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Eye Research Institute
UNIVERSITY OF WISCONSIN–MADISON

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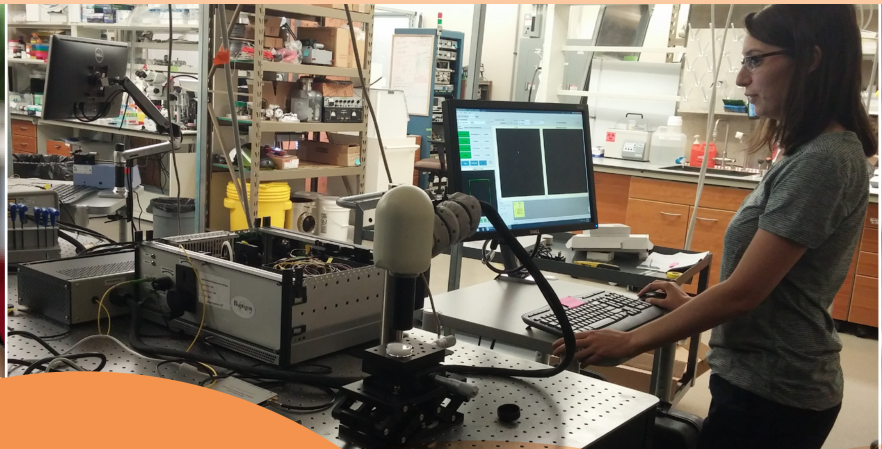


RESEARCH NEWS

A NEW WAY TO SEE INSIDE THE EYE

WITH MARYSE LAPIERRE-LANDRY & DR. MELISSA SKALA

Optical coherence tomography (OCT) is an imaging tool commonly used in the eye for screening, diagnosis and treatment of diseases of the retina and cornea. Used regularly by researchers in the eye and vision community to better understand diseases in the human eye, OCT is also used in multiple animal eye models. OCT can quickly and non-invasively image microscopic structures in the eye without dyes, thereby rendering three-dimensional images of the layers of the retina. Also without using dyes, OCT can produce three-dimensional maps of the blood microvessels in the eye. This "multi-functional" quality of OCT makes it a versatile tool for researchers and clinicians alike. For this reason, researchers in optics and biomedical engineering are developing additional OCT modalities, which if successful could be incorporated in existing instruments and could provide functional contrast. Photothermal optical coherence tomography (PT-OCT) is one of those new modalities, which is currently being developed by Maryse Lapierre-Landry, a graduate student in Dr. Melissa Skala's lab.

Traditional OCT detects changes in refractive index, for example between a tissue layer containing mostly cell nuclei versus a tissue layer containing mostly collagen. Conversely, PT-OCT detects optical absorbers, such as the melanin naturally present in the eye. PT-OCT achieves this added contrast by repeatedly heating the absorbers in the tissue by a few degrees (1-3°C) at a known frequency. This in turn causes a cyclical change in refractive index around each absorber, which is then scanned by the OCT beam. The OCT signal is sensitive to small changes in refractive index, and thereby detects the temperature oscillations. At the post-processing stage, sections of the tissue that are oscillating at the photothermal frequency indicate the presence of absorbers, and their position can be mapped onto the OCT image. Variations in the levels of an absorber such as melanin can occur in multiple diseases of the eye, such as melanoma or age-related macular degeneration, and PT-OCT could eventually be used to study the progression of those diseases.

PT-OCT was initially demonstrated on different types of absorbers in cells, tissue samples such as breast, and in the skin and tumors of living mice. However, Ms. Lapierre-Landry, Dr. Skala, and collaborators were the first to demonstrate PT-OCT in the eye. Collaborators at the Vanderbilt Eye Institute included Dr. John Penn and his graduate student Andrew Gordon. Initial studies were conducted in the eyes of living mice, and established a strong PT-OCT signal from melanin in the retinal pigment epithelium (RPE). In a different experiment, lesions were created at the back of the mice retina using a laser, after which the mice were injected with gold nanoparticles via the tail vein. The presence of new and "leaky" vasculature in the lesion caused the gold nanoparticles to accumulate in the retina, and their presence was detected using PT-OCT.

