Bradley-Herzfeld Catalyst Awards – Summer 2013:

Dengue Virus Drugs that Target the Viral Helicase ($60,000)

David Frick, Ph.D., Associate Professor, Department of Chemistry and Biological Science

David Frick has over 20 years of experience studying how proteins manipulate nucleic acids and their nucleotide building blocks. He studies proteins that viruses synthesize in order to replicate in human cells. Drugs used to treat viral infections typically target viral enzymes. The goal of his work is to develop new treatments for debilitating viruses such as AIDS, hepatitis C, Dengue Fever, and other flaviviruses. His interest in hepatitis C began in 1995 when he was diagnosed with the disease. He started his related research after he received a liver transplant and was cured of hepatitis C in 1999. Dr. Frick's group is now focused on discovering and developing viral helicase inhibitors to better treat HCV and related flaviviruses. Dr. Frick joined the UMW faculty in 2010 after teaching Biochemistry and running a research lab for ten years at New York Medical College.

Unmet Clinical Need for Dengue Fever. Dengue fever is an extraordinarily painful disease colloquially called "breakbone fever." The *Aedes aegypti* mosquito is the primary vector of dengue. While patients typically recover after a few weeks, some progress to dengue hemorrhagic fever or dengue shock syndrome, both of which can be fatal. There are currently no vaccines or antivirals available for dengue virus. Currently, the only method to control or prevent the transmission of dengue virus is to combat the mosquitos to prevent infection. The potential market for Dengue drugs annually is $338 million, with 50-390 million new infections per year. Over 40% of the world's population is now at risk from dengue. The disease is now endemic in more than 100 countries. The threat of a possible outbreak of dengue fever now exists in Europe.

New Use for Small Molecules Designed for HCV. Dr. Frick is seeking to develop a new use for a subset of small molecules that his group previously designed to treat hepatitis C virus (HCV) infection. This group of small molecules are currently protected by an international patent application filed by UWMRF and University of Kansas. During recent studies they discovered that the compounds are even more potent inhibitors of the helicase encoded by the related dengue virus (DENV). Thus far from their set of 88 derivatives, 2 compounds have already been found to be potent specific inhibitors of DENV.

Project Objective – Obtain Key Cell Culture Data. In this project, "Dengue Virus Drugs that Target the Viral Helicase," Frick and his colleagues will test whether the set of compounds can inhibit DENV in cell culture. The ultimate goal is to design a safe therapeutic that could be administered after infection to lessen the severity of Dengue disease or that might be administered to travelers as a prophylaxis. A therapeutic index must be determined for each compound that measures the ability of the compound to inhibit DENV replication in a cell while not killing the cell itself. They will also attempt to isolate DENV that is resistant to the compounds to further show that the molecules are specifically targeting the NS3 helicase in cells. The project deliverables are one or more specific molecular probes that target DENV or related helicases ideally with a potency of less than 1 micro Molar that are specific for DENV helicase and are non-toxic in cell culture. In future studies the probes will be optimized to leads, evaluated in animal models, and further optimized as drugs.

Dr. Frick is working with UWMRF to approach companies interested in discovering drugs for tropical diseases. The multiple disease uses for the compounds are covered in the pending patent application filed with the UWMRF which provides several avenues for potential licensing partners.

Response Inhibition Training Software ($50,000)

Han Joo Lee, Ph.D., Assistant Professor, Department of Psychology

Han Joo Lee's research interests are centered in anxiety disorders, including obsessive-compulsive disorder, social anxiety disorder, and post-traumatic stress disorder, and their clinical manifestations. He conducts studies to investigate the nature of maladaptive cognitive-perceptual information processing (e.g., attentional bias) underlying anxiety problems. Another line of his research is the utilization of web-based techniques in psychological assessment and intervention. Dr. Lee has developed several online assessment systems with his colleagues, including an online diagnostic interview system designed to evaluate individuals presenting with a variety of anxiety problems. Dr. Lee heads the UWM Anxiety Disorders Lab (ADL) which provides a clinical setting in which to study anxiety disorders and their treatments.

Impulse Control Disorder – Trichotillomania. Trichotillomania (TTM) is an impulse control disorder characterized by compulsive hair pulling. TTM typically results in serious consequences including impaired individual functioning, medical problems (e.g., skin infections), and elevated comorbidity with other psychiatric disorders, and it remains one of the most poorly-understood and inadequately-treated psychiatric conditions. There is an urgent need for effective and accessible clinical interventions for TTM, especially for young individuals who suffer from a marked lack of adequate treatment resources despite the early onset of the condition.

