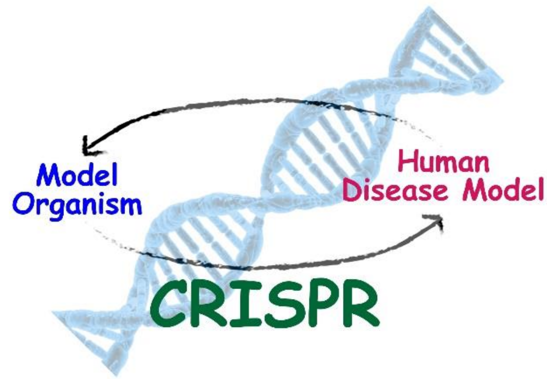
UW2020 Round 4 Project Descriptions

Research

Advancing CRISPR-mediated Genome Editing Technology at UW–Madison to Model Human Disease



This project will establish advanced CRISPR technologies to enable genome editing in multiple mammalian species. Advancing the use of CRISPR-mediated genome editing technology at UW-Madison will accelerate the ability to generate genetically modified animal models of human disease.

Accurately modeling human disease states is critical for the development of new therapeutics. These efforts will promote groundbreaking research across the UW-Madison campus and fundamentally transform our ability to address critical biomedical issues across a wide spectrum of fields.

PRINCIPAL INVESTIGATOR

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CO-INVESTIGATORS

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Robert Redfield, Assistant Professor of Surgery

Krishanu Saha, Assistant Professor of Biomedical Engineering

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Beth Weaver, Associate Professor of Cell and Regenerative Biology

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Xinyu Zhao, Professor of Neuroscience

All-Optical Electrophysiology-Electrophysiology without Electrodes

The field of optogenetics encompasses tools and techniques involving the use of light to control and monitor activity of excitable cells, such as the human brain and heart. These cells are genetically modified to express one or more light-sensitive proteins. This project will develop an all-optical electrophysiology system that will allow researchers to tailor conductances and other biophysical properties of a cell or groups of cells using light.

To realize the full potential of optical voltage clamp, the research team will develop synthetic light activated molecules that will serve as “molecular electrodes” and design a microscope with automated feedback control of illumination. Resulting technology has the potential to be a game changer in the field of optogenetics and the development of future therapeutics. For instance, this all-optical electrophysiology method will allow high-throughput screening of drugs for excitability. The promise of optogenetics is also expected to have a profound impact on development of new therapeutics. Longer-term goals will be to develop this technology for high-throughput screening of therapeutics to treat cardiac and nervous system disorders.

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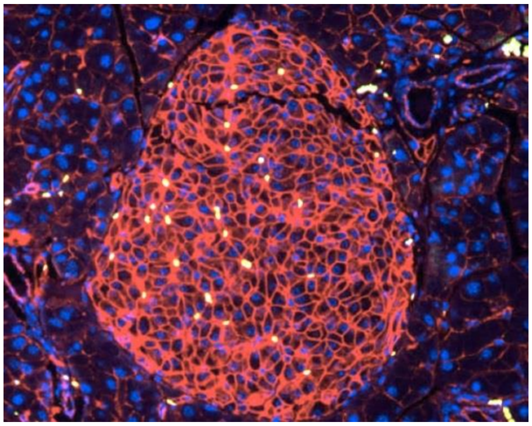
Building a Translational Research Pipeline to Personalize Diabetes Prevention and Treatment



This project establishes the Diabetes Research Accelerator for Wisconsin (DRAW), a data registry and biobank of individuals with diabetes, as a next step toward delivering personalized diabetes care and facilitating interdisciplinary translational diabetes research at UW–Madison.

The long-term goal of this line of research is to improve the health for over 29 million people in the United States with type 1 or type 2 diabetes (T1D or T2D). Over 70% of diabetes patients do not achieve adequate blood sugar control, leading to significantly shortened healthy life and life-altering complications such as blindness, amputation, kidney failure, heart attack, and stroke. Although numerous treatment options and resources are available to help people manage their diabetes, often healthcare providers cannot specifically recommend which treatment is most likely to be effective for a given patient, resulting in a trial-and-error approach. Personalizing diabetes care could support successful early intervention and reduce the costs of failed treatments by addressing a host of biologic, environmental, and psychosocial risk factors. By building the DRAW resource, scientists at UW–Madison can more efficiently expand their ground-breaking work to human clinical populations.

