NEW ADVANCES IN SCIENCE AND ENGINEERING

The Bio-X Fellowships are made possible by various gifts in order to promote interdisciplinary research for promising scientists working on projects that bridge the gap between biology and other fields, such as physics, engineering, computer science, and chemistry.

Researchers are encouraged to work collaboratively with professors in different departments or schools, drawing on expertise campus-wide.

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Inhibitors and activators of proteins can be used to uncover how cells work and to develop new drugs and therapies. The focus of my project is to develop and use computational tools to design modulators specific for particular proteins that will then be experimentally tested.

David Camarillo
Mechanical Engineering, Professor K. Salisbury

My research is in the area of biomedical device innovation, specializing in robotically enhanced surgery. Presently, I am developing technologies for flexible robotic manipulators. These instruments can be tele-operated by a physician or autonomously controlled. My focus is to improve the controllability of such instruments by creating novel algorithms that rely upon solid mechanics models as well as multiple sensory inputs.

Andy Loening
Bioengineering, Professor S. Gambhir Graduated Spr 2006

I'll be working on developing a new class of probes for in vivo receptor imaging consisting of bioluminescent proteins fused to receptor ligands. Preliminary work has focused on optimizing the bioluminescent proteins for this purpose through rational and random mutagenesis approaches. Work is currently ongoing to develop the ligand/bioluminescent fusion proteins and to validate them both in vitro and in vivo.

Leslie Meltzer
Neuroscience, Bioengineering, Professors T. Palmer and K. Deisseroth

My research explores the wiring of new stem cell-derived neurons into intact circuits, using techniques bridging bioengineering, neurosurgery, and computer science. I will investigate the following critical questions:
1) How are new stem cell-derived neurons wired into the adult mammalian brain?
2) How does wiring of new neurons according to these rules impact memory storage in computational neural networks? and
3) How does wiring of new neurons in this way impact memory storage in behaving animals?
I will be working in Prof. Levitt's group developing a novel computational framework to study large-scale protein movements as they explore their energy landscapes. The method will be applied to proteins under experimental study in Prof. Frydman's lab.

We expect that this interdisciplinary collaboration will be very beneficial to both experimentalists and theoreticians as it will help understand particular protein systems and will provide insight into the general mechanisms by which proteins fold and perform their biological functions.

Mechanotransduction, the process by which cells convert mechanical stimuli into cellular signals, is important in many areas of physiology, medicine, and medical device design. The goal of this project is to study the MEC-4 channel complex that mediates sensory mechanotransduction of touch receptor neurons.

Working with Prof. Goodman, we will combine MEMS and biological techniques to characterize the mechanosensitivity of the ion channel and its influence on the cell structure and mechanical property. A bio-molecular model will be developed to describe the mechanism of MEC-4 channel complex as mechanoreceptor and its critical role in the whole-cell behavior.
My research with the Shenoy group involves the design and implementation of neural prosthetics that patients can use. I will be focusing my efforts on the paradigm of point-to-point movements, such as those done by typing on a keyboard. Specifically, I am developing innovative computational models and algorithms that help elucidate how the brain plans and executes movement. I am concurrently working on improving the electronic infrastructure that can support an extremely fast (i.e., realtime) and accurate ‘virtual keyboard’ that would allow a patient to type by planning movements to desired keys at desired times. Finally, I am collaborating with neurosurgeon Dr. Jaimie Henderson to apply our work to a Parkinson’s Disease patient population. I hope to bring all these avenues together to help create a real, useful prosthetic.

I am developing a next-generation whole-genome alignment pipeline in order to harvest the enormous wealth of genomic data that is becoming available; mainly the 12 Drosophila genomes and the impending 20 mammalian genomes. I will use these alignments to predict putative functional elements based on constraint of evolution. The challenge is not only to identify such elements, but to understand how they act in the context of specific biological systems. I am currently investigating new high-throughput experimental techniques to study predicted elements during development of the Drosophila embryo.

I am interested in understanding how ensembles of neurons collectively encode and transmit information, and how this neural activity underlies complex behavior and cognition. Using a combination of behavioral, physiological and computational approaches, I will explore how the brain computes values, how this computation drives decision making, and the applications of this value assessment in the context of neural prosthetic development.
We are exploring new methods to use nanoscale electronics to direct stem cell differentiation in an effort to better understand and control the spatial and temporal events that occur during differentiation. We are developing an active electronic chip that stores signaling chemicals within nano-reservoirs and releases them when activated with an electronic signal.

