THE UNIVERSITY OF MELBOURNE

Department of Optometry and Vision Sciences

RESEARCH PROJECTS 2024

HONOURS, MASTERS, AND PHD

CONTENTS

RESEARCH IN THE DEPARTMENT OF OPTOMETRY AND VISION SCIENCES

The Department of Optometry and Vision Sciences is based in the Faculty of Medicine, Dentistry and Health Sciences (MDHS). Vision science research is multidisciplinary in nature and spans topics from understanding the fundamental workings of the living retina on the microscopic scale to the testing of new therapies in clinical trials. No matter what your major, there are vision research pathways for you. In this brochure we highlight some of the projects available for research students within our Department. If you have a passion for vision science that is not covered specifically in this project set, please contact our researchers to discuss further.

For students who have completed an undergraduate degree a research pathway though an Honours or Master of Biomedical Science is an appropriate research path. For students with a BSc (Hons) or BBiomed (Hons) further scientific training through a three-year PhD, or a 1.5-year Master of Philosophy would be appropriate.

You can also contact the Departmental Honours and Master of Biomedical Science Coordinator, Prof Trichur Vidyasagar on +61383447004 trv@unimelb.edu.au or the Departmental Graduate Researcher Coordinator for PhD and Master of Philosophy related queries, A/Prof Andrew Anderson on +613 9035 9916, aaj@unimelb.edu.au.

FOR FURTHER INFORMATION

HONOURS

http://mdhs-study.unimelb.edu.au/degrees/honours/overview

MASTERS OF BIOMEDICAL SCIENCE

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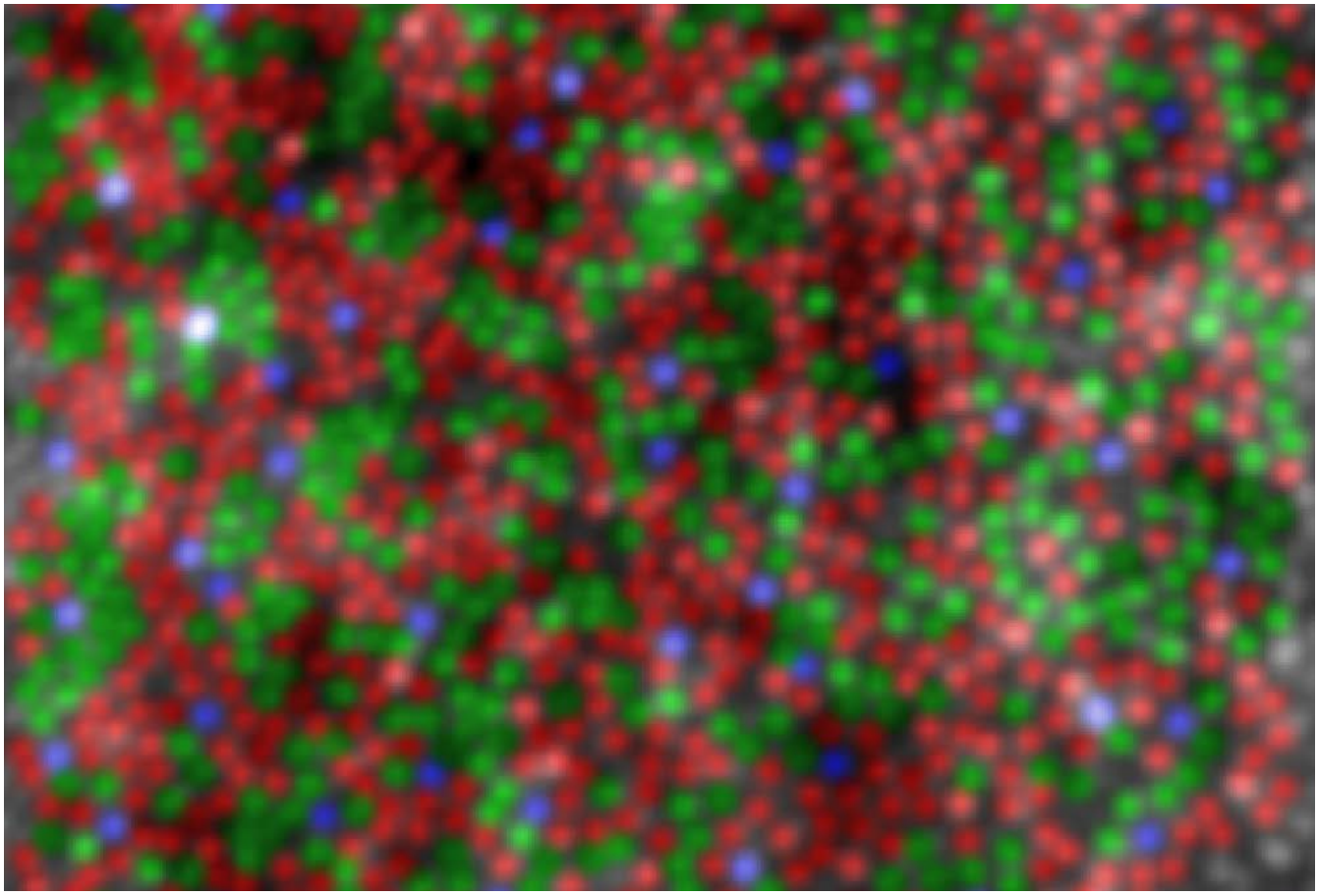
DEPARTMENT OF OPTOMETRY AND VISION SCIENCES

https://healthsciences.unimelb.edu.au/departments/optometry-and-vision-sciences



High-resolution imaging in the living human eye reveals the three classes of photoreceptor cell which combine to produce our sense of colour vision.

ANTERIOR EYE, CLINICAL TRIALS AND RESEARCH TRANSLATION UNIT

LABORATORY HEAD AND PROJECT SUPERVISOR

Name: A/Prof Laura Downie *BOptom, PhD*
Email: ldownie@unimelb.edu.au
Phone: +61 3 9035 3043
Twitter: @DrLauraDownie, @FrontTear_UoM

KEY PROJECT CO-SUPERVISORS

Name: Dr Holly Chinnery *BSc(Hons), PhD*
Email: holly.chinnery@unimelb.edu.au

Name: Dr Sumeer Singh *MOptom, PhD*
Email: sumeer.singh@unimelb.edu.au

Summary of research interests: The *Anterior Eye, Clinical Trials and Research Translation unit* adopts an integrated and innovative approach to research that combines laboratory, clinical and implementation science, as a basis for improving patient outcomes. Our team possess advanced expertise in **anterior eye disease** (including the development and translation of novel ocular diagnostic devices and therapeutics) and **research translation** (to develop and test interventions to improve research dissemination and its implementation in practice). Our collaborators include industry, national and international research groups (including researchers in neurology, endocrinology, immunology, neuroscience and chemical engineering), and the Corneal and Ocular Immunology laboratory (led by Dr Holly Chinnery) on projects combining preclinical and clinical science.

Using tears as a platform for advancing the understanding of disease. This program of research investigates using tears (Figure 1) to provide novel insights into human health. We combine sophisticated clinical techniques with laboratory-based studies to characterise tear film responses in eye and systemic disease. These investigations are the basis for developing new diagnostic and prognostic tests to inform the management of clinical conditions. Some of our recent studies have identified new tear biomarkers for diabetes, dry eye disease and contact lens discomfort, leading to patents and subsequent projects focussed on the commercialisation of these discoveries.

Functional in vivo confocal microscopy (Fun-IVCM) as a window to the immune system. The cornea is the only tissue where sensory nerves and immune cells can be non-invasively imaged in living humans, using high-resolution in vivo confocal microscopy (IVCM). Corneal IVCM (Figure 2) provides unique capacity to assess the immunological effect of disease and exogenous factors on an intact physiological system.

Our team has recently developed a novel method, we term **Functional-IVCM** (Fun-IVCM), to dynamically track corneal immune cell subsets in living humans.

Afforded by the unique transparency of the corneal tissue, using Fun-IVCM we recently captured the first-ever live cell imaging of corneal T cells, dendritic cells and macrophages in response to immune-active stimuli in humans. This research has redefined understanding of the resident corneal immune cell populations, including identifying the presence of T cells in healthy human corneas, and demonstrated changes to their dynamics in acute and chronic inflammation (Downie et al., 2023 PNAS).

Changes to corneal immune cell morphology and behaviour, captured using Fun-IVCM show utility to act as biomarkers of ocular and systemic disease, and inform the development of targeted therapeutics for these conditions.

PROJECT 1: DEFINING THE EFFECT OF CONTACT LENS WEAR ON THE DYNAMICS OF IMMUNE CELLS IN THE HUMAN CORNEA

Using Fun-IVCM, we have shown human corneal immune cells to be a dynamic cell population, however currently little is known about how various stimuli affect their behaviours *in vivo*. This project will investigate how contact lens wear modifies the behaviours of different types of corneal immune cells, to provide new insight into changes in corneal immunology under non-homeostatic conditions in the human eye. This project will involve participant recruitment, clinical examinations, and digital image analysis. It is suitable for Honours, Masters and PhD students.

