Charles E. Kaufman Foundation
2013 Grant Awards

NEW INVESTIGATOR RESEARCH GRANTS
$150,000 over two years ($75,000 per year)

GOAL

The goal of the New Investigator Research Grants is to provide research support for innovative basic scientists in Pennsylvania as they transition into an academic position as a new independent investigator. Proposals are required to address basic (fundamental, pure) questions addressing core principles in biology, physics and chemistry or at the disciplinary boundaries between these fields. Applied or clinical studies will not be supported. Competitive applications are expected to be rich in innovative ideas and approaches with the potential for generating transformative intellectual advances.

NEW INITIATIVE RESEARCH GRANTS
Up To: $300,000 over two years ($150,000 per year)

GOAL

The goal of the New Initiative Research Grants is to stimulate existing investigators with strong records of research accomplishments to establish collaborations that facilitate innovative interdisciplinary approaches towards a common research question and that require expertise beyond that of any single researcher. Investigators may be at different institutions or in the same department and institution, provided that different approaches are combined to address a new research initiative. Proposals are required to address basic (fundamental, pure) questions addressing core principals in biology, physics and chemistry or at the disciplinary boundaries between these fields. Applied or clinical studies will not be supported. Competitive applications are expected to be rich in innovative ideas and approaches with the potential for generating transformative intellectual advances.

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Joel McManus, Ph.D.
Assistant Professor, Department of Biological Sciences
Carnegie Mellon University

Title: High-Throughput Probing of Human lncRNA Structure

Abstract: The human genome has often been referred to as "The Book of Life." Every person's genome contains the instructions needed for their bodies to grow and function. These instructions are stored in molecules of deoxyribonucleic acid (DNA for short) which exist as a double helix structure inside a person's cells. However, in order for these instructions to be read, DNA must first be copied into another molecule called ribonucleic acid (RNA for short), through a process called gene expression. RNA then uses this information to direct the production of proteins and control the expression of genes.
The functions of RNA molecules are largely determined by their molecular structure and interactions with proteins. Traditional experimental approaches to investigate RNA structure are slow and tedious. This project aims to use a novel high-throughput approach to investigate the molecular structures and predict protein binding sites of a particular class of RNAs called large non-coding RNAs (lncRNA for short). This class of recently discovered RNAs has many functions, and the misregulation of lncRNAs have been linked to many human diseases such as cancer and autism. This proposal aims to provide a better understanding of lncRNA structure and function.

Aditya S. Khair, Ph.D.
Assistant Professor, Department of Chemical Engineering
Carnegie Mellon University

Title: Charges, Forces, and Particles in Ionic Liquids

Abstract: This proposal aims to quantify electrochemical and electrokinetic transport in ionic liquids and concentrated electrolytes. These materials offer great promise for use in energy storage and conversion technologies such as ultra-capacitors or solar cells. However, an understanding of their nonequilibrium dynamics under time-dependent voltages, crucial to such applications, is lacking. We will fill this gap in knowledge by utilizing a recently developed model for the electric double layer at an ionic liquid-electrode interface to generate quantitative, experimentally testable models for electrically-driven transport in ionic liquids. Our preliminary results highlight that electrical transport phenomena in such fluids is radically different to that in commonly studied dilute systems, due to the prevalence of electrostatic correlations in ionic liquids and concentrated electrolytes. For instance, we predict electrophoretic velocity reversals — i.e., positively-charged colloids migrate to positively-polarized electrodes! — and drastically shorter time scales for diffuse charge dynamics. The work proposed here focuses on fundamental, paradigmatic electro-chemical and -kinetic phenomena: namely, electrophoresis, colloidal forces, and impedance spectroscopy, which highlight the curious and counterintuitive nature of transport in ionic liquids and concentrated electrolytes.

