Department of Biomedical Engineering

Stony Brook University

BME Biomedical Engineering @ Stony Brook

Research Labs in the Department of Biomedical Engineering

Development and Practical Application of Synthetic Gene Circuits
Gábor Balázsi, Ph.D., Henry Laufer Associate Professor

The goal of my laboratory is to develop synthetic gene circuits (small constructs built from genes and their regulatory regions), and use them for biological discovery and practical applications (such as therapeutic gene expression control). For example, using synthetic gene circuits in yeast cells, we could demonstrate that noise (nongenetic cellular diversity) can aid microbial survival during antibiotic treatment and thereby enable the development of drug resistance. We have designed "linearizer" gene circuits in yeast cells that can tune a protein's level precisely, such that the protein concentration is proportional to an extracellular inducer and uniform within a cell population. We have moved this synthetic gene circuit into mammalian cells and can now tune the expression of a cancer-related genes precisely, to investigate how the level of tumor progression-related proteins affects invasion, migration and other metastasis-related cell behaviors. In the future, similar gene circuits may enable novel approaches to gene therapy. Our research is inherently interdisciplinary, since we use mathematical and computational models in combination with single-cell level measurements to characterize the dynamics of synthetic and natural gene networks, and to understand the cellular and multicellular behaviors they confer.

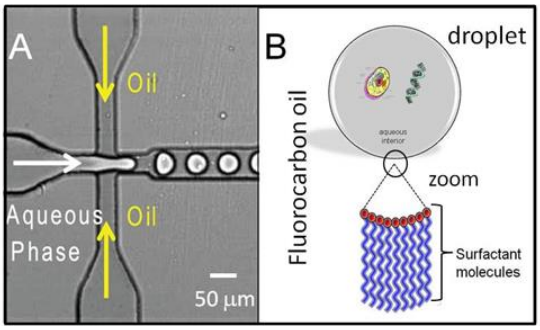
Flow Induced Cardiovascular Pathologies and Optimizing Mechanical Circulatory Support (MCS) Devices
Danny Bluestein, Ph.D., Professor

Prof. Danny Bluestein is a recognized leader in the study of cardiovascular biomechanics, thrombosis, and the thrombogenicity of blood recirculating devices. His research interests include the elucidation of physical forces that regulate cellular function in flowing blood and play a role in cardiovascular disease processes, and translation of this knowledge by using numerical and experimental strategies for: optimizing the performance of blood recirculating devices such as ventricular assist devices and the total artificial heart, enhancing clinical diagnostics of cardiovascular diseases such as calcific aortic disease, aneurysms and vulnerable plaques for improving implantation techniques and clinical outcomes by using patient specific numerical simulations, and developing multiscale modeling and experimental approaches and techniques to describe blood clotting and thrombosis. Students who are interested in cardiovascular biomechanics, in vitro experimental techniques and advanced numerical simulations are welcome to apply.

Graduate student applications are due Jan. 15th, 2016 (https://www.grad.stonybrook.edu/)

Microfluidics for Quantitative and Genomic Biology

Eric Brouzes, Ph.D., Assistant Professor



Our goal is to better describe and understand the role of tissue heterogeneity in normal tissues and in the onset and development of diseases like cancer. Most tissues are comprised of a complex mixture of different cell types, and even cells within a clonal population exhibit a high degree of heterogeneity. However, the detailed behavior of individual cells is obscured in typical measurements which are averaged over cell populations. As a result, it has been difficult to comprehend the functional relevance of this heterogeneity due to the lack of adequate techniques. In order to enable the analysis of tissue heterogeneity we are developing an experimental approach based on droplet microfluidics that allows the manipulation of single cells by suspending them in drops carried in an inert fluid. These drops can then be automatically combined with reaction solutions, interrogated with fluorescent dyes or sorted to carry out sample preparation and analysis. We are combining droplet microfluidics and state-of-the-art molecular techniques like next-generation sequencing to conduct the genomic profiling of tissues at single-cell resolution. This multidisciplinary project will have a direct impact on the basic science of cancer, and at the clinical level by improving the way cancer progression is assessed and monitored.

