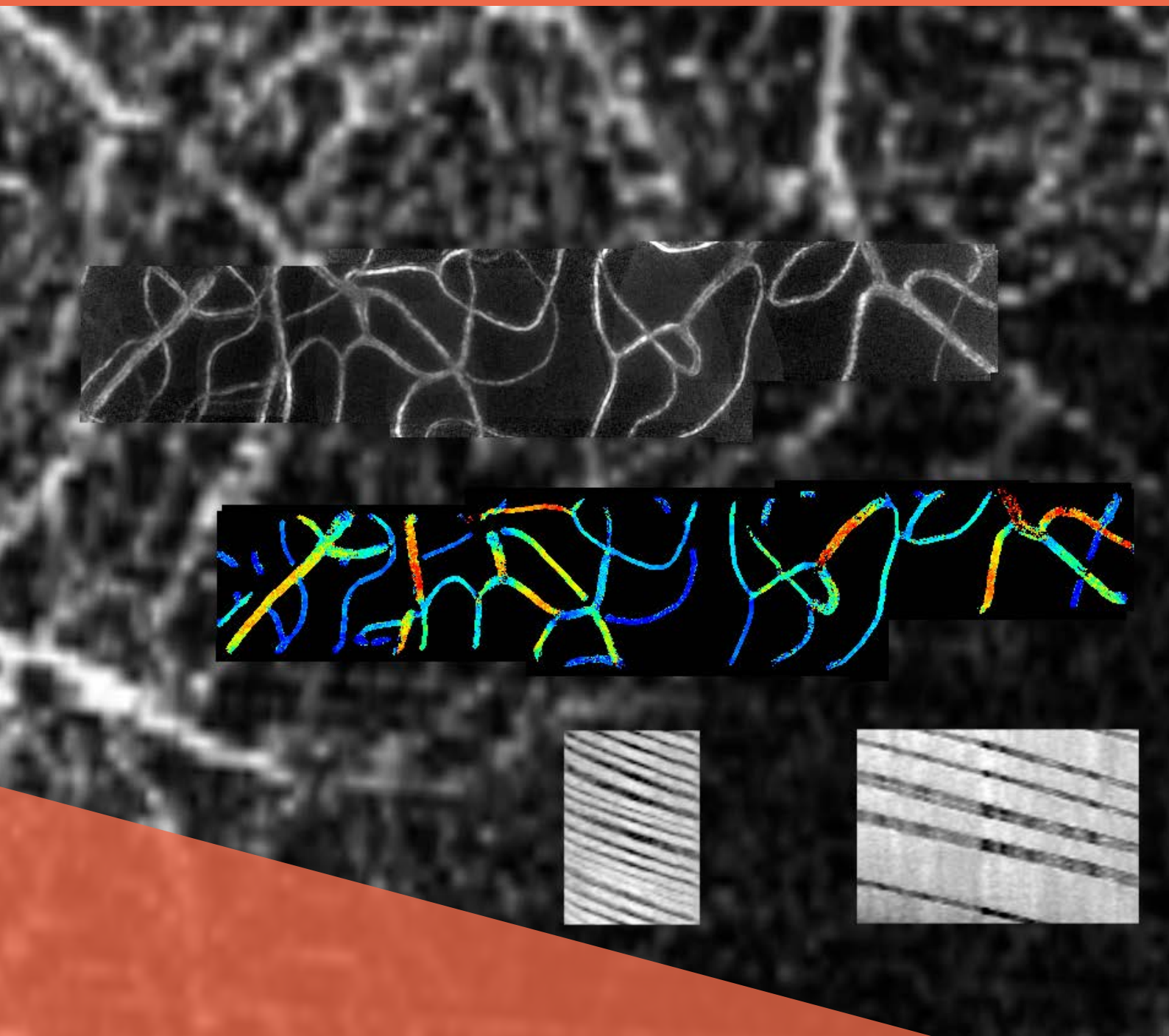
THE UNIVERSITY OF MELBOURNE

Department of Optometry and Vision Sciences

Research Projects 2021

(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 & 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 evaluating the viability of crowdsourcing for research. 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. 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 to four year PhD or a two 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 +61390359916 aaj@unimelb.edu.au .

For further information

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

Masters of Biomedical Science
https://study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/

Masters of Philosophy
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PhD
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Department of Optometry and Vision Sciences
https://healthsciences.unimelb.edu.au/departments/optometry-and-vision-sciences

Clinical Psychophysics Unit

Laboratory Head

Name: Professor Allison McKendrick
Email: allisonm@unimelb.edu .au
Ph: 83447005

Project Supervisors

Name: Dr Bao Nguyen
Email: bnguyen@unimelb.edu.au
Ph: 9035 9979

Website: https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/clinical-psychophysics-unit

Lab blog: http://uomcpulab.wordpress.com/

Summary of lab interests: Our research aims to better understand normal visual processing and damage due to disease. We have specific interests in the study of glaucoma, migraine, and the process of normal ageing. Our applied aims include developing better clinical tests for the assessment of vision loss; determining methods of preventing visual damage, and improving understanding of the consequences of vision loss on performance in natural visual environments and day-to-day tasks. Our current studies use a variety of methods including visual psychophysics (testing visual performance), human electrophysiology and brain and ocular imaging. Our work is highly collaborative with colleagues from ophthalmology, psychology, physiotherapy, neurology and neuroimaging.

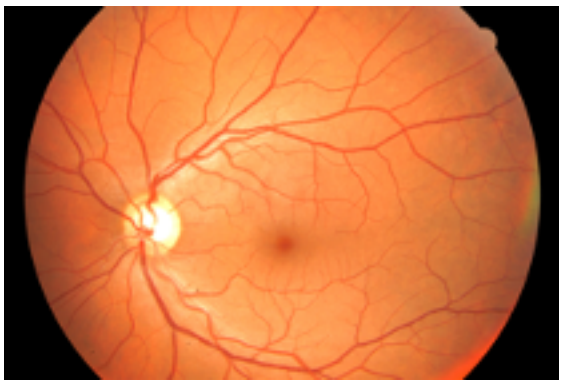
Project 1: Understanding motion perception in peripheral vision

Peripheral vision is very sensitive to visual motion cues. These cues are used to identify objects in our periphery and to segment them from other background features. This project will explore which stimulus features are important to the ability to segment moving objects in our peripheral vision, as well as studying whether individual differences in simple aspects of motion perception predict individual ability to identify moving objects on noisy backgrounds.

PhD student, Juan Sepulveda, measuring motion cues used to identify human movement.