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Michelle Dolinski, Ph.D.
Assistant Professor, Department of Physics
Drexel University

Title: Solid Xenon Bolometers for Radiation Detection

Abstract: Radiation detectors have many practical applications in nuclear medicine, nuclear safeguards, and environmental health and safety. Novel radiation detectors with new properties may ultimately impact one or more of these fields. This proposal is to develop a new type of radiation detector for fundamental nuclear physics research, called a solid xenon bolometer { a high resolution calorimeter where the energy absorber is a xenon crystal cooled to extremely low temperature. Liquid xenon-based radiation detectors have recently become a popular technology in basic nuclear and particle physics research. When radiation interacts with the xenon, charge and light signals are produced. The power of liquid xenon detector technology is in the combination of these two signals, resulting in the ability to reject background signals and improve energy resolution. The microscopic physics of how these detectors work is not well understood, and a great deal of research into liquid xenon energy response is ongoing in the physics community. By detecting a heat signal rather than charge or light, solid xenon bolometers may offer the final piece of the puzzle in understanding xenon detector energy response. The proposed research program would serve as the foundation for the further development of new xenon detector technology.

Sheereen Majd, Ph.D.
Assistant Professor, Department of Bioengineering
Pennsylvania State University

Title: Functional Studies of Multidrug Resistance Transporters at Single-Protein Level

Abstract: Currently, successful treatment of human cancers is severely hindered by the resistance that cancerous cells develop against a wide range of chemotherapeutic drugs (multidrug resistance (MDR) phenomenon). A group of membrane transporters that actively pump these drugs out of cells are believed to be a major cause of this resistance. Most of the clinically used therapeutics interact with these transporters and consequently lose their effectiveness or produce undesired side effects. Despite years of research on these pumps and development of a number of modulators for them, there has been no significant progress in overcoming clinical MDR. New and highly effective strategies to modulate MDR transporters are, hence, urgently needed. Development of such modulators requires a detailed understanding of the mechanism of function of these proteins. To this end, we propose to develop a highly sensitive fluorescent assay that allows studying several different aspects of MDR transporters at the same time under defined conditions. Using this assay, we aim to conduct a mechanistic investigation of the biochemical and biophysical parameters (such as membrane fluidity) that regulate the transport activity of these proteins. Findings of this study may accelerate the rational design of new modulators for MDR pumps to overcome clinical MDR.

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William M. Wuest, Ph.D.
Assistant Professor, Department of Chemistry
Temple University

Title: The Development of Chemical Probes to Study Nucleoside Signaling in Bacterial Biofilms.

Abstract: The proposed research will focus on the development of new antibiotics to curve the increasing percentage of antibiotic-resistant bacteria. Persistent infections, for example within the lungs of cystic fibrosis patients, are typically the result of bacterial biofilms. Biofilms are a lifestyle of bacteria that make them very difficult to treat using currently available antibiotics. New methods to treat a variety of bacterial infections are becoming increasingly important because of the high incidence of antibiotic resistance found in chronic infections. This research seeks to develop new compounds to be used both to treat and also to better understand bacterial biofilms. The compounds that will be created will act as "communication disruptors" of the bacteria's normal activities. If successful, this research would be the first of its kind to specifically kill bacteria within a biofilm. The proposed research is the perfect medium to train graduate and undergraduate students in both chemistry and biology preparing them for future careers in the sciences and medicine.

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Up To: $300,000 over two years ($150,000 per year)

Sergey M. Frolov, Ph.D. (PI)
Assistant Professor, Department of Physics and Astronomy
University of Pittsburgh

W. Vincent Liu, Ph.D. (co-PI)
Associate Professor, Department of Physics and Astronomy
University of Pittsburgh

Title: Topological Quantum Wire Emulators
Amount Adjusted to: $242,310 ($121,155 per year)