Engineering New Treatments for Disease and Injury by Regulating Fate of Bone Marrow Stem Cells

M. Ete Chan, Ph.D., Research Assistant Professor

The research in our laboratory focuses on bone adaptation, mechanotransduction and osteoimmunology in normal and pathological conditions including obesity. Obesity is a disease that, affecting people of all ages, increases the risk of type 2 diabetes (T2D) and bone fracture. With a particular focus on the bone marrow stem cell environment, we utilize a murine model of diet-induced obesity to study how obesity affects bone quality and quantity, as well as the immune system. This study provides insights into the relationship between an increasing adipose burden and dysfunctional changes in bone marrow stem cell populations, immune cells and overall health (*e.g.,* glucose intolerance in T2D) during obesity. Further, we explore the potential of a non-invasive, non-drug treatment, using mechanical signals as a surrogate of exercise, to mitigate these adverse effects by normalizing hematopoietic stem cell differentiation pathways and modulating the mesenchymal stem cell population. Our long-term goal is to understand the underlying mechanism of how stem cells directly or indirectly sense mechanical stimuli, and communicate these signals with neighboring cells in the same niche, which eventually influence the bone and immune health of an individual.

Engineering Smart Molecules & Matrix that Stimulate Soft Tissue Repair and Regeneration

Richard A.F. Clark, M.D., Professor

Our laboratory focuses on the design and development of bioactive peptides and 3-D complex extracellular matrices (ECM) that will enhance soft tissue repair and regeneration. Peptides are assayed for biologic activity in vitro and in vivo for their ability to protect tissue cells and organs from injury, stimulate tissue cell migration and proliferation, and modulate stem cell and tissue cell differentiation. The ECM constructs tethered with bioactive peptides are analyzed for their physical, chemical and immunologic properties by such modalities as goniometry for hydrophilicity, static and dynamic stress and strain for viscoelastic 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. Bioactive peptides and engineered ECM containing peptide biomimetics will also be tested in a variety of animal models before entering into clinical trials. This array of bioactive peptides and 3-D ECM constructs will provide new therapies for soft tissue injury and disease.

Optical Imaging for Physiological and Pharmacological Phenotyping
Congwu Du, Ph.D., Professor

The broad goal of this laboratory is to develop advanced optical instrumentation to detect and characterize the physiological processes in the living biological systems such as brain and heart. More specifically, cutting-edge optical spectroscopy and imaging techniques are developed that permit simultaneous detection of cerebral blood flow, blood volume and tissue oxygenation, as well as intracellular calcium *in vivo*. We are interested in studying drug-induced abnormalities of the brain function. Cocaine is chosen as one of the preliminary drugs for our research applications because it affects cerebral hemodynamcs, metabolism, and neuronal activities in the brain. The mechanisms that underlie cocaine's neurotoxic effects are not fully understood, partially due to the technical limitations of current neuroimage techniques to differentiate cerebrovascular from neuronal effects at sufficiently high temporal and spatial resolutions. To solve this problem, we have developed a multimodal imaging platform that combines multi-wavelength laser speckle imaging, optical coherence tomography, and calcium fluorescence imaging to enable simultaneous detection of cortical hemodynamics, cerebral metabolism, and neuronal activities of animal brain *in vivo*, as well as its integration with microprobes for imaging neuronal function in deep brain regions *in vivo*. Promising results of *in vivo* animal brain functional studies demonstrate the potential of this novel multimodality approach to compliment other neuroimaging modalities (e.g., PET, fMRI) for investigating brain functional changes such as those induced by drugs of abuse.

Hemodynamics and Cellular Engineering
Shmuel Einav, Ph.D., Professor

The primary role of this laboratory is to study basic physiological flow phenomena, both experimentally and numerically, as well as cellular and tissue engineering as applied to the vascular system, and to suggest ways of improving the functioning of cells, tissues and organs in the body. These physiological flows include blood flow in the heart, blood flow in arteries, veins and the microcirculation, air flow in the respiratory airways, and urine flow in the kidney and urethra. This laboratory simulates systems through the use of computers, assisting life scientists to better understand physiological functions without having to rely entirely on living systems as experimental models. The use of mathematical analysis helps minimize animal experimentation. Other projects are the investigation of hemodynamics as a regulator of vascular biology, the mathematical modeling of the dynamic response of mammalian cells, the role of flow and the associated shear stress on vascular endothelial biology, prosthetic circulatory devices and the tissue engineering of blood vessel substitutes. We also evaluate critical conditions that lead to failure of biological organs, such as the heart and the coronary circulation, failure of circulatory prosthetic devices as stents, heart valves and grafts. To facilitate in vitro and in vivo studies, the laboratory develops new investigative techniques, noninvasive diagnostic methods, and advance, multi-dimensional numerical modeling.

