2018 ICB SABRE Project Descriptions

ICB Systems and Synthetic Biology Projects

Stochastic Biological Oscillators, Circadian Rhythms, and Cognition

Linda R. Petzold, Depts. of Mechanical Engineering and Computer Science

Sleep and wakefulness are fundamental dimensions of neural activity. Their dysregulation has been implicated in numerous diseases, as well as in difficulties in learning and memory formation. Yet, the physiological consequences of fatigue and its effects on cognitive performance are poorly understood. In this project we seek to better understand the neural mechanisms giving rise to wakefulness, and to search for biomarkers to predict fatigue. With this improved understanding, we expect to be able to suggest ways in which the productivity and safety of workers and soldiers might be improved.

Functional magnetic resonance imaging (fMRI) highlights the regions of the brain that are most active, while the subject is performing a given task. In this research project, the student will use machine learning tools and techniques to develop a system to predict what each subject was doing, from their fMRI signal. Scientific American (October 2013) described this as “mindreading.”

Engineering Synthetic Cellulose-degrading Complexes from Gut Fungi in S. cerevisiae

Michelle A. O'Malley, Dept. of Chemical Engineering

Renewable biofuels derived from plant biomass are an attractive alternative to petroleum-based fuels for the US Army. However, problems associated with substrate recalcitrance in the depolymerization of lignocellulose have prohibited biofuel development. In order to realize the potential of cellulosic materials as an energy source, it is necessary to develop new technologies to convert crude sources of cellulose in plant biomass to sugar. To address this issue, much may be learned by studying nature, particularly microbiomes where high efficiency biomass breakdown regularly occurs. For example, anaerobic gut fungi found in the digestive tract of large herbivores are among the most efficient degraders of lignocellulose on earth. This project aims to discover novel cellulose-degrading enzymes from anaerobic gut fungi and to engineer synthetic multi-protein enzyme complexes (cellulosomes) for the conversion of plant biomass into biofuels. The SABRE intern will learn microbiology techniques coupled with biochemistry analysis to screen how these protein complexes interact, and then use these interactions to drive the assembly of synthetic enzyme complexes.

Macromolecular Design from Sequence-Activity Analysis

Irene A. Chen, Dept. of Chemistry & Biochemistry

The overall goal of this synthetic biology project is to improve the design and discovery of functional RNAs and to study the integration of functional RNAs into synthetic cells. RNAs are highly interesting components for synthetic biology, as they possess a broad and expanding palette of known functions. One may envision a synthetic cell in which all metabolism is carried out by a minimal number of RNA components; indeed, such cells are thought to have been an ancient form of life. We study the evolution of functional RNAs during in vitro evolution and their encapsulation into artificial cells.

As a part of the ICB SABRE program, we will analyze the course of an in vitro evolution experiment for protein enzymes, in which a zinc-finger scaffold was lost and a new, non-biological fold emerged. New protein folds discovered during in vitro evolution are likely to be simpler and more evolvable than biological folds, which are the product of billions of years of evolution. Successive generations of the selection will be characterized by high-throughput sequencing combined with bioinformatic analysis. We are particularly interested in understanding how this transition occurred in the protein fold, and in characterizing any additional new folds that were generated.

ICB Bio-inspired Materials Projects

Reflectin-inspired, Lightweight, Tunably Reconfigurable Photonic Materials

Daniel E. Morse, Dept. of Molecular, Cellular & Developmental Biology

We recently discovered the remarkable molecular mechanism that squids use to quickly change color for camouflage and signaling under the sea. The key to this mechanism is the way that the “reflectin” proteins respond to a signal from the brain, changing their structure and configuration to drive rapid changes in the brightness and color of light reflected from subcellular structures in specialized cells in the skin. We now are “translating” this discovery to develop a new class of tunably reconfigurable polymers and lightweight devices that can change their color in response to electrical signals for a wide range of applications.

Building on these findings, we aim to (1) to genetically engineer and biochemically analyze the cloned recombinant reflectin proteins to identify the structural determinants that are minimally required for signal-activated reconfigurability driving the dynamic tunability of photonic behavior; and (2) translate these findings to develop a practical, readily engineered and inexpensive synthetic, tunably reconfigurable material that can used for a wide range of applications requiring lightweight dynamically tunable electro-optical materials. Research will involve the close integration of experimental and quantitative studies.

