The Next Step

Call the departments listed, or visit our website to find out projects details, plus information on just how CEAS is meeting the challenges of the future head-on.

Applied Mathematics and Statistics
631-632-8270

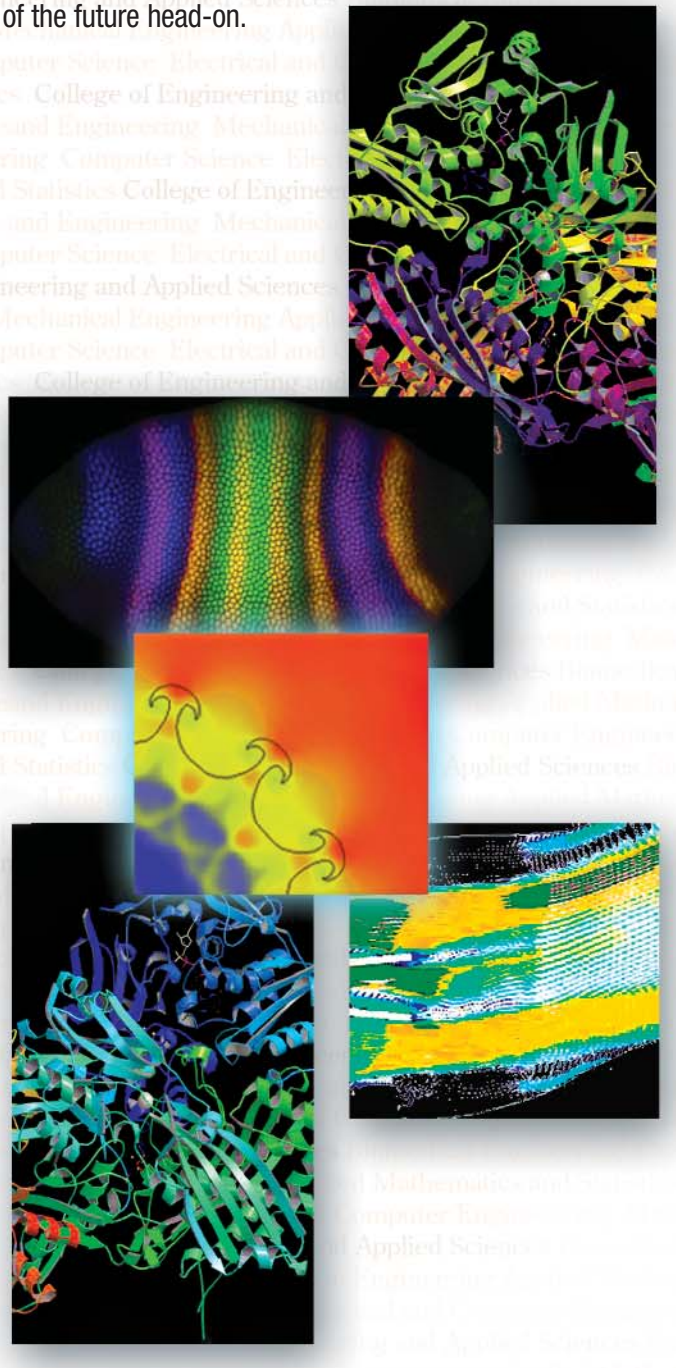
Biomedical Engineering
631-444-2303

Computer Science
631-632-8470

Electrical and Computer Engineering
631-632-8420

Materials Science and Engineering
631-632-8484

Mechanical Engineering
631-632-8340



CEAS
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Stony Brook University
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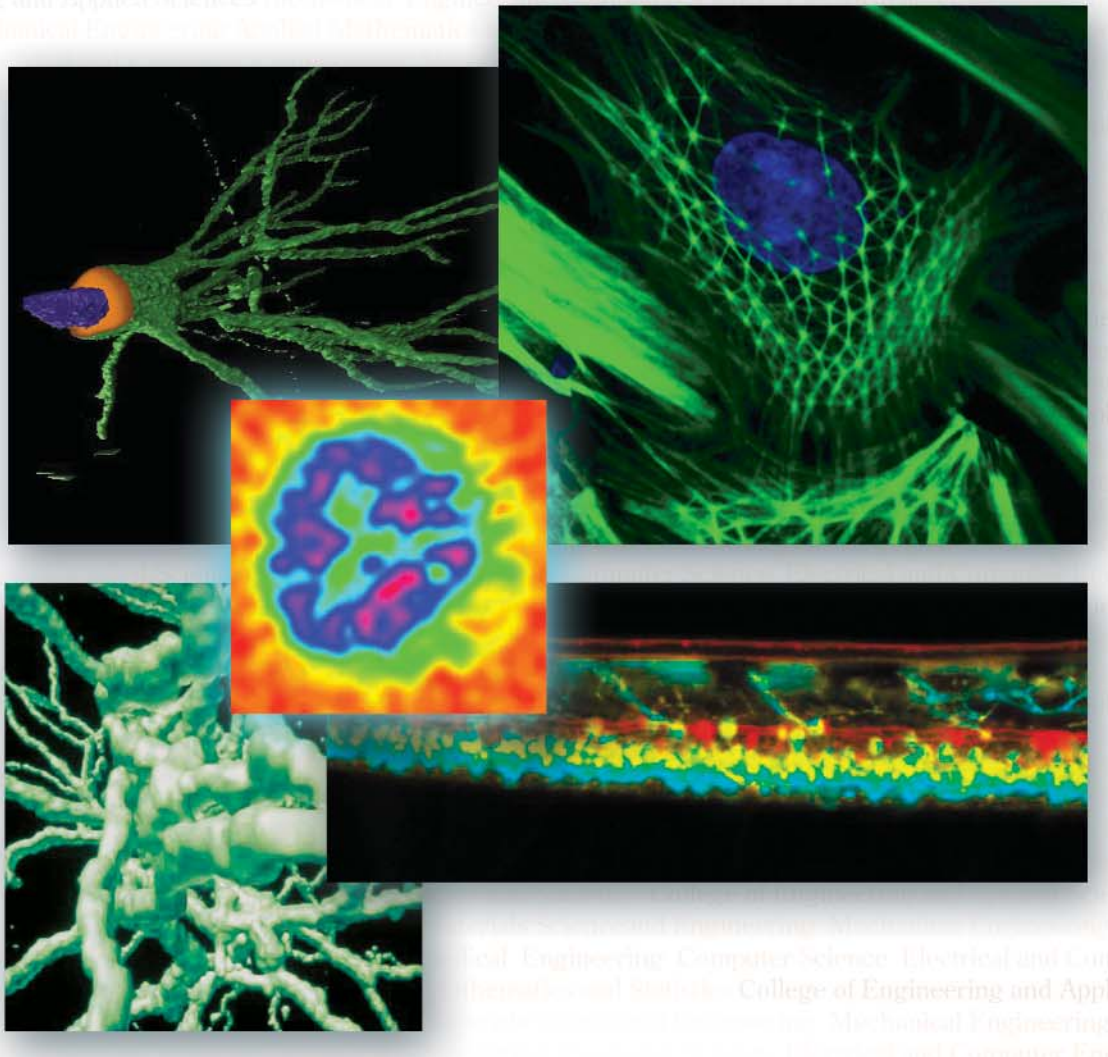
STONY BROOK
STATE UNIVERSITY OF NEW YORK

COLLEGE OF ENGINEERING AND APPLIED SCIENCES

COLLEGE OF ENGINEERING AND APPLIED SCIENCES

STONY BROOK BIOMEDICAL TECHNOLOGY:

The Source and the New Frontiers



Biomedical-Related Sponsored Projects

STONY BROOK
STATE UNIVERSITY OF NEW YORK

Revolutionizing the Future in Medicine

Biomedical Research and Engineering is at the forefront of science and medicine in the 21st century. While the 20th century was characterized as the age of specialization, the 21st century has begun at a point where creative contributions and major advances are made at the interface of different fields. In addition to attracting many of the brightest young minds nationwide, Biomedical Technologies highlight the importance of crosslinkage activities, and provide an excellent model for interdisciplinary research.