Computerized Cognitive Training for Treatment of TTM. One promising therapeutic approach is to improve cognitive problems believed to contribute to TTM using a computerized cognitive retraining method. Research has indicated impaired response inhibition (RI), the ability to inhibit inappropriate but potent response, is a cognitive feature that is characteristic of TTM, and RI is considered to be an important target of cognitive retraining. Dr. Lee has conducted a line of research that aims to develop a cognitive retraining program designed to reduce TTM symptoms by improving RI capabilities. Response Inhibition Training (RIT) has been designed as a simple video game consisting of 30 increasingly difficult levels, offering individualized training for practicing RI. Dr. Lee's preliminary outcome study (funded by the Trichotillomania Learning Center) showed that children with TTM who received an 8-session RIT intervention in the UWM Psychology Clinic improved in TTM symptoms to a greater degree, relative to children assigned to the waitlist control condition. Further, continuing improvement was observed during the 1-month follow-up period after RIT was completed.

Developing a Web-Based Response Inhibition Training System. Building on Dr. Lee's existing research, this project, "Developing Online Response Inhibition Training for Individuals with Trichotillomania," proposes to develop and test a web-based version of RIT to examine its effect and feasibility as an effective, accessible, and portable online self-help intervention for TTM. Fifty children with TTM will be randomly assigned to (a) online 8-session RIT (n=25), or (b) 1-month waitlist condition (n = 25). The study will test the hypothesis that online RIT will show greater improvement in TTM symptoms and RIT capabilities at post-treatment and 1-month follow-up assessments, compared to the waitlist condition. This study is expected to generate important data that will guide the development of an accessible, cost-efficient, and effective cognitive intervention for individuals suffering from TTM.

Exploring Commercial Pathways for Treatment. This study will provide validation needed to explore several pathways to commercialize the proposed RIT intervention. These include a web-based clinical intervention services using a secure online system or a downloadable application which could be accessed on mobile devices.

Commercialization of Advanced Weather Forecasting System ($19,000)

Paul Roebber, Ph.D., Professor, Department of Mathematical Sciences

Paul Roebber is the Founder of Innovative Weather, Professor of Atmospheric Sciences in the UWM Department of Mathematical Sciences, and Associate Dean of the UWM School of Freshwater Sciences. His research in synoptic meteorology has led to improvements in operational tools used by the National Weather Service, Weather Eye, Inc., and WE Energies. Dr. Roebber's background includes experience in mesoscale numerical model prediction, private forecasting, and editing the journal of Weather and Forecasting. He has been the recipient of the American Meteorological Society's Editors Award, the UWM Research Foundation Senior Faculty Award, and the Distinguished Undergraduate Teaching Award.

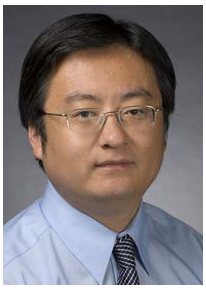
Innovative Weather – An Innovative Model for Service and Education. Innovative Weather is a 24/7 forecast service provider created by Dr. Roebber based at the University of Wisconsin-Milwaukee. The staff consists of advanced meteorology students, led by Roebber and Mike Westendorf. The team provides customized forecasts targeted toward their client's specific business needs that go beyond the information found forecasts from the National Weather Service. Innovative Weather serves a diverse roster of clients throughout the Midwest and east cost in fields that include energy, transportation, education, and broadcasting.

New Algorithms Produce More Accurate Predictions and Commercial Value. Dr. Roebber has developed a new method for making forecasts of weather variables (including, but not limited to, air temperature). In one study, he showed that this method can produce next day temperature forecasts which are 20% more accurate than the best existing technique (available from the US National Weather Service), a skill advantage that would translate to approximately $3 million dollars of cost savings per year for an energy utility servicing an area the size of the state of Ohio. Roebber has gone on to extend this method to fully probabilistic forecasts and showed a performance advantage in extreme value forecasts of up to 32% compared to a national ensemble forecast system. Features of the method include: (1) speed – enables decisions incorporating uncertainty to be made in real-time; (2) improved accuracy – forecasts are more accurate than industry benchmarks; (3) reliable and efficient – produces consistent results and requires interpretation by only one skilled forecaster for maximum benefit; (4) transferable – while the method has been developed for weather forecasting, it is generalizable to any kind of forecast setting.