Project 2: Outer retinal structure and function in people who suffer episodic migraines

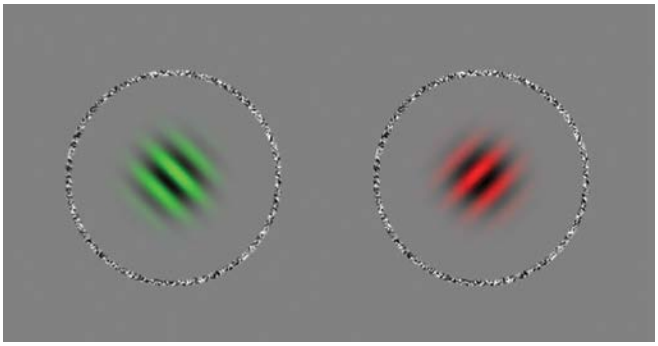
Migraine headaches can be associated with visual dysfunction at the time of an attack, but also in between migraine attacks. This study will consider whether there is evidence for anomalies in outer retinal structure and function. This project will be an analytical study of data collected in young and otherwise healthy people with normal vision who suffer from episodic migraines, compared to people who do not regularly get headaches. This study will contribute to our understanding of how migraine may impact on the visual system.



Retina of an individual who suffers from migraines

Project 3: Does caffeine influence perceptual eye dominance plasticity?

Caffeine is a widely used psychostimulant that is associated with increased acetylcholine in the brain. Acetylcholine is a neuromodulator that plays an important role in the processing of visual information. In particular, acetylcholine and the cholinergic system are thought to be involved in adult brain plasticity, which can be measured by temporary patching of one eye for a few hours. A recent study showed that perceptual eye dominance plasticity is reduced with pharmacological administration of donepezil (an acetylcholine enzyme inhibitor) in healthy human observers. Here, we test whether temporarily manipulating caffeine levels has a similar effect on perceptual eye dominance plasticity.



Binocular rivalry stimuli, commonly used to infer visual system plasticity. The red and green stimuli are presented to each eye separately, with the combined percept swapping regularly from one to the other (rivalrous percept).

Recent related publications from our team:

1. Chan YM, Pitchaimuthu K, Wu Q-Z, et al. Relating excitatory and inhibitory neurochemicals to visual perception: A magnetic resonance study of occipital cortex between migraine events. *PLoS One* 2019;1-13.

2. Nguyen BN, Hew SA, Ly J, et al. Acute caffeine ingestion affects surround suppression of perceived contrast. J *Psychopharmacol* 2018;32:81-88.

3. Sepulveda JA, Anderson AJ, Wood JM, McKendrick AM. Differential aging effects in motion perception tasks for central and peripheral vision. J Vis. 2020;20(5):8.

4. Nguyen BN, McKendrick AM. Foveal and parafoveal contrast suppression are different: mechanisms revealed by the study of healthy ageing. *Journal of Vision* 2016;16(3):10.

Optological Laboratory

Laboratory Head

Name: Assoc. Prof. Andrew Anderson
Email: aaj@unimelb.edu.au
Ph: +613 9035 9916

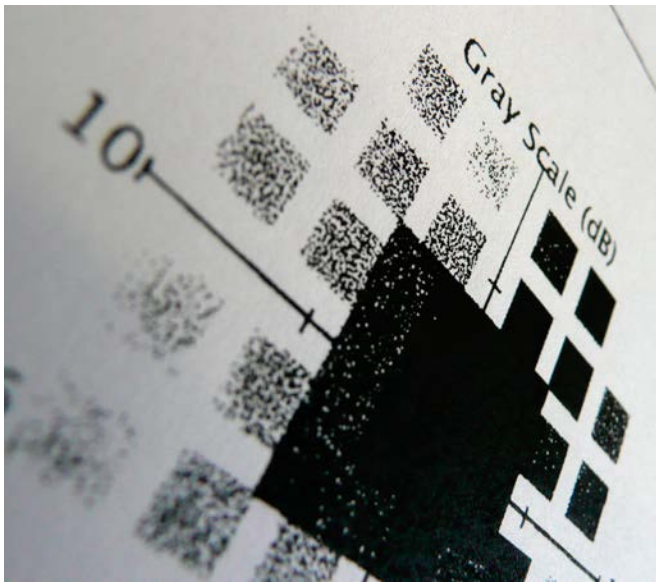
https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/optological-laboratory

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: 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 stabilization mechanisms improve our ability to do a very common task – making fine judgement of relative motion between objects in the world.



Selected Publications:

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.

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.

Mahjoob M, Anderson AJ (2019). Contrast discrimination under task-induced mental load. *Vision Res* 165:84-89.

Anderson AJ, Chaurasia AK, Sharma A, Gupta A, Gupta S, Khanna A, Gupta V (2019). Comparison of rates of fast and catastrophic visual field loss in three glaucoma subtypes. *Invest Ophthalmol Vis Sci* 60(1):161-167.

The Retinal Observatory

(Imaging cellular structure and function in the living human retina)

Laboratory Head

Name: Associate Professor Andrew Metha
Email: ametha@unimelb.edu.au
Ph: 9035 9783

Project Supervisors

Name: Dr Phillip Bedggood
Email: pabedg@unimelb.edu.au
Ph: 9035 9979

https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/imaging-retinal-cells-human-unit/individual-photoreceptors-in-the-human-eye

Our broad research aim is to understand the fundamental workings of the living retina on the microscopic scale: how this works normally and how this becomes compromised in sight-debilitating diseases such as diabetes. We combine a range of novel investigative tools including high-spatiotemporal resolution non-invasive retinal imaging, psychophysics, and computational modelling.

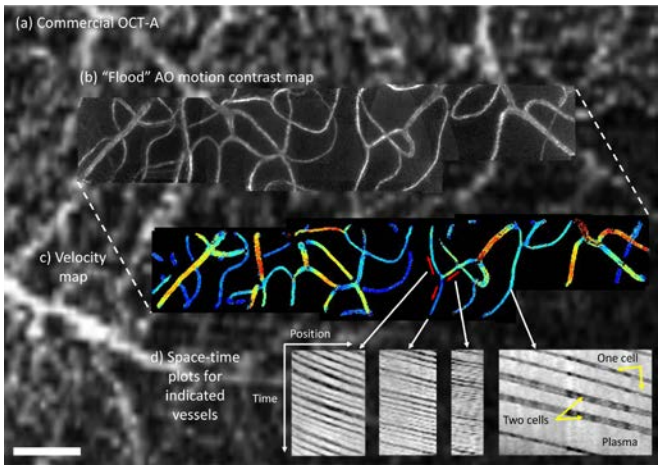
Our current research projects make use of high speed, multi-spectral adaptive optics to visualize the smallest neurons and blood vessels that is possible to see in in living human eyes. We study the dynamics of flow and oxygen exchange at the level of individual red blood cells, and the cascade of optical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

Project 1: Keeping neurons alive in the living human eye: single red and white blood cell flow through retinal capillary networks

With newly-developed adaptive optics (AO) retinal imaging, we can now visualize the finest capillaries in the eye and watch the passage of single red and white blood cells through vascular networks. These are the networks that keep your retina healthy, and which fail in diseases such age-related macular degeneration and diabetes. The fine details of blood flow patterns have not yet been fully documented because blood flows very quickly - and also because the retina is designed to be transparent, making it hard to obtain high contrast images without risking light damage. 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 who wish to learn about and apply optical and image processing skills to questions of basic human physiology with immediate clinical applicability.