College of Engineering and Applied Sciences (CEAS) is ideally situated to lead efforts on campus that will attract the participation of faculty from all the departments. To encourage novel cross-disciplinary approaches toward discoveries in many areas of biomedical science and engineering, individual researchers, as well as research groups and centers from across CEAS, are teaming together and collaborating with their peers at such fields as structural and computational biology, health sciences, electrical and neural networks, information and wireless technology, materials and tissue, biotechnology, biosensors and bioinstrumentation, and as magnetic and ultrasound imaging. The relative proximity of all these units, the medical center, and the campus itself, are conducive to intellectual journeys and exploratory science of all kinds.

The current projects, which are listed here, are a strong witness to the deep involvement of the entire college in the Biomedical-related effort. Together with scientists from Brookhaven National Laboratory and Cold Spring Harbor, two of the nations leading research centers linked to SBU, CEAS is conducting a wide spectrum of Biomedical Engineering activities. A large part of this revolution is the entrance of molecular cells, which leads medical engineering in new directions. The Human Genome project and Nano-Technology brings the need to develop experimentally based computational models and tools to address problems ranging from regulation of gene expression and sub-cellular and cellular interactions, to tissue and organ function. In response, distinctions between scientific disciplines have begun to blur, fueling cross-fertilization of ideas between life scientists, physical scientists and engineers. CEAS' duty is to organize this reservoir of information, and change it into quantitative data that will integrate with real biological systems.We are constructing the building blocks that will enable biologists to implement this Information System and work with it.

This publication provides an up-to-date summary of CEAS activities in biomedical-related fields. Our research activities interface with Federal, State and local agencies, as well as New York State and Long Island institutions.We already hold a strong, nationwide position in this activity, and with additional external support we will thrive to explore new fields and get involved with new endeavors.

Yacov Shamash, Dean

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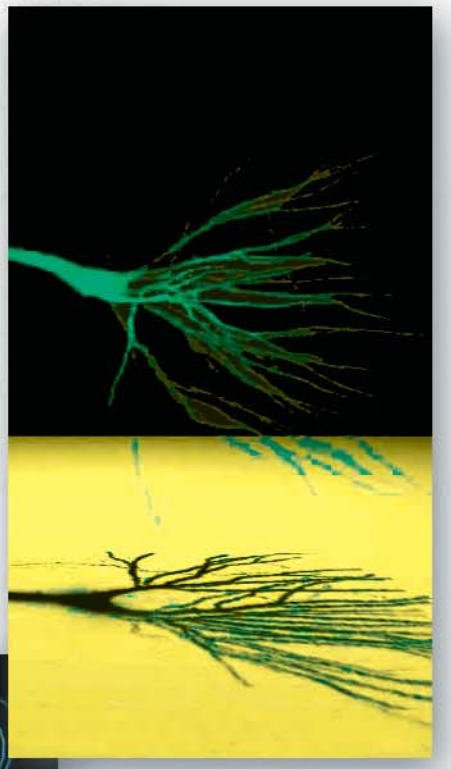


Applied Mathematics and Statistics

Gene Regulation and Biological Pattern Formation

Prof. John Reinitz

We are engaged in a long term project to characterize the dynamics (physiology) of the segment determination process and control of transcription in the fruit fly (Drosophila melanogaster) by means of an integrated approach that utilizes experiment, computation, and mathematics. The major goal of our work is to achieve an integrative understanding of the segment determination process as an emergent property of a network of genes, a copy of which is present in each of many cells. We are also engaged in making models of transcriptional control which are designed to predict the physiological action and expression patterns of modular enhancers from knowledge of their constituent binding sites. Both problems are being approached using an approach called ``Gene Circuits''. The Gene Circuit method has four parts: 1) Construct a theoretical model, 2) obtain gene expression data, 3) fit the model to the data by large scale numerical optimization, and 4) learn new biology from the model. In addition to shedding new light on fundamental biological problems, we have developed new algorithms in support of points 2 and 3 above. With respect to expression data, these include new methods of image segmentation, registration, classification, and background removal. These data have been placed on the web in a modern bioinformatics database (http://flyex.ams.sunysb.edu/FlyEx). With respect to large scale optimization, we have developed both a new parallel simulated annealing algorithm as well a new Lagrangian Optimal Steepest Descent optimizer. (NIH)

Nano-Structured Thin Silicon

Prof. Charles Fortmann

This project is investigating the use of nano-engineered silicon structures for site specific pharmaceutical delivery. This project spans the range from theoretical material engineering to actual material generation. The project involves an agent simulation of the life cycle that abandons the deterministic rate equation approach to model various cellular cyclic systems (e.g., metabolic cycle) using independent, non-deterministic agents performing the various interconnected: reactions, diffusions, energy production (and consumption) and feedback circuits. (SPIR, Sensor CAT and Solar Physics Corp., Biota LLC)

Docking of Proteins

Prof. Ilya Vakser

The research in our lab focuses on molecular modeling in the context of structural genomics and bioinformatics. The major goals are to develop approaches to the modeling of protein interactions and to design procedures for reconstruction of the network of connections between proteins in a genome. The number of protein-protein interactions in a genome is significantly larger than the number of individual proteins. Moreover, most protein structures will be models of limited accuracy. Thus the structure-based methods for building this network have to be (a) fast, and (b) insensitive to significant inaccuracies of modeled structures. The primary current objectives are: (1) accurate prediction of the structure of protein complexes, (2) docking in genome-wide databases of modeled protein structures, and (3) integrated environment for docking methodology development and applications. The long-term goals are to understand the fundamental principles of protein interaction and to create a structure-based description of genomes. (NIH)

Suffolk County Mental Health Project

Prof. Steve Finch

This is a prospective study of the progression of mental illness among psychotic subjects who were first hospitalized in Suffolk County. Research in progress is investigating which, if any, medicines given to bipolar subjects are associated with earlier first remission of illness and longer period of first remission. The principal finding is that subjects who use mood stabilizing drugs (lithium, tegretol, and related medicines) sporadically have longer times to first remission of illness and subjects who have been prescribed an anti-depressant medication also take longer times to achieve first remission. Additionally, subjects who have earlier age of onset of illness take longer to achieve first remission. Another aspect of the project is whether bipolar subjects, who have been administered anti-depressant medications, are more likely to "switch"; that is, to have a manic episode while taking the anti-depressant medication or within thirty days of the cessation of the anti-depressant. (NIH)