Dr. Skala and Ms. Lapierre-Landry moved from Vanderbilt University to the University of Wisconsin last year, and have established collaborations with McPherson Eye Research Institute members to develop PT-OCT for clinical applications. Additional research is needed to make PT-OCT a faster, more user-friendly system with a wider range of contrast agents, which is the current focus of Maryse Lapierre-Landry's graduate work in the Skala Lab. The added contrast of PT-OCT has the potential to provide three-dimensional, non-invasive molecular imaging in the eye. In the future, this technology could facilitate automatic RPE segmentation to study diseases such as age-related macular degeneration, and could also increase contrast on OCT images during macular surgery.

FROM THE DIRECTOR:

Dear Friends of the McPherson Eye Research Institute,

The eye is one of the most complex and specialized organs in the body. When it works well it is a marvel, although like many aspects of our health we rarely think about it until it begins to fail us. When it does fail, we look first to available treatments, some of which can be quite effective (cataract surgery, for example). However, treatments are too often unavailable or disappointing. In these situations, it is common to look to the biological sciences for direction and help – and indeed, our McPherson ERI biologists have seen and taken part in many exciting advances over recent years. That being said, a single discipline, no matter how broad, can only take us so far in isolation. As this issue of *Insights* underlines, fields beyond biology are critical to understanding how the eye works and how to fix it when it succumbs to disease or injury. McPherson ERI members in biomedical engineering, psychology, neuroscience, computer science, and a host of other disciplines are on the front lines of today's most important advances in vision science. I'm pleased that the work of two such scientists, Melissa Skala (Biomedical Engineering) and Bas Rokers (Psychology) are featured in these pages.

The across-the-campus (and well beyond) reach of the Institute is arguably our greatest strength. There is general acknowledgement at most institutions that the majority of transformational research advances will be made in multifaceted collaborative teams, but few research organizations have the structure or spirit to make it a reality. Fortunately, UW-Madison in general is far ahead of most institutions in putting this awareness into practice. Two months ago, I spoke about stem cell applications for blinding disorders at the National Eye Institute (NEI) in Bethesda, MD. I was introduced by NEI director Dr. Paul Sieving, who commented that the McPherson Eye Research Institute is a model for future vision research organizations, as it eliminates artificial boundaries and brings together the range of expertise and ideas necessary to overcome obstacles to therapeutic and technological development. I could not have said it better myself.

And our results bear this out. McPherson ERI-affiliated labs continue to receive noteworthy awards, such as a recent NEI grant to Drs. Nader Sheibani, Chris Sorenson, and Daniel Albert to study diabetic retinopathy using a new type of imaging technology; a defense department award to Dr. Andreas Velten's lab to develop ways to "see around corners"; and another NEI grant to our Retinal Stem Cell Program (comprised of biologists and engineers) for a project to replace photoreceptor cells in the eye. In addition, Dr. Hongrui Jiang was given the 2017 Research to Prevent Blindness Stein Innovation Award to create implantable sensors to register pressure constantly inside the eye of glaucoma patients.

I am amazed by the creativity and drive of our individual researchers, but even more so for their enthusiasm for working together. They have more ideas than they have time to pursue, and certainly more ideas than can be supported in the current funding environment – which is where the help of our extended McPherson ERI community comes in. We're very grateful for the assistance that we receive; among other things, it is essential in creating collaborative networks that can then be supported by larger federal grants. Thank you, and we will continue to share our progress and successes with you in the future.

David M. Gamm, MD, PhD

RRF Emmett A. Humble Distinguished Director, McPherson ERI
Sandra Lemke Trout Chair in Eye Research

RESEARCH NEWS

FROM *LOOKING* TO *SEEING*

BAS ROKERS, KAREN SCHLOSS & ARI ROSENBERG

Eye and brain function are intricately linked. The brain requires the eyes to look, but the eyes require the brain to see. McPherson ERI member-researchers in psychology and neuroscience, disciplines that study the mind and brain, are critically important to understanding many issues in vision function and dysfunction. Bas Rokers, Associate Professor in the Department of Psychology at UW-Madison, is an exemplar of the UW-Madison's strength in these fields.