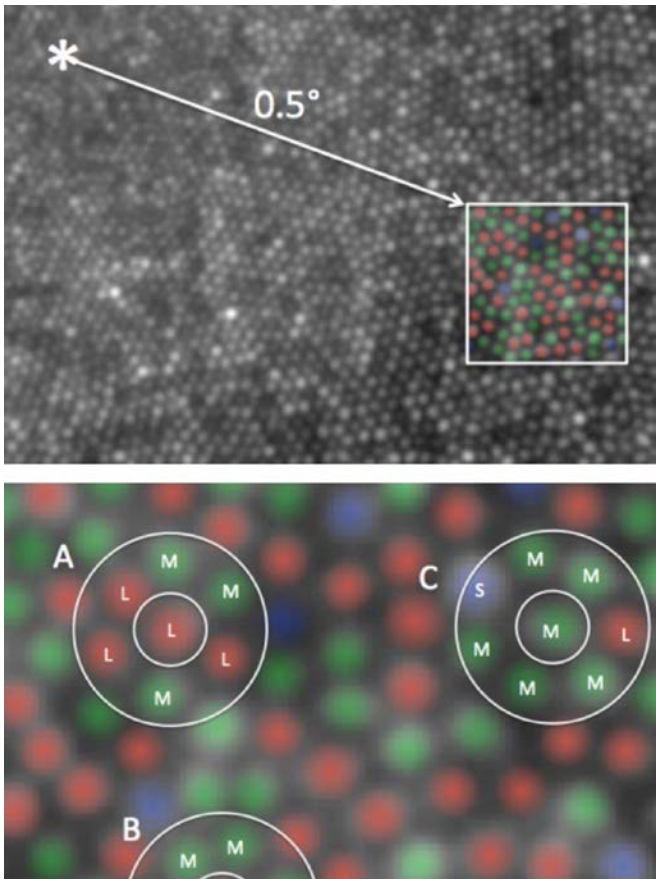


Tracking single-file blood cell flow though the retinal capillary network

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!

Text BoxUsing psychophysical methods to record behavioral responses to stimulating either single cells or specific cell arrangements, an exciting ARC-funded project exists 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.



Targeting single cone photoreceptors to investigate inputs to midget ganglion cells

Project 3: Methods to improve the measurement of visual performance

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. *Clinical Experimental Optometry*, *103*(1), 112-12).

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. Scientific reports, 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).

Ocular Physiology Laboratory

Laboratory Head

Name: Bang Bui
Email: bvb@unimelb.edu.au
Ph: +61 3 83447006

Project Supervisors:

Dr Christine Nguyen
Email: christine.nguyen@unimelb.edu.au
Ph: +61 3 9035 3186

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

Da Zhao
Email: da.zhao@unimelb.edu.au
Ph: +61 3 8344 1484

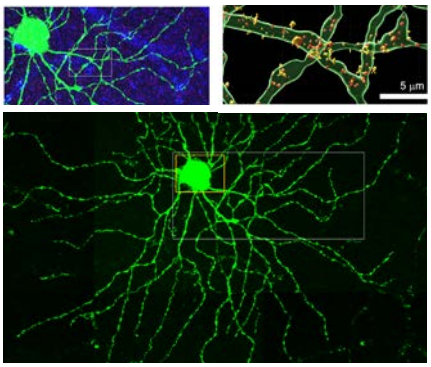
https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/ocular-physiology-lboratory

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

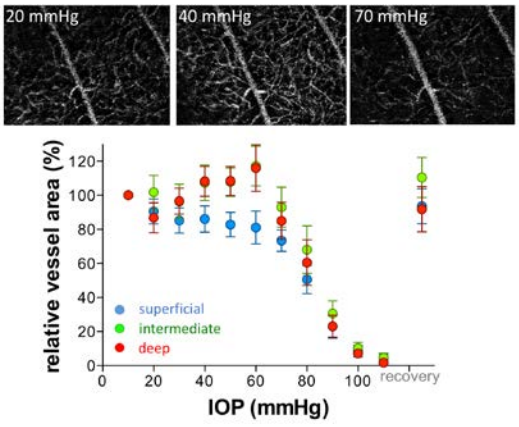
Our investigations of glaucoma hope to shed light on how the cells that connect the eye to the brain, the retinal ganglion cells are able to adapt to changes in their local environment. When such adaptation mechanisms fail ganglion cells undergo programmed cell death. Ganglion cells have to cope with constant changes in the pressures in and around the eye; intraocular pressure, blood pressure and intracranial pressure. As the eye gets older the capacity to cope with stress is diminished, but at the moment we dont understand why this occurs. In order 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 quantifying their function and relating this to changes in dendritic morphology and expression of membrane pressure sensors.

The figure top left shows a ganglion cell in a mouse eye, that we can co-stain for synapses to better understand why ganglion cells are affected by high eye pressure.



Project 2: Studies of retinal vascular autoregulation

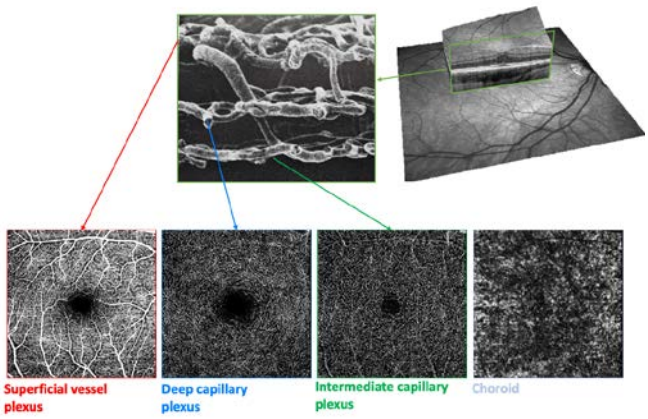
The retina and brain are the most highly energy demanding tissues in the body. In the retina, the need for optical clarity and many neurons for good vision comes at the expense of fewer blood vessels as well as the lack of ways to store energy. The retina is completely dependent on a stable blood supply to deliver oxygen and glucose. In the retina there are three major vascular beds (superficial, intermediate and deep) that entirely locally controlled to respond to normal fluctuations in blood and eye pressure. This control system is known as vascular autoregulation and involves not only the cell lining the blood vessel walls (endothelial cells) but also neurons and supporting glial cells (astrocytes and microglia). The failure of autoregulation has been implicated in retinal disease such as diabetes and glaucoma. In these studies, we will employ optical coherence tomography imaging to assess autoregulation in animal models of retinal diseaseresponse to changes in pressure. response to changes in pressure.



