron acceptors, including soluble toxins, such as Uranium(IV). *Shewanella*’s unique regulatory pathways controlling its respiration and metabolism are believed to be highlighted by knockout strains that exhibit an atypical performance in a MFC. Through transposon mutagenesis, a 4,608 strain knockout library of AS92 *Shewanella* was constructed and optically screened for strains showing increased rates of anaerobic Fe(III) reduction. Strains with heightened metal reduction rates were tested in MFCs and sequenced to determine genotype. Linking *Shewanella*’s knockout genes to their phenotypes will aid in mapping unknown gene networks and validate network inference models, which can be used to create better antibiotics, predict the targets or mechanisms of drugs, and rationally engineer *Shewanella* for efficient water treatment and bioremediation systems.