McPherson
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UNIVERSITY OF WISCONSIN–MADISON

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AI Helps Broaden Access to Diabetic Retinopathy Care

Roomasa Channa, MD

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Making Sense of Colors

Karen Schloss, PHD

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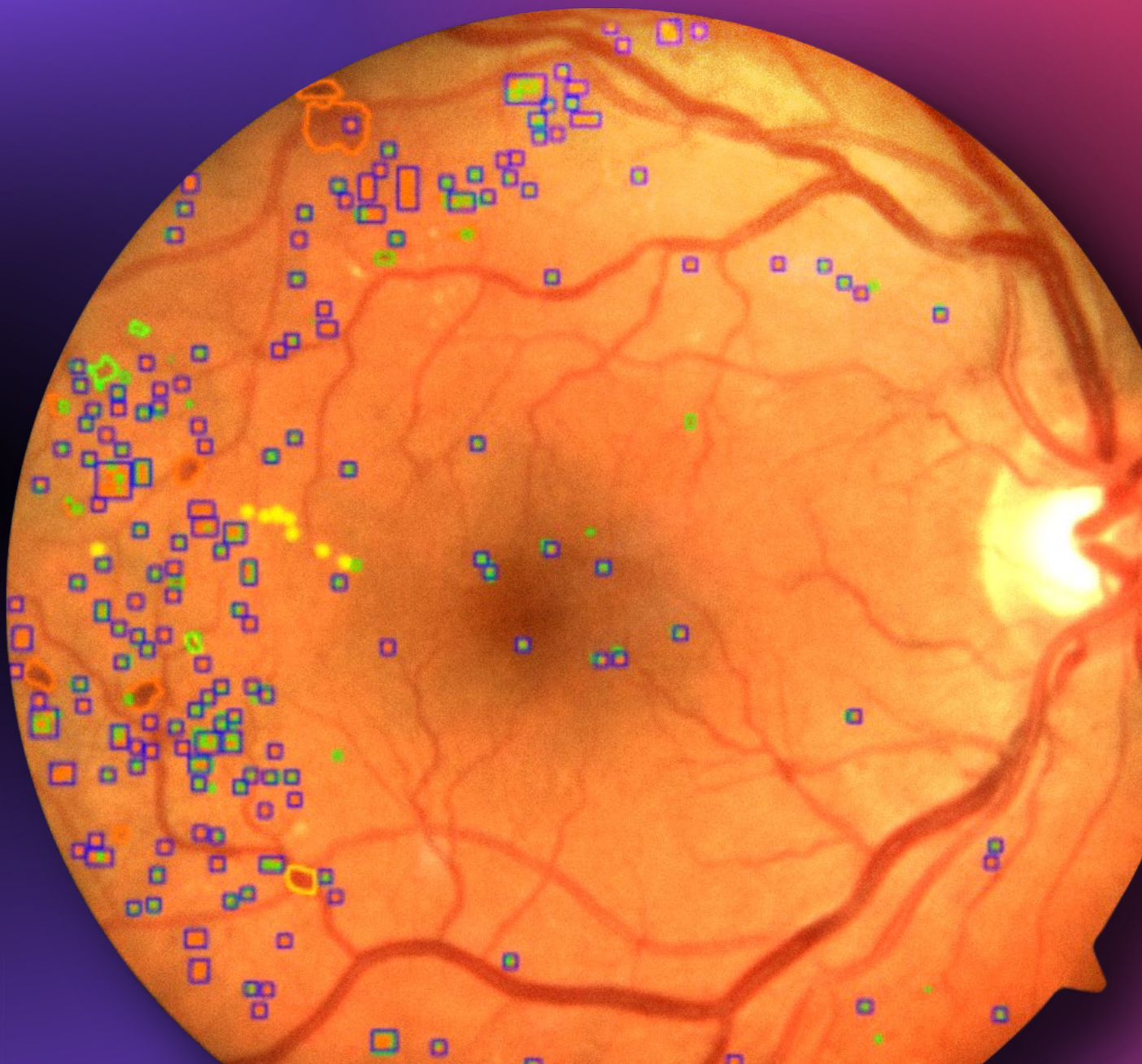