Higher eye pressure changes the blood vessels in the living eye, which we measure using optical coherence tomography. By looking at the vessel at different retinal depths we can see that the superficial vessels (blue) respond differently to intermediate (green) and deeper (red) vessels.

Project 3: Developing a clinical test of vascular autoregulation

As we better understand how blood vessels in the eye work to supply blood when needed, we use this information to help us develop better clinical tests for detecting blood vessels that don't work as they should. Optical coherence tomography angiography can be used in the laboratory as well as in the clinic. By using a flickering light stimulus we challenge the blood vessels to dilate, in order to get more blood to support the increased communication between retinal neurons that occurs with lights repeatedly turning on and off. Using this approach we may be able to identify eyes that have regions of blood vessels that do not respond as they should. We believe that this will help us detect earlier those eyes that might go on to develop vision loss.



Optical coherence tomography angiography can help us to discern key blood vessel layers in the retina.

Recent related publications from our team:

1. Grant ZL, Whitehead L, Wong VHY, He Z, Yan RY, Miles AR, Benest AV, Bates DO, Prahst C, Bentley K, Bui BV, Symons RC, Coultas L. Blocking endothelial apoptosis revascularises the retina in a model of ischemic retinopathy. J Clin Invest. 2020:127668.

2. Zhao D, He Z, Wang L, Fortune B, Lim JKH, Wong VHY, Nguyen CTO, Bui BV. Response of the Trilaminar Retinal Vessel Network to Intraocular Pressure Elevation in Rat Eyes. Invest Ophthalmol Vis Sci. 2020 ;61(2):2.

3. Zhao D, Wong VHY, Nguyen CTO, Jobling AI, Fletcher EL, Vingrys AJ, Bui BV. Reversibility of Retinal Ganglion Cell Dysfunction From Chronic IOP Elevation. Invest Ophthalmol Vis Sci. 2019;60(12):3878-3886.

4. Liu G, Cull G, Wang L, Bui BV. Hypercapnia Impairs Vasoreactivity to Changes in Blood Pressure and Intraocular Pressure in Rat Retina. Optom Vis Sci. 2019;96(7):470-476.

5. Li F, Hung SSC, Mohd Khalid MKN, Wang JH, Chrysostomou V, Wong VHY, Singh V, Wing K, Tu L, Bender JA, Pébay A, King AE, Cook AL, Wong RCB, Bui BV, Hewitt AW, Liu GS. Utility of Self-Destructing CRISPR/Cas Constructs for Targeted Gene Editing in the Retina. Hum Gene Ther. 2019;30(11):1349-1360.

Ocular Biomarker Laboratory

Laboratory Head

Dr Christine Nguyen
Email: christine.nguyen@unimelb.edu.au
Ph: +61 3 9035 3186

Project Supervisors:

A/Prof Bang Bui
Email: bvb@unimelb.edu.au
Ph: +61 3 8344 7006

Prof Cassandra Szoeke
Email: cszoeke@unimelb.edu.au
Ph: +61 3 8344 1835

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

Dr Da Zhao
Email: da.zhao@unimelb.edu.au

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

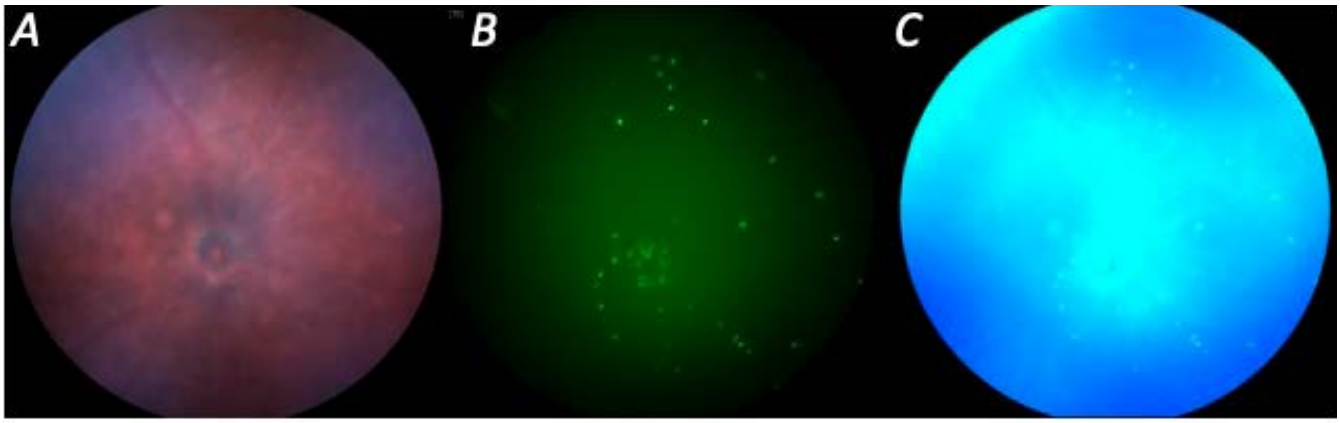
Summary of lab interests: The eye affords a unique opportunity to gain insights into what is occurring in the brain. It is the only place in the body where neurons and blood vessels can be directly visualised. Moreover, neurological diseases such as Alzheimer's disease, Parkinson's disease and multiple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

Project 1: Imaging Parkinson's disease in the eye

Diagnosis of Parkinson's disease is a difficult and lengthy process. A hallmark of Parkinson's is alpha-synuclein deposits in the brain but the skull makes these difficult to detect. Interestingly, in our lab and others, alpha-synuclein has been identified in the retina, an outpouching of the central-nervous-system. The aim of this project is to provide proof-of-principle that it is possible to image alpha-synuclein in the mouse retina. Given the clear optics the eye, we will fluorescently tag an antibody and directly image them in living animals. The capacity to develop early, specific biomarkers for PD is pivotal for development of treatments.

