Bradley-Herzfeld Catalyst Awards – Summer 2014:

Controlled Language Software – Exploratory Project ($12,905)

Dave Clark, Ph.D., Associate Professor, Department of English

Scott Graham, Ph.D., Asst. Professor, Department of English

William Keith, Ph.D., Professor, Department of English

Entrepreneurial Team from UWM's English Department. Dave Clark's research focuses on content management, information design, the rhetoric of technology and writing pedagogy. Collaborators Scott Graham and William Keith have complementary research interests that include focus on specific disciplines such as medical communication. This team brings an entrepreneurial perspective to their work in the Department of English in UWM's College of Letter and Science. Together they are working to create the Innovation Policy and Communication Center that will be housed at the new UWM Innovation Accelerator facility adjacent the County Medical grounds – putting the team in close proximity to key customers including GE Healthcare and the Medical College of Wisconsin. The goals of this center include research on innovation communication, and this proposal is aligned closely with that goal.

Controlled Natural Languages Bring Order to Complex Communications. "Controlled natural languages" are attempts to standardize complex, idiosyncratic languages – a movement that began in the 1970's to make legal and government jargon more clear and understandable. Some companies have developed their own controlled languages for specialized purposes like technical documentation and marketing communications (e.g., Caterpillar Technical English and IBM's Easy English); there are examples of entire industries pursuing the same goal (e.g., Simplified Technical English of the Aerospace and Defense Industries of Europe). As organizations become more globalized and technology domains become more specific, there is an increasing need for this sort of standardization of languages.

Need for Improved and Less Expensive Controlled Natural Language Tools. Traditionally, organizations rely on time-consuming editing to enforce organizational style guides, but contemporary technology can make the production of controlled language more efficient, more accurate, and more consistent. And yet while there are a handful of software products that can assist an organization with controlled language efforts, for small- and medium-sized organizations with controlled language needs, existing products are 1) too specialized (focusing exclusively on a particular function, like style correction, or on a particular role, like marketing or technical documentation), 2) too expensive, costing hundreds of thousands of dollars.

Pilot Project to Explore Customers and Tools. Support for this project will allow Dr. Clark and his collaborators to explore an affordable, customizable solution to industry needs for automated control of language style, clarity, and translation readiness. They will look broadly at the market and work in detail with a few targeted customers to understand their requirements and the dynamics of bringing such tools to market. Several local and regional clients who have indicated a possible interest in the product. The team has also identified a specific Small Business Innovative Research (SBIR) grant opportunity and will explore that along with support from other sources such the Ideadvance program which supports university-based innovators in the customer discovery process.

Proof of Concept Testing for Asthma Therapy ($50,000)

Doug Stafford, Ph.D., Director, Milwaukee Inst. for Drug Discovery, Dept. of Chemistry and Biochemistry

James Cook, Ph.D., Professor, Department of Chemistry and Biochemistry

Alexander Arnold, Ph.D., Assistant Professor, Department of Chemistry and Biochemistry

Doug Stafford came to UWM to create the Milwaukee Institute for Drug Discovery (MIDD) which helps bring UWM discoveries in chemistry and biochemistry to market faster. He has over 20 years of experience in biomedical product companies, is inventor on over a dozen biomedical patents, formed numerous public and private research collaborations, and participated in the development of several entrepreneurial businesses. As MIDD Director, he identified the opportunity to collaborate with Dr. James Cook and Dr. Alexander Arnold to investigate the use of Dr. Cook's library of compounds in the treatment of asthma and inflammation of the lungs.