From the Director

Dear Friends of the McPherson ERI,

Fall 2024 sees the McPherson Eye Research Institute achieve an important milestone. Our ability to fund new and exciting vision research will reach an all-time high with the introduction of the Grant Accelerator Program (GAP), an annual funding mechanism that will jumpstart early-stage projects that address "gaps" in knowledge, technology, and treatments. You can read more about GAP below. It's important to note that this program—and many others—wouldn't exist without our generous donors. Dr. Alice McPherson, whose estate gift will largely fund the GAP awards, has been joined by others whose passion for vision research has been unwavering. We are very thankful for this support.

It is often overlooked that every FDA-approved treatment that finds its way to patients requires laboratory research. The purpose of this foundational research is to develop ideas, perform experiments, and interpret and distribute results so that others can critically assess their merit. Just as you need information to make informed medical decisions, we need information to develop effective medical therapies. The two scientists profiled in this issue of ***InSights*** are experts at collecting and analyzing different types of information, and their work has recently yielded fascinating results. Dr. Roomasa Channa works with artificial intelligence (AI) to understand ways in which underserved communities can receive better care for diabetic retinopathy, a blinding disease that is growing at an alarming rate. Dr. Karen Schloss's lab investigates how to present data so that it is more easily understood, focusing on color-coding of information. Both Dr. Channa and Dr. Schloss exemplify the Institute's commitment to rigorous research and to clear dissemination of results to the broadest possible audience.

This season also marked a critical milestone for my own lab's research, with FDA clearance obtained to start (hopefully in 2025) the first clinical trial to treat retinitis pigmentosa with iPS cell-derived photoreceptors. Over 15 years ago, my lab embarked on research to determine whether authentic human photoreceptors can be made from these stem cells. Through countless studies, we discovered that they can, and now we are on the cusp of seeing whether they are a safe and effective means to help patients. Staying in touch with the McPherson ERI through our newsletters and website (vision.wisc.edu) remains the best way to hear about advances from all Institute scientists, which we will continue to share as quickly and freely as possible.