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Umberto Tachinardi, Associate Dean for Biomedical Informatics

Chi-Liang Eric Yen, Associate Professor of Nutritional Sciences

Communication Ecologies, Political Contention, and Democratic Crisis

The 2016 presidential campaign demonstrated the critical role mass media and social media play in American elections, driving themes and messages of campaigns and distributing information and misinformation to the electorate.

This project examines how growing polarization and fragmentation in the Wisconsin media ecology, as reflected in talk radio, local news, political advertising and social media, contributed to ideological and partisan political divides in the state. It will also study under what conditions the flow of information in the Wisconsin media ecology encourage citizens across the ideological spectrum to retrench into "echo chambers" that amplify highly partisan messages of party leaders and pundits within state politics.

The project research team, its students, and partners have gathered social media, public opinion, news coverage, and qualitative data on Wisconsin since 2010. The team has retrieved millions of tweets concerning Wisconsin politics, accessed 42 waves of Wisconsin surveys from the Marquette University Law School Poll, gathered news content from local newspapers and broadcast outlets, and conducted dozens of interviews with Wisconsin citizens, reporters, and political elites. The team will integrate these data with tracking of talk radio and political advertising content to create unified datasets that combine electoral messaging, news coverage, partisan media, social networking, and public opinion data to reconstruct the political and communication ecology of our state.

PRINCIPAL INVESTIGATOR

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CO-PRINCIPAL INVESTIGATORS

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Michael Wagner, Associate Professor of Journalism and Mass Communication

Christopher Wells, Associate Professor of Journalism and Mass Communication

Development of a Forecast-based Flood and Health Risk Management System to Support Advanced Disaster Preparedness

This project will develop a novel forecast-based interactive online flood and health risk management system to support advanced disaster preparedness. To accomplish this, the research team will couple global flood and health risk prediction models and establish proactive management strategies, plans, and alternatives.

Development of an actionable flood and health risk prediction framework has the potential to radically improve existing disaster management practices, and save lives and resources by providing advanced preparedness and response strategies.

The team will work closely with the International Federation of the Red Cross and disaster management experts in Ethiopia, Peru, and Mozambique.

PRINCIPAL INVESTIGATOR

Paul Block, Assistant Professor of Civil and Environmental Engineering

CO-PRINCIPAL INVESTIGATORS

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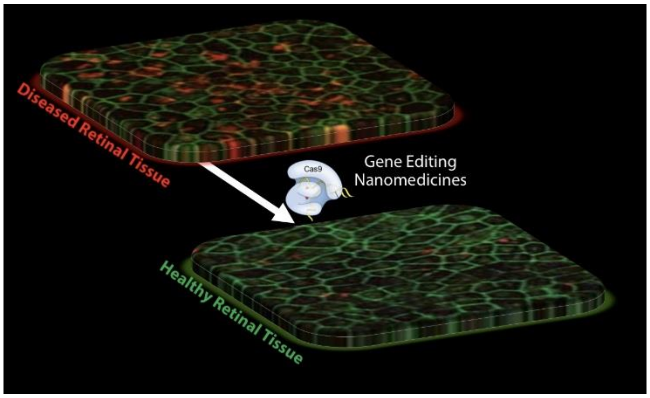
Donald Moynihan, Georgetown University's McCourt School of Public Policy

Jonathan Patz, Professor and Director of the Global Health Institute

Justin Sydnor, Associate Professor of Actuarial Science, Risk Management and Insurance

Stephen Vavrus, Senior Scientist at the Nelson Institute Center for Climatic Research

Gene Editing Nanomedicines to Correct Pathogenic Mutations in Retinal Pigmented Epithelium



Bioengineering advances have now made it feasible for precision gene editing directly in patient tissues with the goal of not only treatment, but of a cure. In this project, the priority is genetic disorders that inflict the eye, specifically the retinal pigmented epithelium (RPE) that surrounds the retina.

Existing state-of-the-art approaches to edit cells within human tissues have significant limitations both with respect to safety and efficacy. The nanomedicine approach of this project is anticipated to overcome these limitations and will set the foundation for a new paradigm in developing genomic medicine.