Figure 1: After non-invasive collection, human tears are analysed using a range of cutting-edge techniques, to quantify parameters such as viscoelasticity, protein composition and lipid content. These studies are the foundation for developing novel lab-on-a-chip tests for ocular and systemic disease.

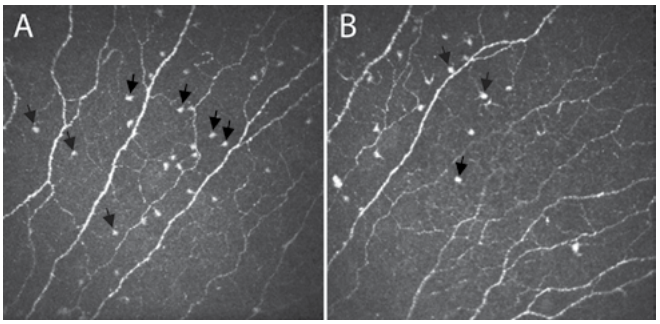


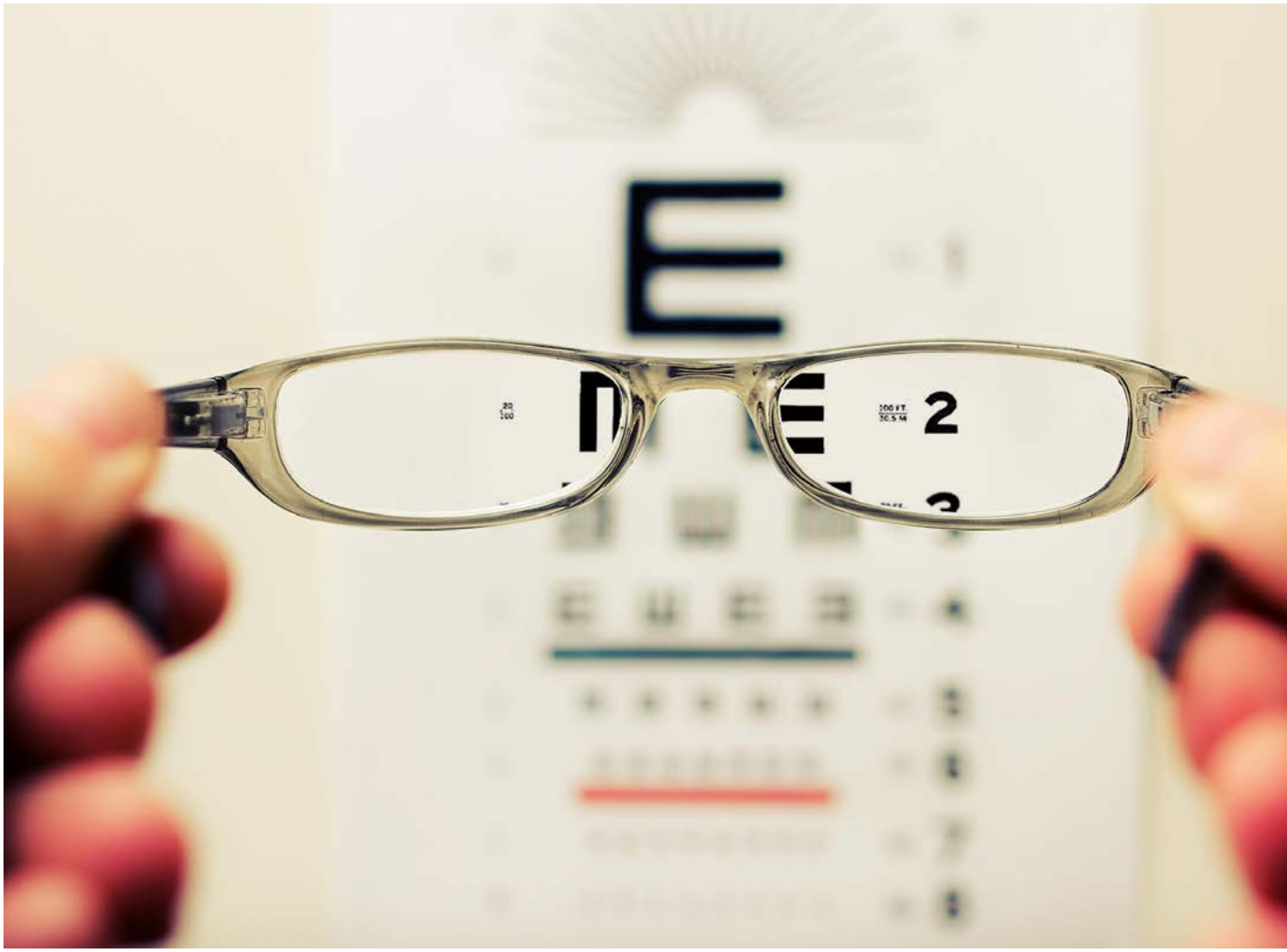
Figure 2: Laser-scanning confocal microscopy images from the central cornea of a person with peripheral neuropathy, at (A) baseline and (B) after eight weeks of oral prednisolone treatment, showing a reduction in the density of putative immune cells (white trapezoid-shaped cell bodies).

PROJECT 2: EXPLORING THE EFFECTS OF OMEGA-3 FATTY ACID SUPPLEMENTATION ON THE RETINAL VASCULATURE IN TYPE 1 DIABETES

Building on our previous studies showing that omega-3 fatty acid supplements promote corneal nerve regeneration in people with type 1 diabetes, this project will investigate the effects of these supplements on the retinal microvasculature. High-resolution images of the retinal vasculature were captured using optical coherence tomography angiography (OCT-A) from participants with type 1 diabetes who participated in a randomised, placebo-controlled clinical trial. Omega-3 fatty acids modulate systemic inflammation, and high dietary intakes can reduce the risks of severe diabetic retinopathy. However, the effects of these supplementation on the retinal vasculature architecture has not yet been comprehensively studied. This project will involve development and implementation of new image analysis protocols, to investigate whether omega-3 fatty acids modulate retinal vascular density and architecture in people with type 1 diabetes. It is suitable for Honours students.

SELECTED RELATED PUBLICATIONS FROM OUR TEAM:

1. Downie LE, Zhang X, Wu M, … Mueller SN, Chinnery HR. Redefining the human corneal immune cell compartment using dynamic intravital imaging. *Proc Natl Acad Sci U S A* 2023; In press.
2. Britten-Jones AC, Kamel JT, et al. Investigating the neuroprotective effect of oral omega-3 fatty acid supplementation in type 1 diabetes (nPROOFS1): a randomized, placebo-controlled trial. *Diabetes* 2021;70(8):1794-1806.
3. McDonnell A, Lee JH, Makrai E, Yeo LY, Downie LE. Tear film extensional viscosity is a novel potential biomarker of dry eye disease. *Ophthalmology* 2019;126(8):1196-8.
4. Gad A, Vingrys AJ, Wong CY, Jackson DC, Downie LE. Tear film inflammatory cytokine upregulation in contact lens discomfort. *Ocul Surf* 2019;17(1):89-97.



CLINICAL VISION RESEARCH AT THE AUSTRALIAN COLLEGE OF OPTOMETRY

PROJECT SUPERVISOR

Name: Dr Marianne Coleman
Email: mecoleman@unimelb.edu.au
Twitter: @MPOrthoptics

Summary of research interests: This strand of research based at the National Vision Research Institute is focused on undertaking clinically oriented vision research, including public eye health, aimed at improving the health and well-being of the community. The Australian College of Optometry sees over 60,000 Victorians annually across the region who live with socioeconomic disadvantage, which in turn is a risk factor for health inequalities. Projects are centred around providing an evidence base to support the care of these groups, including children and families, older adults, people living with disability and those residing in aged care facilities.

FOCUS AREA 1: BINOCULAR VISION

Binocular vision helps us in many ways that we take for granted. Problems with depth perception can affect our ability to judge distances, complete precise hand-eye tasks and move around confidently. If our eyes are not coordinated, this can lead to symptoms of eye strain or distressing double vision, increasing risk of falls and affecting day to day tasks. This research program focuses on the clinical measurement of depth perception and binocular vision, in people of all ages, with and without other long-term conditions.