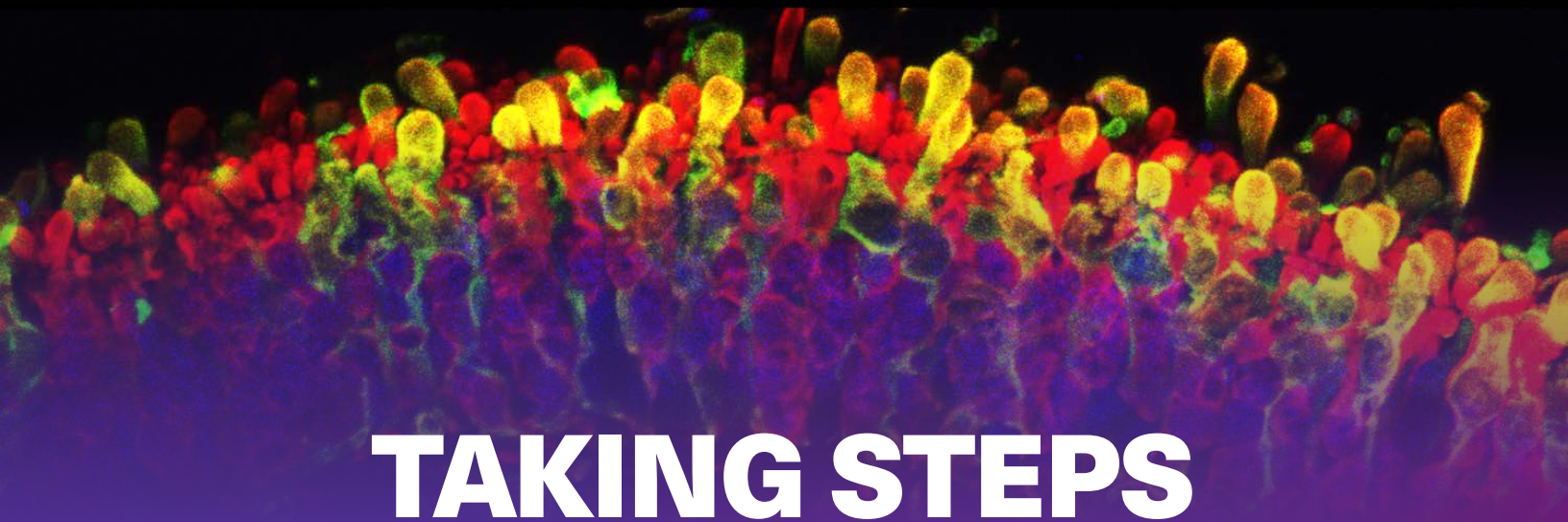
Thank you for your help and interest,

RRF Emmett A. Humble Distinguished Director

Professor, Department of Ophthalmology and Visual Sciences

Sandra Lemke Trout Chair in Eye Research
McPherson ERI Sandra Lemke Trout Chair in Eye Research

A section of photoreceptors grown from induced pluripotent stem cells in the Gamm Lab.



TAKING STEPS TO RESTORE VISION

Launching a Stem Cell Clinical Trial for Retinitis Pigmentosa

Stem cell-derived photoreceptor replacement therapy has been one of the goals of Dr. David Gamm's lab for a decade and a half, beginning with the development of a process to create human photoreceptor cells (cones and rods) from induced pluripotent stem cells (iPSCs). In September 2024, the FDA approved a plan to begin initial human trials using iPSC-derived photoreceptors for individuals with advanced forms of retinitis pigmentosa.

BlueRock Therapeutics LP, a wholly owned subsidiary of Bayer, Inc., will manage the trial, and has licensed the cell therapy (termed OpCT-001) from Opsis Therapeutics and FUJIFILM Cellular Dynamics, which supported the research, development, and manufacturing of OpCT-001. Trial participants will be enrolled in multiple locations, with the goal of beginning the trial in at least one location in 2025. In the press release announcing FDA clearance, Amit Rakhit, Chief Development and Medical Officer at BlueRock Therapeutics, noted, "We believe that OpCT-001 has potential to restore vision in people living with primary photoreceptor diseases and look forward to working with the ophthalmology community in initiating our Phase 1/2a clinical study."

Of note, photoreceptors are also lost in macular degenerative diseases like AMD, Best disease, and Stargardt disease, but these conditions also require replacement of retinal pigment epithelium (RPE) cells. Efforts are well underway to develop products to address these diseases as well, so stay tuned.

MIND THE GAP

Introducing the Grant Accelerator Program

The McPherson ERI has just introduced an exciting new grant program for our Principal Investigators and their labs: **The Grant Accelerator Program (GAP)**. This new program provides significant seed funding—more than the Institute has ever awarded in the past—thanks to a gift from the Estate of Dr. Alice McPherson, along with generous support from the Van Vreede McPherson ERI Greatest Needs Fund and the Robert A. Brandt Macular Degeneration Fund. GAP Awards will support innovative research that advances knowledge of the visual system and/or applies such knowledge to protect or restore vision.

In this inaugural year of the program, McPherson ERI will be offering up to six $50,000 GAP awards to support a wide range of vision research at UW-Madison, as well as one additional $50,000 AMD GAP award specifically designated for research in age-related macular degeneration. GAP funds are intended to allow researchers to explore promising new research avenues that are not yet at the stage to be funded by the National Institutes of Health (NIH). Oftentimes, the most novel and potentially impactful ideas never get off the ground because they lack enough data to be competitive for NIH funds. GAP provides funds to get these projects going. Importantly, GAP complements the Institute's existing Grant Summit Program (GSP), which is designed to help well-established research projects reach new heights.