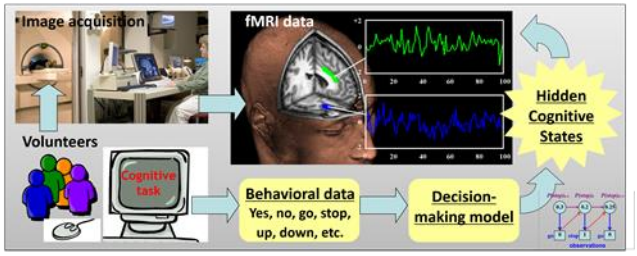
Flow Patterns and Flow Coordination in the Microcirculation.

Mary D. (Molly) Frame, Ph.D., Associate Professor, Vice-Chair, Director of the Undergraduate Program

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 new 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 (flow mediated dilation). In the normal resting state, flow distribution into successive branches along a central feed occurs with most flow (red blood cells, RBC) going to the first branch and successively less for sequential branch arterioles. This RBC distribution is linked to the total area of tissue fed by downstream capillaries, and ensures a uniform oxygen delivery. In inflammatory states, the flow distribution is significantly altered; RBC are shunted through the central feed with most flow going to the furthest most branch downstream. Oxygen delivery is not uniform. Further, both gap junctional activity and flow sensing are impaired. This occurs in a wide range of inflammatory states that includes: diabetes, obesity, pharmacologically induced inflammatory states, and inflammation that accompanies thermal wounds. Ongoing work targets the molecular basis for these abrupt and significant changes in flow distribution. The arterioles at this level are ~2 times the diameter of the RBC – hence they are large particles relative to the size of the tube in which they travel (the arteriole). The 3-D architecture of the arteriolar branch point affects how easily the RBC passes to that branch. Additionally, at this level the flow itself is viscous driven, with a low inertial component (Re <1). The independent impact of the flow properties and the particle:tube dimensions is studied in vitro in microchannels, where the relevant rheological factors can be scaled and controlled. 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.

Integration of Functional Connectivity, Model-based Neuroimaging, and Control-system Engineering Applied to Neural Circuits

Jaime S. Ide, Ph.D., Research Assistant Professor



Broadly, our research is focused on the application of machine learning and pattern recognition techniques in neuroimaging, functional connectivity of the brain, and computational modeling of decision-making. Our current goals are twofold. 1) Integration of functional connectivity, and model-based neuroimaging. Although many advances have been made in functional connectivity analysis and model-based fMRI separately, little has been done to integrate both into a single framework. Therefore, we aim to characterize the brain functional connectivity by employing latent variables that are dynamically estimated using probabilistic graphical models such as Bayesian networks, and hidden Markov models. 2) Control-system engineering applied to neural circuits. Most of the investigations of the brain's connectivity have focused on some sort of correlation analysis, which only describe brain interactions in a static manner. Therefore, we still lack an understanding of the rich dynamics behind interacting brain regions. We are using tools from control theory to model and predict the dynamics of human brain activity. The successful application of Bayesian modeling, and control techniques in brain connectivity analysis will open up a large venue of research in clinical applications, and make available useful tools for neuroscientists.