Detection of Bio-Pathogens in the Blood Serum

Prof. Wei Zhu

Diagnosis of cancer and other ailments from a drop of blood in your doctor's office? With no invasive or surgical testing? A recent breakthrough has moved this dream closer to reality. We have developed a statistical methodology for the detection of ovarian cancer with a 100% success rate of detection, based on analysis of mass spectrograph data taken from blood serum, using publically posted data sets maintained by NCI. This methodology has a strong potential for application to other biomarkers in the blood serum. The idea has two steps, and builds on earlier work of Petricoin et al. The hardware, or physical measurement step, is by a mass spectrometer. This machine looks at blood fractions and trace proteins and records mass (in relation to charge). Of course there are many hundreds of thousands of these signals ("markers"). The second step, addressed here, is to find the needle in the haystack. Which markers distinguish a normal patient from one with ovarian can cer? This is a problem in statistics and its solution enables the diagnostic procedure. The statistical problem is solved using diagnostic data, that is, blood samples from patients with know diagnosis, having ovarian cancer or normal. The data is divided in half, one half to train the statistics and the other half to test the conclusions. All markers are assessed for their ability to distinguish between normal and afflicted patients in the training set. About 150 markers show a statistically unusual pattern of difference between these populations. This number depends on the resolution power of the mass spectrum equipment. Selection of six or so of the markers from the 150 identified defines the test. A subject with a positive reading on these six markers is diagnosed with ovarian cancer. When the test is applied to the testing set, 100% accuracy results. (Long Island Cancer Center)

Neural Imaging

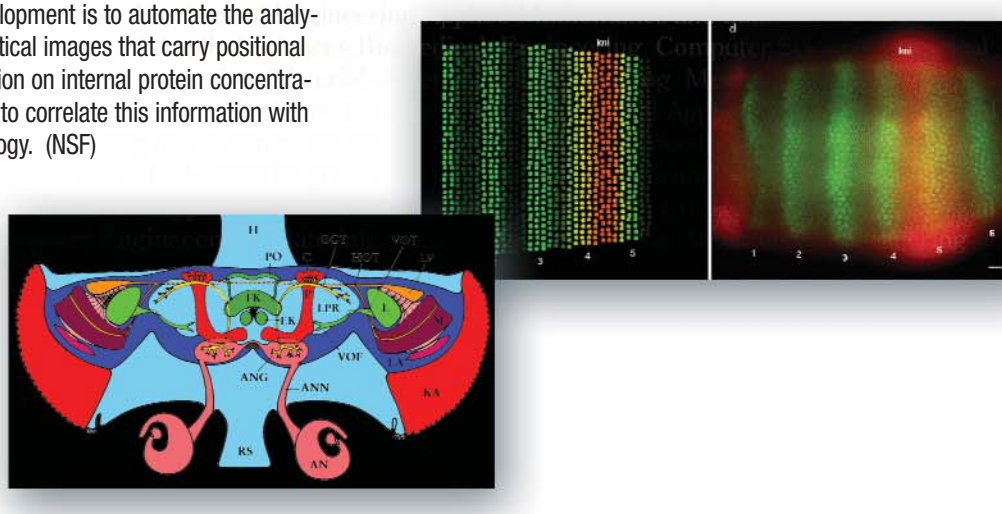
Prof. Brent Lindquist

We have developed a prototype, 3DMA-Neuron, of the next generation of computational algorithms that provide automated feature recognition, to advance the analysis of optical images used extensively in the study of three dimensional neuron morphology. Laser scanning microscopy, employing fluorescent marker proteins, has proved to be a revolutionary tool in modern neuroscience, routinely producing large numbers of three dimensional images. Current analysis of these images relies on computer aided technology that requires the human eye to perform critical feature detection while tracing slice-by-slice through an image. This leads to severe restrictions in the number and size of data sets that can be analyzed, and remains inherently prone to fatigue- and habituation-related bias. The prototype software targets automated tracing of dendritica arbors and detection of dendritic spines (post synaptic termini). These algorithms have been developed in close collaboration with neuroscience laboratories at Cold Spring Harbor and Mt. Sinai School of Medicine. One current thrust of the development is to automate the analysis of optical images that carry positional information on internal protein concentration and to correlate this information with morphology. (NSF)

Modeling of Bio-Molecules

Profs. James Glimm and Yuefan Deng

The central problem for molecular dynamics (MD) simulations of protein structure is the disparity between time scales for atomic vibrations and those for conformational changes. Typical time scales for conformational changes are not known, but have been estimated as of the order of a micro sec. The time step in an MD all atom simulation is of the order of a femtosec, so that billions of time steps may be needed. This simple fact illustrates the central difficulty in the direct all atom simulation of structural biology. We have developed new tools applicable to a special purpose computer to be located at BNL, which allow the all atom simulation of molecular dynamics for a greatly extended time period, up to 10 micro sec. This algorithm will allow exploration of new regimes of biology in the binding of proteins, and their biological functions. (BNL)



Brain Imaging

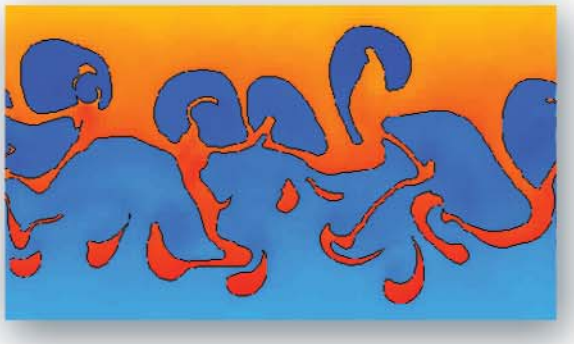
Prof. Wei Zhu

A major goal of statistical analysis in brain research is to extract from a vast amount of brain image data (PET and MRI) the essential features that characterize brain functions. We are developing two novel approaches for such analysis: (1) correlational and path analysis to uncover brain functional networks, and (2) coefficient of variation (CV) – a measure of brain regional variability or heterogeneity. These analyses are being implemented in BrainMiner, an interaction brain functional analysis and visualization tool. Correlational and path analysis: the correlations in brain activity are calculated on the basis of predefined anatomical regions-of-interest (ROI's). The correlation coefficient is then employed to quantify similarity in response, for various regions during an experimental setting. To account for anatomical variability, each test subject's volumetric brain data is first transformed into a common anatomical coordinate system (the Talairach-Tournoux space). Measuring brain functional variability: it is well known that the two most essential statistics are mean and variance. In ROI-based brain functional studies, the analysis of the regional mean is a fully developed practice; however, the same is not true for the variability. We have developed the analysis for brain functional homogeneity/heterogeneity based on the coefficient of variation (CV). The CV is the ratio of the standard deviation to the mean. It is a measure of regional variability independent of the underlying measurement unit. We have applied such analysis to the comparison of brains affected by Alzheimer's disease with normal brains. Our results indicate that such analysis is providing new insight into disease etiology and additional information on diagnosis. (BNL)