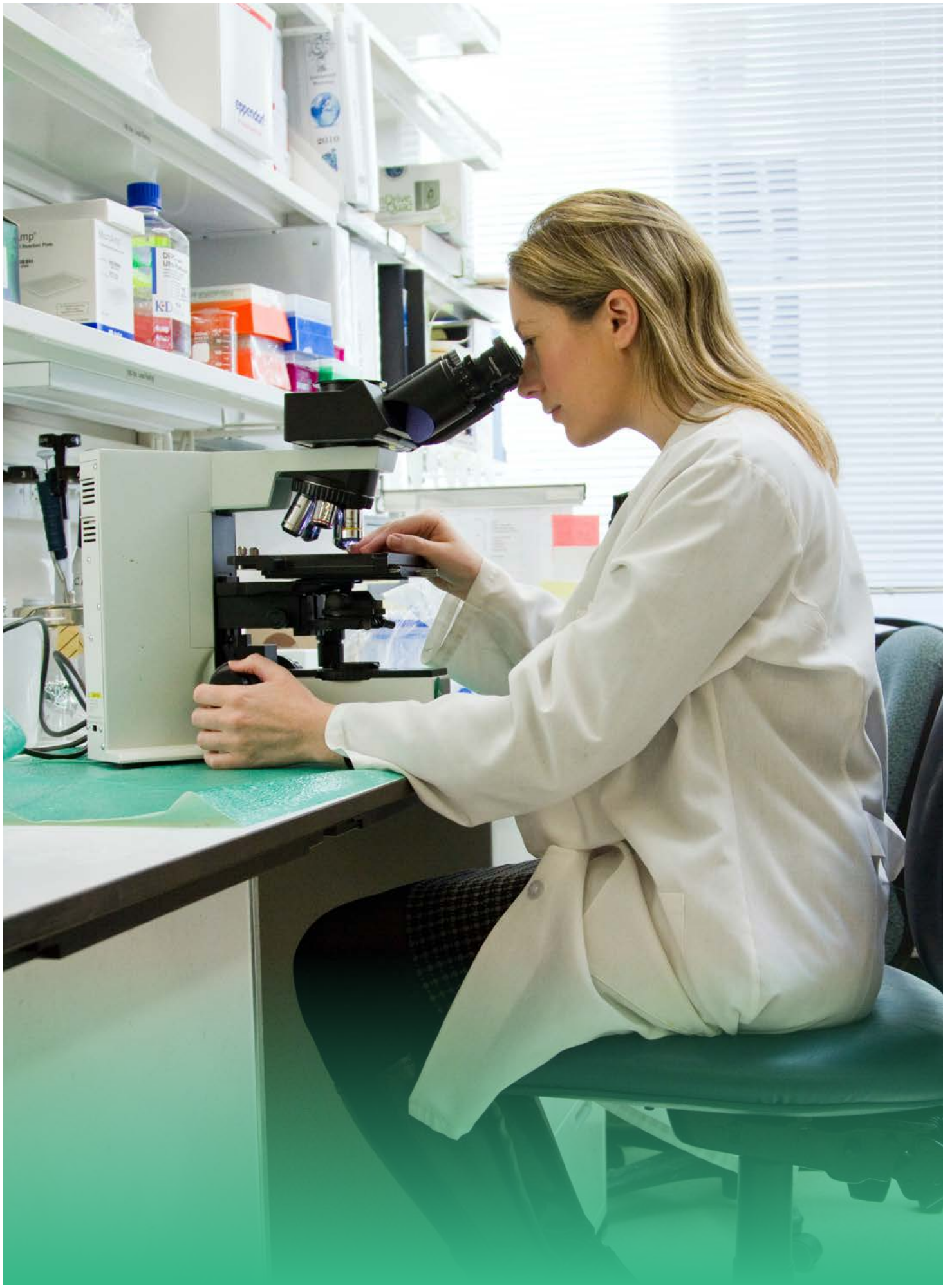
FOCUS AREA 2: AMBLYOPIA

Amblyopia, or 'lazy eye', is the most common cause of treatable sight loss in young children, occurring in approximately 2% of Australians growing up. Untreated amblyopia has been associated with poor reading scores, fine motor coordination difficulties and low self-esteem in children and young people. Early diagnosis and treatment results in better visual outcomes, but problems with visual processing and depth perception can remain, even after successful treatment. Many aspects of how children respond to amblyopia treatment are still poorly understood. This program of mixed methods research focuses on the clinical diagnosis and treatment of amblyopia in children, to generate more evidence on barriers to successful amblyopia treatment and design adaptive treatment protocols to maximise visual function in amblyopia.

FOCUS AREA 3: LOOKING AFTER OLDER EYES

Older adults are at greater risk of developing eye conditions that threaten sight, yet only half of older adults in Australia attend for regular sight tests. Poor vision in older adults is a significant risk factor for falls, and through impact on ability to engage in daily activities and socialising, is associated with increased risk of depression and cognitive decline. Maximising eyesight for older adults with other co-morbidities such as diabetes, dementia or cardiovascular disease is therefore an important step in maintaining quality of life and independence, thus the optometrist can make an important contribution to integrated care for these conditions that is yet to be fully recognised. This program focuses on the role of routine eye examinations for older adults living with long term conditions.

Data collection at Insomnia Gaming Festival.



CORNEAL AND OCULAR IMMUNOLOGY

LABORATORY HEAD

Name: Dr Holly Chinnery
Email: holly.chinnery@unimelb.edu.au
Phone: +61 3 9035 6445

CO-SUPERVISOR

Name: A/Prof Laura Downie *BOptom, PhD*
Email: ldownie@unimelb.edu.au
Phone: +61 3 9035 3043

Name: Dr Mengliang Wu
Email: mengliang.wu1@unimelb.edu.au

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/corneal-and-ocular-immunology-unit

Summary of lab interests: We investigate the structural, physiological and immunological interplay between immune cells and other non-immunological structures such as sensory nerves and epithelial cells in the cornea during homeostasis and disease. Techniques used in our lab include in vivo clinical imaging of the cornea, ex vivo confocal microscopy and 3D image reconstruction and molecular biology and protein assays. We also collaborate closely with A/Prof Laura Downie, who leads the *Anterior Eye, Clinical Trials and Research Translation Unit.*

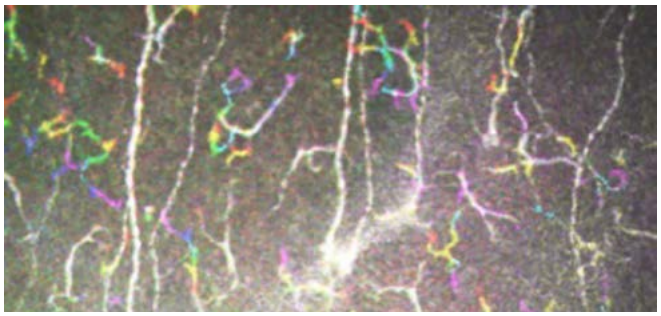


Figure 3: Fun-IVCM image of the human corneal epithelium which was captured dynamically. Colour-coded time lapsed image reveals stable immune cells and nerves (white) and motile immune cells (T cells, coloured).

PROJECT 1: USING FUNCTIONAL IN VIVO CONFOCAL MICROSCOPY (FUN-IVCM) TO EVALUATE IMMUNOLOGICAL CHANGES IN THE DISEASED CORNEA

The human cornea is the only tissue in the body where immune cells such as T cells and dendritic cells can be non-invasively visualised in situ. Using our newly-developed functional in vivo confocal microscopy (Fun-IVCM), the morphology and dynamic behaviour of immune cells can be visualised in the cornea of living humans. However, little is known about how these immune cells react to changed extracellular matrix. This project will investigate the distributional, morphological and dynamic behavioural features of immune cells in human corneas with structural and biomechanical alteration (keratoconus), and correlate these findings with clinical signs and symptoms. This project will provide new insight into how immune cells interact with keratocyte and collagen in the cornea.

PROJECT 2: CORRELATING IMMUNE CELL MORPHOMETRY WITH MARKERS OF CELLULAR ACTIVATION IN THE MOUSE CORNEA

We have recently demonstrated using in vivo confocal microscopy that corneal immune cells change their shape and size in response to local inflammatory stimuli. It is unclear how the changes in cell shape and size relate to function and maturation. In this project, mouse models of corneal inflammation will be used to correlate morphological changes in immune cell populations with alterations in cell surface markers indicative of cell activation. These findings will provide clinically translatable information that will shed light on the functional relevance of morphological changes to immune cells in the human cornea. This project will involve animal handling, clinical imaging, ex vivo confocal microscopy, flow cytometry and 3D image reconstruction and image analysis. This project would be suitable for Honours, Masters or PhD students.