This project will use advances in biomaterials to generate nonviral, synthetic nanocarriers of CRISPR-Cas9 gene editing machinery for targeted delivery to the RPE. Such research would generally expand the types of tissues that could be edited and hence the spectrum of disease where genomic medicine could have an impact. This hypothesis will be tested to precisely edit pathogenic point mutations *in vivo* within transgenic mouse disease models and in patient-derived, induced pluripotent stem cell (iPSC)-based disease models.

PRINCIPAL INVESTIGATOR

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CO-PRINCIPAL INVESTIGATORS

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David Gamm, Associate Professor of Ophthalmology and Visual Sciences and Director of the McPherson Eye Research Institute

Improving Outcomes for Incarcerated Parents and their Children through Enhanced Jail Visits

This project will develop an innovative multidisciplinary approach to bring about transformative change in the lives of incarcerated mothers and fathers, at-home caregivers, and children through enhanced visits. Although family visits in jail are a key opportunity to maintain parent-child relationships and decrease recidivism for incarcerated individuals, several studies have linked children's visits to jails with elevated child behavior problems and anxiety. Low-income children of color are disproportionately affected by parental incarceration.

The short-term innovation is to develop and examine the feasibility, acceptability, and preliminary efficacy of a multi-level intervention strategy to improve family visits between children and a parent who has been incarcerated in the Dane County Jail in Wisconsin. The intervention will focus on fostering positive family interactions through coaching during jail and home visits, creating family friendly and child appropriate spaces for jail visits, and promoting other correctional systems and facility-level changes that support child-parent contact such as offering in-home visits via laptops.

The long-term goal is to evaluate a well-designed intervention to improve behavioral outcomes and family relationships for children with incarcerated parents as well as reduce recidivism for incarcerated fathers and mothers.

PRINCIPAL INVESTIGATOR

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CO-PRINCIPAL INVESTIGATOR

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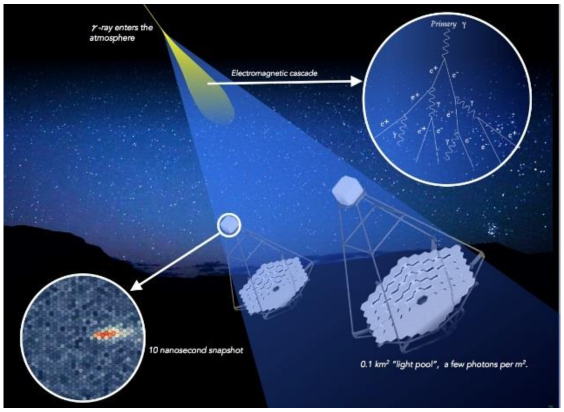
Instrument Development to Study the Highest Energy Photons in the Universe



The highest energy photons in the universe are gamma rays that carry essential information capable of answering leading questions in astrophysics and particle physics. This proposal will support development of low-noise, nanosecond-resolution electronics for very-high-energy gamma-ray astronomy. The technology will enable detection of single optical photons produced by astrophysical gamma rays. Thanks to an innovative technique combining aspects of astronomy and particle physics, it is possible to detect gamma rays from the ground, when they collide with Earth's atmosphere and produce a fleeting (a few billionths of a second in duration) flash of blue Cherenkov light. The technology development can be exploited by the international Cherenkov Telescope Array (CTA) project. When complete, CTA will consist of a large array of telescopes that will be specially instrumented to exploit the Cherenkov technique.

These activities lay the groundwork for significant University of Wisconsin involvement in this highly visible and intellectually rich international project. The Cherenkov Telescope Array will investigate some of the most important mysteries at the heart of multi-messenger astronomy, including the origins of gravitational waves and astrophysical neutrinos, and the nature of dark matter.

PRINCIPAL INVESTIGATOR

Justin Vandenbroucke, Assistant Professor of Physics

CO-INVESTIGATOR

John Gallagher, Professor of Astronomy

Maternal Breathing Dysfunction during Pregnancy Increases Risk for Psychiatric Disorders in Her Offspring: A Paradigm-Shifting Concept

Each year, over half a million women develop sleep disordered breathing (SDB) by the third trimester. SDB is characterized by recurrent partial or complete cessation of breathing during sleep causing pathologic drops in blood oxygen levels, often hundreds of times each night. SDB is a potent inflammatory stimulus, inducing chronic inflammation that, in turn, causes many illnesses in individuals with SDB. There is a growing scientific consensus that maternal inflammation increases susceptibility to autism, which raises a profound question: Is the recent explosion in autism related to the growing incidence of SDB during pregnancy?