Schizophrenia

Prof. Nancy Mendell

Research interests include development of statistical methods for linkage analysis of complex diseases. Specific interests are in disease related traits or "endophenotypes" and quantitative risk factors. These are traits which occur at a higher frequency or are associated with a different distribution in the affected individuals and their family members than that observed in the general population. They are often show better aggregation in families than the disease itself and hence genetic linkage studies of these endophenotypes are more powerful for identifying disease susceptibility genes than studies of the disease itself. The focus of this research has been in the area of schizophrenia for which several promising endophenotypes have been identified. The methodological focus has been on developing methods for genetic analysis of these traits. Other areas of interest include incorporation of Bayesian methods into the analysis on immunogenetic data and evaluating the effects of behavioral and life style changes on health. (McClean Hospital)



Toxicology

Prof. Hongshik Ahn

We conduct statistical analysis of toxicology in collaboration with scientists at the National Center of Toxicology. We have developed statistical methods for testing the carcinogenic potential of drugs and other chemicals used by humans. In this project, age-adjusted trend tests for the tumor incidence rate have been investigated. We also have investigated modified experimental designs to reduce the cost of drug developoment. Finding an optimal design with a shortened study duration will be of great economic and medical value. (NIH)

Biomedical Engineering

Biomechanical Based Etiology of Low Back Pain

Prof. Partap Khalsa

Recent findings from the Somatosensory Spine Research Laboratory have shown that certain spine ligaments could provide a biomechanical basis for spine proprioception. A theory of low back pain due to non-traumatic mechanical causes posits that mechanically sensitive neurons innervating the ligamentous joint capsules in the spine are necessary for accurate encoding of spine motion. Inaccurate "feedback" from these neurons may result in altered coordinated muscle control of the vertebra during normal motions, eventually resulting in pain. We have found that joint capsule plane strains provide a reliable code that could be used by proprioceptive neurons to encode spine motion. (NIH)

Angiogenesis Induced by a Biodegradable Microparticle VEGF DNA Delivery System

Prof. Weiliam Chen

Recent in vivo experiments have demonstrated that a biodegradable microparticle formulation intended for prolonged VEGF DNA delivery is capable of inducing angiogenesis in hindlimb muscle 4, 12 and 18 weeks after injection. This sustained DNA delivery system will ensure the continual presence of VEGF to facilitate the maturation of newly formed blood vessels and thus their persistence. The VEGF DNA microparticles will be used to induce angiogenesis in porcine chronic ischemic myocardium. In collaboration with Drs. Fu-Pen Chiang, Irvin Krukenkamp and Adam Saltman, Computer Aided Speckle Interferometry (CASI) and Multi-Channel Electromapping (MCEM) are being used to evaluate the functional recovery of revascularized myocardial tissue after VEGF DNA microparticles injection, and perhaps resolve some of the controversial issues about therapeutic angiogenesis. (NIH)

Flow Induced Cardiovascular Pathologies

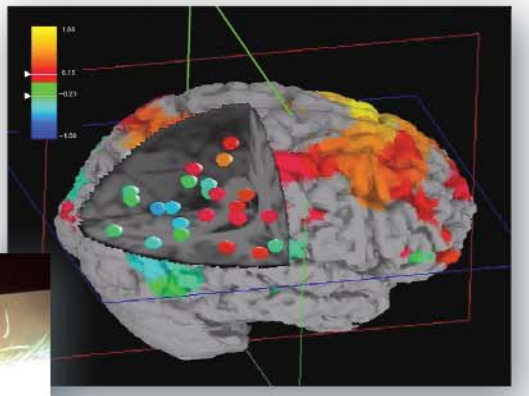
Prof. Danny Bluestein

Despite major progress, cardiovascular diseases remain the leading cause of death in the western world. One of the major culprits in cardiovascular disease and in devices designed to treat or restore impaired cardiovascular function is the non-physiologic flow pattern that enhances the hemostatic response mainly through platelet activation. Platelets have long been regarded as the preeminent cell involved in physiologic hemostasis and pathologic thrombosis. An innovative technique for measuring flow induced platelet activation has been developed, and its utility demonstrated in experiments conducted in recirculation devices (models of arterial stenosis, Left Ventricular Assist Device (LVAD), and mechanical heart valves). The mechanisms by which the non-physiologic flow patterns induce platelet activation and generate free emboli, that enhance the risk of cardioembolic stroke, was demonstrated in vivo with mechanical heart valves implanted in the sheep model. The results of this research will aid in elucidating physical forces that regulate cellular function in flowing blood, and may be applied to improve the design of blood recirculating devices and to develop more potent drugs for treating cardiovascular diseases. (NSF, AHA, FAMRI)

Discovery of Molecular Mechanisms in Chronic Atrial Fibrillation

Prof. Anil Dhundale

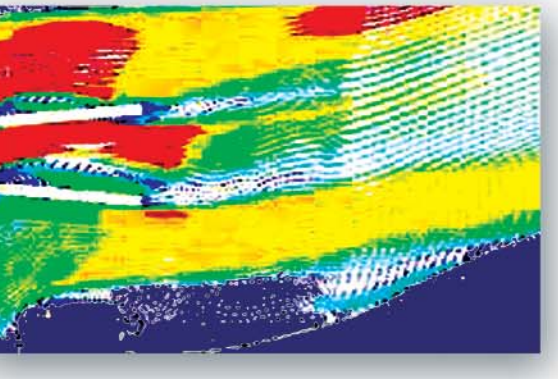
Atrial fibrillation is the most common cardiac arrhythmia seen in cardiology practice today. At Stony Brook University Hospital cardiovascular surgeons perform hundreds of open heart surgery each year as well as investigate vascular disease. A collaboration, between Adam Saltman (Surg), Glenn Gaudette (BME and Surg), Kenny Ye (AMS) and Anil Dhundale (BME and CfB), is exploring the molecular basis of chronic atrial fibrillation utilizing DNA microarray technology. An initial broad survey of 12,265 genes has offered clues to the genes differentially regulated in a disease which affects over 3 million patients in the United States alone. Beyond characterization of this mechanism is the discovery and validation of potential diagnostic and therapeutic gene targets for drug discovery, and the long term goal to identify pharmaceuticals specifically targeted to treatment of this devastating disease. (NIH, NYSTAR)



Nanostructured Materials for Bioseparation, Drug Delivery and Biosensors

Prof. Helmut H. Strey

Nature's ability to assemble simple molecular building blocks into highly ordered materials, such as those found in cell membranes, cell nuclei, cytoskeleton, cartilage, or bone presents many fascinating and unanswered questions. We are interested in how to tune the interactions of water-soluble building blocks so as to induce their self-assembly into useful microstructures much needed for the next generation of controlled drug delivery, biosensors and DNA sequencing applications. In particular, we are working on long-range ordered polyelectrolyte-surfactant microemulsions that are used as templates for solid nanoporous materials using polymerization and/or cross-linking strategies. Such materials, because of their well-ordered porous structure, will allow more efficient molecular separation and drug delivery. In addition, we are developing biosensors that are based on biopolymer chiral liquid crystals and quantum dot colloidal crystals. In both cases the softness of the systems allows the induction of a strong optical response to external stimuli. Such sensors should be able to quantitatively detect and measure analyte concentrations at hormonal levels. (NSF, NIH)



Non-Invasive Diagnostic for Osteoporosis

Prof. Yi-Xian Qin, Ph.D.