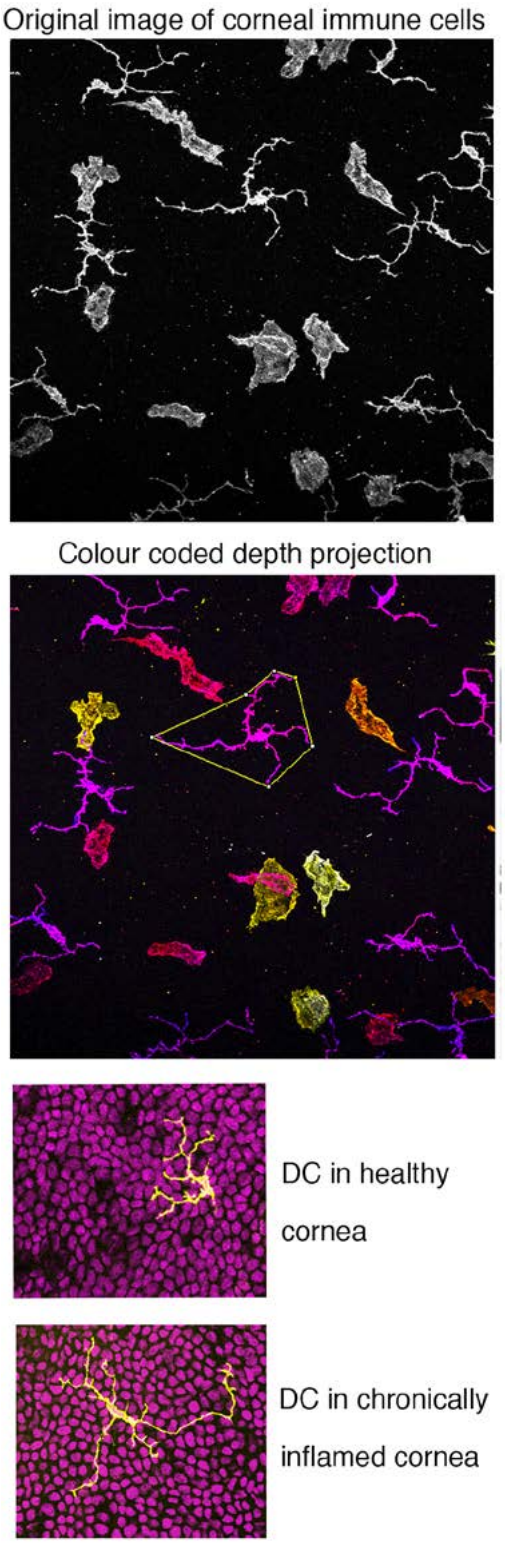


Figure 4: Resident immune cells (dendritic cells and macrophages) in the mouse cornea. Shape and size analyses can provide insight into functional alterations in the immune cells.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Downie LE, Zhang X, Wu M, … Mueller SN, Chinnery HR. Redefining the human corneal immune cell compartment using dynamic intravital imaging. *Proc Natl Acad Sci U S A* 2023; In press.
2. Chinnery HR, Zhang XY, Wu CY, Downie LE. Corneal immune cell morphometry as an indicator of local and systemic pathology: A review. Clin Exp Ophthalmol. 2021 doi: 10.1111/ceo.13972. Epub ahead of print. PMID: 34240800.
3. Jiao, H., L. E. Downie, X. Huang, M. Wu, S. Oberrauch, R. J. Keenan, L. H. Jacobson and H. R. Chinnery. 2020. Novel alterations in corneal neuroimmune phenotypes in mice with central nervous system tauopathy. J Neuroinflammation 17(1): 136.
4. Wu, M., L. E. Downie, L. M. Grover, R. J. A. Moakes, S. Rauz, A. Logan, H. Jiao, L. J. Hill and H. R. Chinnery. 2020. The neuroregenerative effects of topical decorin on the injured mouse cornea. J Neuroinflammation 17(1): 142.
5. Jiao H, Naranjo Golborne C, Dando S, McMenamin PG, Downie LE & Chinnery HR. 2020. Topographical and morphological differences of corneal dendritic cells during steady state and inflammation. Ocul Immunol Inflamm 28(6): 898-907.

OCULAR BIOMARKER LABORATORY

LABORATORY HEAD

Name: A/Prof Christine Nguyen
Email: christine.nguyen@unimelb.edu.au
Phone: +61 3 9035 3186

PROJECT SUPERVISORS

Name: Prof Bang Bui
Email: bvb@unimelb.edu.au
Phone: +61 3 8344 7006

Name: Dr Pei Ying Lee
Email: py.lee@unimelb.edu.au

Name: Dr Vickie Wong
Email: vickie.wong@unimelb.edu.au
Phone: +61 3 8344 1484

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/ocular-biomarker-laboratory

Summary of lab interests: The eye affords a unique opportunity to gain insights into what is occurring in the brain. It is the only place in the body where neurons and blood vessels can be directly visualised. Moreover, neurological diseases such as Alzheimer's disease, Parkinson's disease and multiple sclerosis have been shown to exhibit changes in the eye which can be measured with currently available clinical tools and emerging technologies.

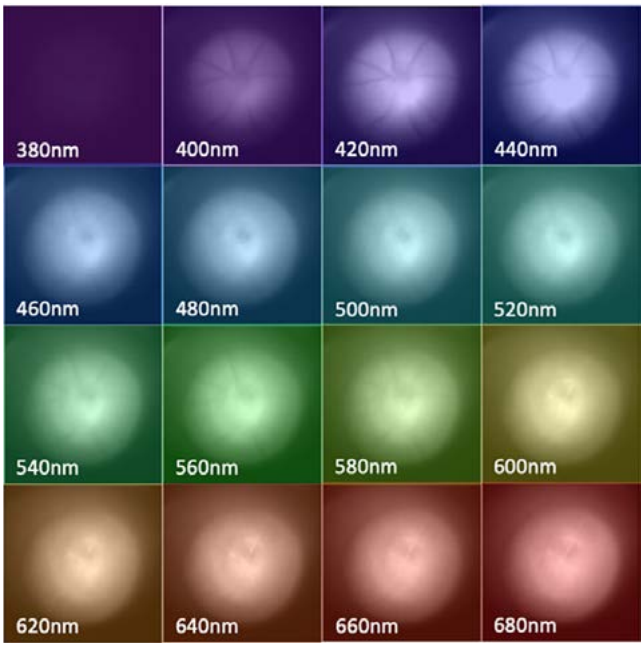


Figure 5: In vivo hyperspectral imaging in a live mouse eye.

PROJECT 1: AN EYE ON PARKINSON'S DISEASE: CHARACTERISING TOXIN-INDUCED CHANGES IN THE RETINA

Exposure to environmental toxins can increase an individual's risk of Parkinson's disease. Given the neuronal similarities in the eye and brain it is not surprising that these toxins also effect the retina. Our group has shown that a toxin that modify energetic demand (MPTP) can modify retinal measures that can also easily be conducted in patients. The current project will build on this work and characterise retinal imaging changes in another toxin-induced mouse model (rotenone) of oxidative stress. In this manner, the project will form the building blocks for testing whether common clinical retinal assessments (optical coherence tomography, hyperspectral imaging, electroretinography) may be useful for early detection of Parkinson's disease.

PROJECT 2: EYE AS A WINDOW TO PARKINSON'S DISEASE: HUMAN DATA ANALYSIS

Parkinson's disease needs to be detected earlier in order for new treatments aimed at neuroprotection to be effective. The eye can serve as a "brain on a stalk" and provide a window into cortical changes whilst being simple and inexpensive to measure. This project will analyse visual measures conducted on control and Parkinson's disease patients in order to examine which may be the most sensitive to differentiate between the two groups. This will pave the way for early biomarkers of Parkinson's disease that can assist with future development of novel treatments.

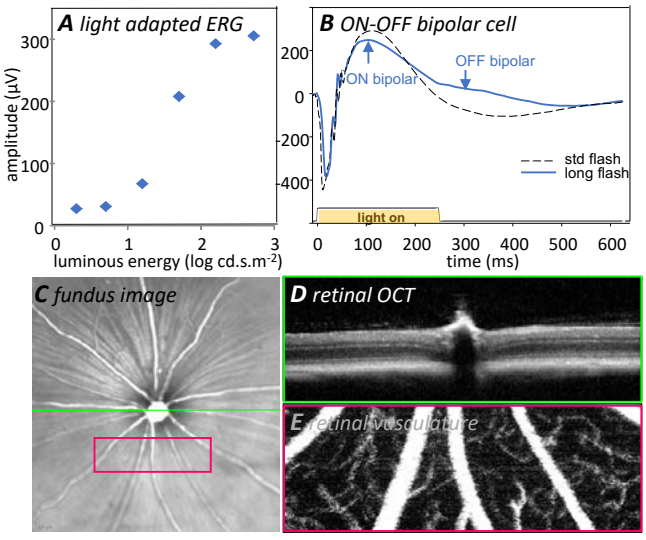


Figure 6: Functional and structural assessment of retinal health in Parkinson's disease.

PROJECT 3: AN EYE ON PARKINSON'S DISEASE: CHARACTERISING ALPHA-SYNUCLEIN CHANGES IN THE RETINA

A hallmark of Parkinson's disease is deposition of a key protein, alpha-synculein in the brain. These proteins are also found in the eye and our group has shown their presence can modify retinal measures which can also easily be conducted in patients. The current project will build on this work and characterise retinal imaging changes in a mouse model of alpha-synculein overaccumulation at early and late stages of disease. In this manner, the project will form the building blocks for testing whether common clinical retinal assessments (optical coherence tomography, hyperspectral imaging, electroretinography) may be useful for early detection of Parkinson's disease.

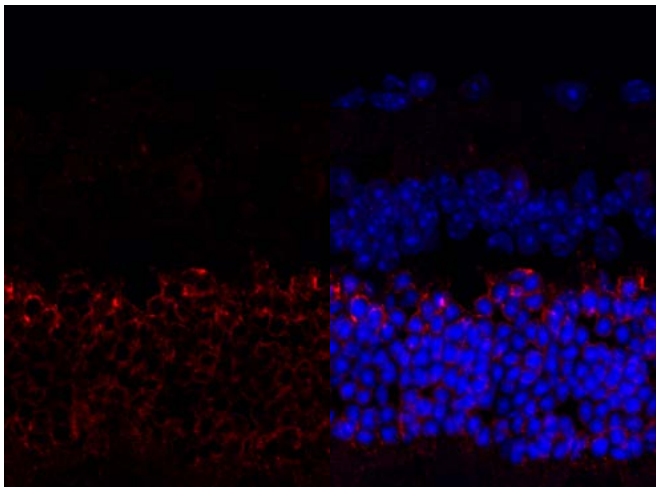


Figure 7: Alpha-synuclein (red) a hallmark of Parkinson's disease in the retina.