How might SDB increase risk for ASD? Fetal brain immune cells, known as microglia, are essential partners in neurodevelopment because they prune excess and imprecise connections in the brain. Shortly after birth, an explosion of connections occurs as the newborn begins to interact with the environment; throughout early childhood, these are gradually trimmed down by microglia to adult levels. This process refines brain connections so that only the most meaningful remain, and superfluous or inefficient connections are removed. ASD is in part a disorder of too many connections, suggesting that normal microglial pruning is disrupted. Since a process known as epigenetics directly links the environment to cell function, we propose that maternal SDB initiates epigenetic alterations in microglia that suppress critical refinement of brain connections.

This project will determine if maternal SDB during pregnancy causes autism-like behavior in the offspring and identify associated epigenetic marks in microglia that impair their pruning activities. These studies will reveal new targets to enable early diagnosis and therapeutic intervention for neurodevelopmental disorders. Because maternal SDB also causes SDB in her offspring, it may also predispose to a multitude of other adult illnesses associated with SDB, including cancer, hypertension, diabetes, obesity, kidney disease, heart disease, stroke, and neurodegenerative disorders.

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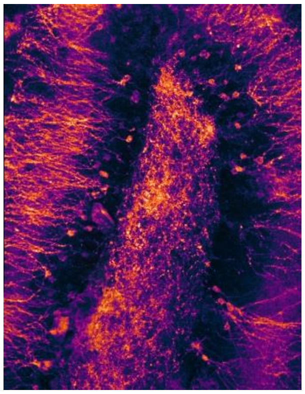
Toxoplasma Infection and Brain Function



The neurobiological impacts of infection by *T. gondii* are almost completely unknown, despite the fact that this parasite establishes a life-long infection in the brains of about one third of the world's human population. In Wisconsin, 4-12.4 percent of children are infected, with a roughly five-fold higher rate on farms. Recent studies have raised concerns about mental health and toxoplasmosis, with reports of links to schizophrenia, depression, and suicide.

A multidisciplinary approach is the only way we will learn how toxoplasmosis influences mental health. This project brings together leaders in microbial science, neuroscience, and computational biology to address this need. This project will generate the first detailed anatomical study of *T. gondii* infection of the brain, telling us which brain regions and cell types are targeted. It also will generate a detailed profile of the impact of *T. gondii* on gene expression in an infected host. A final goal of the project is to determine how infection alters the electrical activity of neurons and establish the functional impact of changes in gene expression. The results will be synthesized into a comprehensive picture for how *T. gondii* modifies the brain of its host, providing valuable insights and a first meaningful step toward understanding how toxoplasmosis affects behavior and mental health.

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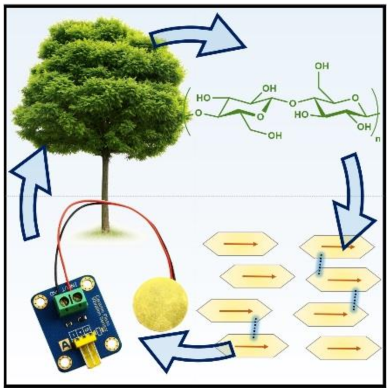
Transforming Wood into a Green, Renewable Electronic Material



This project will develop flexible piezoelectric materials (e.g., ultrasonic transducers for medical imaging, tactile sensors for surgery, actuators for precision motors, and accelerometers for electronics) based on cellulose that are green and that outperform current state-of-the-art piezoelectric materials. Cellulose is naturally generated by plants such as trees, cotton, and hemp or from microbes such as bacteria, algae, and fungi. It is the most abundant natural polymer on earth and provides a sustainable, green resource that is renewable, degradable, biocompatible, and cost effective.

Current commercially employed piezoelectric materials such as polyvinylidene fluoride (PVDF) are non-degradable. The nanocellulose-based piezoelectric materials that will be developed here will be highly renewable and highly biodegradable, thereby dramatically improving environmental sustainability and reducing the accumulation of electronic waste in landfills.