Understanding the Mechanism of Transmembrane Electron Transfer and its Influence on Intercellular Communication and Biofilm Diversification

Guillermo C. Bazan, Depts. of Chemistry & Biochemistry and Materials

This project concerns how to change the electronic and catalytic properties of microorganisms. Essentially, molecular species have developed that insert into membranes and allow microbes to be efficiently incorporated into bioelectronic devices. One can thereby improve the extraction of energy from wastewater and impact microbial production of commercially relevant metabolites. Depending on the shape of the synthetic molecules, one can find instances where they exhibit antimicrobial properties—an important consideration in view of the emergence of drug-resistant bacteria. For other molecular structures, one finds that membrane modification leads to acceleration of whole-cell catalyzed chemical reactions.

A useful undergraduate research project concerns the synthesis of new COEs using the modular approach already reported by our group. These syntheses are relatively straightforward and would enable education of organic chemistry techniques. Once in hand, the new COEs can be used to modify microorganisms, of which various yeasts are simplest by virtue of their larger size. Intercalation within membranes can be confirmed by using confocal fluorescence microscopy. If time permits, the preparation of microbial fuel cells and the impact of modification by the presence of COEs can also be carried out.

Anisotropic Nanostructured Materials for Electrochemical and Photovoltaic Energy Conversion and Storage
Bradley F. Chmelka (Dept. of Chemical Engineering) and Songi Han (Dept. of Chemistry & Biochemistry)
Novel anisotropic membranes that exhibit high and controllable macroscopic orientational order are being developed with ion-conduction and/or light-harvesting properties that target Army applications in energy generation, efficiency, storage, and management. Using a new approach to processing inorganic-organic hybrid materials, novel functionalized membranes are being fabricated with highly anisotropic properties that are expected to significantly improve ion, electron, and/or reactant transport and, accordingly, the electrochemical or photophysical properties of devices into which they are integrated. Emphasis is on synthesizing, integrating, and optimizing nanostructured PR-functionalized membranes for light-activated ion-conduction in bio-hybrid fuel cells and batteries and developing new composite heterojunction photovoltaic materials.

Nanostructured surfactant-silica materials that incorporate PR guests are promising for macroscopic solar-to-electrochemical energy conversion and storage. A main objective of the ICB SABRE project is to understand the efficiencies and rates at which PR guests in nanostructured silica convert solar energy. As the surfactants strongly interact with PR guests in nanostructured materials, we hypothesize that material compositions (e.g., the types and concentrations of stabilizing surfactants, inorganic frameworks, their surface hydrophobicities, and light-responsive guest species) and material structures (e.g., nanochannel dimensions and periodicity, surface interactions, alignment of the light-responsive guest species, etc.) will influence the solar energy conversion abilities of PR guests. The experimental approach for understanding this includes synthesizing materials with various surfactant compositions and investigating these materials by using time-resolved UV-visible spectroscopy and macroscopic electrochemical tests.

Bio-inspired Photonic Surfaces for Broadband IR Detectors, LEDs, and Lightweight, Flexible Solar Platforms
Michael J. Gordon, Dept. of Chemical Engineering
The goal of our project is to develop an easy, scalable, and defect-tolerant surface coating method that mimics the variable refractive index behavior of the moth-eye to manipulate the optical behavior of surfaces. In addition, we seek to understand how structuring surfaces with sub-wavelength features can be used to control reflection and transmission of visible and infrared light at material interfaces for applications in optics, imaging, photo-detection, and solar energy harvesting.

The ICB SABRE student will assist researchers in the development and characterization of anti-reflective surface coatings that mimic the graded refractive index behavior of the moth eye. In addition, we seek to understand how structuring surfaces with sub-wavelength features can be used to reduce reflection and enhance transmission of infrared and visible light at material interfaces for applications in optics, photo-detection, imaging, and solar energy harvesting.

3D Printing of Bio-enabled, High Performance Hydrogels
Craig J. Hawker, Depts. of Chemistry & Biochemistry and Materials
Following the motto “making more with less,” nature has succeeded in making strong, light and dynamic materials from a very limited set of building blocks. Compared to synthetic materials, these natural building blocks cannot be prepared on industrial scale. We propose to develop synthetic building blocks that are readily available and rival natural systems in their utility for self-organization to build ordered structures in the length scale of nano- and micro-meters. This will enable complex functions, normally only associated with natural systems, to be realized for synthetic systems with building blocks based on commercially available starting materials.

The basis of the ICB SABRE project is to develop new synthetic strategies for discrete polymer building blocks that allow a degree of structural control previously only found in natural systems. Together with the selective introduction of chemical functionalities, the assembly of such well-defined building blocks into ordered supramolecular structures will ultimately lead to the development of advanced bio-inspired materials that have properties that match or exceed those found in nature.

Topology and Shape Optimization of Energy-Dispersive Cellular Structures
Frank W. Zok, Dept. of Materials
Protection of Army personnel against impacts and distributed impulsive loads from blasts in combat environments requires use of lightweight compressible materials that both dissipate energy during crushing and reduce the pressure level of blast waves to non-lethal levels. The goal of the present program is to identify, develop and assess new paradigms in materials and topological designs that offer potential for high-energy absorption and effective pressure attenuation. Emphasis is on bio-inspired periodic lattice concepts.