PROJECT 4: PARKINSON'S DISEASE: USING A RETINAL STRESS TEST TO UNCOVER EARLY METABOLIC CHANGES

One of the earliest pathological changes in Parkinson's disease are changes to metabolism. Retinal photoreceptors are the most highly metabolic tissue per weight in the body and hence they form a logical location to examine early Parkinson's changes. By challenging the retina with light (akin to a photographic flash) retinal metabolism can be probed in mice with or without Parkinson's at various disease stages. This will shed light on whether retinal metabolic changes may be an early marker of Parkinson's disease and improve our understanding of its pathogenesis. The capacity to develop early, specific biomarkers for Parkinson's disease is pivotal for the development of treatments.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Tran KKN, Wong VHY, Lim JKH, Shahandeh A, Hoang A, Finkelstein DI, Bui BV, Nguyen CT (2022). Characterization of retinal function and structure in the MPTP murine model of Parkinson's disease. Sci Rep 12:7610.
2. Nguyen CT, Hui F, Charng J, Velaedan S, Van Koeverden A, Lim JK, He Z, Wong VHY, Vingrys AJ, Bui BV, Ivarsson M (2017). Retinal biomarkers provide "insight" into cortical pharmacology and disease. *Pharmacology and Therapeutics.* 175: 151-177.
3. Lim JKH, Li QX, Ryan T, Bedggood P, Metha A, Vingrys AJ, Bui BV, Nguyen CT (2021). Retinal hyperspectral imaging in the 5xFAD mouse model of Alzheimer's disease. Sci Rep 11:6387.
4. Lim JK, Li QX, He Z, Vingrys, AJ, Wong, VHY, Currier N. Mullen J, Bui BV, Nguyen, CT (2016). The Eye as a Biomarker for Alzheimer's Disease. *Front Neurosci* 10, 536.

OCULAR PHYSIOLOGY LABORATORY

LABORATORY HEAD

Name: Prof Bang Bui
Email: bvb@unimelb.edu.au
Phone: +61 3 8344 7006

PROJECT SUPERVISORS

Name: A/Prof Christine Nguyen
Email: christine.nguyen@unimelb.edu.au
Phone: +61 3 9035 3186

Name: Dr Vickie Wong
Email: vickie.wong@unimelb.edu.au
Phone: +61 3 8344 1484

Name: Dr Pei Ying Lee
Email: huif@unimelb.edu.au
Phone: +61 3 8344 1484

Name: Dr Flora Hui
Email: py.lee@unimelb.edu.au
Phone: +61 3 8344 5884

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/ocular-physiology-lboratory

Summary of lab interests: Our laboratory is interested in understanding the causes of retinal and optic nerve injury in diabetes and glaucoma. We are also interested in developing new ways to clinically detect eyes at risk of vision loss from these conditions.

PROJECT 1: UNDERSTANDING HOW PRESSURE AFFECTS GANGLION CELLS IN GLAUCOMA

Our investigations of glaucoma hope to shed light on how the cells that connect the eye to the brain, the retinal ganglion cells, adapt to stress such as the change in pressure in and around the eye. When adaptation mechanisms fail, ganglion cells can die. Whilst it is known that as the eye gets older the capacity to cope with stress diminishes, however we don't fully understand why this occurs. To study how ageing and other risk factors impact the capacity for retinal ganglion cells to cope with stress we have developed both acute and chronic model of intraocular pressure elevation. We will study ganglion cell responses to stress by relating their function (using electroretinography), structure (using imaging) and cell morphology to a range of cellular processes that help ganglion cells to work better (e.g., communication with support cells, autophagy for self-repair, energy supply).

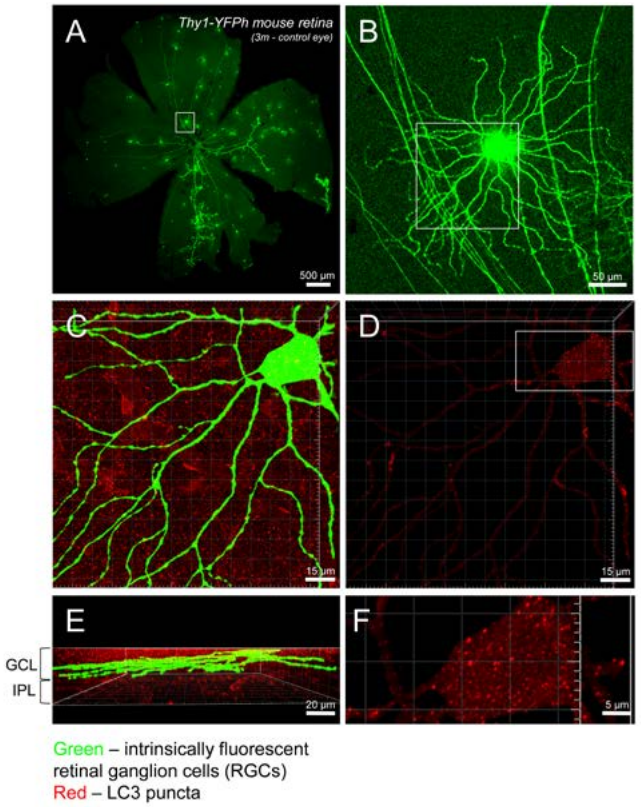


Figure 8: Using a transgenic mouse line where optic nerve cell are fluorescent we can study how injury affects certain proteins only in these cells.

PROJECT 2: CLINICAL STUDIES OF RETINAL VASCULAR AUTOREGULATION

The retina and brain are the most highly energy demanding tissues in the body. The need for optical clarity means that little energy is stored and as such the retina is completely dependent on a stable blood supply for oxygen and glucose. Local control mechanisms stabilise flow to three major vascular beds (superficial, intermediate and deep). This local control system is known as vascular autoregulation and involves cells lining the blood vessel walls (endothelial cells) as well as neurons and supporting glia (astrocytes and microglia). Failure of autoregulation is thought to contribute to vision loss in retinal disease such as diabetes and glaucoma. In these studies, we will employ optical coherence tomography imaging to assess autoregulation in people with retinal disease such as diabetes and glaucoma.

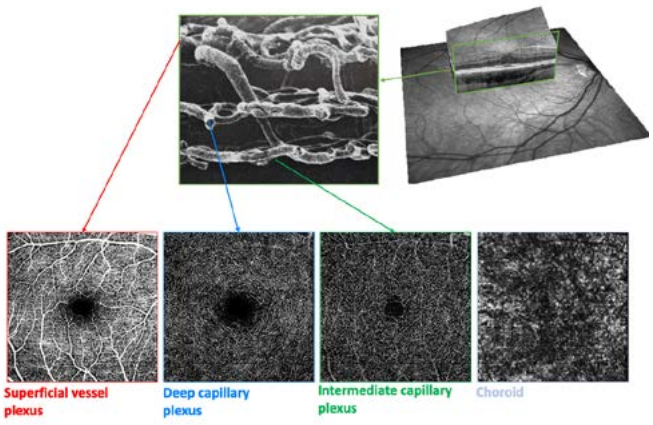


Figure 9: Using non-invasive imaging we can study the vessel layers in the living eye.

PROJECT 3: DEVELOPING OCULAR BIOMARKERS OF EPILEPSY

Epilepsy is a chronic neurological condition that causes an individual to experience recurrent seizures. It is the most common neurological disorder, affecting about 4% of Australians. Many of the channels that are dysfunctional in the brain are also manifest in other sensory systems. This means that the eye and its response to light might be useful to detect and monitor the condition. in this project we will assess the electrical response of the eye to light, called the electroretinogram, in murine models of epilepsy to establish the optimal protocol for assessing channel dysfunction in subtypes of epilepsy. We will use these protocols to assess the effect of standard of care and new drugs. This work is critical in developing a laboratory platform for drug testing with significant potential to inform the development of clinical tools for children with epilepsy.

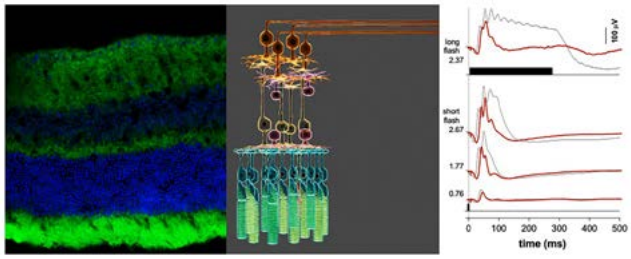


Figure 10: Using a non invasive measure of retinal function the electroretinogram, we can use the retina to better understand and test drugs for epilepsy, in this case when it arises from HCN1 epilepsy.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Zhao D, Pinares-Garcia P, McKenzie CE, Bleakley LE, Forster IC, Wong VHY, Nguyen CTO, Scheffer IE, Reid CA, Bui BV. Retinal Dysfunction in a Mouse Model of HCN1 Genetic Epilepsy. J Neurosci. 2023 Mar 22;43(12):2199-2209.
2. Lee PY, Zhao D, Wong VHY, Chrysostomou V, Crowston JG, Bui BV. The Effect of Aging on Retinal Function and Retinal Ganglion Cell Morphology Following Intraocular Pressure Elevation.Front Aging Neurosci. 2022 May 12;14:859265.
3. Heriot WJ, Metha AB, He Z, Lim JKH, Hoang A, Nishimura T, Okada M, Bui BV. Optimizing retinal thermofusion in retinal detachment repair: achieving instant adhesion without air tamponade. Ophthamol Sci. 2022 2:100179.