Project 2: The retina as a window to Alzheimer's disease: a prospective study

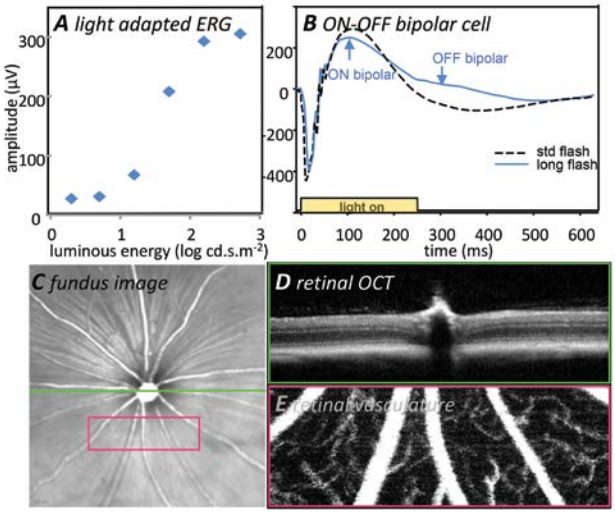
Retinal ganglion cells and their axonal projections form part of the central nervous system and are uniquely suited to direct visualisation and imaging. In Alzheimer's disease, reports using 3D retinal scans (optical coherence tomography) have suggested that the retinal nerve fibre layer is thinned in patients with advanced dementia. More recently, there has been suggestion that the inner plexiform layers of the retina are thickened in people with early Alzheimer's. This project is part a longitudinal study known as the Women in Healthy Ageing Project and will correlate optical coherence tomography measures to mental health status from depression to dementia. In this manner the project will evaluate whether the time course of retinal measurements is potentially useful as a topographical biomarker for Alzheimer's disease.



Alpha-synuclein imaging in the eye A. Retinal photograph B. following injection of a fluorescently labeled tag, alpha-synuclein (green spots) can be visualised. C. A combination image where some retinal detail and tagged alpha-synuclein can be simultaneously viewed

Project 3: A marker for Parkinson's disease? ON- OFF- electroretinography assessment

Emerging evidence indicates that changes to the electrical response from the retina (electroretinogram) may reflect changes in cortical disease such as Parkinson's disease. Studies have shown dampening of the electroretinogram in Parkinson's disease patients that reverse with current gold standard treatment with levadopa. Indeed, dopamine has multiple roles in the retina including light adaptation and ON-OFF bipolar cells responses but light adaptation can be time-consuming and ON- OFF- responses have been difficult to measure. This study aims to apply a novel analysis approach recently shown to differentiate ON and OFF bipolar cell responses to electroretinography recordings from patients and animal models with Parkinson's disease. Such an approach will aid understanding of whether assessment of the ON-OFF- system is an informative marker for Parkinson's diseas.



Functional and structural assessment of retinal health in animals models of neurodegenerative disease

Project 4: Examining neuroinflammation in a model of Parkinson's disease

Neuroinflammation is central to the pathophysiology of Parkinson's disease, however it is challenging to measure in vivo. Assessment in peripheral systems (such as blood) may be indicative but are limited due to the distinct inflammatory pathways found within the central nervous system. It is established from Parkinson's disease human post- mortem substantia nigra tissue, that microglia become activated and release specific proinflammatory cytokines that lead to neurodegeneration. The eye is an out- pouching of the brain and literature indicates that 3 dimensional scans of the retina show thickening which is typical of active inflammation. What has not been examined are inflammatory markers which correspond to these changes. This project aims to examine this link in a mouse model of Parkinson's disease.

Recent related publications from our team:

1. 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.

2. 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.

3. Habiba U, Merlin S, Lim JKH, Wong VHY, Nguyen CT, Morley JW, Bui BV, Tayebi M. Age-Specific Retinal and Cerebral Immunodetection of Amyloid-beta Plaques and Oligomers in a Rodent Model of Alzheimer's Disease. *J Alzheimers Dis* 2020

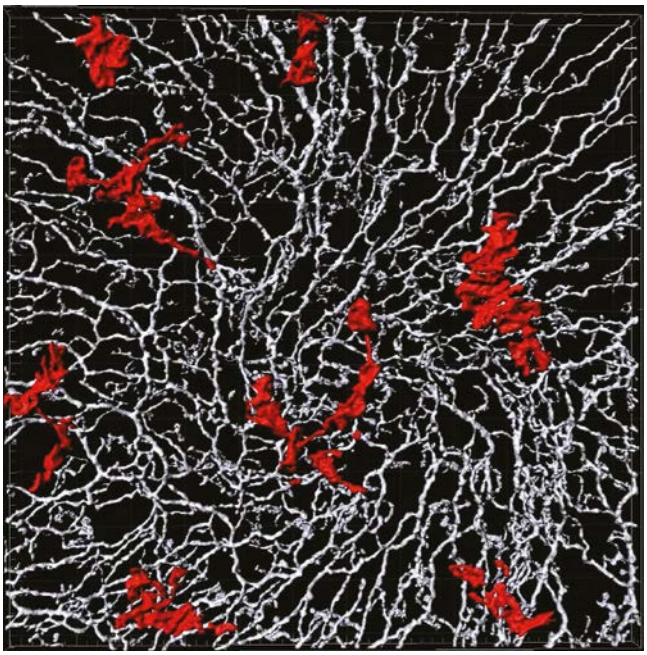
4. Shahandeh A, Bui BV, Finkelstein DI, Nguyen CT. Therapeutic applications of chelating drugs in iron metabolic disorders of the brain and retina. *J Neurosci Res* 2020

Corneal and Ocular Immunology

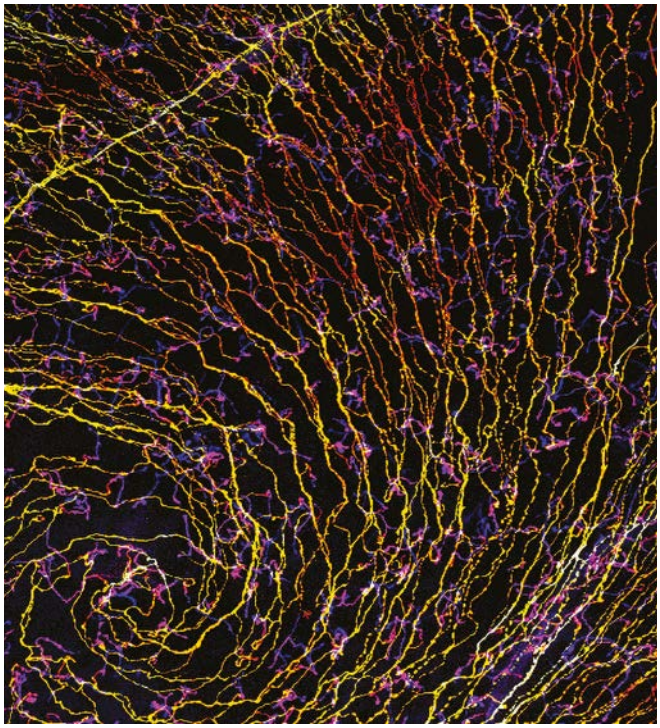
Laboratory Head

Name: Dr Holly Chinnery
Email: holly.chinnery@unimelb.edu.au
Ph: 9035 6445

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 Dr Laura Downie, who leads the Anterior Eye, Clinical Trials and Research Translation Unit in DOV.