Early diagnostic of osteoporosis allows for accurate prediction of fracture risk and effective options for early treatment of the bone disease. New ultrasound technology, based on focused transmission and reception of the acoustic signal, has been developed which represents the early stages of development of a unique diagnostic tool for the measure of both bone quantity (density) and quality (strength). These data show a strong correlation between non-invasive ultrasonic prediction and micro-CT determined bone mineral density ($r>0.9$), and significant correlation between ultrasound and bone stiffness ($r>0.8$). Ease of use, the non-invasive, non-radiation based signal, and the accuracy of the device, this opens an entirely new avenue for the early diagnosis of metabolic bone diseases. (NIH, NSBRI, USAMRC, Whitaker)

Molecular Mechanisms of Bone Regeneration

Prof. Michael Hadjiargyrou

To identify the vast array of genes involved in the bone regeneration process (i.e. fracture healing), we constructed a PCR-select cDNA library consisting of induced clones pooled from RNA isolated from the fracture calluses at day 3, 5, 7, and 10, and subtracted against RNA derived from an intact, control bone (includes cartilage and bone marrow). Subsequently we have sequenced ~5,000 cDNA clones and examined their identities via bioinformatic analyses. Further, bioinformatic analyses are being carried out to determine the expression levels of each gene during the progression of the healing callus, as well as to functionally cluster the thousands of novel genes identified. This knowledge will facilitate a greater understanding in our ability to elucidate the process of bone development and regeneration and identify ideal gene candidates for possible therapeutic intervention. (NASA, NIH)

Engineering a Smart Matrix for the Enhancement of Wound Healing in the Skin

Prof. Richard A.F. Clark

We focuse on constructing 3-D complex extracellular matrices (ECM) that simulate normal soft tissue ECM and corrupt ECM as found in chronic wounds, diabetes and the elderly, and that are engineered for tissue repair and regeneration or for tissue augmentation. The ECM constructs are analyzed for their physical, chemical and immunologic properties by such modalities as goniometry for hydrophilicity, static and dynamic stress and strain for viscolastic material properties, atomic force microscopy for Young's elastic moduli and surface topography; HPLC, mass spectroscopy, gel permeation chromatography and gel electrophoresis for chemical analysis; and fluorescence immunoassays for immunologic epitope mapping. In addition, cell interactions with the 3-D ECM constructs are examined at the transcriptional, protein and functional level as judged by real-time PCR, DNA microarray analyses, Western blots, proteomics, quantitative fluorescence microscopy, and cell viability, migration and proliferation assays. Special in vitro systems have been created to quantify sprout angiogenesis, epithelial sheet migration and neurite axon extension. Engineered ECM will also be tested and a variety of animal models and hopefully some construct will enter into clinical trials. This robust array of 3-D ECM constructs and assays thereof, we believe, will provide new insight into connective tissue pathobiology and new therapies for chronic wounds and soft tissue dysfunction. (NIH)

Genetic Variations Determine the Skeleton's Sensitivity to Anabolic Signals

Prof. Stefan Judex

The structure of the adult skeleton is determined, in large part, by its genome. Recent data by Dr. Judex indicate not only a genetic basis for bone architecture, but also that the sensitivity of bone tissue to both anabolic and catabolic stimuli is influenced by subtle genetic variations. Using different strains of mice, this study showed that stimuli which are strongly anabolic in the skeletal tissue of one cohort, failed to initiate a response in other strains. Similarly, signals which stimulated resorption of bone from one strain failed to initiative a response in other strains of mice. Extrapolated to humans, these results may in part explain why prophylaxes for osteoporosis are not universally effective, yet also indicate that there may be a genotypic indication of people who are at reduced risk of suffering from the disease. (NSF, NSBRI, Whitaker)

Regional Mechanical Function in the Ischemic Heart

Prof. Glenn R. Gaudette

Coronary artery disease generally leads to regional ischemia (no nutritive supply), resulting in a decrease in regional mechanical function. Currently, available techniques do not offer the high spatial resolution needed to determine the heterogeneous mechanical function of the heart. A method has been developed to determine regional function in the heart. This method is a whole field technique that offers high spatial resolution and is used to investigate the effects of regional ischemia on heart function. Various strategies used in the operating room to protect the heart undergoing cardiac surgery are also being investigated. This includes determining the restoration of mechanical function by angiogenesis, a process that involves new blood vessel formation. (NYSTAR, NIH)

Flow Patterns and Flow Coordination in the Microcirculation

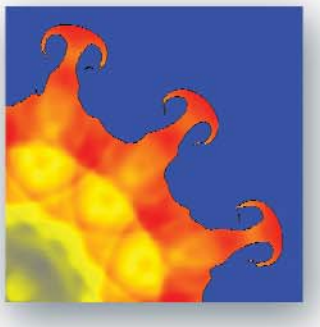
Prof. Mary D. (Molly) Frame

Our emerging understanding of oxygen delivery to the tissues is that the blood flow within the smallest arterioles is tightly organized within repeating networks across the tissue. Central to this emerging paradigm are the concepts of vascular communication between the beginning and end of the network (via gap junctions), and its relation to flow sensing by the vascular endothelium. Different types of microvascular flow patterns can be triggered by direct stimulation of the focal adhesions (alpha-v-beta-3 integrins, i.e., wound healing), compared to adenosine (i.e., metabolic change), compared to nitric oxide (i.e., inflammation), hence we can control the flow patterns. Goals of this work are in vitro construction of transplantable microvascular networks, using bionanotechnology to create the sturdy scaffolding, and verification of nanofabricated drug delivery units within the vasculature. Equally important are mechanotransducti on of the physical forces associated with flow change (i.e., wall shear stress), the pharmacologic signal transduction systems involved, and the molecular basis for the committed step that ensures healthy flow delivery. Our work employs computational modeling of the fluid mechanics, the physiology of arteriolar network blood flow (in vivo and in vitro), and precise genomic manipulation of key proteins in healthy and vascular disease states. (NIH, AHA, Whitaker)

Early Detection of At-Risk Patients for Sudden Cardiac Arrest

Prof. Ki Chon

The cardiac autonomic nervous system is responsible for maintaining proper homeostasis, or balance, of the cardiovascular system. One of our major areas of research is to detect, quantify, and interpret differences in dynamic characteristics of the cardiac autonomic nervous system between normal and diseased subjects, in an attempt to find a marker for increased risk of sudden cardiac death. Identifying and quantifying differences in the dynamic characteristics of autonomic function between normal and diseased conditions may lead to a better understanding of the role of autonomic function imbalance in diseased conditions, and should have important clinical diagnostic and prognostic applications. Another active research area is the development of computational modeling approaches to understand differences in dynamics of renal autoregulatory mechanisms between normotensive and hypertensive conditions. For both areas of research, we are developing novel linear and nonlinear signal processing techniques that can be successfully applied to achieve the research objectives. (NIH)



A Cell & Tissue Structure and Function as Defined by Laser Scanning Endoscopy (LSE)