This research may lead to a new class of electronic materials derived from an abundant renewable resource with the potential for a transformative impact on the electronics industry and for new biomedical applications. The results obtained in this project will also provide a strong foundation to position the campus to become a leader in nanocellulose-based materials research.

PRINCIPAL INVESTIGATOR

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COLLABORATOR

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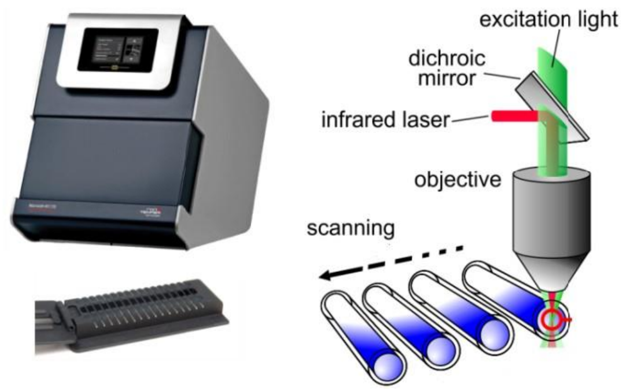
Infrastructure

Accelerating Lead Optimization to Clinical Application Using Microscale Thermophoresis to Quantify Molecular Interactions



This project supports the purchase of a Monolith NT.115pico instrument for use in analyzing molecular interactions. UW–Madison has an urgent need for a general and sensitive method to detect and quantify molecular interactions, such as small molecule-protein, protein-protein, and oligonucleotide-protein binding affinities. Key applications include using the instrument to screen libraries of potentially bioactive compounds and as a quantitative binding assay in fundamental biological, biochemical, and biophysical research. The Monolith instrument uses a new technology based on the movement of biomolecules along a temperature gradient.

The Monolith instrument will support UW researchers as they conduct in-depth mechanistic studies of small molecule/drug target interactions, develop cancer immunotherapeutics, and partake in other related basic and translational research. The addition of the Monolith instrument to the campus capabilities will be critical to the research community since current instrumentation for binding assays on campus either requires a fairly significant amount of sample, or only provides quantitative information for a limited number of molecular interactions. The instrument will be housed and run by trained staff at the UW Medicinal Chemistry Center (MCC) within the School of Pharmacy.

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CO-PRINCIPAL INVESTIGATOR

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Jennifer Golden, Assistant Professor of Pharmaceutical Sciences and Associate Director of the UW Medicinal Chemistry Center

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Douglas McNeel, Professor of Medicine

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Manish Patankar, Professor of Obstetrics and Gynecology

Paul Sondel, Professor of Pediatrics

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Michael Sussman, Professor of Biochemistry and Director of the Biotechnology Center

Douglas Weibel, Professor of Biochemistry, Biomedical Engineering and Chemistry

Yongna Xing, Associate Professor of Oncology

Wei Xu, Professor of Oncology

John Yin, Professor of Chemical and Biological Engineering and Systems Biology Theme Leader at the Wisconsin Institute for Discovery

Acquisition of an Illumina NovaSeq Next Generation DNA Sequencer for UW–Madison

DNA sequencing capabilities at UW–Madison will get a boost from this project, which supports the purchase of a 'next generation' DNA sequencer, the Illumina NovaSeq. The Illumina NovaSeq provides 15 times the sequence throughput at almost half the cost as the campus' older instrument. This upgrade in hardware for the Illumina platform of sequencers, which performs work for hundreds of laboratories on campus, is required to maintain state of the art critical service to researchers and clinicians in colleges, centers and departments all over UW.

The HiSeq 2500 purchased in 2013 has in the past five years performed 2,531 sequencing runs from samples provided by 240 different campus faculty investigators in departments, centers and colleges all over campus. Equally important, this instrument will be operated in an established core facility that meets the needs of the campus research community with technology that is fundamental to a majority of modern basic and translational experiments performed in the biological sciences.

DNA sequencing is a need that is now almost as ubiquitous as computers at UW-Madison, for everything from forensics to disease treatment as well as basic molecular, cellular and organismal research in the biological sciences. With the future of personalized medicine already upon us, and the large potential of clinical uses for DNA sequencing to provide rapid diagnosis and individualized disease treatments, this instrument will not only help campus researchers, but also, will contribute to improving the health of citizens all over this state.