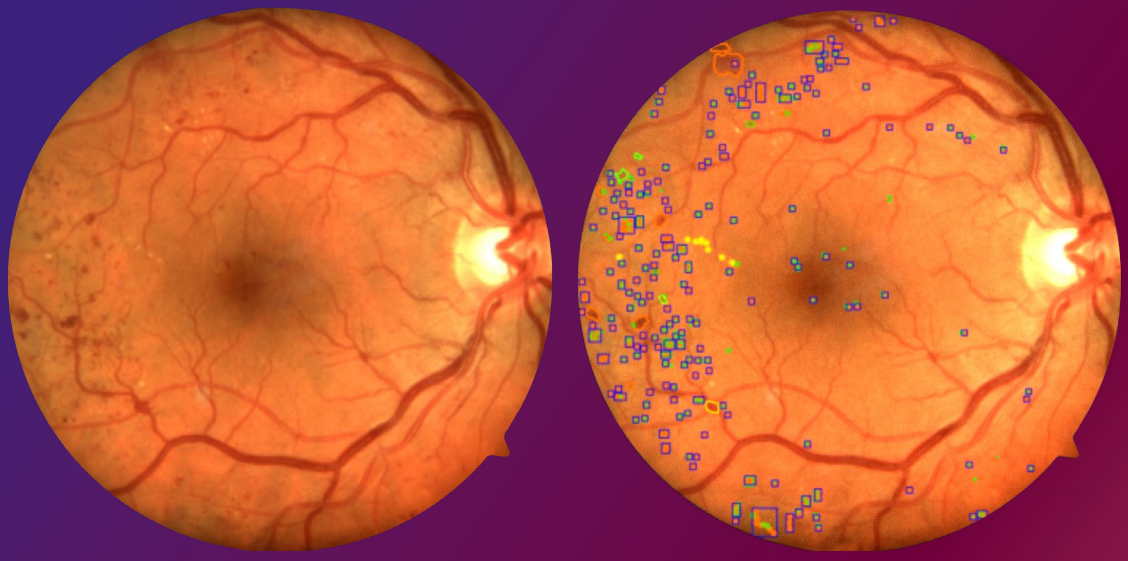
EQUAL VISION

Employing Artificial Intelligence (AI) to reduce disparities in the diagnosis and treatment of vision loss

Dr. Roomasa Channa is a retina surgeon with a research focus on preventing vision loss from diabetes. Throughout her career, her clinical work has been the inspiration for her research. As a trainee, one of her first patients on call was a young African-American woman from inner city Baltimore. She presented to the emergency room with sudden vision loss and headaches, thinking she was having a migraine. Dr. Channa noted that one of the patient's eyes was full of blood, and the other had the classical findings of advanced diabetic retinal disease. The patient was unaware that she even had diabetes and severely uncontrolled blood sugars.

Diabetes is the leading cause of vision loss among working aged adults in the U.S., but Dr. Channa has long thought that advanced diabetic eye disease is preventable with screening and early detection. However, as the number of patients with diabetes increases, it has become burdensome to both patients and providers to perform the annual eye screenings recommended by the American Diabetes Association and the American Academy of Ophthalmology. This burden is disproportionately higher for patients from socioeconomically disadvantaged backgrounds due to inequities in our health system. Solving the problem of poor access to eye care became Dr. Channa's driving research interest and coincided with growing interest in ophthalmology to use artificial intelligence to address this problem.

Diabetic retinal diseases have very characteristic findings on retinal images (pictures your eye doctor routinely takes to document how your retina looks), findings that were established at the Wisconsin Reading Center. These readily identifiable indicators make it possible to train a computer to do the repetitive task of searching these images for characteristic abnormalities. Currently, we have multiple AI programs that can automatically detect diabetic retinopathy from retinal images. Dr. Channa's lab analyzes the ability of these AI approaches to prevent vision loss from diabetes, which is needed to maximize their effectiveness in the clinic.



A retinal scan of a patient with diabetic retinopathy. In the image on the right (and on the cover of this issue), diabetic retinopathy lesions are outlined by an AI algorithm. Image courtesy of Roomasa Channa, MD.