This chip will allow us to extend the spatial and temporal control of soluble signals down to an individual cell for unprecedented control over the local cellular environment.

The goal of my project is to examine the dopaminergic neuron associated neural circuitry in fruit fly (Drosophila) models of Parkinson's disease, using a combination of genetics, electrophysiology, behavioral analysis and computational modeling approaches.

Ion atmospheres play an important role in the function and formation of tertiary structure in charged nucleic acids. However, current understanding of electrostatics around nucleic acids is poorly understood. My research is focused on advancing the theory of nucleic acid electrostatics, the creation of computational tools to model these effects, and experimental verification of new theories. Research in this area may lead to new drug designs, molecular sensor designs, and increased knowledge of gene regulation.
Musculoskeletal modeling and simulation tools are powerful resources for both basic research and clinical applications. However, current models incorporate a major simplification by representing muscles as single lines following the effective line of action. In my research I will develop a modeling pipeline that incorporates diffusion tensor magnetic resonance imaging to create three-dimensional finite element models of muscle representing the geometry and architecture of muscle fibers. These models will be used to explore the functional implications of altered muscle architecture and to simulate surgical treatments designed to treat movement abnormalities.

The powerful potential of stem cell therapy motivates a better understanding of the basic mechanisms regulating developmental biology. The role of mechanical and electrical forces in the adult physiology and pathology has been well documented, and I am interested in what clues these phenomena may hold for generating robust, terminally differentiated stem cells. The pluripotent capacity of human embryonic stem cells makes them an attractive source for cell-based myocardial therapy. Specifically, the delivery of cardiac myocytes, which constitute 70-80% of the adult myocardium, may restore tissue viability and function to ischemic tissue damaged by a heart attack. My research is motivated by the limitations of current methods to derive cardiac myocytes from stem cells. The aim is to increase the differentiation yield of cardiac myocytes through electromechanical conditioning and ultimately the in vivo performance of myocardial cell-transplants.

I am researching the application of artificial muscles to robotics and prosthetics through a novel manufacturing method. Electric motors lack many of the dynamic characteristics of biological muscle, limiting their use in biomimetic devices. Electroactive polymer actuators are a promising alternative, with muscle-like performance, light weight, low cost, and silent operation. I am developing methods for fabricating these actuators using shape deposition manufacturing, which allows customized geometries, heterogeneous materials, and embedded components. With the help of Professor Scott Delp, biomechanical modeling and analysis can be applied to these actuators, inspiring the next generation of dynamic, agile machines.
Cartilage is a complex tissue, capable of withstanding large compressive loads during everyday activities. Determining the mechanical properties of articular cartilage is important for understanding how the tissue behaves in vivo, how the tissue properties might change with age, injury, or disease, and also how we might try to replicate the function of cartilage using tissue engineered constructs. The first step of my research is to develop a robust and computationally-efficient method to calculate cartilage material properties using creep or stress-relaxation indentation experiments. The next step is to develop non-invasive methods to determine the cartilage properties using magnetic resonance imaging.
It is increasingly appreciated that protein function is not strictly related to its three-dimensional structure of the folded state, but to its structural dynamics. Conformational changes occur in various biological events: protein folding upon the presence of appropriate ligand, protein–molecule recognition, enzyme catalysis and etc. Noting that these events are critical in maintaining normal metabolism, understanding protein structural motion is important in drug and protein design. However, there is no experimental technique existing that allows us to observe all proteins at atomic level in real time. Although NMR spectroscopy enables the visibility of dynamic properties of proteins, protein size is limited. Much effort has been paid to developing computational methods. But neither the problem is close to solved nor the solutions are accurate enough for practical usage. I would like to study protein structural dynamics using computer science and statistics techniques, starting from short loops, I will begin loop modeling and flexible protein docking.

Bio-X Endowed Graduate Fellowships 2006

Namiko Abe
Paul Berg Biomedical Fellow
Neurosciences
Professor T. Meyer

Although phosphoinositides (PIs) represent a minor fraction of cellular lipids, they are integral components of cell membranes. Recent evidence suggests that PIs have not only a structural role but may also act as important second messengers during membrane trafficking events. My laboratory in collaboration with Tom Wandless’s group has recently developed a chemically-inducible translocation strategy to rapidly synthesize or degrade specific PIs at the plasma membrane. I plan to make improvements upon this chemical strategy while developing new bioengineered probes to manipulate levels of different PIs in specific membrane compartments. I will then use these tools to investigate the role of specific PI species in various steps of receptor-mediated endocytosis as well as the synaptic vesicle cycle.