Prof. Yingtian Pan

2D and 3D cross-sectional optical imaging of biological tissue at close to cellular resolution (e.g., 10um) and at depths of 1-3mm can have significant impacts on noninvasive or minimally invasive clinical diagnosis of tissue abnormalities, e.g., tumorigenesis. Laser scanning endoscopes, based on optical coherence tomography (OCT), have been developed and tested on a wide variety of tissues both *ex* and *in vivo*. Results based on animal and human studies show that LSE can provide morphological details correlated well with excisional histology, suggesting its potential for optical biopsy or optically guided biopsy to reduced negative biopsies in clinical practice. Research is focused on early-stage epithelial cancer detection, diagnosis of cartilage injury and healing, and assessment of engineering tissue growth. In addition, studies of skin dehydration, geriatric incontinence and laser/biochemical attack to the eye using OCT and light microscopy. (NIH, Whitaker)

Prevention of Osteoporosis by Low-level Mechanical Stimuli

Prof. Clinton Rubin

Results show that the application of extremely low level strains to animals and humans will increase bone formation, and thus may represent the much sought after "anabolic" stimulus in bone. More than 15 years of research into non-invasive, non-pharmacological intervention to control osteoporosis, was referenced in Dr. Rubin's recent paper published in the journal *Nature* (August 9, 2001; 412:603-604). Dr. Rubin's studies suggest that gentle vibrations on a regular basis will help strengthen the bones in osteoporosis sufferers and increase bone formation. (NIH, NSBRI, NASA, NYSTAR, Whitaker)

Complex Systems Analysis of Emotion and Cognition for the Study of Mental Illness

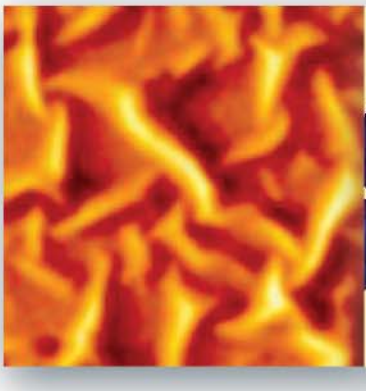
Prof. Lilianne R Mujica-Parodi

Dysregulation of the neural limbic system, associated with modulation of autonomic arousal and emotion, is thought to play a key role in schizophrenia, bipolar disorder to anxiety disorders. However, effective testing of these models in patients is limited by the challenge of developing a biosystems analysis that can successfully integrate causes and effects across many different biological systems in the human, including neural, autonomic, endocrine, and cognitive. In particular, it is prohibitively complicated to take into account compensatory and feedback mechanisms employing standard mathematical methods of data analysis. Our laboratory, in collaboration with Dr. Charles Peskin at the NYU Courant Institute of Mathematical Sciences and Dr. Bruce McEwen at the Laboratory for Neuroendocrinology of Rockefeller University, has been developing a complex systems approach to limbic regulation that will integrate the neural, autonomic, endocrine, and cognitive components of l imbic regulation. This work uses algebraic iterative data-fitting techniques to describe and simulate relationships between all four components, including the effects of perturbation to one or more components. Separate projects apply this research to both a healthy population as well as to patients with schizophrenia and panic disorder, modeling the contribution of each component in the developing symptomology of the disease. As part of these projects, our lab also aims to develop improved methodologies in the areas of functional MRI imaging of the limbic structures as well as nonlinear complexity analysis of heart-rate variability. (NIH)

Ca2+ Sensing and Cardiac Arrhythmogenesis

Prof. Emilia Entcheva

Calmodulin is a ubiquitous cytosolic protein in the heart, sensing and mediating Ca2+ dependent processes. Using a model system of cardiac cell networks and adenoviral constructs (supplied by Dr. Yue @ Johns Hopkins), Dr. Entcheva has optically mapped electrical activity in the conditions of normal and mutated calmodulin. A dramatic action potential prolongation was observed when mutation occurred at the C-terminus. Differential effects on the propagation velocity and on the patterns of reentrant activity were observed with different calmodulin mutants. These preliminary results suggest a much more profound role than previously perceived (and predicted by computer models) for the calmodulin-mediated Ca2+-dependent ionic processes. This work potentiates several interesting possibilities for the involvement of calmodulin in the intercellular communication in the heart, and may lead to unique diagnostics and/or therapeutics for early stage cardiovascular disease. Such studies are instrumental in our understanding and possible treatment of arrhythmias. (AHA, Whitaker Foundation)



Computer Science

Visualization/Massive: Multiresolution, Adapative, Subdivision Surfaces for Interactive Visualization and Exploration

Prof. Hong Qin

This research initiative aims to develop new theoretic, algorithmic, computational, and software techniques within the mathematically rich and broadly applicable deformable models paradigm, with an ambitious goal to further revolutionize deformable models and promote them as a valuable visualization and exploration tool. The outcome of this project is of direct benefit to bio-medical image analysis and processing. (NSF)

Point Based & Image Based Volmetric Rendering & Detail Modelling for Volume Graphics

Prof. Klaus Mueller

Texture Synthesis to Extend the Visual Realism of Medical Surgical Simualtors Volume data obtained with MRI and CT scanners only provide limited tissue detail. Histological slides, micro-CT, and confocal microscopy can provide the missing detail, but these data are usually only available for small tissue samples. Our texture synthesis techniques will be able to use all the available data to synthesize a patient for virtual medical surgery on the fly. (NSF/Career)

Model Based Design and Verification of Embedded Systems

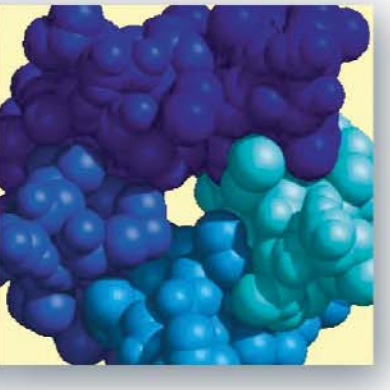
Prof. Radu Grosu

Embedded systems are hybrid digital-analog systems where the digital part monitors and controls the behavior of the analog part. Embedded systems abound in telecommunications, systems biology, aerospace/military, automotive industries, etc. This project investigates efficient model based techniques for the analysis and design of embedded systems. (NSF/Career)

Gene Design and Bioinformatic Approach for Vaccines and Therapeutic Phages

Prof. Steve Skiena

We are investigating algorithms which exploit the redundancy of the genetic code to design safer and more effective therapeutics. The genomic sequence tag (GST) approach, pioneered by my collaborators at Brookhaven, promises to make the analysis of complex microbial communities possible for the first time. We are developing bioinformatics approaches to increase the sensitivity of the technology and extend it to analyze the vast majority of organisms which have not yet been sequenced. There are numerous common viral diseases against which vaccines have not been developed, or for which vaccines can be potentially dangerous (e.g. smallpox). This project studies the potential of improving, or developing novel, therapeutic agents such as vaccines by redesigning genes so they code for identical proteins as in the original agent, but in different ways. Viral strains can be weakened by introducing mutations that alter translational efficiency and RNA secondary structure without affecting protein coding so as to create better vaccine candidates. We will also investigate a proposed class of anti-bacteriological agents, called bacteriophages, seeking to improve their ability to combat pathogenic infections. (NSF/ITR, BNL)