An artificial intelligence algorithm guides the operator to acquire a high-quality image and detects the presence/ absence of referable diabetic eye disease.

Table-top camera.

A screening result is available within a few minutes.

The model developed in Dr. Channa's lab is called the Care Process for Preventing Vision Loss from Diabetes (CAREVL) model, and it has already determined that AI-based eye screening (as opposed to traditional in-person screening at an eye doctor's office) could prevent severe vision loss in an additional 27,000 patients with diabetes across the U.S. The effect could be further increased 3-to-4-fold by optimizing "next steps" in the care process, such as following up with recommended eye treatments. Based on this and previous work, the Channa Lab designed a screening strategy termed AI-BRIDGE (Artificial Intelligence-Based point of caRe, Incorporating Diagnosis, schedulinG, and Education) to address the problem of poor adherence with screening and eye care follow-up.

The AI-BRIDGE strategy begins with eye imaging and identification of eye disease in primary care clinics using AI-based analysis. It then facilitates follow-up by providing patients with culturally-adapted education regarding diabetic eye disease, and then helping local clinics schedule eye appointments. An upcoming multi-center clinical trial, funded by a 5-year, $4.7 million R01 grant from NIH/NEI, will test whether the AI-BRIDGE screening strategy improves diabetic eye care access across different racial and ethnic groups compared to standard approaches.

The implementation of AI-based eye screening in underserved settings has been challenging, and there is the risk that pervasive eye care disparities will be worsened if AI-based screening is adopted by only large academic centers, and ignored in other settings. Dr. Channa's upcoming multi-center trial will include underserved primary care clinics and work to seamlessly integrate this technology into their busy workflows. Ultimately, the trial will assess whether AI screening technology can decrease racial, ethnic, and socioeconomic disparities in vision loss.

Dr. Channa's lab also employs AI to study how retinal damage first begins in diabetes, with the goal of halting it as soon as possible. For example, the initial effects of high blood sugar may not affect the blood vessels of the retina like most researchers assume; rather, it may alter the retinal cells themselves. With the help of computer scientists at UW-Madison, she is leading a prospective trial at the UW Department of Ophthalmology and Visual Sciences that uses AI to analyze retinal images with the goal of uncovering changes in diabetic retinal disease before they are visible to human examiners.

Taken together, Dr. Channa's comprehensive, cutting-edge research provides great hope to a nation striving to address a rapidly growing burden of vision loss from diabetes in all segments of our population.

Schloss Lab members walked through the Chazen Museum in Madison as their unique way of participating in Cycle for Sight 2024. Dr. Schloss is fourth from the right.

MAKING SENSE OF COLORS

Have you ever tried to interpret a weather map so that you could decide whether to wear your rain boots or snow boots, but had trouble figuring out what the colors meant? Or perhaps you have had the experience of standing in front of several bins in a restaurant with a tray full of trash and recyclables, and had to awkwardly pause to figure out which color bin was for paper vs. trash? If so, then you were using visual reasoning to determine the meaning of perceptual features (in this case, colors) to make rapid judgments about how to behave in the world around you.

Sometimes visual reasoning feels easy, but other times understanding the meaning of visual features can feel like an unnecessarily difficult struggle. Such struggles can be an annoyance or distract us from critical tasks that require quick action.

The Schloss Visual Reasoning Lab works to understand how people interpret perceptual features, like color, in order to make the world easier to navigate and more enjoyable to experience. Their research, led by McPherson ERI member Professor **Karen B. Schloss, PhD** (UW-Madison Department of Psychology and Wisconsin Institute for Discovery), is guided by a core premise: When designers create information visualizations (e.g., maps, graphs, diagrams, and signs), they communicate messages by representing concepts in perceptual features. For example, in a map of rainfall across the state, a designer may communicate that there will be more rainfall in Madison than Milwaukee by using darker colors. (The term “designer” refers to anyone who creates visualizations to communicate messages, including scientists, business professionals, or even middle school students at science fairs). On the receiving end, when observers interpret visualizations, they draw conclusions from their observations. Communication is successful when the messages sent by the designer are accurately and efficiently received by the observer.