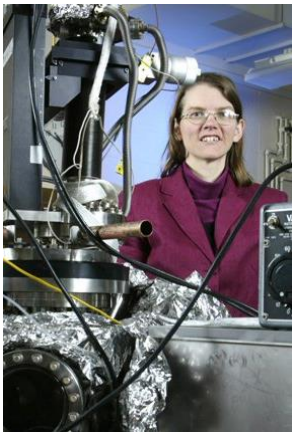
Novel Compounds for the Treatment of Asthma and Inflammation. The Cook laboratory has synthesized a library of compounds selective for several different gamma-amino butyric acid type A receptors (GABAAR). These important receptors are known to be prevalent in the brain, but some of the subtypes were recently found to also be present in airway smooth muscle (ASM) found in the lung and in inflammatory cells. This led Stafford to idenify the opportunity to use Cook's compounds in treatement of asthma. Alexander Arnold's laboratory is working on developing cell lines to screen these receptors, bringing a strong complement to the team. The concept is the subject of a pending patent application filed by the UWM Research Foundation.

Market for Asthma Drugs. The significance of asthma is reflected in an estimated global prevalence of 245 million persons, with nearly 25 million afflicted in the US alone (about 8.2% of the population). It is the most common chronic disease of children with disparate impact in US minority populations. High disease prevalence results in an estimated US health care cost burden of $56 billion (in 2007). The growing problem of asthma demands better therapeutic strategies to control symptoms and costs. The global market for asthma and chronic obstructive pulmonary disease (COPD) prescription drugs was valued at $34.9 billion in 2011. This figure is projected to reach $47.1 billion in 2017.

Project Objective – Obtain Key Animal Data. This project will help the team to obtain key *in vivo* testing in several rodent asthma models for proof of concept. This data will be key to leveraging funding for the next steps – including a $2 million NIH grant that UWM is currently pursuing with collaborators at the Medical College of Wisconsin and Columbia University.

Important Steps Toward Commercialization. Despite the growing appreciation of GABAAR signaling in asthma cell types, a strategy that targets GABAAR responses in the lung has not previously exploited. Animal studies are crucial to determine *in vivo* efficacy and druggability data needed to demonstrate pharmacological proof-of-concept. Without animal data, it is extremely difficult to engage with potential biotech and pharmaceutical partners or licensees. The support will aid in determining whether this approach will provide a new non-steroidal alternative to the numerous asthma sufferers worldwide.

Advancing a New Semiconductor – Graphene Monoxide ($30,000)

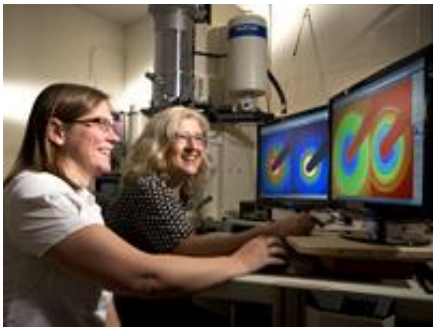


Carol Hirschmugl, Ph.D., Professor, Department of Physics

Dr. Carol Hirschmugl is a professor in the Department of Physics at UW-Milwaukee with a doctorate from Yale University and over 20 years of experience in physics research. She is the director of the Laboratory for Dynamics and Structure at Surfaces and an expert in the study of surface adsorbates on epitaxial and bulk oxide systems, focusing on environmentally and technologically relevant problems. More broadly, she has interest in research involving material science and evolving biological specimens. The discovery of a new semiconducting material, graphene monoxide, has led to new promising research in her lab and other labs across campus.

Graphene Monoxide – The Semiconductor of Future Electronics. The age of silicon electronics is nearing an end as silicon reaches its physical limits. This has sparked global research into finding a carbon-based semiconducting successor. While some carbon-based semiconductors have been developed, they have poor electrical performance and are difficult to economically manufacture on a commercial scale. The continued development of graphene monoxide, a carbon-based semiconductor discovered at UWM, may lead to applications in electronics and flexible circuits.