Abstract: Relativistic quantum mechanics dictates that for each type of particle there should exist an antiparticle. For example, a positively charged positron is an antiparticle of a negatively charged electron. There also exists a theoretical possibility of a particle that is its own antiparticle – known as the *Majorana fermion* after Ettore Majorana's work in the 1930's. Such hypothetical elementary particle has been actively searched for in the context of neutrino physics, supersymmetry, and dark matter but it remains elusive. Alternative ideas have been put forward in condensed matter physics community in the past few years, showing that rather than being discovered blindly in nature, Majoranas can be engineered in transistor-like devices as quasi-particles, which are the collective modes of electrons similar to waves on water. The path of Majorana's ideas through these different fields of physics has been reviewed by Nobel laureate Frank Wilczek in a popular article 'Majorana returns' (Nature Physics, 2009). The rapidly expanding race for Majorana quasi-particles is motivated not only by their fundamental importance, but also by the promise of topological quantum computing. The most prominent approach, 'a Kitaev chain', prescribes how to generate Majoranas in a chain of atoms paired into an exotic topological superconductor. This project will explicitly realize a Kitaev chain following an approach that draws from two physics research fronts: ultracold atomic gases and semiconductor nanoelectronics. We will build a chain of artificial atoms (quantum dots) in a semiconducting nanowire, and map the Kitaev model onto our solid state quantum emulator. The sizes of artificial atoms and their coupling strength will be fully tunable making our emulator a powerful platform for studying not only Majorana particles, but beyond, for discovery of currently unknown fundamental topological phases of matter.

Veronica Hinman, Ph.D. (PI)
Associate Professor, Department of Biological Sciences
Carnegie Mellon University

Jonathan Minden, Ph.D. (co-PI)
Professor, Department of Biological Sciences
Carnegie Mellon University

Bruce Alan Armitage, Ph.D. (co-PI)
Professor, Department of Chemistry
Carnegie Mellon University

Danith H. Ly, Ph.D. (co-PI)
Associate Professor, Department of Chemistry
Carnegie Mellon University

Title: Developing a Sea Star Model for Regenerative Biology

Abstract: Humans have little capacity to regenerate. However, human tissues could potentially be reengineered if the mechanisms controlling this process in animals that do regenerate were well enough understood. Unfortunately the genetically tractable organisms, e.g. *Drosophila* and *C.elegans,* that have driven much of our knowledge of development have little regenerative capacity. Regenerative biology thus remains highly unexplored. While vertebrate animals and humans in particular have generally poor regenerative capabilities, members of their closest invertebrate phylum, sea stars, have extraordinary abilities to regenerate. The sea star larva is a newly emerged model system for understanding the regulatory mechanisms of cell specification during early development. This proposal will be capitalize on and extend this knowledge to take advantage of the inherent biology of this organism to develop it as model system for understanding cell specification during regeneration. In this proposal we will profile the changes in gene expression and protein modification during early regeneration and begin to build gene regulatory network models of this process. An integral component of this proposal is also to develop enhanced tools for manipulating gene function and analyzing gene expression in regenerating larvae. These tools are also likely to be widely useful for any developmental model system.

Christine D. Keating, Ph.D.
Professor of Chemistry
Penn State University

Theresa Mayer, Distinguished Professor of Electrical Engineering & Materials Science & Engineering
Penn State University

Title: Probing the Role of Interparticle Forces in the Collective Behavior of Particle Assemblies

Abstract: The properties of individual molecules within biological assemblies such as lipid membranes or protein complexes are often stimuli-responsive. For example, a conformational change may occur upon binding that consequently alters the structure of the overall assembly, effectively amplifying the response of the molecule(s) directly involved in the binding events. This type of control over the interactions between components of synthetic, inorganic assemblies would be a powerful step towards increased functionality and responsiveness in these materials, and could have far-ranging implications in nanophotonics, chemical and biological sensors, and energy. In this *New Initiatives* proposal, Profs. Keating and Mayer combine diverse expertise to generate systems in which a fundamental materials property, particle polarizability, is controlled in real-time by optical illumination. Complementary experimental model systems will be investigated to probe the effect of this materials property change

on two important classes of interaction forces and its impact on particle organization within assemblies. We anticipate observing rich phase behaviors based on mixtures of different particle types in which particle subpopulations are selectively altered to vary their interaction potentials. Cooperative responses to material structure such as a stimulus-induced phase change are of fundamental interest and are exciting in the longer-term as reconfigurable materials.