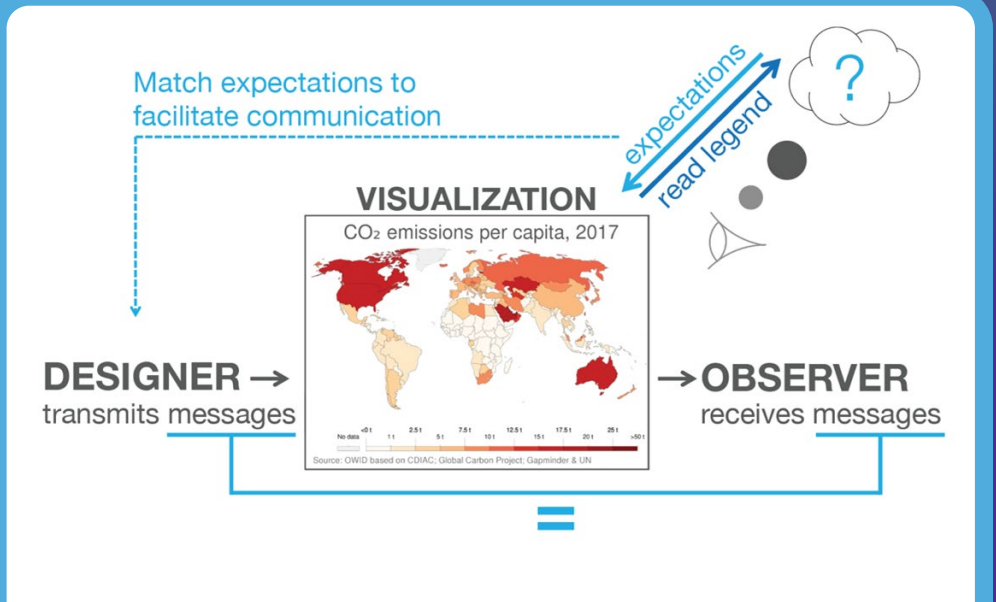
You may ask, if visualizations include legends or labels that say what the colors mean, can't observers simply read the legends/labels and receive the exact message that the designer intended? However, it's not so simple. Research from the Schloss Lab has shown that observers bring prior expectations to their interpretations—for instance, biases about how colors should be used to convey information—and they have more difficulty interpreting visualizations that violate those expectations, even with legends/labels. By understanding these expectations, designers can create visualizations that are easier to interpret and thus help the observer receive the message that was intended by the designer.

The Schloss Lab has studied several factors that contribute to expectations about how colors help convey concepts. One factor is "direct" associations—the degree to which individual colors are associated with concepts (such as oranges associated with fire and blues associated with glacial ice). Another factor is "relational" associations—the degree to which color relations are associated with conceptual relations, such as darker colors being associated with larger magnitudes in data. In work led by former graduate student Melissa Schoenlein, the team developed new methods to predict people's expectations of color meaning, even when these two factors conflict. And in work led by current graduate student Kushin Mukherjee, the group developed methods to predict conditions in which colors can represent concepts on their own (without legends/labels). The results not only inform visualization design, but also have led to new psychological theories about how the human mind can find meaning from basic perceptual features like color.

Having established their approach by studying color, the Schloss Lab recently received support from the National Science Foundation to test their theories in new domains, including textures that people can see or touch. This new research avenue offers exciting potential to improve communication for individuals with visual impairments, who may rely on touch rather than vision to glean information from the world.