Project Objectives – Commercial Value from Characterization and Applications. This "gap fund" award builds on a previous Catalyst Grant (2012) with objectives targeted toward commercialization. Previous theoretical and nano-scale experimental characterization has led to initial interest from industry, but electrical characterization of larger samples (100's of milligrams) is needed to prove the feasibility for their applications. This project will bridge the commercial gap by having graphene monoxide evaluated by industry, and demonstrate its use in practical electronics. The objectives include: (1) measurement electrical properties of the material to generate key current-voltage charts and of field-effect transistors constructed with a graphene monoxide composite; (2) characterization of materials during the manufacturing process to help optimize fabrication parameters leading to better reproducibility of the material; (3) testing the feasibility of the material in inks, transistors, and sensors.



Impactful Gap Fund - Building a Commercial Partnership. The UWM Research Foundation has worked with Dr. Hirschmugl and her colleagues to identify potential partners to help realize graphene monoxide as a new material for the semiconductor industry. Companies have expressed interested if larger amounts of material are available to evaluate. A particular company is interested in not only evaluating the material but also in building a collaborative partnership while Dr. Hirschmugl works towards further characterization and scale-up of graphene monoxide.

In Vivo Efficacy Testing for New Cancer Therapy ($60,000)

Xiaohua Peng, Ph.D., Assistant Professor, Department of Chemistry and Biochemistry

Dr. Xiaohua Peng conducts interdisciplinary research which focuses on nucleic acid chemistry and its applications in other fields including drug discovery, DNA diagnostics, and nanotechnology. Her laboratory investigates the role of DNA damaging agents and their effect on tumors. The goal of this work is to discover novel anti-tumor drugs that cause less damage to normal cells in the body. Dr. Peng's current research focuses on distinctive features of the tumors that are normally not present in healthy surrounding cells. These features are low levels of oxygen and high levels of oxidative stress or free radicals – properties that have led to the development compounds known as "pro-drugs" because they remain largely inactive until they reach their target and become activated. In 2010 she received a research award from the National Institutes of Health, and in 2012 she was awarded a Shaw Scientist Award from the Greater Milwaukee Foundation.

Novel Compounds Activated by Hydrogen Peroxide. Cancer cells are known to exhibit high levels of hydrogen peroxide (H_2O_2) as compared to normal cells. The Peng lab has synthesized novel pro-drugs that are activated upon entering an environment, such as a tumor, with high levels of H_2O_2. Her compounds were initially screened by the National Cancer Institute against sixty human tumor cell lines, and leukemia and breast cancer cells were most sensitive to her pro-drugs. Preliminary results using leukemic lymphocytes obtained from patients versus healthy lymphocytes show that one compound can kill cancer cells while normal lymphocytes are less affected. Dr. Peng's group has demonstrated *in vitro* that activation of her pro-drugs by H_2O_2 leads to DNA damage in the tumor cells which ultimately leads to tumor cell death. Since leukemia is less likely to lead to tumor formation, the Peng lab will next focus on the effectiveness of the pro-drugs in a breast cancer tumor model.

Project Objective – Obtain Key Data in Mouse Tumor Model. The UWM Research Foundation has filed a patent application on Dr. Peng's novel pro-drugs for cancer treatment. The first application covering a subset of compounds was quickly allowed by the patent office, supporting the novelty of her work. In previous applications to the Catalyst Grant Program, reviewers identified the need for more *in vivo* data for lead compounds, and in this application she has focused on that end by partnering with Dr. Alexander Arnold to design cellular and *in vivo* experiments for proof of concept that her pro-drug compounds can reduce tumor size.

Market and Commercialization Opportunities. Breast cancer is second only to skin cancer in terms of the number of American women affected. It is the second leading cause of cancer death in women, exceeded only by lung cancer. Chemotherapy is one of the most important treatments for breast cancer. It is used before and after surgery and for advanced cancer that has spread outside the breast and underarm area. The global market for breast cancer drugs was $10.2 billion in 2011 and is expected to reach $11.2 billion by 2016. DNA damaging drugs are some of the most widely used breast cancer drugs. These agents are effective against rapidly dividing cancer cells, because they interfere with DNA replication and transcription, stall cell division, and/or induce cell death. However, many normal cells also divide very quickly, thus, most anti-cancer drugs have serious side effects. Free radical-activated anti-cancer drugs developed in this proposal have great potential to increase the selectivity of cancer therapy, and this reduces the side effects. With the data gathered from this Catalyst support, the team will be in a better position to biotech and pharmaceutical companies that have shown interest but insist on seeing *in vivo* data.