Medical Imaging Diagnostics Technologies: Novel Algorithms and Softare Technologies for Sample-based Graphics

Prof. Arie Kaufman

The major goal of this project is to enhance the commercialization of research, specifically medical imaging diagnostic technologies. The project is focusing on developing novel algorithmic and software technologies for robust, near real-time, 3D computer visualization for diagnostic applications. The specific activities include: centerline generation, volume rendering, interactive navigation measurements, user interface, automatic segmentation, electronic biopsy, computer aided detection, and clinical applications in Virtual AAA (abdominal aortic aneurysm) angiography, calcium scoring, and virtual bronoscopy. We focus on an innovative modeling and rendering primitive, called the O-buffer, for sample-based graphics, such as images, volumes, and points. Another goal is to develop algorithm and tools for 3D navigation and visualizationi for medical imaging applications, and specifically for electronic colon cleansing means and fast navigation technologies for virtual colonscopy. (NSF/CCR, NIH/NCI, NYSTAR)

Imaging the Awake Animal Brain and Functional Neuroimaging

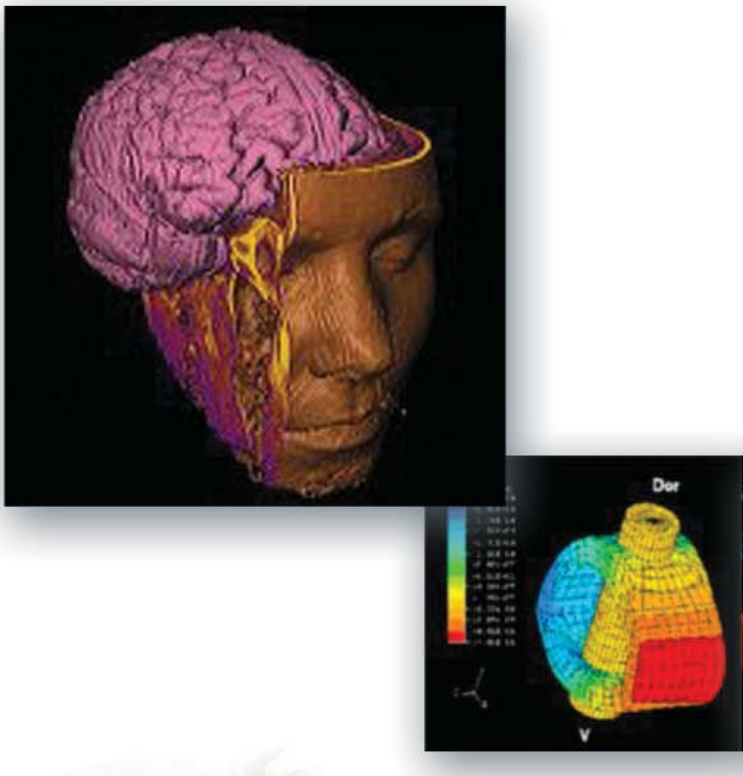
Prof. Dimitrios Samaras

Visual tracking of a small animal inside a PET brain scanner. This will allow the exact position of the animal's brain to be known at all times, as necessary to correct the scanned brain images for animal motion and be able to reconstruct brain activity. Functional Neuroimaging of three dimensional volumetric brain images acquired by the 4 Tesla magnetic resonance image scanner at BNL, using Statistical Parametric Mapping. Investigation of machine learning of fMRI responses. (BNL)

A System for Discovering Bioengineered Threats by Knowledge Based Driven Mining of Toxin Data

Prof. Michael Kifer

The goal of the project is to establish a Toxin Knowledge Base - a bioinformatics resource focused on molecular information about toxins and other virulence factors that are the natural products of biological and potential biological warfare agents. (ARO/BNL)



Electrical and Computer Engineering

High Throughput Ultra-Sensitive DNA Sequencing Machines

Prof. Vera .B. Gorfinkel

The main goal of the proposed project is to bring our novel DNA sequencing instrument from the research stage via the development stage to the pilot project testing stage. The instrument development will be carried out at Stony Brook, and sequencing technology development will be carried out at Cold Spring Harbor Laboratory (CSHL). (NIH/NCHGR)

Development of 4-Color Automated DNA Sequencing Machine Based on Asynchronous Network Operation

Prof. Serge S. Luryi

The goal is to develop the network structure and the basic modules of an automated sequencer comprising more than 1,000 capillary lanes. (NIH/NCHGR)

Current Bio-related Projects at the Sensor CAT

Charles Fortmann (AMS)

Agent simulation of the cell life cycle

Perena Gouma (MSE)

Selective Electronic Noses for Medical and Homeland Security Applications

Mikhail Gouzman (ECE)

Neurosurgical Image Enhancement System

Novel spectroscopic device for biological research

Miriam Rafailovich (MSE)

Development of a Chip Based System for Rapid Biological Antigen Detection

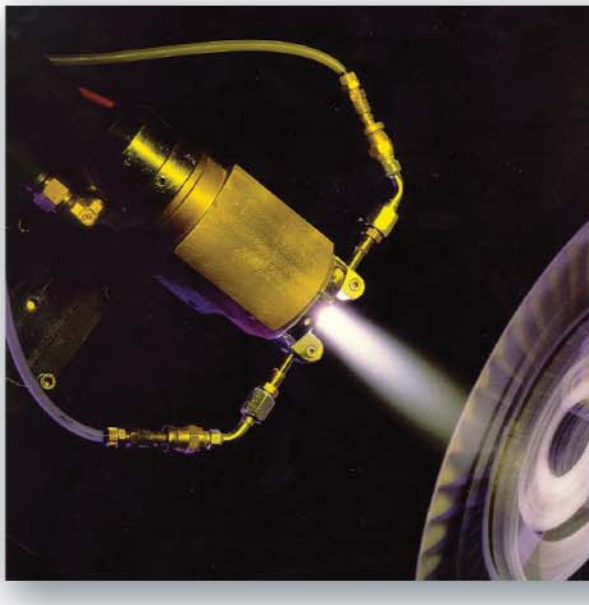
Arthur Suits (Physics)

Imaging Tandem Mass Spectrometry for Biomedical Applications

Wei Zhao (Radiology)

Evaluation of the Imaging Performance of an Amorphous Selenium Flat Panel Detector for Digital Mammography

Large area flat panel digital x-ray imaging device based on the active column sensor concept



Materials Science and Engineering

Protein Self Organization and DNA Electrophoresis on Surfaces

Prof. Miriam Rafailovich

Tissue engineering requires the ability to precisely organize cells and accurately reproduce their natural physical environment. Tissue function depends not only on morphology but also on the conditions in the physical environment. This environment is determined by the structure and composition of the extracellular matrix (ECM), which contains numerous proteins and polysaccharides essential for cell adhesion and motility. The structure of these components is usually known when they are in isolated in solution or in bulk crystalline form. Tissue engineering relies on the ability to adsorb cells to surfaces and hence the structure of ECM proteins adsorbed on these surfaces is more relevant than the bulk structures. One major obstacle is most of the ECM proteins require the presence of the cell membrane in order to self assemble into their natural fibrilar state. This increases the complexity of the system, which makes it very difficult to isolate individual factors that would allow us to make quantitative models of the protein surface self-assembly process. Structures of the ECM have not been previously reproduced in vitro. Spontaneous fibrillogenesis of several proteins can be induced on surfaces if they are coated with polyelectrolyte polymers such as sulfonated polystyrene. Once the proteins formed fibrils, they self-assembled into a regular periodic network comprised of ordered nanoscale substructures. A similar multi-tiered lattice was produced naturally by cardiac fibroblast cells when deposited directly onto the same polytelectrolyte coated surfaces. This observed lattice was similar to the natural structures formed by these proteins when they self assembled in the ECM adjacent to surfaces. These polymer coated surfaces can serve as "laboratories on a chip" to enable us to study the factors involved in assembling proteins from the ECM onto surfaces and the effect of their organization on cell adhesion and DNA separation on nanopatterned surfaces. (NSF)