OPTOLOGICAL LABORATORY

LABORATORY HEAD

Name: A/Prof Andrew Anderson
Email: aaj@unimelb.edu.au
Phone: +613 9035 9916

PROJECT SUPERVISORS

Name: A/Prof Christine Nguyen (*co-supervisor for Project 1, from the Ocular Biomarker Laboratory*)
Email: christine.nguyen@unimelb.edu.au
Phone: +61 3 9035 3186

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/optological-laboratory

The Optological Laboratory non-invasively investigates how the human eye and brain function, both in normal observers and those with eye disease. Although our understanding of neuroscience has been greatly enhanced through electrophysiological recordings from individual neurons and through computer imaging of gross neural activity across the brain, such information only tells us part of how the brain and eye work. Ultimately, we also need to understand how the eye and brain behave in response to various forms of information, and to ascertain what functional limits exist in processing such information. By combining results from a range of studies – including electrophysiological, imaging and behavioural studies – a more complete understanding of neuroscience be achieved.

Our laboratory uses a range of techniques to determine how the eye and brain behave, many of which can be classed under the general heading of psychophysical methods. Sometimes our investigations involve visual targets used in clinical tests of vision, allowing us to better understand how such tests work and allowing more effective clinical tests to be developed. Other investigations use customised visual stimuli and special experimental protocols to examine how the eye transmits information to the brain, and also how the brain processes this information in order to make decisions. The laboratory is well equipped to undertake a wide range of behavioural experiments and so can address a broad range of behavioural questions, both in the clinical and basic sciences.

PROJECT 1: EXAMINING A NOVEL, COMPUTERISED TEST OF COLOUR VISION FOR DETECTING & MONITORING DISEASE

A decreased ability to distinguish between colours can occur in both eye (e.g., glaucoma) and systemic (e.g., Parkinson's) diseases. Because of this, measuring a person's colour discrimination ability can be an important tool in both testing for, and monitoring the progression of, diseases. Although commercial computer displays can render colours accurately, they do have limitations for performing clinical assessments of colour vision. Here, we will investigate a different type of colour vision test aimed at overcoming these limitations, with the hope of making accurate colour vision assessment cheaper and more accessible, and potentially available via telehealth services.

PROJECT 2: DO THE MECHANISMS THAT PREVENT OUR NOTICING SMALL EYE MOVEMENTS IMPROVE OUR ABILITY TO JUDGE SMALL MOVEMENTS IN THE WORLD?

Even when we stare intently at a small target, our eyes are constantly in motion. This results in images that continuously move on our retina. Powerful perceptual stabilisation mechanisms prevent our noticing this motion, however. Whilst this means our world doesn't appear to incessantly jiggle around, does this actually improve our ability to see things? This project will investigate whether perceptual stabilisation mechanisms improve our ability to do a very common task – making fine judgement of relative motion between objects in the world.

SELECTED PUBLICATIONS:

1. Park ASY, Bedggood PA, Metha AB, Anderson AJ (2019). The influence of perceptual stabilisation on perceptual grouping of temporally asynchronous stimuli. *Vision Res* 160:1-9.
2. Sepulveda JA, Anderson AJ, Wood JM, McKendrick AM (2020). Differential aging effects in motion perception tasks for central and peripheral vision. *J Vis* 20(5):8.

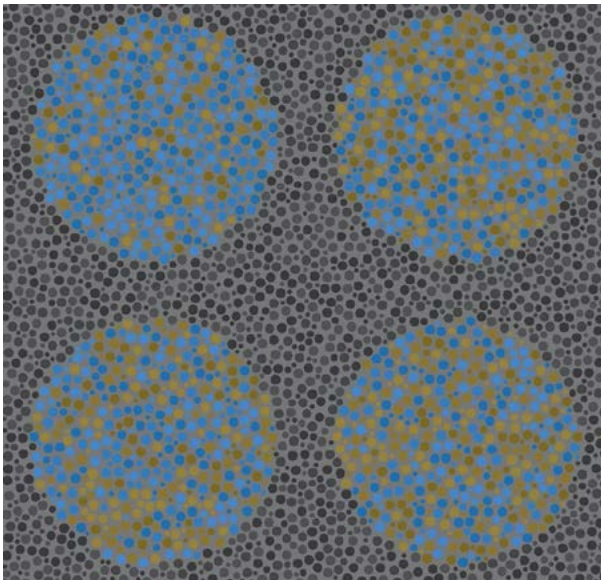


Figure 11: Novel digital colour vision tests.

OPO
The retest distribution of the visual field summary index mean deviation is close to normal

THE RETINAL OBSERVATORY

(IMAGING CELLULAR STRUCTURE AND FUNCTION IN THE LIVING HUMAN RETINA)

LABORATORY HEAD

Name: A/Prof Andrew Metha
Email: ametha@unimelb.edu.au
Phone: 9035 9783

PROJECT SUPERVISORS

Name: Dr Phillip Bedggood
Email: pabedg@unimelb.edu.au
Phone: +61 3 9035 9979

The broad research aim of the Retinal Observatory is to observe the structure and function the living retina on the microscopic scale, so as to figure out what it is doing and how. We work collaboratively with other groups in the Department and throughout the University to observe how the retina works under normal circumstances, and how this becomes compromised in sight-debilitating diseases such as diabetes and inherited retinal degenerations. To achieve these aims, we combine a range of investigative tools including high-resolution non-invasive retinal imaging, psychophysics, and computational modelling.

Our current research projects make use of high speed, multi-spectral adaptive optics to visualize the smallest neurons and blood vessels that is possible to see in living human eyes. We study the dynamics of blood flow and oxygen exchange at the level of individual red and white cells, and the cascade of optical and physiological events that occur when a photoreceptor interacts with light.

This requires a multi-disciplinary approach and so we welcome motivated students across all fields (e.g., Mathematics, Physics, Computer Science, Engineering, Biology, Psychology), who are interested in contributing to our innovative programs of research.

PROJECT 1: KEEPING THE EYE ALIVE: CHARACTERIZING THE PULSATILE NATURE OF SINGLE RED AND WHITE BLOOD CELL FLOW THROUGH RETINAL CAPILLARY NETWORKS

With newly-developed adaptive optics (AO) retinal imaging, it is now possible to visualise the finest capillaries in the eye and watch the passage of single red and white blood cells through its fine web of vascular pipes. These are the networks that keep your retina healthy, and which fail in diseases such age-related macular degeneration and diabetes. The exact details of blood flow patterns have not yet been fully documented – even in healthy eyes – because blood flows very quickly. Also, because the retina is designed to be transparent, it has been difficult to obtain high contrast images without risking light damage. However, with the recent lifting of these technical issues, a novel project emerges to characterize aspects of normal flow such as: cell deformability during flow; variation in flow velocity through different parts of the network; and the influence of the cardiac cycle on flow pulsatility.

This project would suit Honours Students and Graduate Researchers who wish to learn about and apply optical and image processing skills to questions of basic human physiology with immediate clinical applicability.

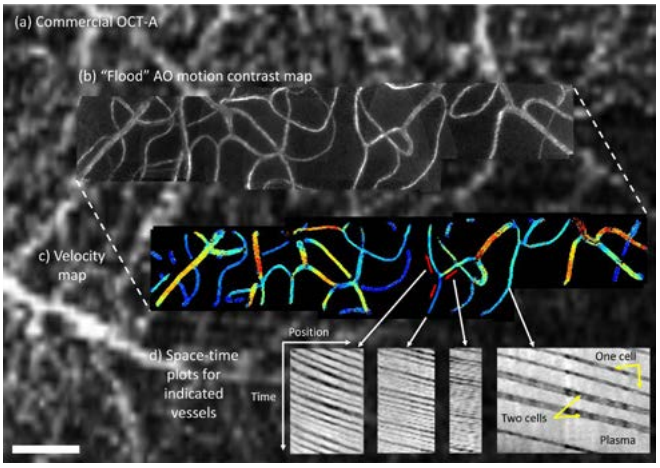


Figure 12: Tracking single-file blood cell flow though the retinal capillary network.

PROJECT 2: WIRING THE RETINA FOR HUMAN VISION - A SINGLE-CELL BEHAVIOURAL APPROACH

The normal human retina is tiled with a mosaic of about 110 million rods and 6 million cone photoreceptors of 3 types that are sensitive to long (L), middle (M) and short (S) wavelengths of light. These 116 million photoreceptors converge to a mere 1 million axons that form the optic nerve connecting the eye and brain. The retina itself is responsible for much more than image detection, but is involved in substantial processing of visual information as well!

Using psychophysical methods to record behavioral responses to stimulating either single cells or specific cell arrangements, this project aims to establish precisely how signals from 3 types of cone photoreceptor are organised within the receptive fields of retinal ganglion cells whose fibers exit the eye, and how this impacts the information conveyed for spatial and colour perception.