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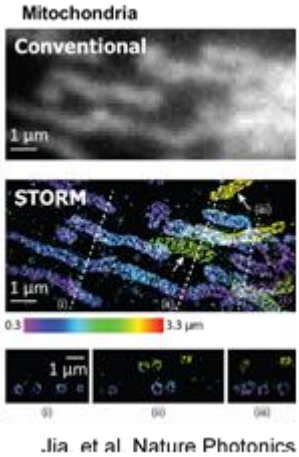
Optical Bioimaging at the Nano Scale

Shu Jia, Ph.D., Assistant Professor



Super-resolution fluorescence imaging techniques have overcome the optical diffraction limit (~λ/2) of conventional fluorescence microscopy, allowing visualization of biological structures and processes with near-molecular-scale resolution. In recent years, these emerging techniques have significantly empowered studies in molecular, cellular and neurobiology. However, the complexity of biological systems ranges from small structures organized at molecular precision to large volumes of connected networks extending across multi-cellular organisms. This poses a strong desire for imaging systems that possess spatial resolution at the sub-cellular or molecular level, temporal resolution that captures rapid bio-dynamics, and imaging depth that penetrates deep tissues. To address these challenges, the Jia Laboratory works on the forefront of super-resolution optical microscopy, developing and applying advanced biophotonic tools to study complex, dynamic biological systems at the nanometer scale. Specifically, our research aims to develop a host of methods that enable the extraction of structural, molecular and functional information from intact tissues and organisms, including optical wavefront engineering, single-molecule biophysics, adaptive optics, light-sheet microscopy, large-data processing, advanced instrumentation, nano-fabrication, etc. These projects employ interdisciplinary knowledge across physics, engineering and biomedicine. In collaboration with researchers at Stony Brook University and elsewhere, we hope our technologies would provide new insights and solutions to challenges in biological and ultimately clinical research.

Regulation of Musculoskeletal Quantity and Quality

Stefan Judex, Ph.D., Professor

Research in the Integrative Skeletal Adaptation and Genetics Laboratory focuses on the identification of precise parameters that define skeletal tissue quantity and quality and their perturbation to applied physical stimuli. To this end, state of the art imaging techniques (e.g., microCT or synchrotron infrared spectroscopy) are combined with molecular (e.g., RT-PCR), genetic (e.g., QTL), and engineering techniques (e.g., finite element modeling) to determine genes, molecules, forces, as well as chemical and structural matrix properties. An example for a recent study includes the demonstration that extremely small amplitude oscillatory motions (~ 100μm), inducing negligible deformation in the matrix, can serve as an anabolic stimulus to osteoblasts in vivo, producing a structure that is mechanical stronger and more efficient to withstand forces. Recent results also indicate that there is 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. The identification of the specific chromosomal regions that modulate this differential sensitivity is in progress. Clinically, our studies may lead to the development of effective diagnostics, prophylaxes and interventions for osteoporosis, without side-effects and tailored towards the genetic make-up of an individual.

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Virtual Instrumentation Technology in Biomedical Engineering

Wei Lin, Ph.D., Research Associate Professor

Our research focuses are on the applications of embedded system in wireless medical devices and the high performance computing (HPC) in biological data analysis. Embedded system is the core of wearable wireless healthcare technology and capable of collecting, preprocessing and real time streaming of biomedical signals. Our work is on the development of the architecture of wireless module that takes the advantage of the ubiquitous Wi-Fi network and the wireless sensor network technology using IEEE 801.15.4 standard. The wireless module and its interface with the interface to the electronic health records (HER) system can significantly change the current healthcare model with broader coverage and less cost. HPC is the solution to dramatically reduce the computation analysis time in processing the huge biological data set generated by the latest diagnostic technologies. Our work is to develop an adaptive computation environment using the Field Programmable Gated Array (FPGA) technology to create solution specific computation models on the chip. This will allow maximal parallel data processing in a pure hardware setting and eliminate the unwanted overhead operations by the operating system. This technology can cut processing time by over 95% and has wide applications in areas such as image processing and informatics.

Complex Systems Analysis of Neural Limbic Dysregulation in Schizophrenia.

Lilianne R Mujica-Parodi, Ph.D., Associate Professor

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, and anxiety disorders. However, effective testing of these models in patients is limited by the challenge of developing analytical methods that can successfully integrate causes and effects across neural, autonomic, and endocrine components of the human arousal response. This laboratory uses simultaneous measurements (functional MRI, heart rate variability, electrodermal activity, continuous blood sampling) to quantify the excitatory and inhibitory inter-connections between all three components using system identification techniques adapted from control systems engineering. Validation of this systems approach through testing of normal variability in the healthy population, as well as testing of patients with mental illness, has direct applications for development of prodromal (pre-symptomatic) diagnostic devices and novel pharmaceutical treatments for schizophrenia.