Bertrand Lui
Lubert Stryer Fellow
Bioengineering
Profs. J.R. Cochran and J.R. Swartz

The goal of my research is to develop a technology platform which combines yeast surface display and cell-free protein synthesis to engineer proteins for enhanced biological efficacy. It will be demonstrated by evolving epidermal growth factor, which plays a role in the healing process and has great therapeutic potential for wound repair and regenerative medicine.

Daniel Kimmel
Affymetrix Fellow
Neurobiology
Prof. B. Newsome

As you read these words, your nervous system is coordinating countless small eye movements to different locations on the page. The problem for your oculomotor system is how to encode this information in an efficient, accurate, and decipherable way. A computer system would encode movement commands as a series of binary numbers, whose meaning is universally interpretable and independent of the rate at which the code is transmitted. The nervous system is distinct in that the neural code is highly sensitive to the timing of information—unlike the Morse code, in which the mere occurrence of a "beep" carries less information than whether the beep was long or short in duration. My research harnesses the oculomotor system to understand the temporal dynamics that encode the planning, selection, and execution of eye movements.
Kelsey Clark  
Neurosciences  
Professor T. Moore

My research focuses on the neural basis of attention, and the relationship between attention and working memory. How are certain regions or objects selected for attention, and how does this selection influence their representation in sensory areas? Which neural circuits and neurotransmitters underlie this attentional modulation of sensory signals? How does attention bias subsequent representation in working memory? To address these questions we are using electrophysiological and pharmacological techniques in a visual working memory paradigm.

Frances Lau  
Electrical Eng.  
Profs. C. Levin & M. Horowitz

I am designing and building an ultra-high resolution Positron Emission Tomography (PET) system dedicated to breast cancer imaging. PET is a non-invasive, in-vivo, molecular imaging technology that has shown promise for early and accurate identification of breast cancer due to its unique ability to visualize increased biochemical changes in malignant tissue well before structural changes occur. My focus is on applying techniques from circuit design and signal integrity to develop data acquisition electronics that read out and process the small signals detected while meeting the demanding data rate and noise requirements.

Jennifer Hicks  
Mech. Engineering  
Professor S. Delp

My primary research focus is applying biomechanical modeling and simulation to study human movement, particularly to improve the treatment of walking abnormalities in children with cerebral palsy. In my graduate work so far, I have developed methods to simulate a common skeletal deformity found in patients with cerebral palsy and the effect of this deformity on muscle function during walking. My current research projects include quantifying the effect of crouched gait postures on the ability of muscles to support the body against gravity and developing statistical learning algorithms to predict treatment outcome in children with movement disorders.

Cory McLean  
Computer Sci.  
Prof. G. Bejerano

Evolution of cis-regulatory elements may drive the majority of anatomical evolution, yet the mechanisms of cis-regulation of gene expression are poorly understood. I have uncovered a number of interesting non-coding genomic regions within vertebrates using the computational tools of high-performance computing, statistics, and natural language processing. I am also investigating roles for machine learning in the discovery of a genomic signature of cis-regulatory elements. Additional transgenic experiments will be performed in collaboration with the Kingsley laboratory.
Rebecca Taylor
Mechanical Engineering
Professors E. Kuhl and B. Pruitt

Rebecca is developing both microfabricated and macro-scale electromechanical systems for both electrical and mechanical stimulation and monitoring of stem cell-based cardiac tissue constructs. Her research aims to utilize these systems for 1) characterization of stem cell differentiation to cardiac myocytes in response to electrical and mechanical stimulation 2) constitutive modeling of coupled electromechanical behavior of cardiac myocytes, and 3) the development of continuum mechanics based predictive models of tissue growth.

Larry Wang
Materials Science & Engineering
Professors S. Heilshorn and A. Spakowitz

The goal of my research project is to understand the structural and behavioral characteristics of quaternary protein structure using the coat-vesicle protein clathrin. This study employs two major approaches in parallel: development of a theoretical model using Brownian dynamics simulation to predict quaternary structure and in vitro self-assembly experiments to observe and control the quaternary structure.

The choice of clathrin as our model protein system stems from its well-studied functional characteristics and biological significance. Clathrin proteins perform their biological functions by self-assembling into cages, and recent reports have begun to elucidate the structure of the individual clathrin molecule and have provided a more detailed static picture of the in vivo assembly. A good understanding of the static elementary structural composition provides an appropriate foundation for looking at the dynamic interactions of clathrin quaternary structure.