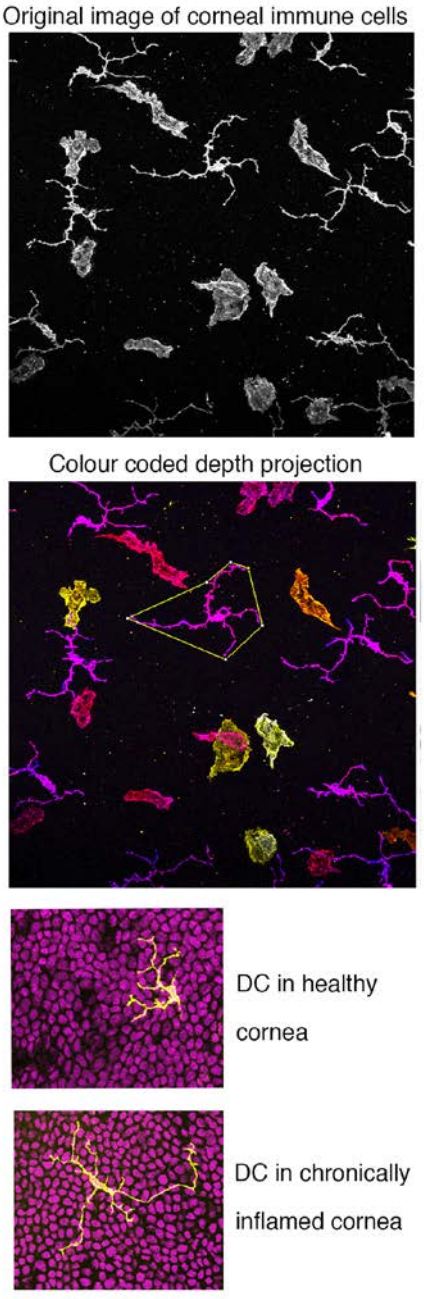
Corneal macrophages living just beneath the corneal epithelial nerve plexus.



Corneal nerves forming a whorl pattern in the central epithelium

Project 1: Time course of sensory nerve recovery after epithelial injury

Following corneal epithelial injury, the regeneration of the corneal nerves is a slow process, often taking months to recover. However, despite this slow recovery process, the cornea appears structurally normal, with the epithelial cells and tissue architecture appearing clear and healthy. We propose that this is due to differential rates of recovery of different nerve plexi. This project will quantify the regeneration rates of nerves and measure neuropeptide secretion in distinct regions of the cornea after injury. Techniques include animal handling, clinical imaging, confocal microscopy, protein assays, 3D image reconstruction and image analysis. This project would be suitable for Honours, Masters or PhD student.



Resident immune cells (dendritic cells and macrophages) in mouse cornea. Shape and size analysis reflect functional alterations in immune cells.

Project 2: Correlating immune cell morphometry with markers of cellular activation in the mouse cornea.

Recent clinical studies have demonstrated using in vivo confocal microscopy that corneal immune cells change their shape and size in response to local and systemic inflammatory diseases. 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.

Recent related publications from our team:

1. 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.

2. 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

3. Jiao H, Naranjo Golborne C, Dando S, McMenamin PG, Downie LE & Chinnery HR. 2019. Topographical and morphological differences of corneal dendritic cells during steady state and inflammation. Accepted for publication in *Ocular Immunology and Inflammation* .

4. Downie LE, Naranjo Golborne C, Chen M…Chinnery HR et al. Recovery of the sub-basal nerve plexus and superficial nerve terminals after corneal epithelial injury in mice. *Exp Eye Res* 2018; 171: 92-100.

Anterior Eye, Clinical Trials and Research Translation Unit

Laboratory Head

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

Project Supervisors:

Name: Dr Holly Chinnery *BSc(Hons), PhD*
Email: holly.chinnery@unimelb.edu.au
Ph: 9035 6445

http://healthsciences.unimelb.edu.au/research2/optometry-and-vision-sciences-research/aect-and-rt-unit

Summary of lab 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 Chinnery) on projects combining pre-clinical and clinical science.

Anterior eye biomarkers of ocular and systemic disease: This program of research investigates using the anterior eye, in particular 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 ocular 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.

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.

Research translation: This research focuses on improving patient outcomes by identifying, synthesising and promoting implementation of the best-available evidence in eye care practice.

We are currently undertaking several projects that are developing new clinical tools and digital platforms to support evidence-based practice, in areas such as dry eye disease and age-related macular degeneration. We have developed a free, online platform (in collaboration with A/Prof Michael Pianta) called CrowdCARE, (Crowdsourcing Critical Appraisal of Research Evidence crowdcare.unimelb.edu.au), which uses crowdsourcing to support evidence-based practice. CrowdCARE has the capacity to redefine how clinicians discover and use appraised research evidence, through its capacity to: teach critical appraisal, enable critically appraised research to be shared amongst a global interdisciplinary community, and facilitate contributions and access to an evolving stream of appraised research.

Project 1: Understanding the dynamics of corneal immune cells in the human eye

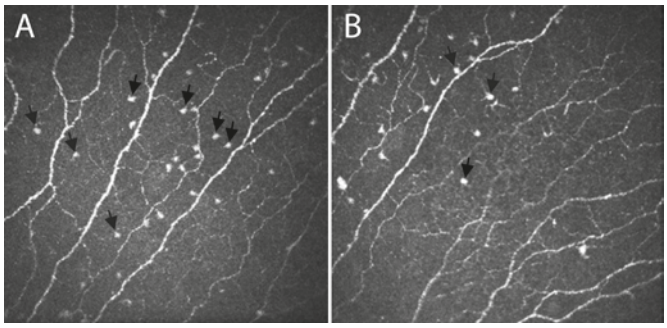


Figure 2: Laser-scanning confocal microscopy images from the central cornea of a person with peripheral neuropathy, at (A) baseline and (B) after eight weeks of oral prednisolone treatment, showing a reduction in the density of putative dendritic cells (white trapezoid-shaped cell bodies).