Physics and Biology: A Materials Science Approach Joint Project with the CNRS

Prof. Andrew Gouldstone

The lung is a vital organ that undergoes high volume changes during breathing. As such strains are part of its function; healthy operation is directly linked to its mechanical behavior. The mechanics of inflation and deflation (i.e. bulk behavior) of the lung have been studied in the physiological and clinical literature. The mechanical behavior of the lung in shear is less well-understood, especially its plastic behavior. This property is ostensibly linked to atelectasis (localized collapse of alveoli) when applied shear strains are sufficient to bring neighboring alveolar surfaces into contact, at which point they are held by surface tension. A quantitative, multi-scale understanding of this phenomenon would be useful for physiological analysis and prediction of chronic and acute breathing disorders, respectively. In addition, a micromechanical understanding of alveolar collapse would likely facilitate the design of safe and conservative ventilation strategies for its reversal. In this investigation, the criteria for plastic deformation in the mammalian lung will be determined, by recourse to instrumented indentation. This project will be led by an engineer and a physiologist; new mechanics principles will be applied to biological materials, but all results will be grounded and guided by an atmosphere of physiologic relevance. (NSF/International)

Selective Electronic Noses for Medical and Homeland Security Applications

Prof. Perena Gouma

This project involves the development of advanced, selective chemosensor arrays for the detection of chemical and biological warfare agents as well as for the fabrication of sensing probes for breath analysis of pathogens. The elements we use are nanocomposite metal oxides and bio-doped materials. (NYSTAR)

Biomaterial High Stress Applications

Prof. Christopher C. Berndt

Biomaterial is a material intended to interface with biological system to evaluate, treat, augment or replace any tissue, organ or function of body. The biomaterial, made of polymer, metal, ceramics or mixture of these, may be used to replace an organ (heart valve or bone), a joint (I.e. a knee, hip or finger), or be used to interact with the body temporarily (contact lens, drug delivery system). Hydroxyapatite (HA) {Ca10(PO4)6(OH2)} and bioactive glasses (P2O5-Na2O-CaO-SiO2) are group of biomaterials used in bone fixation and replacement since the inorganic part of the living bone has the similar chemistry. Unfortunately, neither HA or bioactive glass has the mechanical properties that are required for high stress applications. However, when they are coated on a materials with good mechanical properties such as titanium and its alloys, HA or bioactive glass coatings provide bonding with living bone in the body environment in very short period of time. In the current study, air plasma sprayed HA and bioactive glass coatings are examined to develop and understand the potential for new biological applications. (NIST)

Mechanical Engineering

High-Speed, Full 360 Degree, 3-D Imaging Technique for Applications in Anthropometry

Prof. Peisen Huang

Anthropometry, as the science of measuring the human body, has numerous applications in biomedical research and clinical practices. For example, by measuring the 3-D shape of breasts and identifying their asymmetries in volume distribution, it is possible to detect breast cancer in its early stage. Traditional techniques for anthropometry include contact, laser scanning, stereophotogrammetry, and moiré contouring. While these techniques vary in measurement speed and resolution, none of them is fast enough to measure 3-D shapes of living objects, such as beating heart and breathing thorax, with high accuracy. Our long-term goal is to develop a novel high-speed 3-D imaging technique that will fill this gap. The specific aims of the proposed research are:

1. Develop a high-speed 3-D imaging system based on a digital fringe projection technique.
2. Develop a high-speed, full 360º, 3-D imaging system using multiple projectors and cameras.
3. Apply the developed high-speed 3-D imaging systems to lung function study.

First, the basic technique of high-speed 3-D imaging based on digital fringe projection will be developed. Fringe patterns will be digitally created by software and projected to the object by a digital projection system. Phase shifting will be implemented digitally by software to significantly improve measurement resolution. High-speed imaging will be realized through rapid phase shifting of the fringe patterns and synchronized fringe projection and image capture. Once the basic technique is developed, it will then be extended to full 360º 3-D imaging by using four digital projectors and four CCD cameras. Parallel fringe projection, image capture, and image processing will be used to maintain the high-speed capability of the system. Issues such as how to connect the four surface patches together to form a continuous 3-D surface contour will be addressed. Finally, the developed system will be applied to lung function study. Both normal healthy subjects and patients with lung disease will be imaged. The effectiveness of lung volume reduction surgery (LVRS) will be evaluated. The technique developed in this research should have numerous other medical as well as engineering applications. (NIH)

Magnetosome Detection for RAMBS: Remotely Addressable Magnetics-Based Biochemical Sensors"

Prof. Jon Longtin

We propose to study magneto-optical and magnetic sensors for the detection of magnetosomes in magnetotactic bacteria. The sensor system will be comprised of magnetic field coils, magnetic filtering for concentrating the bacteria, sensors and associated optics and electronics. Two distinct measurement techniques will be investigated during the course of this project, with the main emphasis on the first, the magneto-optical Faraday Effect. The second will focus on optical attenuation of laser light passing through the bacteria, though very strong scattering may render this approach unsuitable.

Assessing Regional Heart Function Using FAST

Prof. Fu-Pen Chiang

It is proposed to integrate the speckle technique and the fringe projection technique developed by the PI to assess the regional function of the heart by measuring its regional deformation. (NIH)

CSF Pulsatile Dynamics

Prof. Lili Zheng

Hydrocephalus, commonly found among infants and children, is a serious neurological disorder in which CSF accumulates around the brain. The accumulation of CSF is a direct result from the rate of CSF drainage being less than the rate of producion of CSF. The ventricles, which are the center for CSF production, enlarge as a result of the excess fluid and put pressure on the surrounding tissue. This increase in pressure around the brain is life threatening. The treatment of Hydrocephalus is to drain CSF from the ventricle using a device called a shunt. This treatment is based on the understanding of the CSF dynamics - volume pressure relationship. Recent MRI revealed that CSF exhibits pulsatile features. Based on this observation, we have developed a new model that simulates CSF pulsatile dynamics and helped explain many hydrocephalus disease related phenomena, which cannot be explained using traditional models. The advanced understanding of the CSF pulsatile dynamics has provided new basis for hydrocephalus treatment that has been proved to be effective. This work has been published in *Pediatric Neurosurgery* to reveal new understanding in pulsatile dynamics of cerebral spinal fluid. It is expected that advanced understanding of the CSF dynamics might also lead towards better treatment of other CSF related diseases. (Dana Foundation and Homer Holland Brain Child Foundation)