A central question in visual perception is how the flat images received by the two eyes are transformed into our experience of the three-dimensional world in the brain. Research in the Rokers Vision Laboratory is targeted at understanding the neural mechanisms that make that possible. Identifying these mechanisms will help us understand the cause of visual impairments such as amblyopia (commonly known as lazy eye) and motion blindness.

Like many McPherson ERI-affiliated scientists, Dr. Rokers collaborates with colleagues in multiple fields both across the UW-Madison campus, and in other institutions in the U.S. and globally. On this page, you'll see a sampling of the research projects in the Rokers Vision Laboratory.

Virtual reality

New technologies, such as virtual and augmented reality, provide unique opportunities to bridge the gap between fundamental research in the laboratory, and an understanding of visual perception and navigation in the three-dimensional world. In collaboration with Dr. Karen Schloss at the Wisconsin Institutes for Discovery, Dr. Rokers has initiated the Virtual Brain Project. The goal of this project is to understand the factors that facilitate effective perception and navigation in novel (virtual reality) environments. In addition to identifying these factors, this work may produce effective educational tools for neuroscience instruction.

Figure 2: Virtual Reality (VR) as a tool for education. VR provides unprecedented opportunities to learn about complex, otherwise inaccessible environments, such as the human brain. However, a number of barriers to widespread adoption remain. For example, novice users find it challenging to navigate and remain oriented in virtual environments. The Rokers laboratory is investigating the role of implicit cues, such as color. In the example depicted here, they used an ecologically-inspired color scheme, using greener colors for more inferior parts of cortex, and bluer ones for more superior parts to mimic the color of the natural environment (i.e., blue sky and green grass).

Neural basis of perception

Multiple visual cues inform us about the motion of objects in our environment. For example, small differences between the two eye's images provide valuable information about an object's motion in three dimensions. However, when we close one eye, an object's changing size can still tell us that it is approaching. In collaboration with Dr. Ari Rosenberg in the Department of Neuroscience, researchers in the Rokers lab work on identifying the brain regions in which these visual cues are processed and combined. This work may ultimately pinpoint the cause of cortical deficits such as motion blindness.

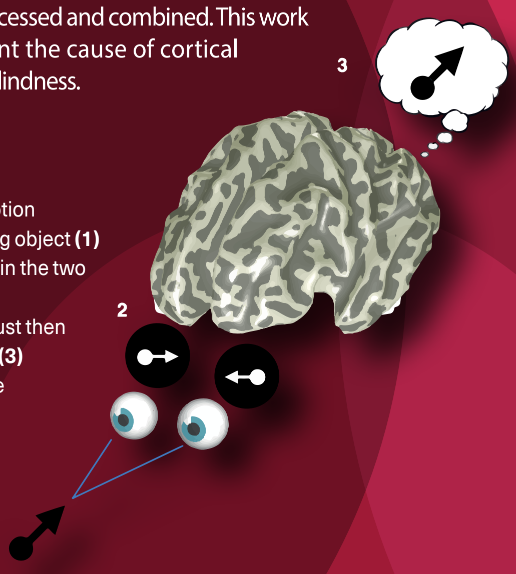


Figure 1: Illustration of motion perception. An approaching object **(1)** produces different images in the two eyes **(2)**.
Visual areas in the brain must then reconstruct object motion **(3)** based on information in the two images. Failure in this reconstruction will lead to motion blindness. Research in the lab aims to identify the cause of such failures.

Neural basis of visual disorders

Many visual disorders are caused by abnormal visual input to the brain, either during development (in the case of amblyopia) or during adulthood (in the case of glaucoma). Dr. Rokers has developed new techniques to identify the neural consequences of such abnormal visual input, and has identified the neuro-anatomical signatures of these disorders in the human brain. This work is central to the diagnosis of visual dysfunction and the assessment of novel therapies for vision recovery.