Commercial Prototype of New Low-Cost Spectroscopy System ($28,095)

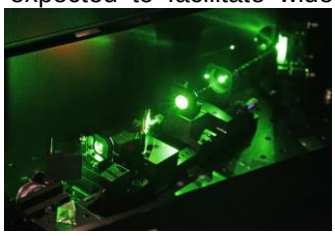
Valerica Raicu, Ph.D., Associate Professor, Department of Physics

Valerica (Vali) Raicu is Chair of the UWM Department of Physics and an accomplished researcher. He has also grown into the role of faculty entrepreneur since launching Aurora Spectral Technologies (AST) in 2010. His work serves as a model for the positive interaction between research, teaching and commercialization of technology. The Company funded research in Raicu's laboratory, helped support graduate students and has donated equipment that helps his team continue with fundamental discoveries. The strong coupling between his university research program and the company also helped Raicu secure a National Science Foundation (NSF) Partners for Innovation Grant that provided more than $1 million over three years to help link UWM researchers with other discovery and instrumentation companies.

Tools for Drug Discovery. Raicu's work focuses on creating tools that support drug discovery. A significant roadblock to efficient drug design is the lack of information regarding the structure of a drug target (usually, a membrane receptor) prior to optimizing a potential compound suspected to bind to and modify its function. A Bradley Catalyst Grant in 2009 helped him develop an instrument that addresses this. It employs a optical process of *two-photon excitation* of fluorescent molecules which include light sensitive "tags" to help researchers measure activity and interaction; the instrument delivers full-color fluorescence images with unparalleled sensitivity (i.e., 100 times higher than that of comparable technology). This has opened the way to rapid probing of the quaternary structure of fluorescently labeled proteins in living cells, before and after treatment with various natural and artificial ligands (i.e., drugs), using a process of energy transfer between two abutting fluorescent proteins.

Commercializing Drug Discovery Tools. This *two-photon* technology has been patented by the UWM Research Foundation, and Aurora Spectral Technologies has made it the building block of their Optical Micro-Spectroscopy (OptiMiS) product that relies on ultrashort-pulse lasers for the excitation of fluorescent samples. Raicu's experience in the company has led to numerous conversations with potential customers of AST and scientific collaborators; these discussions have revealed the need for a product providing the same hyperspectral technology but equipped with continuous wave lasers (CW) which results in a dramatically less expensive system.

A New Approach to Produce a Low-Cost System. In this proposal, Raicu proposes a novel new approach that will building on the existing technology platform and yield similar results using a low-cost laser technology instead of the more expensive laser technologies required by the current system. The goal of the project is to design and construct the commercial prototypes that connects the light source to the scanning part of the OptiMiS module. This is expected to facilitate wide adoption of this technology by individual investigators and thus accelerate the process of structure-informed drug-design and spur a new revolution in protein-quaternary structure determination *in vivo*.



Accessing New Markets. The new commercial prototype is expected to dramatically expand AST's customer base by reaching beyond large, well-funded, and not so numerous imaging facilities in order to give single-investigator labs access to cutting-edge technology. Current as well as new private investors in the company are expected to contribute additional funds so that the sales efforts of the company may be scaled up. Much of the prior art has been developed in the past using a Bradley Catalyst Grant as well as a large NSF Partnerships for Innovation grant awarded to Raicu. Additional return on investment is expected by positioning the company and UWM for successful extramural funding applications, such as through the Small Business Innovative Research (SBIR) grant mechanism.