In this ICB SABRE project, we are pursuing new paradigms in structures and topological designs that offer potential for high-energy absorption and effective pressure attenuation. The work combines fabrication, testing and analytical and numerical modeling.

Field-Assisted 3-Dimensional Printing of Bio-inspired Hierarchical Materials
Matthew R. Begley, Depts. of Mechanical Engineering and Materials
This work will develop 3D-printing technologies for the deposition of two-phase materials consisting of particles (spheres or fibers) in fluid 'inks' with a high degree of control over particle handling both spatially and temporally. The goal is to manufacture composites with structural complexity similar to that of biological materials (such as exoskeletons or wood) that possess intricate microstructures that cannot easily be replicated by traditional manufacturing techniques. Our approach, using acoustically-assisted print nozzles, can achieve print lines with varying composition and microstructure that can be tuned "on the fly" using simple piezoelectric actuators that control particle orientation within the print nozzle.

In the ICB SABRE program, we will develop printing strategies and characterization of ink materials for fiber-based composite printing, with the goal of 3D-printing composite structures with precisely-controlled alignment and local composition. We will investigate the effect of printing parameters (including acoustic excitation conditions), ink composition (including factors to control ink rheology such as filler chemistry and volume fraction), and nozzle geometries, that optimize microstructural control in printed parts.

Theoretical and Experimental Investigations of Energy-Dispersive Cellular Nanostructured Polymeric Materials
Glenn H. Fredrickson, Depts. of Materials and Chemical Engineering
Our project aims to develop new polymer materials with a cellular nanostructure that possess unique combinations of recoverable elasticity, high modulus, high strength and toughness, inspired by the byssal cuticle of the marine mussel. The platform for this work is an unusual block polymer: a "mikto-polymer" produced by coupling homopolymer and diblock copolymer arms into a radial (star-shaped) architecture. The hard-tough-strong-elastic materials we seek are expected to be useful in the fabrication of advanced soldier protection equipment.

The ICB SABRE student will participate in the theoretical component, a project titled "Computational Studies of Cellular Nanostructured Polymers." This project aims to develop a new type of bio-inspired elastic polymer expected to have unusual morphology and mechanical properties that could be transformative in soldier protection systems. Specifically, we seek to identify new types of nonlinear block copolymers ("mikto-polymers") that when blended with other polymers will exhibit an equilibrium nanoscale morphology resembling cells of a foam, but with a hard material inside the cells and a soft material comprising the walls. The intern will assist a graduate student researcher in performing field-theory based simulations to explore the relationship between the molecular parameters of a mikto-polymer blend (compositions, architectures, molecular weights) and its equilibrium morphology. The project will provide experience with state-of- the-art computational methods in polymer science and serve to develop reporting and presentation skills.

ICB Biotechnology Tools Projects

Fundamental Development of Novel Nanomaterials for Biomarker Detection
Sumita Pennathur (Dept. of Mechanical Engineering), Luke Theogarajan (Dept. of Electrical & Computer Engineering) and Carl D. Meinhart (Dept. of Mechanical Engineering)
We aim to develop a painless wearable sensor with individually actuated microcantilever arrays for continual monitoring of soldier interstitial fluid. This will revolutionize solider health and monitoring, and allow for unique, handheld, field-deployable sensors for the Army that can detect a variety of threat agents. We will be collaborating with the Edgewood Chemical and Biological Center (ECBC) for miRNA, protein and bacteria-based sensors to put on the chemical sensor for nove electrochemical detection.

Microtechnology has the potential to revolutionize bioanalytical systems. The ICB SABRE student will be exposed to the potential of MEMS and microfluidic systems and perform fundamental experiments characterizing not only our fabricated microneedles but also benign biosensing within our needle tips using a combination of experimental techniques. These techniques include epifluorescent microscopy, image analysis, current monitoring, potentiostat measurements, and data analysis. The summer intern will not only be trained on equipment and techniques, but also use them to produce useful data towards efficient electronic-based biosensing.

Exploring Key Design Parameters Exploited by Naturally Occurring Chemoperception Systems
Kevin W. Plaxco (Dept. of Chemistry & Biochemistry) and Tod E. Kippin (Dept. of Psychological and Brain Sciences)
Our goal is to mimic biology's ability to continuously and quantitatively monitor specific molecules directly in complex, flowing samples, such as the continuous monitoring of drugs and metabolites in the blood. To achieve this we are developing several integrated and complementary technologies based on naturally occurring counterparts. These are: 1) conformation-linked signaling, which provides a means of transducing biomolecular binding events into specific, not-easily-fooled output signals, and 2) the development of filtering and differential measurement approaches that reduce fouling and correct the baseline drift that inevitably occurs in complex environments. Our ultimate goal is to develop biosensors capable of real-time measurements of multiple biomolecules directly in the most complex of sampling environments, including in effluent streams, in bioreactors, and in the human body.