Extracting Commercial Value from Greater Accuracy. The UWM Research Foundation has worked with Dr. Roebber to identify a number of interested commercial partners. However, what is lacking is a real-time prototype, using weather data for a specific site, which can demonstrate the operational value of the approach to prospective clients. This project, "Development of a Client Demonstration Temperature Forecast System," will develop customized algorithms for a specific site – Chicago, Illinois – and a prototype website which will allow prospective customers to compare the model against their existing standards. These critical steps will help demonstrate the viability to prospective clients.

Nano-Manufacturing Method for High Capacity Batteries ($52,000)

Chris Yuan, Ph.D., Assistant Professor, Department of Mechanical Engineering



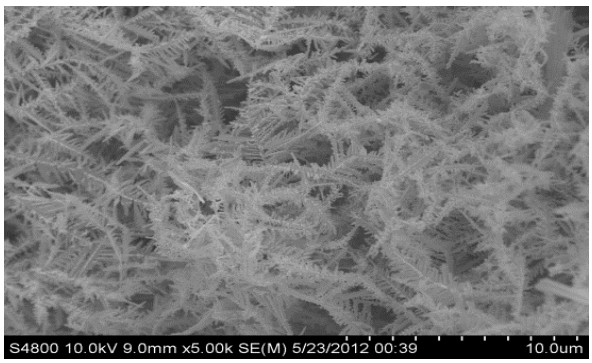
Chris Yuan is an Assistant Professor in the College of Engineering and Applied Science and recently received the 2013 SME Outstanding Young Manufacturing Engineer Award. He is also Director of the Department of Energy Industrial Assessment Center at UWM. Yuan is an upcoming researcher with a specific expertise in materials applied to solar and battery cell technology.

Energy Storage Challenges. Consumer electronics and advanced vehicle power systems are among the most challenging applications for compact energy storage. Lithium ion batteries are increasingly used in these applications, but their use is limited by storage capacity. The capacity of lithium ion batteries using the current graphite anode technology limited to 372 mAh/g, but theoretical predictions for lithium ion batteries indicate that capacity could be increased to more than 11 times that value. Frost and Sullivan projects that this market will exceed $20 billion by 2016. To achieve this potential, manufactures must address storage capacity as well as poor stability, low capacity retention and poor ability to scale manufacturing processes.

A Li-ion Approach with Manufacturing in Mind. Lithium-ion battery researchers have developed solutions that yield high capacity storage, but these solutions are accomplished using exotic materials and specialized nano-scale manufacturing techniques that are not cost effective or feasible on a commercial scale. Yuan and his colleagues have approached development of a lithium ion battery electrode while being mindful of the manufacturing resources and techniques available in industry. They have been able to demonstrate a battery with capacity as high as 3850 mAh/g using manufacturing methods that start with bulk silicon and metal-assisted chemical etchants commonly used in other industry manufacturing processes.

The team has worked closely with UWM industry partners, including Johnson Controls, to better understand market needs and has identified that while they have promising results and a favorable method for manufacturing on a large scale, their electrode still needs improvements in capacity retention. High capacity retention allows for long battery life and a more consistent power supply required for digital electronics. Low capacity retention is related to the degradation of the electrode as the lithium ions force the electrode to expand and contract during battery cycling. A clear path has been set for improving the capacity retention through modifications to the nano-structure of the electrode as well as coating techniques.

Project Objective – Increasing Capacity Retention. The goal of this project, "A Novel Silicon Nano-Manufacturing Method and Structure for High Capacity Lithium Ion Battery," is to enhance the energy capacity retention to achieve a commercially viable battery electrode. Yuan and his team will seek to enhance capacity retention through the design and fabrication of various silicon electrodes based on their established manufacturing method, through carbon coating and atomic layer deposition techniques. They will collect performance results of the newly developed electrodes in lithium-ion battery cells, and continue to work with UWM industry partners for insight and access to battery cell manufacturing equipment. This project can result in significant strides towards a commercially viable battery electrode for the lithium-ion battery industry.



Yuan's silicon-silver dendrite structure, shown here in a scanning electron microscope image, can improve capacity of lithium ion batteries while minimizing the volumetric expansion problems that plague other technologies.