Kitchner Wilson
Bioengineering
Professors J. Wu and P. Yock

My research focuses on characterizing human embryonic stem cell differentiation and transplantation, with a specific focus on cardiovascular tissue regeneration. I am using genomic and proteomic methodologies such as DNA microarrays and highly sensitive protein arrays to better understand the regulatory networks that govern stem cell behavior, as well as in vivo molecular imaging techniques to assess their engraftment in mouse models of disease.

Of particular interest is the cardiac stem cell “niche”, or microenvironment within heart tissue, that promotes their regenerative capacity.
It is well documented that bone responds to changes in load with corresponding changes in size and density. My lab believes that Oscillatory Fluid Flow (OFF), generated by pressure gradients in the lacunar canicular network, is a potent physiological signal that is recognized by bone cells as an anabolic stimulus. While it is known that bone cells respond to fluid flow with various intracellular chemical responses, the actual mechanism that transduces the physical extracellular signal to a chemical intracellular one is not yet known.

I am hoping to determine the actual molecules that take part in this conversion from a mechanical signal to a chemical one. My hypothesis is that this mechanotransduction event could be linked to integrins and the phosphorylation of Focal Adhesion Kinase (FAK). FAK is a good candidate for a mechanotransduction molecule in bone cells because it has both structural and enzymatic function and has proved relevant in mechanotransduction in other cell types.

Adam Grossman
Professors T. Sanger, S. Delp and K. Shenoy

Adam will study children with severe movement disorders in order to generate hypotheses as to the biological cause for their disorders. He will collect data from each child—ranging from simple MRI and CT scans to more complex kinesthetic analyses. The data will help shed light on the specific locations in the brain that may be malfunctioning. Using this information, Adam will design further experiments to test these hypotheses and provide insight for better treatments and potential cures for these diseases.

In particular, Adam is interested in determining how and why deep brain stimulation is an effective treatment for some dystonic children and what parameters of the stimulation can be adapted to optimize the benefits of DBS in these children.
Virginia will be working in Dr. Sanger’s group to develop a theoretical model for human motor learning. In particular, she is interested in studying motor learning in children and young adults. Various aspects of motor learning will be explored and will help shed light on the important elements of motor learning. Virginia will also study children with severe movement disorders in order to learn more about the missing pieces that leads to various motor learning deficits. Using this information, she will study “correction” methods to compensate for the missing pieces in light of the model. With a greater understanding of the motor learning deficits, Virginia hopes to develop medical devices and training paradigms to help children with movement disorders learn and further develop their motor skills.

Mindy Chang

Professor T. Moore

I am interested in using signal processing and computational modeling approaches to understand neural circuits. My current project involves population analysis of neurons in the visual cortex that encode color and orientation information. Future research will focus on mechanisms of visual attention in modulating neural representations of sensory input.

Stephen Lee

Professor J.R. Cochran

The Cochran lab uses directed evolution and yeast display to create novel protein mutants for therapeutics in wound healing and cancer applications. Stephen’s current project investigates mutants of human epidermal growth factor (EGF), a protein involved in both of these pathways. In vitro assays are being used to study the migratory and proliferative effects of EGF on murine and human fibroblasts. His goal is to demonstrate an EGF mutant with improved migration and proliferation over wildtype to ultimately test in mice in vivo. Stephen holds a bachelor’s of science degree in biology from MIT.

Prasheel Lillaney

Professor R. Fahrig

Prasheel is a second year graduate student in the BioE department working at the Lucas Center under Dr. Rebecca Fahrig on the XMR project. The goal of the project is to build a hybrid X-Ray/MRI system that will allow Interventional Radiologists more versatility in how they approach various procedures that require MR or X-Ray guidance, while still maintaining the image quality and performance offered by a conventional MRI or X-ray system.

Prasheel is currently working on modeling the electron beam optics in X-ray tubes and determining how the electron beam is affected by the presence of the strong MR fringe field. He also is working on developing different X-ray tube motor designs that would allow for better tube performance in the hybrid system.
Angela Wu

Angela graduated from the University of California, Berkeley with a major in bioengineering with an emphasis in Computational and Biomedical Systems Engineering, and a minor in electrical engineering and computer science. During her undergraduate years, she mostly worked in the Lee BioPOEMS Lab at UC Berkeley, testing and characterizing a BioMEMs microfluidic patch clamp device that was developed by the group. She also spent a summer at the Hong Kong University of Science and Technology.

At Stanford, Angela plans to further her knowledge of bioengineering principles and applications, and she hopes to do her PhD research on microfluidic and bio-electronic devices for medical applications.