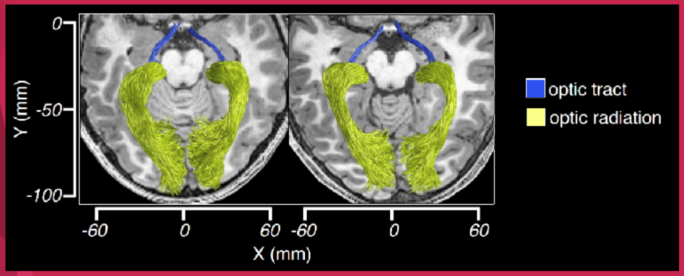
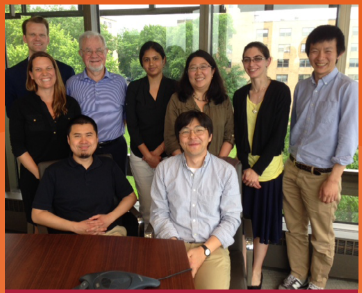


Figure 3: Identifying the neural basis of visual disorders. Novel neuroimaging techniques now make it possible to identify visual pathways in the living human brain. Using these techniques, Dr. Rokers has shown systematic impairments in the optic radiation of individuals with amblyopia (lazy eye). Dr. Rokers is now using the same techniques to understand the neural consequences of other visual disorders, such as cataracts and glaucoma. This work will be instrumental in the future diagnosis, prognosis and treatment of visual disorders.

Walsh Research Travel Awards: In Appreciation of Opportunities

With McPherson ERI Advisory Board member and donor David Walsh, his son John, and daughter Molly, six 2015-2017 recipients of McPherson ERI/David G. Walsh Research Travel Awards met over lunch to talk about their respective research pursuits. In casual, seminar style, each trainee gave a synopsis of project goals and advances, responding to questions and sharing insights with the Walsh family—regarding research specifics, opinions on current or possibly future innovations, and the value of conference involvement. Interactions were stimulating, informative, and enjoyable!

Initiated in 2011 with donations from the David G. Walsh family, this travel award provides funds for graduate students and postdocs from MERI members' research groups to attend conferences and present vision-related research findings. From 2011 through 2013, just a single award was given each year. But generous donations from the Walsh family and friends and help from Cycle for Sight funds increased the number of awards to four per year from 2014 through 2017. Through a competitive application process, nineteen McPherson ERI trainees have now received Walsh Research Travel Awards – expanding their meaningful research connections. We are grateful!

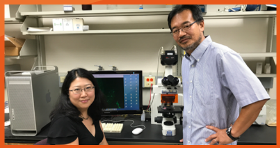


Back, L to R: John Walsh, Molly Walsh, David Walsh, Girijha Rathnasamy, Wei-Hua Lee, Jacqueline Fulvio, Kazuya Oikawa; **Front, L to R:** Eric Nguyen, Seung Heon Yoo

2017 Vision Research Trainee Grant Recipients

The McPherson Eye Research Institute's first grant opportunity for trainees—*the Vision Research Trainee Grant*—was established this year to give trainees experience writing grant applications, to augment their professional development, to advance vision research in McPherson ERI member groups by funding trainee research, and to encourage the next generation of vision scientists. Two one-year grant awards of $3000 each have been funded by the Institute's annual Cycle for Sight event, which raises money to support research by McPherson ERI members.

The Institute's Research and Leadership Committees are pleased to announce the 2017 recipients of *Vision Research Trainee Grants*, with congratulations!



Wei-Hua Lee, a postdoctoral researcher in Professor Aki Ikeda's lab in the Department of Medical Genetics, will pursue a project discerning "**The molecular mechanism regulating mitochondrial dynamics through TMEM135.**"

Hilary Miller, a graduate student in Professor Vanessa Simmering's lab in the Department of Psychology—and in collaboration with Professor Heather Kirkorian in the Department of Human Development and Family Studies, will explore "**The role of visual attention and language in spatial cognitive development.**"

THURSDAY, OCTOBER 12, 2017

9th Annual Vision Science Poster Session & Lecture

Poster Session
3:00PM to 5:30PM

Atrium, Health Sciences Learning Center (HSLC)
750 Highland Ave
UW-Madison

Registration opens late August

SAVE THE DATE
12TH
OCT 2017

Distinguished Guest Lecture

At 5:45PM, HSLC Room 1335

Professor Steven Seitz
University of Washington, Seattle
Department of Computer Science and Engineering
Google Scholar, Google Corporation