A key component of the proposed ICB SABRE program is to develop sets of related redox reporters (molecules that give up electrons easily and can thus be used to generate a signal) that report at different potentials (and thus can be monitored simultaneously), and yet exhibit otherwise identical chemistry (e.g., degrade with the same rate). Using these, we hope to fabricate sensors that contain an internal calibration control, obviating the need for calibration before or after measurements.

ICB Cognitive Neuroscience Projects

Action Selection Under Time-Pressure
Scott T. Grafton, Dept. of Psychological and Brain Sciences
Effective tactical operations require a soldier to make complex decisions while operating a broad range of systems under extreme environments. This work focuses on defining patterns of brain activity as well as responses of the autonomic nervous system that are indicative of potential performance failures. Experiments are performed with healthy subjects as they make decisions under time pressure combined with different sources of stress such as fatigue, distraction, large incentives or losses and noisy environments. The goal is to develop new approaches for training and to identify brain or peripheral nervous system monitoring tools.

The Action Lab of Dr. Grafton hosts undergraduate students interested in learning to map human brain function using both magnetic resonance imaging and electroencephalography. The student will learn how to operate the MRI scanner and perform EEGs in healthy normal volunteers. They will learn basic data analysis and the identification of brain activity that is task specific. They will be matched with a laboratory member to work on an ongoing project in action recognition, planning or decision-making. This is a great opportunity to work with human subjects, learn state of the art brain mapping methods and advanced image analysis.

Neural Indicators of Optimal and Adaptable Decision-Makers
Michael B. Miller, Dept. of Psychological and Brain Sciences
We explore ways in which neuroscience can improve decision-making. Decisions to take action on the battlefield must often be made quickly, in rapidly changing environments, and on the basis of uncertain evidence. Under such circumstances, it is crucial that decision-makers adapt their criterion for taking action to the current situation (e.g., being cautious about pulling the trigger when civilians are present). We use neuroimaging techniques to identify and predict individual differences in decision-making. We also are developing neuroscientific tools to monitor effective criterion placement in real-time and to directly intervene with prefrontal cortex functioning in order to optimize decision performance.

Cognitive Neuroscience Embedded in Large-Scale Models of Systems Dynamics
Jean M. Carlson, Dept. of Physics
We develop theoretical systems-level models and data-driven analysis of anatomical architecture and cognitive function in the human brain, thereby describing human motor control, dynamic evolution of network organization, anatomical connectivity patterns, and responses to risk and pressure across a range of cognitive conditions. Through the application of tools from control theory and dynamical systems engineering, we integrate anatomical architecture, cognitive function, and behavioral performance into a theoretical framework that suggests approaches for efficient training, optimal decision-making, and resource allocation under relevant Army scenarios. These advances may further enable the identification of biomarkers for cognitive flexibility, fatigue, and performance under pressure, and may help capture important aspects of human cognition for the development of adaptable machine systems.

Potential ICB SABRE participants will investigate the application of complex systems analysis to the study of anatomical and functional brain architecture. The proposed study will expose the intern to techniques drawn from control and systems engineering, complex network analysis, and statistical analysis for the theoretical and computational modeling of complex biological systems. Critical research investigations would address the relationships between brain anatomy and dynamic activity, measured via DSI and fMRI neuroimaging techniques, and the constraints imposed by this structural and functional brain architecture on behavioral and external variables such as cognitive flexibility, reaction time, and performance in high-pressure situations.

Identifying the Neural Biomarkers of Adaptive Cognition Under Fatigue and Stress
Barry Giesbrecht, Dept. of Psychological and Brain Sciences
Successful, goal-directed behavior requires a cognitive system that is both highly flexible to one's ever-changing internal goals and adaptive to external physical and psychological stressors. The primary objective of this project is to use cutting-edge methods from cognitive neuroscience to identify the neural mechanisms of adaptive and maladaptive cognitive states under conditions of changing task demands, physical fatigue, and mental stress. Understanding these mechanisms will not only provide key insights into the adaptive nature of cognition, but they will also provide avenues for the development of strategies to both enhance adaptive cognition and mitigate the cognitive impairments caused by stress. ICB SABRE students are trained in experimental design and control using MATLAB, measurement of human performance and brain activity electroencephalography and functional magnetic resonance imaging), and data analysis and presentation skills.