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

Yingtian Pan, PhD, Professor

2D and 3D cross-sectional optical imaging of biological tissue at close to cellular resolution (e.g., 2-10um) 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 endoscopy based on optical coherence tomography (OCT), has been developed and tested on a wide variety of tissues both *ex vivo* and *in vivo*. Encouraging results based on animal and in vivo clinical studies show that LSE can provide morphological details correlated well with excisional histology, suggesting its potential for optical biopsy or optically guided biopsy to enhance clinical diagnoses of epithelial cancers (e.g., bladder cancer). Current research of Dr. Pan's lab is focused on in vivo noninvasive early epithelial cancer detection, diagnosis of skin healing, and noninvasive assessment of engineering tissue growth. In addition, Dr. Pan's lab studies geriatric incontinence, label-free cerebral microvascular hemodynamics, and brain activation and dysfunction.

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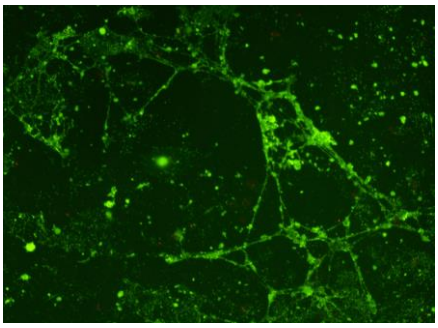
An Ultrasound-based Diagnostic for Osteoporosis.

Yi-Xian Qin, Ph.D., Professor

Early diagnostic of osteoporosis allows for accurate prediction of fracture risk and effective options for early treatment of the bone disease. A new ultrasound technology, based on focused transmission and reception of the acoustic signal, has been developed by Dr. Qin and his team 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 ($r>0.8$). Considering the ease of use, the non-invasive, non-radiation based signal, and the accuracy of the device, this work opens an entirely new avenue for the early diagnosis of metabolic bone diseases.

3D Biomimetic Electrospun Scaffolds for Microvascular Tissue Engineering and Platelet Mediated Cardiovascular Diseases

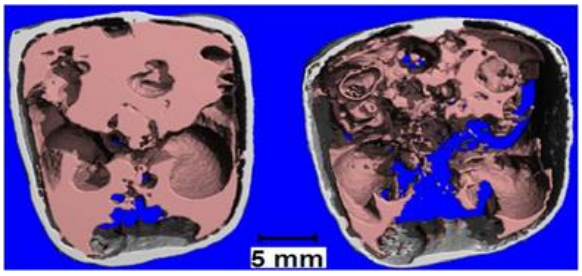
David A. Rubenstein, Ph.D., Associate Professor



Emerging evidence suggests that tissue engineering scaffolds needs to be designed to have topographical, chemical and mechanical properties similar to the innate extracellular matrix. Our lab makes use of electrospinning (single polymer, coaxial, composites and multijet electrospinning) to design scaffolds with specified properties. In particular, we have designed new methods to improve the mechanical strength of electrospun scaffolds, while maintaining biological properties of the scaffolds, which promote endothelial cell growth into tube-like structures. Our current approaches include the use of 3D culture systems, with supporting cells, to accelerate microvascular growth. We have the ability to comprehensively determine the compatibility of novel materials with the vascular system. Cardiovascular diseases remain to lead to the most deaths in the United States. Our belief is that many of these diseases accelerate due to altered platelet-endothelial cell interactions. The success of low dose aspirin as a means to slow the progression of cardiovascular diseases, through reduced platelet functions, is well accepted. Our lab use a combination of in vitro, ex vivo and in vivo techniques to characterize the progression of cardiovascular diseases in response to tobacco smoke, disturbed shear stress, advanced glycation end products (e.g. diabetes) and hyperlipidemia. Our work may be able to identify new therapeutic targets for disease intervention by inhibiting platelet function.