In vivo confocal microscopy (Figure 2) is a high-resolution imaging technique that permits direct visualisation of corneal nerves and immune cells (dendritic cells) in the living human eye. The cornea is the only tissue in the body that permits this non-invasive, in vivo observation of peripheral nerves and immune cells. Corneal dendritic cells are known to be a dynamic cell population, however there is currently a lack of understanding with respect to how their density change over time. This project will investigate the fundamental dynamics of dendritic cell responses in the healthy cornea, in order to provide insight into the repeatability of this metric, as a marker of corneal inflammation.

This project will involve participant recruitment, clinical examinations, and digital image analysis. It is suitable for Honours, Masters and PhD students.

Project 2: Is crowdsourcing a valid approach to evaluating research quality?

Before we 'trust' a research study, we need to consider how it has been performed, and evaluate its potential weaknesses and/or biases. This process, called critical appraisal, enables us to assess the quality of a scientific paper. This is a potentially time-consuming task, which is an established barrier to it being routinely performed. Using data contributed to our online crowdsourced critical appraisal platform (CrowdCARE), the major aim of this project is to evaluate the quality of the data generated using crowdsourcing, with a focus on the appraisal of laboratory-based studies.

This project will engage researchers and students to contribute critical appraisals, and involve considerable data evaluation and statistical analysis. It is suitable for Honours and Masters students.

Recent related publications from our team:

1. 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.

2. Downie LE, Wormald R, Evans J, et al. Analysis of a systematic review about blue light-filtering intraocular lenses for retinal protection. *JAMA Ophthalmology* 2019;137(6):694-7.

3. 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.

4. Pianta MJ, Makrai E, Verspoor KM, Cohn TA, Downie LE. Crowdsourcing critical appraisal of research evidence (CrowdCARE) was found to be a valid approach to assessing clinical zresearch quality. *J Clin Epidemiol* 2018;104:8-14.

5. Downie LE, Gad A, Wong CY, et al. Modulating contact lens discomfort with anti-inflammatory approaches: a randomized controlled trial. *Invest Ophthalmol Vis Sci* 2018;59(8):3755-66

Visual and Cognitive Neuroscience Laboratory

Laboratory Head

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

Project Supervisors:

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

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

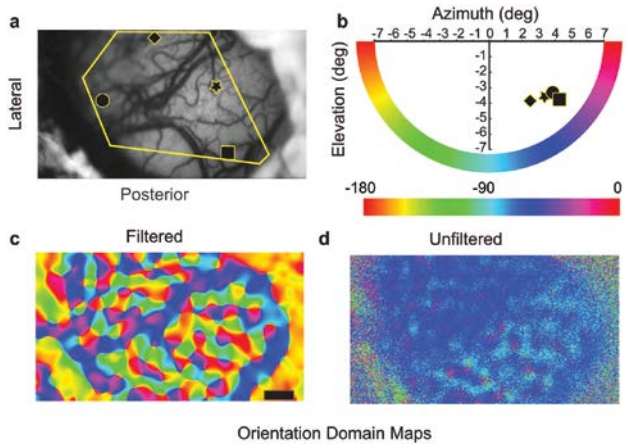
https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research/visual-and-cognitive-neuroscience-laboratory

Summary of lab interests: Our laboratory is interested in understanding the neural basis of visual perception, attention and memory.

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.

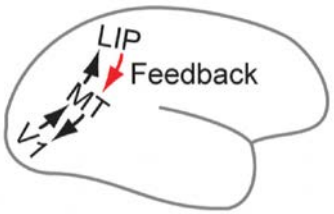
Understanding this microcircuit is important to understanding how the brain makes sense of the external world. In our lab, we examine the microcircuit of the primary visual cortex in anaesthetised cats and macaques, to shed new light on this problem. In these studies, we use a combination of single electrodes, 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.

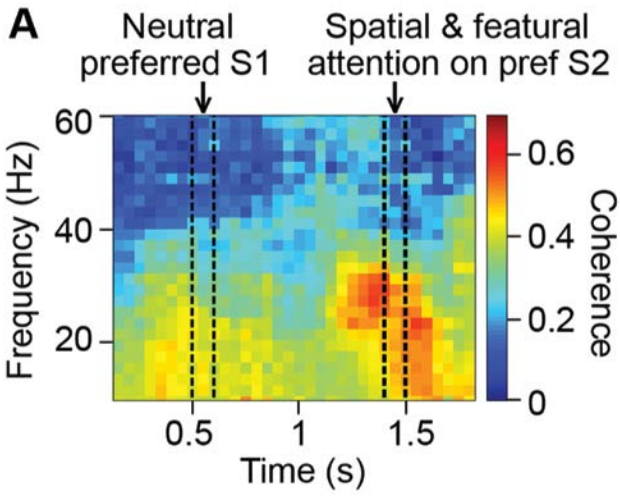


Orientation Domain Maps

Project 2: Neural Mechanisms of Top-down Attention and predictive coding

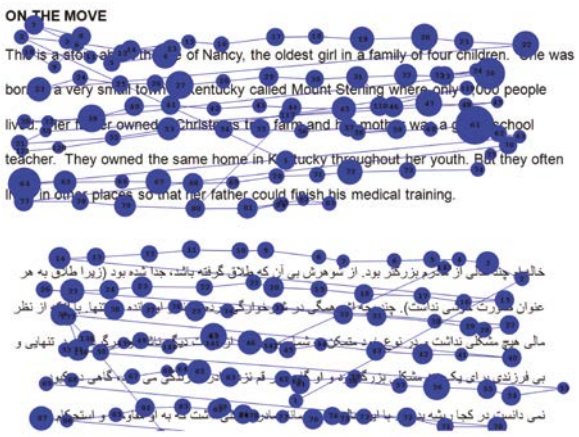
How does the brain manage to attend to a specific object or region of visual space when it is confronted with innumerable objects? How are we able to pick out a face in a large crowd, often so effortlessly? Such focussing of attention is known to involve some specific areas of the brain, but how these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





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 recently found the visual attention efficiency to differ substantially between people and it is related both to reading speeds and to the functional size of the primary visual cortex. We are now exploring these relationships further using visual psychophysics and functional brain imaging in the dyslexic population and also comparing reading of scripts written from left to right (as in English) with those written from right to left (as in Farsi).



Publications of the team relevant to current interests:

1. Archer K, Pammer K & Vidyasagar TR (2020). A temporal sampling basis for visual processing in developmental dyslexia. *Front Human Neurosci.*, Vol. 14, Article No.213. doi: 10.3389/fnhum.2020.00213.