Murtaza Mogri

Murtaza graduated with a double major in Bioengineering/Biotechnology and Math/Computer Science from UC San Diego, where he focused on bioinformatics and systems biology. Since he had a budding interest in neuroscience, he spent a year at the NIH studying the mechanism of rhythm generation in the respiratory control system and developing software to analyze neuronal activity. His current research interest is in neuroengineering, specifically the study of neural circuit dynamics using computational and experimental techniques.
Sheng Ding
(1 year award)

Sheng Ding is currently working on enzymatically crosslinked protein polymer hydrogels. She has successfully created a novel family of genetically engineered ‘protein polymers’ that are crosslinked into hydrogels by trasglutaminase enzymes (TGs). Advanced genetic engineering technology will be used to develop protein-based ‘block copolymers’, and thus special blocks of peptide sequences can be incorporated to further modify structures, mechanical properties and bioactivities of the protein hydrogels. This novel kind of hydrogels will have broad applications in tissue engineering, for instance, cell replacement therapies for diabetic patients, regeneration of the central nervous system, etc. Her research will lead to novel biomaterials that are superior to currently available biomaterials, in aspects of biocompatibility, customizable controllable hydrogel architecture, and versatile property manipulation.

Jayodita Sanghvi

As an undergraduate, Jayodita strived to get a broad range of research experiences, which eventually led her to a PhD program in bioengineering. At MIT, Jayodita worked in Prof. William Thilly’s lab for four years where she analyzed Japanese and American pancreatic cancer mortality data to gain an understanding of environmental risk. She also worked in Prof. Robert Langer’s lab for two years trying to develop a universal system for binding proteins to micropatterned hydrogels that could be used for tissue engineering and to improve various experimental techniques. Over summers, she conducted research at various places including, thyroid hormone research at Yale Medical School and tuberculosis research Astra Zeneca in India. Currently, she is doing a summer rotation at Stanford in Prof. Markus Covert’s lab, studying the oscillations of the transcription factor, NF-kB in and out of cells’ nuclei.

Jacob Hughey

While at Vanderbilt, I worked for three years under the guidance of John Wikswo at the Vanderbilt Institute for Integrative Biosystems Research and Education. My research as well as my senior design project centered around helping to develop a microfluidic platform to study T cell signaling pathways. I also spent one summer at Georgia Tech for a nanotechnology REU, working on new techniques for synthesizing core/shell nanoparticles. Last summer I was at the Department of Microsystems Engineering in Freiburg, Germany, where I characterized the performance of pneumatic micro-mirrors and enjoyed the World Cup. At Stanford, I hope to use microfluidics to contribute to our understanding of complex biological systems.

Min-Sun Son

At Washington University, I worked with Dr. Frank Yin on uniaxial stretching of human aortic endothelial cells on a silicon membrane. My main project involved working out a protocol in order to investigate the effects of cyclical stretching in real time on the cell orientation and shape index. I also helped in the research of studying the mechanical and chemical response to stretching of alpha actinin knockout and rescued cells. Through my research and studies as an undergrad, biomechanics has become an area of great interest for me and I would like to continue in this field. However, I would like to expand and also work on the tissue level and the application side of research.
During my undergrad years, I developed computational tools for neuroscience research at Rice University and Baylor College of Medicine. I helped implement an indirect method to deduce the distributions of ion channels based on calcium fluorescence data from neurons in /in vitro /slices. The tools I worked on make this process possible by using simulations involving morphologically realistic neurons.

At Stanford, I hope to partake in the many research opportunities available in biomedical computation.

Tiffany will be designing small molecule probes for in vivo imaging of apoptosis. Because apoptosis takes place through activation of caspases, she will develop a bioluminescence imaging system that can directly image the activation of the caspases in vivo.

This imaging system will allow convenient real-time detection of specific caspase activation during cell apoptosis. This will help our understanding of roles of apoptosis in a myriad of physiological processes and facilitate screening for both anti- and pro-apoptosis agents for therapy.

Sergey’s research will involve the use of single-molecule Fluorescence Resonance Energy Transfer (sm-FRET) to explore the folding dynamics of RNA.

In the Herschlag and Chu labs, Sergey will use synthetic and characterization techniques to determine distance changes between labeled sites on a ribozyme molecule. In addition, simulations of the data will be performed to predict and test folding pathways for mutant ribozymes.
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**Bio-X Program**

To learn more about the Bio-X Program at Stanford, please visit the Bio-X website at:

http://biox.stanford.edu

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Brochure designed and edited by F. Sincock