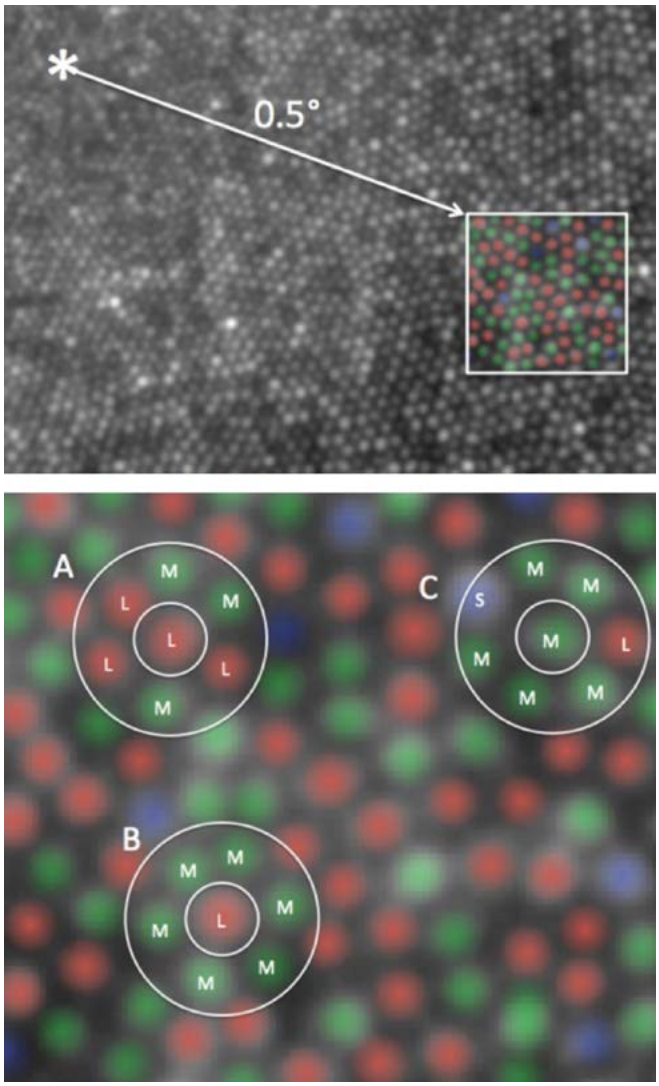


Figure 13: Targeting single cone photoreceptors to investigate inputs to midget ganglion cells.

PROJECT 3: IMPROVING THE EFFICIENCY, ACCURACY AND ROBUSTNESS OF HUMAN VISUAL PERFORMANCE MEASURES

Measurements of human visual performance are important both to understand the basic science behind vision and for diagnosis of blinding eye diseases. The methods currently used to measure visual performance in the clinic and laboratory are time-consuming, which limits the amount of information that can be gained in a given test session. This Honours project will evaluate the use of alternate testing strategies designed to improve test efficiency, and determine whether such improvements can be obtained whilst avoiding the introduction of inaccuracy or bias. Specifically, the project asks whether: 1) the reported degree of certainty of participant's responses be used to determine visual threshold more quickly than assessing the accuracy of responses alone; and 2) the degree to which cueing participants to direct their attention to a smaller part of the visual field can improve the reliability of their responses. This information may have immediate clinical applicability for improving standard clinical perimetry (visual field testing) for diseases such as glaucoma and maculopathy, and also for making more efficient laboratory investigations of precise retinal cell sensitivity.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Bedggood, P., & Metha, A. (2020). Adaptive optics imaging of the retinal microvasculature. Clin Exp Optom 103(1): 112-122.
2. Duan, A., Bedggood, P. A., Metha, A. B., & Bui, B. V. (2017). Reactivity in the human retinal microvasculature measured during acute gas breathing provocations. Sci Rep 7(1), 2113.
3. Bedggood, P., & Metha, A. (2013). Optical imaging of human cone photoreceptors directly following the capture of light. PloS One 8(11).

VISUAL AND COGNITIVE NEUROSCIENCE LABORATORY

LABORATORY HEAD

Name: Professor Trichur Vidyasagar, *MBBS, PhD*
Email: trv@unimelb.edu.au

PROJECT SUPERVISORS

Name: Dr Ekaterina Levichkina, *PhD*
Email: ele@unimelb.edu.au

Name: Dr. Yamni Mohan, *PhD*
Email: mohan.y@unimelb.edu.au

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/visual-and-cognitive-neuroscience-laboratory

Summary of lab interests: Our laboratory is interested in understanding the neural basis of visual perception, attention, memory and how they relate to complex functions such as reading.

PROJECT 1: FUNCTIONAL MICROCIRCUITRY OF THE VISUAL CORTEX

Different areas of the cerebral cortex have fairly similar morphological structures regardless of their specific functions, suggesting that there is a universal cortical microcircuit which is involved in transforming the inputs.

Understanding this microcircuit is important to understanding how the brain makes sense of the external world. In our lab, we examine the microcircuit of the primary visual cortex in anaesthetised cats and macaques, to shed new light on this problem. In these studies, we use a combination of single electrodes, multi-electrode arrays and optical imaging of intrinsic signals to examine the cortical inputs, responses of individual neurons and groups of neurons, to shed new light on this problem. We also study the feedback influences from higher areas on early visual areas.

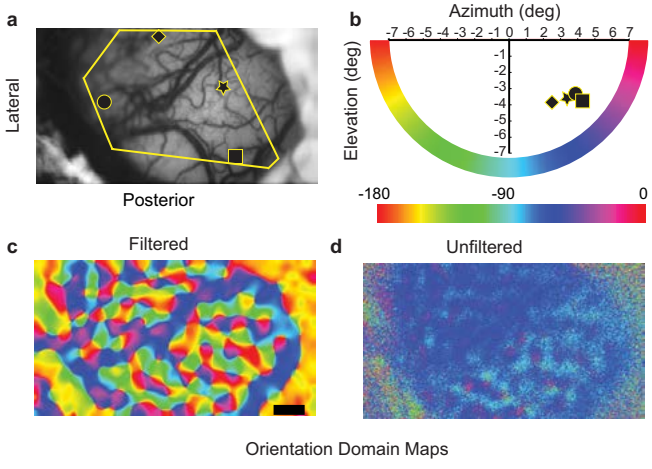


Figure 14: Imaging and functional studies to understand how vision is organised in the brain.

PROJECT 2: NEURAL MECHANISMS OF TOP-DOWN ATTENTION AND PREDICTIVE CODING

How does the brain manage to attend to a specific object or region of visual space when it is confronted with innumerable objects? How are we able to pick out a face in a large crowd, often so effortlessly? Such focussing of attention is known to involve some specific areas of the brain, but how these interact with each other has been largely unknown. In these experiments on trained macaques, we record from multiple brain areas implicated in visual attention, to characterise the distributed processing that occurs with attention.

With these experiments, we also seek to test an influential new model that suggests that the brain makes conscious or unconscious predictions about what it expects to see in the external world and updates these expectations using any mismatches with sensory inputs.

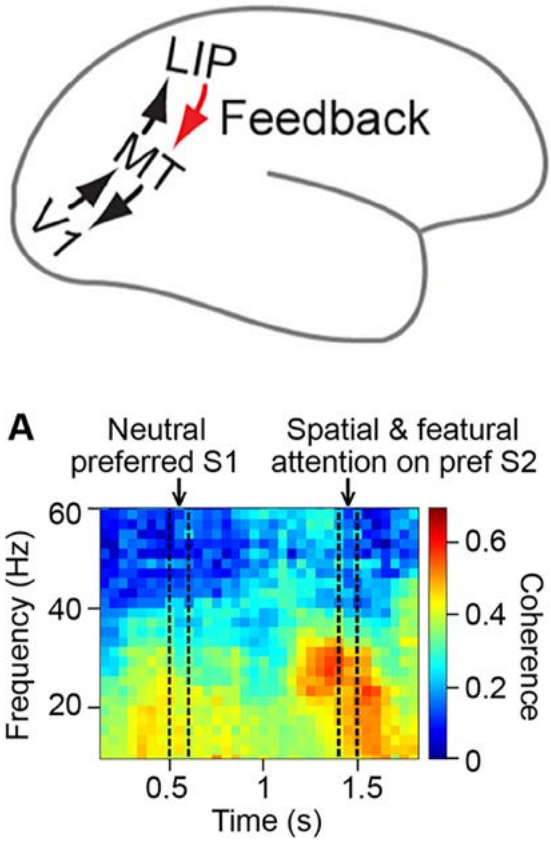


Figure 15: Studies of how connections between brain areas mediate visual attention.

PROJECT 3: VISUAL ATTENTION, READING AND DYSLEXIA

The basic cause of specific reading disability, commonly known as dyslexia, has been a matter of intense debate for decades. Reading is a relatively recent activity in human history and so it is very unlikely that humans have evolved a specific brain region or circuitry devoted to reading, but we probably use for reading brain functions that evolved for a different purpose. Our lab has been working on the idea that one such critical brain function is the visuo-spatial attention network usually used in focussing attention at a visual field location for object identification. We are now exploring these relationships further using visual psychophysics in both normal readers and the reading impaired. Drawing on our experience from physiological studies of neural oscillations, we are also investigating how auditory rhythms, including certain types of music, may influence visual attention and reading performance.