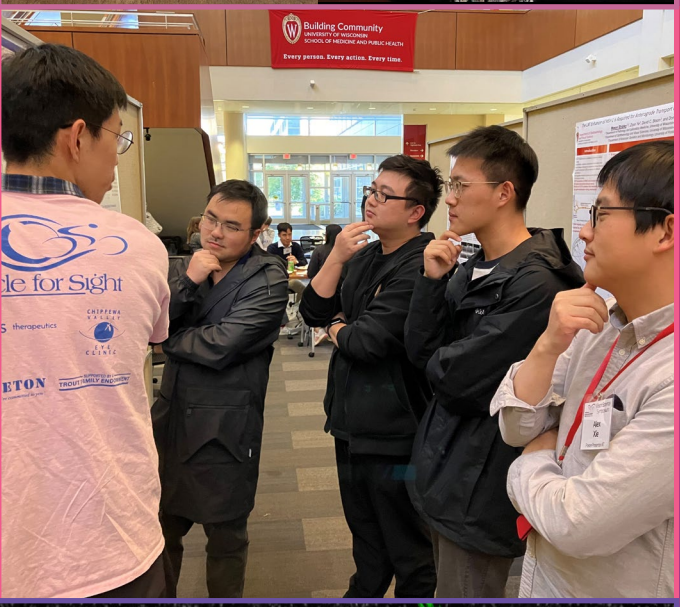
Funding: ***This work has been supported by several awards from the McPherson Eye Research Institute (MERI), the UW-Madison Office of the Vice Chancellor for Research (OVCR), and the National Science Foundation (NSF).***

The Schloss Lab aims to synchronize the designer's intent with the information received by the observer. Image courtesy of Karen Schloss, PhD.



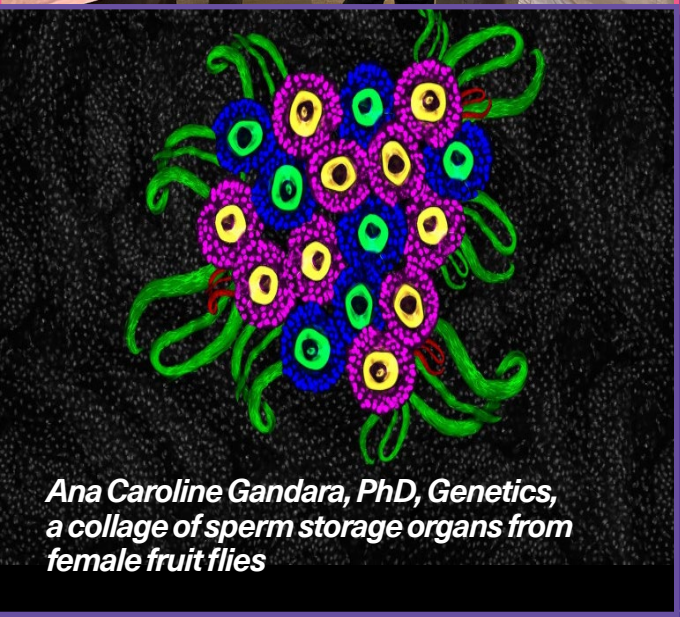
2nd Annual Sandra Lemke Trout Lecture

Goldis Malek, PhD (Duke University), delivered the annual Sandra Lemke Trout Lecture as a Grand Rounds talk in collaboration with the Department of Ophthalmology & Visual Sciences, on Friday, September 13th. Dr. Malek's talk on potential therapeutics for AMD was very well attended, and widely viewed online as well.



16th Annual Vision Science Symposium

McPherson ERI's annual vision science poster session and Distinguished Lecture took place on Friday, October 25th, and drew a large audience of grad students, postdocs, and PIs to the HSLC Atrium. Sönke Johnsen, PhD (Duke University) spoke on *Three Tales from the Sea: How Our Cognitive and Sensory Biases Affect Our Study of Vision.*



Ana Caroline Gandara, PhD, Genetics, a collage of sperm storage organs from female fruit flies

Cool Science Image Contest Exhibit 2024

Winning images from this annual contest, sponsored by UW Strategic Communication and the McPherson ERI (with support from Promega), will hang in the Mandelbaum & Albert Family Vision Gallery on the 9th floor of the Wisconsin Institutes for Medical Research through January 10th, 2025.

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