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Jean-Michel Ane, Professor of Bacteriology and Agronomy

David Baum, Professor of Botany

Kristen Bernard, Professor of Pathobiological Sciences

Qiang Chang, Associate Professor of Genetics and Incoming Director of the Waisman Center

Mike Cox, Professor of Biochemistry

Cameron Currie, Professor of Bacteriology

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John Doebley, Professor of Genetics

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David Eide, Professor of Nutritional Sciences

Catherine Fox, Professor of Biomolecular Chemistry

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Thomas Givnish, Professor of Botany

Michael Gould, Professor of Oncology

Rick Gourse, Professor of Bacteriology

Daniel Greenspan, Professor of Cell and Regenerative Biology

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Shawn Kaeppler, Professor of Agronomy

Ned Kalin, Professor of Psychiatry

Yoshi Kawaoka, Professor of Pathobiological Sciences

Paul Koch, Assistant Professor of Plant Pathology

Jason Kwan, Assistant Professor of Pharmacy

Jennifer Laffin, Associate Professor of Cytogenetics

Dudley Lamming, Assistant Professor of Endocrinology

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Ramamurthy Mahalingam, Assistant Professor of Agronomy

Patrick Masson, Professor of Genetics

Gillian McLellan, Assistant Professor of Surgical Sciences

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Phil Simon, Professor of Horticulture

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Rupa Sridharan, Assistant Professor in Cell and Regenerative Biology and Wisconsin Institute of Discovery

Garret Suen, Associate Professor of Bacteriology

Susan Thibeault, Professor of Otolaryngology

William Tracy, Professor of Agronomy

Raghu Vemuganti, Professor of Neurological Surgery

Donald Waller, Professor of Botany

Thea Whitman, Assistant Professor of Soil Science

Marvin Wickens, Professor of Biochemistry

Mostafa Zamanian, Assistant Professor of Pathobiological Sciences

Jing Zhang, Professor of Oncology

Xinyu Zhao, Professor of Neuroscience and the Waisman Center

Data Science Hub for UW–Madison

This project will launch a campus-wide Data Science Hub (DSHub), paving the way for an eventual Data Science Institute. The goal of DSHub is to coordinate and execute a campus-wide data science strategy that fills critical gaps and supports data science growth and cross-fertilization.

In the last decade, data science has gone from the "big data" fad to a mission-critical enterprise need. DSHub will increase visibility of UW–Madison as a major data science destination, provide unified leadership to advance campus expertise in data science, enable big funding opportunities, foster researcher training in data science, coordinate and strategize development of educational tools for data science degree programs, support domain scientists doing data science, foster cross-disciplinary methodological research in data science, and develop data science outreach to Wisconsin.

PRINCIPAL INVESTIGATOR

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AnHai Doan, Professor of Computer Science

Kristin Eschenfelder, Professor of iSchool

Michael Ferris, Professor of Computer Science

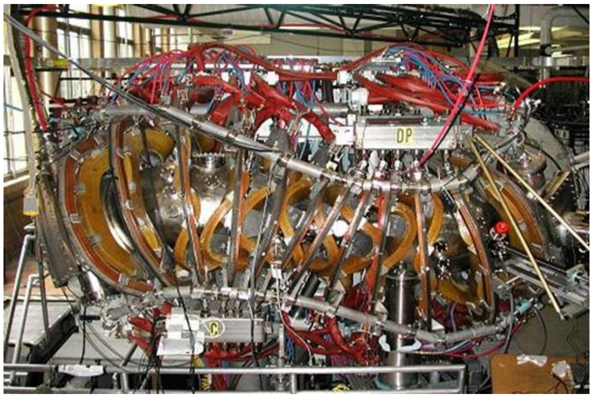
Lauren Michael, Research and Computing Facilitator at Wisconsin Institute for Discovery

Robert Nowak, Professor of Electrical and Computer Engineering

Paul Rathouz, Professor of Biostatistics and Medical Informatics

Eric Wilcots, Professor of Astronomy

Fusion Energy Research at the Next Frontier: Integrating Optimized Plasma Confinement with Interdisciplinary Science and Engineering



The next grand challenge in fusion energy sciences is the understanding and control of the interactions between high temperature plasmas and the surrounding solid material systems under extreme conditions. This project will define the mission, scope, and pre-conceptual design of a new magnetic plasma confinement facility to enable studies on plasma confinement optimization with the coupled plasma-materials interface at requisite heat and particle fluxes.