Driving Mesenchymal Stem Cell Fate by Low Intensity Mechanical Signals as a Non-Drug Treatment for Osteoporosis and Obesity

Clinton Rubin, Ph.D., SUNY Distinguished Professor and Chair



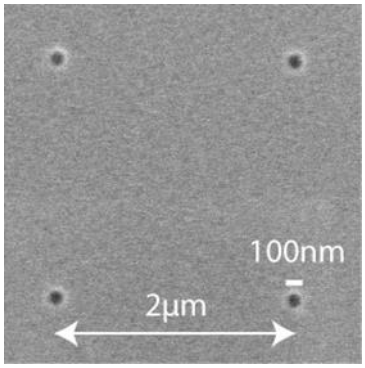
Encouraging results show that the application of extremely low level strains to animals and humans will increase bone formation, and thus may represent the much sought after "anabolic" stimulus in bone. More than 20 years of research into non-invasive, non-pharmacological intervention to control osteoporosis suggest that gentle vibrations on a regular basis will help strengthen the bones in osteoporosis sufferers and increase bone formation. In his study, adult female sheep treated with gentle vibration to their hind legs for 20 minutes daily

showed almost 35% more bone density. Clinical trials have been completed on post-menopausal women, children with cerebral palsy, and young women with osteoporosis, all with encouraging results, including the anabolic nature of the signal to the musculoskeletal *system*, and improvement in posture and balance. In expanding the research platform into other physiologic systems, current work demonstrates that these low-level signals influence mesenchymal stem cell differentiation, such that their path to adipocytes is suppressed, and markedly reduces adipose tissue, providing the foundation for a non-drug strategy for the treatment of obesity and diabetes. These mechanical signals ultimately may represent a means of rescuing both mesenchymal (and their ability to regenerate tissue), and hematopoietic stem cell populations (and their ability to fight disease).

Nanobiosystems for Medical Diagnostics, Therapeutics & Tissue Regeneration
Balaji Sitharaman, Ph.D., Associate Professor

Our laboratory seeks to integrate nanotechnology with the biological sciences and clinical medicine to achieve significant advances in simultaneous molecular diagnostics and therapeutics (theragnosis), drug delivery, and bioengineering. Towards these ends, our research interests involve a multidisciplinary approach for the development of functional (electronic, optical, magnetic, or structural) bionanosystems as contrast agents for molecular imaging, as carriers for drug delivery, and as structural scaffolds for tissue engineering. Our current projects capitalize on the unique properties of carbon nanobiomaterials to develop a) advanced contrast agents (CAs) for molecular magnetic resonance imaging (MRI), b) nanocomposites to improve the physical and biological (osteoconduction and osteoinduction) properties of polymer scaffolds for bone tissue engineering and c) non-viral vectors for gene transfection. We have exploited the potential of Gd-based carbon nanostructures: Gd@C_{60} metallofullerenes (gadofullerenes) and Gd@Ultrashort-tubes (gadonanotubes) as a new generation of advanced CAs for MRI and shown them to have efficacies up to 100 times greater than current clinical CAs. Our recent studies show that they are particularly well suited for passive (magnetic labels for cellular MRI) and active (pH sensitive probes for cancer detection) MRI-based Molecular Imaging. Single-walled carbon nanotubes (SWNTs) have been proposed as the ideal foundation for the next generation of materials due to their excellent mechanical properties. We have dispersed SWNTs and ultra-short SWNTs into fumarate-based polymers to form nanocomposite scaffolds that exhibit mechanical properties far superior to the polymers alone and are osteoconductive as well osteoinductive. Our research work involves material synthesis techniques, physico-chemical characterization techniques, tissue culture and *in vivo* studies.