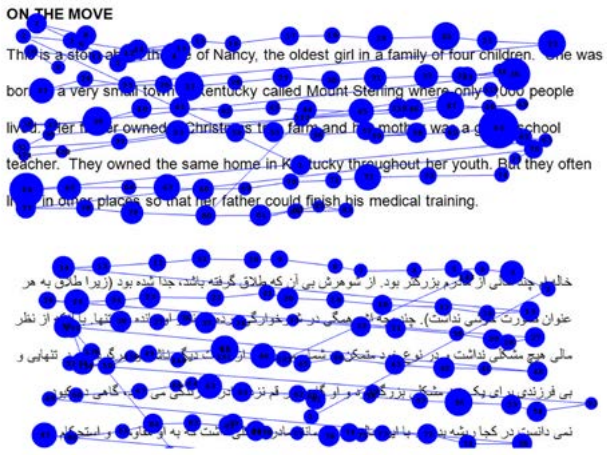


Figure 16: Understanding how we move our eyes to read might help us understand the reasons underlying reading difficulties.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Esghaei M, Treue S, Vidyasagar TR. (2022) Dynamic coupling of oscillatory neural activity and its roles in visual attention. *Trends in Neurosci*. 45(4):323-335.
2. Nguyen BN, Kolbe SC, Verghese A, Nearchou C, McKendrick AM, Egan GF, Vidyasagar TR. (2021) Visual search efficiency and functional visual cortical size in children with and without dyslexia. *Neuropsychologia,* 155, 178819.
3. Levichkina E, Kermani M, Saalmann YB, Vidyasagar TR. (2021) Dynamics of coherent activity between cortical areas defines a two-stage process of top-down attention. *Exp Brain Res*. 239, 2767-2779.
4. Archer K, Pammer K & Vidyasagar TR (2020). A temporal sampling basis for visual processing in developmental dyslexia. *Front Human Neurosci*. Vol. 14, Article 213.
5. Mohan YS, Jayakumar J, Lloyd EKJ, Levichkina E & Vidyasagar TR. (2019) Diversity of feature selectivity in macaque visual cortex arising from limited number of broadly-tuned input channels. *Cerebral Cortex*, 29: 5255-5268.
6. Vidyasagar TR, Eysel UT. (2015) Origins of feature selectivities and maps in the mammalian primary visual cortex. Trends in Neurosciences. 38(8), 475-485.
7. Vidyasagar TR & Pammer K. (2010) Dyslexia: a deficit in visuo-spatial attention, not in phonological processing. Trends Cognitive Sci. 14(2):57-63.
8. Saalmann YB, Pigarev IN, Vidyasagar TR. (2007) Neural mechanisms of visual attention: how top-down feedback highlights relevant locations. Science 316(5831): 1612-1615.

VISION OPTIMISATION LABORATORY

LABORATORY HEAD

Name: A/Prof Lauren Ayton
Email: layton@unimelb.edu.au
Phone: +61 3 8344 3441
www.linkedin.com/in/drlaurenayton

PROJECT SUPERVISORS

Name: Dr Ceecee Britten-Jones
Email: ac.brittenjones@unimelb.edu.au

Summary of lab interests: In recent years, there have been a number of interventions developed for vision loss and blindness. From gene therapy to bionic eyes, all treatments require thorough evaluation of visual function pre- and post-intervention, as well as an understanding of the impact of the treatments on a person's life.

Our team works on clinical vision and psychosocial assessments of people who receive such vision interventions. We have developed and run clinical studies for retinal prostheses (bionic eyes), gene therapy, and other low vision aids (including sensory substitution devices). Our aim is to ensure that every person is able to make the most of the vision they have.

The lab maintains strong collaborations with engineers (University of Melbourne, Bionics Institute, Swinburne University, Cornell University USA), neurologists (Harvard University, USA), ophthalmologists (Royal Victorian Eye and Ear Hospital, Centre for Eye Research Australia), visual function experts (Oxford University, UK) and basic scientists (University of Melbourne) to assist in the development of new treatments.

Currently, we are collaborating on a project to develop Australia's first ocular gene therapy for an inherited retinal disease; designing new software algorithms for electronic and audio-based low vision aids; developing novel imaging techniques to identify raised intracranial pressure and running natural history studies to identify biomarkers of retinal degenerative disease. We are also involved in industry-sponsored clinical trials, including gene therapy for age-related macular degeneration, and an oral anti-oxidant for Usher syndrome, the most common cause of dual vision and hearing loss.

PROJECT 1: DEVELOPMENT OF NEW VISION TESTS FOR VISION RESTORATION CLINICAL TRIALS

This project, in collaboration with clinicians at the University of Oxford and ophthalmologists from the Centre for Eye Research Australia, will develop and validate new methods of measuring low vision in patients who may be eligible for treatments such as gene therapy and stem cells. At present, there is a lack of gold standard test protocols for low vision testing, and this project will provide important data on the validity of new tests.

PROJECT 2: NATURAL HISTORY OF INHERITED RETINAL DISEASES (VENTURE REGISTRY)

A large study in our group is focusing on the collection of data on the natural history of inherited retinal diseases in Australia and New Zealand. A number of research projects into imaging biomarkers, genotype/phenotype correlations and visual function measures in this population are available.

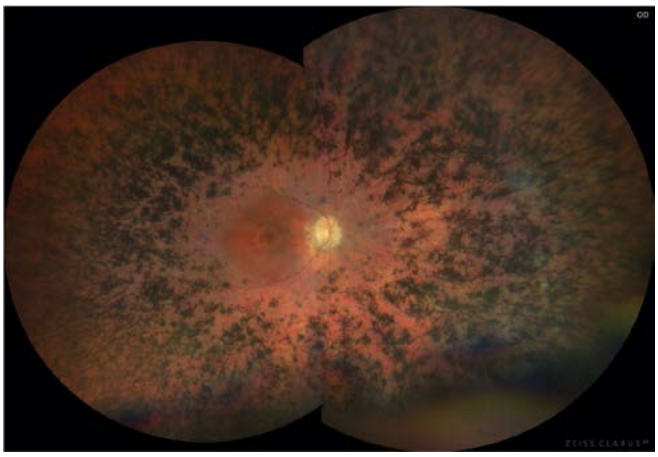


Figure 17: A retinal fundus photo of a person with X-linked retinitis pigmentosa, a form of inherited retinal disease that we focus on in our research.

PROJECT 3: EVALUATION OF ADVANCED LOW VISION TECHNOLOGIES

Historically, low vision aids were low-tech, such as magnifying glasses and high-powered spectacle lenses. However, recent advances have led to a proliferation in high-tech alternatives, such as the iPhone, text-to-speech software and spectacle-mounted camera systems. This research program is investigating the efficacy and uptake of these technologies, and comparing to the more traditional options for patients with conditions such as age-related macular degeneration.

RECENT RELATED PUBLICATIONS FROM OUR TEAM:

1. Britten-Jones AC, O'Hare F, Edwards TL, Ayton LN for the VENTURE Study Consortium. *The Victorian Evolution of Inherited Retinal Diseases Natural History Registry (VENTURE study): Rationale, methodology, and initial participant characteristics.* Clinical and Experimental Ophthalmology 2022; accepted 16 May 2022.
2. Britten-Jones AC, Gocuk SA, Cichello E, O'Hare F, Hickey DG, Edwards TL, Ayton LN. *The safety and efficacy of gene therapy treatment for monogenic retinal and optic nerve diseases: A systematic review.* Genetics in Medicine 2022; 24(3):521-534.
3. Mack HG, Chen FK, Grigg J, Jamieson RV, De Roach J, O'Hare F, Britten-Jones AC, McGuiness MB, Tindell N, Ayton LN. *Potential participant perspectives on ocular gene therapy in Australia: Protocol for a national survey*. British Medical Journal Open 2021; 11(6): e048361.
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5. Petoe MA, Titchener SA, Kolic M, Kentler WG, Abbott CJ, Nayagam DAX, Baglin EK, Kvansakul J, Barnes N, Walker JG, Epp SB, Young KA, Ayton LN, Luu CD, Allen PJ, for the Bionics Institute and Centre for Eye Research Australia Retinal Prosthesis Consortium. *A second generation (44-channel) suprachoroidal retinal prosthesis: Interim clinical trial results.* Translational Vision Science & Technology 2021; 10(10):12.

CONNECT WITH US

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DEPARTMENT OF OPTOMETRY AND VISION SCIENCES

HONOURS COORDINATOR
Prof Trichur Vidyasagar
+613 8344 7004
trv@unimelb.edu.au

MASTER OF BIOMEDICAL SCIENCE COORDINATOR
Prof Trichur Vidyasagar
+613 8344 7004
trv@unimelb.edu.au

GRADUATE RESEARCHER COORDINATOR
A/Prof Andrew Anderson
+613 9035 9916
aaj@unimelb.edu.au

WEBSITE
healthsciences.unimelb.edu.au/departments/optometry-and-vision-sciences

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