A key feature of this initiative will be the coupling of this expertise with elements of the material science and advanced manufacturing research communities on campus and elsewhere. An additionalgrand challenge in fusion energy sciences is understanding and controlling the anomalous transport of energy and particles arising from saturated nonlinear turbulence in magnetically confined fusion plasmas. This is done here by careful design of the externally controlled 3-D magnetic fields. At the same time, interactions between these high temperature plasmas and the surrounding solid material systems must be managed under extreme conditions. This is an environment rich in physical phenomena with relevance and applications far beyond the fusion energy goal. With its expertise in plasmas, material sciences and high-temperature environments, the UW–Madison can lead academic research over the next decade to address this challenge.

PRINCIPAL INVESTIGATOR

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CO-PRINCIPAL INVESTIGATORS

Raymond Fonck, Professor of Engineering Physics

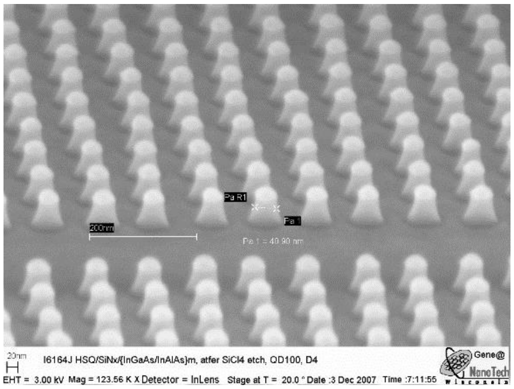
Chris Hegna, Professor of Engineering Physics

John Sarff, Professor of Physics

Oliver Schmitz, Associate Professor of Engineering Physics

Carl Sovinec, Professor of Engineering Physics

State-of-the-Art, Reactive-Ion-Etching Instrument for Nanofabrication of Devices at UW–Madison



UW-Madison has established itself as a national leader in the area of nano-structured semiconductor materials and devices. This project provides acquisition of a reactive-ion etching (RIE) system to allow researchers on campus to further push the envelope on the emerging fields of semiconductor nano-fabrication and nano-manufacturing.

The etching system, called APEX SLR, working in conjunction with existing UW capabilities and strengths in materials synthesis and nano-patterning (newly acquired advanced electron-beam lithography system), will provide unique opportunities to UW-Madison for advancing materials and device development for the next generation of electronic and optoelectronics applications, such as ultra-low power dissipation lasers, extended- wavelength response detectors, and ultrahigh-efficiency multi-junction solar cells. This system will be housed in the Wisconsin Center for Applied Microelectronics (WCAM) cleanroom facility.

PRINCIPAL INVESTIGATOR

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COLLABORATORS

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Thomas Kuech, Professor of Chemical and Biological Engineering

Jack Ma, Professor of Electrical and Computer Engineering

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The UW*LandLab* - a Place for Ecological Solutions to Land Use Problems

The UW*LandLab* will be a space where innovative solutions to complex land use challenges are explored, interrogated, and planned. The UW*LandLab* will build and provide a sustainability process that brings together science-based knowledge, decision-support tools, and innovative stakeholder engagement to help solve problems and make decisions about land use with community partners. Critical to this endeavor, partnerships and trust will be cultivated and nurtured via reciprocal site visits, listening sessions, and collaborative data exploration.

For example, land management solutions to the environmental problems caused by modern agriculture have been well-known for decades, but considerable social, political, and economic resistance has impeded their implementation. How do we configure and incentivize landscapes that produce healthy food, feed, fiber, and fuel while simultaneously helping to purify water, stabilize climate, and enhance biodiversity? Solutions that simultaneously improve all of these criteria exist, but must be explored in a collaborative, collegial manner where tradeoffs and synergies are acknowledged, mitigated, and agreed upon by stakeholders. Using data, models, expertise, and facilitated engagement, the UWL*andLab* will position itself as a space where people with conflicting world views, goals, and expertise can come together to engage in discussion and design processes that arrive at enduring and effective land-use strategies.

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