Nano- and Microtechnologies
Helmut H. Strey, Ph.D., Associate Professor
Director of the Graduate Program



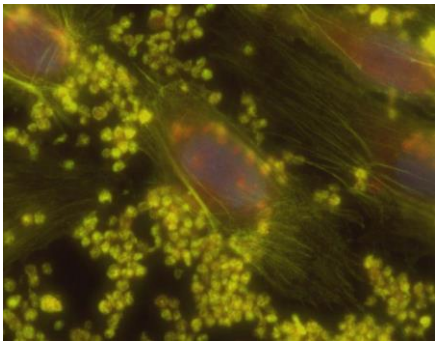
My lab is interested in developing micro- and nano-technologies for quantitative biology. Specifically, we are working on microfluidic chips to capture mRNA from single cells to measure their gene expression profiles. Single cell gene expression analysis is becoming increasingly important as a tool to understand gene regulation, cell differentiation and the development of disease states. For example, in stem-cell research, important questions are: How does cell differentiation alter the gene expression profiles? What is the sequence of gene activations that ultimately leads to a change in cell lineage? Such questions can only be addressed by observing gene expression at the single cell level because of the heterogeneous nature of cell populations. In addition, we are developing nanocavity arrays for high-throughput single-molecule experiments to

study the dynamics of protein-protein interactions. Protein–protein interactions play key roles in many cellular processes and their affinities and specificities are finely tuned to the functions they perform. In recent years, it has become clear that many important biological processes are controlled by protein-protein interaction with weak interactions. In this context intrinsically disordered proteins (IPDs) are especially important since they seem to bind fast, but also dissociate fast, resulting in a large dissociation constant. IDFs are often central in cell signal transduction, transcription and translation and often bind many different binding partners to form large complexes (e.g. p53 interacts with over 100 other proteins). Methods to characterize the formation of such multi-protein complexes are urgently needed because altered binding of IDFs are linked to several human diseases such as cancer (α-Fetoprotein, p53, BRCA-1), neuro-degenerative disorders (α-Synuclein, Amyloid-beta), Cardiovascular Disease (Hirudin), and Type II Diabetes (Amylin).

Advancing Instrumentation for Nuclear Medicine Imaging
Paul Vaska, Ph.D., Professor

Medical imaging techniques have undergone substantial growth in recent years, in both the research and clinical arenas. The standard anatomical imaging modalities of computed tomography (CT) and magnetic resonance imaging (MRI) have been complemented by quantitative functional approaches like positron emission tomography (PET) and single photon emission computed tomography (SPECT). Our lab develops new instrumentation and processing techniques not only to enhance the functional capabilities of PET, but also to combine it with synergistic modalities such as MRI to provide unprecedented, multidimensional information for cancer diagnosis, brain research, and many other applications. We have developed a miniaturized brain scanner for rodents (RatCAP) which avoids the potentially confounding effects of general anesthesia in rat brain studies, and even allows for the simultaneous study of behavior along with neurochemistry by PET. We have also developed new approaches for very high spatial resolution in PET, including a solid-state imager using cadmium zinc telluride (CZT) which achieves sub-mm resolution, and a monolithic scintillator detector with depth-encoding capability via a novel maximum likelihood positioning algorithm. And we have developed multiple imaging systems for simultaneous imaging with PET and high-field MRI, including a rodent brain scanner, a whole-body rodent system, and a prototype clinical breast imager. The research encompasses the development of new detector materials and concepts, low-noise microelectronic signal processing, high-throughput data acquisition methods, Monte Carlo simulation, and new data processing techniques to optimize the extraction of quantitative information from the PET data.

Hemodynamics, Coagulation and Mechanotransduction in Cardiovascular Diseases
Wei Yin, Ph.D., Assistant Professor



Cardiovascular disease is the leading cause of death in the United Sates, and coronary artery disease is the most common type of cardiovascular disease. Shear stress induced by altered blood flow plays an important role in the initiation and development of atherosclerosis, the major reason for coronary artery disease. Circulating platelets and vascular endothelial cells are very sensitive to their mechanical environment; any change can affect their functions and interactions significantly. The major research interest of our group is to investigate how altered blood flow and stress distribution affect platelet and endothelial cell functions and lead to cardiovascular disease initiation. Computational fluid dynamics modeling, along with *in vitro* and *ex vivo* experiments are carried out to study platelet and endothelial cell responses under physiologically relevant dynamic flow conditions. Biomarkers,

mechanotransduction pathways, as well as complement activation associated with platelet and endothelial cell activation are of great interest to us. We also work on computational models to describe platelet coagulation kinetics and platelet adhesion to injured blood vessel wall under dynamic flow conditions.

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