2. 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.

3. Vidyasagar TR & Levichkina E (2019). An Integrated Neuronal Model of Claustral Function in Timing the Synchrony Between Cortical Areas. *Front Neural Circuits*, Vol. 13:3. doi: 10.3389/fncir.2019.00003.

4. Kermani M, Verghese, A, Vidyasagar TR (2018) Attentional asymmetry between the visual hemifields is related to habitual direction of reading and its implications for debate on cause and effects of dyslexia. Dyslexia. 24(1):33-432.

5. Levichkina E, Saalmann YB, Vidyasagar TR (2017) Coding of spatial attention priorities and object features in the macaque lateral intraparietal cortex. *Physiological Reports*. 5(5).

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. Jayakumar J, Roy S, Dreher B, Martin P & Vidyasagar TR (2013). Multiple pathways carry signals from short wavelengths-sensitive ("blue") cones to the middle temporal (MT) area of the macaque, J. Physiol (Lond), 591, 339-352.

8. Vidyasagar TR & Pammer K (2010). Dyslexia: a deficit in visuo-spatial attention, not in phonological processing. *Trends Cognitive Sci., 14*(2):57-63.

9. 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: Dr Lauren Ayton
Email: layton@unimelb.edu.au
Ph: 8344 3441

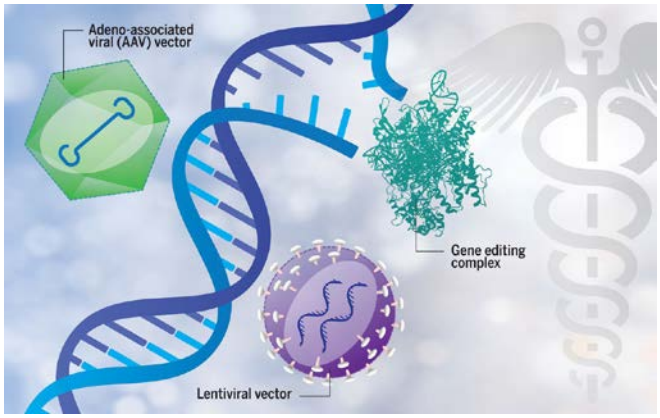
www.linkedin.com/in/drlaurenayton

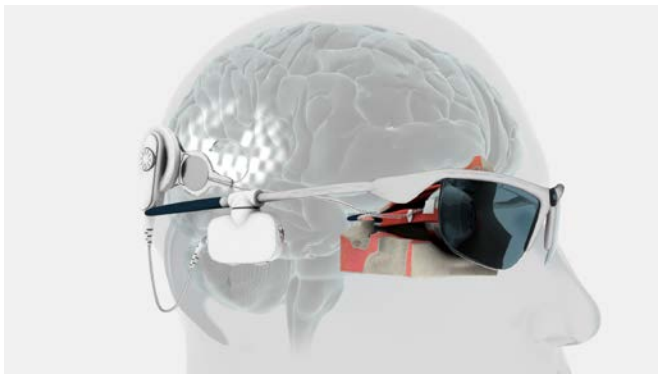
Summary of lab interests: In recent years, there have been a number of interventions developed for vision loss and blindness. From gene therapy to bionic eyes, all treatments require thorough evaluation of visual function pre- and post-intervention, as well as an understanding of the impact of the treatments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





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. For example, one avenue of interest in this area is colour vision measures.

Project 2: Natural History of Inherited Retinal Diseases

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.

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. Ayton LN, Rizzo JF, Bailey I et al. The Harmonization of Outcomes and Vision Endpoints in Vision Restoration Trials (HOVER) consensus document. Transl Vis Sci Technol 2020; In press.

2. Kvansakul J, Hamilton L, Ayton LN, McCarthy CD, Petoe MA. Sensory augmentation to adi training with retinal prostheses. Journal of Neural Engineering 2020; In press.

3. Ayton LN, Blamey PJ, Guymer RH, Luu CD, Nayagam DAX, Sinclair NC, Shivdasani MN, Yeoh J, McCombe MF, Briggs RJ, Opie NL, Villalobos J, Dimitrov PN, Varsamidis M, Petoe MA, McCarthy CD, Walker JG, Barnes N, Burkitt AN, Williams CE, Shepherd RK, Allen PJ, for the Bionic Vision Australia Research Consortium. First-in-human trial of a novel suprachoroidal retinal prosthesis. PLOS One 2014; 9(12): e115239.

4. Bentley SA, O'Hare F, Murphy GC, Finger RP, Luu CD, Keeffe JE, Guymer RH, Ayton LN. Psychosocial assessment of potential retinal prosthesis recipients. Clinical and Experimental Optometry 2019; 102(5):506-12.

5. Finger RP, McSweeney SC, Deverell LA, O'Hare F, Bentley SA, Luu CD, Guymer RH, Ayton LN. Developing an instrumental activities of daily living tool as part of the Low Vision Assessment of Daily Activities (LoVADA) protocol. Investigative Ophthalmology and Vision Science 2014; 55(12): 8458- 8466

Notes

Notes

THE UNIVERSITY OF MELBOURNE

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

If you are interested in vision research, here is your road map:

Step 1: Inform yourself of the research going on in the Department of Optometry and Vision Sciences from this brochure and/or from the webpages of the different research labs (https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research)

Step 2: Contact one or more lab heads for potential supervision in the area/s you may be interested in, after emailing them with your latest statement of results.

Step 3: After mutual tentative agreement for potential supervision, go to the faculty website for application to either Honors or Masters (https://study.unimelb.edu.au/fac/courses/undergraduate/bachelor-of-biomedicine-degree-with-honours or https://healthsciences.unimelb.edu.au/research-groups/optometry-and-vision-sciences-research respectively)

If you think you are eligible to apply for a Research Higher Degree, there is either an MPhil of PhD option that you may like to consider. (https://study.unimelb.edu.au/find/courses/graduate/master-of-philosophy-mdhs-health-sciences/ or https://study.unimelb.edu.au/find/courses/graduate/doctor-of-philosophy-medicine-dentistry-and-health-sciences/ respectively)

Honours Coordinator
Prof Trichur Vidyasagar

+ 61 3 8344 7004

trv@unimelb.edu.au

Master of Biomedical Science Coordinator
Prof Trichur Vidyasagar

+ 61 3 8344 7004

trv@unimelb.edu.au

Graduate Researcher Coordinator
A/Prof Andrew Anderson

+61 3 9035 9916

aaj@unimelb.edu.au

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

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