MANCHESTER 1824

The University of Manchester

Virtual Research Showcase

10th July 2020

Programme and Presentations

Manchester Vision Network Friday 10th July 2020

Session Chair	Co-chair					
Chris Dickinson		**9.30-9.45**	**INTRO/WELCOME**			
Riccardo Storchi	Rob Lucas	**9.45-10.30**	**Annette Allen**	**Keynote**	**Form vision from melanopsin in humans**	
Ian Murray		**10.30-10.45**	Research Award Presentation			
Paul Warren	David Foster	**10.45 -11.00**		Oral	**Marina Gardasevic**	BrighterTime – a smartphone app to determine the effects of ambient lighting on human performance
		11.00-11.15		Oral	**Paul Warren**	Visual decision-making under risk: Robustness to outcome valence?
		11.15-11.30		Oral	**Neil Parry**	Anomalous pupillary responses to M-cone onsets are linked to LM ratio
		11.30-11.45		Oral	**Jasna Martinovic**	Emergence of crowding: the role of contrast and orientation salience
		11.45-12.00		Oral	**Jasleen Jolly**	Inner retinal thickening affects microperimetry thresholds in the presence of photoreceptor thinning in patients with *RPGR* X-linked retinitis pigmentosa
Chris Dickinson	Fiona Cruickshank	**12.00-12.10**		Poster	**Qing Wen**	WITHDRAWN
		12.10-12.20		Poster	**David Green**	Gene expression variability is associated with incomplete penetrance in inherited eye disorders
		12.20-12.30		Poster	**Victoria Rimmer**	Lysozyme and lactoferrin modulate virulence in keratitis-causing Pseudomonas aeruginosa
		LUNCH BREAK				
David Foster		**13.15 - 14.00**	**Paul McGraw**	**Keynote**	**Changes in visual sensitivity during fixation**	
Chris Dickinson	Riccardo Storchi	**14.00-14.10**		Poster	**Zeinab Tirandaz**	The problem of shadows: real-world scene matching by merging superpixels
		14.10-14.20		Poster	**Ben Hamblin-Pyke**	Differences in Perception of Emotion from Dynamic and Static Faces – Testing a Novel Methodology
		14.20-14.30		Poster	**Daniel Poole**	Visual and auditory timing in autistic adults
		14.30-14.40		Poster	**Lucy Evans**	Does the radial speed bias depend on eccentricity?
Rob Lucas	Hema Radhakrishnan	**14.40-14.55**		Oral	**Phillip Wright**	Rhodopsin and altered rhodopsin constructs as a bipolar cell targeted optogenetic therapy
		14.55-15.10		Oral	**Beatriz Bano-Otalora**	Daytime light enhances the amplitude of circadian output in a diurnal mammal
		15.10-15.25		Oral	**Jess Rodgers**	Using a bistable animal opsin for switchable and scaable optogenetic inhibition of neurons
		15.25-15.40		Oral	**Riccardo Storchi**	A high dimensional quantification of the mouse defensive behaviours reveals enhanced diversity and stimulus specificity
Paul Warren		**15.45 - 15.50**	Award of presentation prizes			

Keynote Lecture from the winner of the Janus Kulikowski Annual Research Award for the most outstanding output from a researcher within the Manchester Vision Network

Annette Allen

Form vision from melanopsin in humans

It is approximately 15 years since the discovery of a third class of retinal photoreceptor—intrinsically photosensitive retinal ganglion cells (ipRGCs)—which respond to light thanks to their expression of melanopsin. In that time, it has become clear that ipRGCs are specialised to provide a signal of long-term light intensity and are critical for reflex light responses (entraining the circadian clock, regulating pupil size). However, there is now emerging evidence, that melanopsin also contributes to the processes of visual perception.

To address the question of whether melanopsin is a third origin of form vision, we have developed new multi-primary visual displays comprised of up to 5 distinct spectral channels, which allow independent control of up to five photoreceptors. Using this new technology, we find that melanopsin can be used by the human visual system to detect low spatiotemporal frequency patterns, and in turn, that it adjusts the appearance of a range of everyday images. Together, these data identify melanopsin as a new potential origin for aspects of form vision.

10.45 Gardasevic

Title: BrighterTime – a smartphone app to determine the effects of ambient lighting on human performance

Authors: Marina Gardasevic*, Annette Allen & Robert Lucas
*presenting author

Affiliations: The University of Manchester

Abstract
Ambient light levels have a profound impact on human physiology, most well-studied is their ability to modify parameters under circadian control. However there is discrepancy in the literature over the effect of ambient light levels on human performance. To address this uncertainty we have developed a smartphone application: BrighterTime. BrighterTime presents tasks measuring alertness, short-term memory and visual search performance whilst subsequently using the smartphone's inbuilt hardware to record ambient light levels. Additionally we have included gamified versions of the tasks to improve participant engagement and optimise detection capabilities. After conducting pilots we have optimised our tasks for duration, participant acceptance and ability to detect differences in performance and present preliminary results on the effects of ambient light levels. BrighterTime will enable us to expand on published work in laboratory settings and understand the effects of light on the brain in the field. By collecting large sample sizes with a wide range of naturally experienced light levels BrighterTime will allow us to fully appreciate these effects. This could potentially inform on the effects of artificial indoor lighting and contribute to the development of intelligent lighting systems.

11.00 Warren

Visual decision-making under risk: Robustness to outcome valence?

Paul A. Warren
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University of Manchester

Introduction. Cognitive decisions are subject to *the framing effect* – choices between uncertain gain outcomes are risk averse, whereas choices between loss outcomes are risk seeking. Here framing effects are investigated using a visual decision-making task. **Method.** In two experiments, participants observed a dot on a random walk until it disappeared behind the inner edge of a surrounding annular occluder. They then set the angular location and extent of a 'catcher' on the outer edge to predict its point of re-emergence. Probability of catching the dot was manipulated by varying the uncertainty in the random walk. Reward points were allocated for catches, decreasing linearly with catcher size but penalty points were imposed for missing the dot. By adjusting rewards and penalties it was possible to generate different outcome valence conditions involving loss, gain and mixed outcomes. **Results.** Across all conditions, average catcher size was close to that of an ideal decision-maker, determined using Monte Carlo simulation. There was some limited evidence for sensitivity to outcome valence, although this was inconsistent across experiments. **Significance.** Visual decision-making in this task is remarkably good, suggesting appropriate encoding of trajectory variability, robustness to outcome valence and application of value maximizing decision-making.

11.15 Parry

ANOMALOUS PUPILLARY RESPONSES TO M-CONE ONSETS ARE LINKED TO LM RATIO

Neil Parry[1], Ian Murray[2], Xian Li[2], Elena Rodrigo-Diaz[2]

1Vision Science Centre, Manchester Royal Eye Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK
2Visual Sciences Lab, School of Health Sciences, Faculty of Biology Medicine and Health, University of Manchester, Manchester, UK

Background. Increasing M-cone stimulation induces a conspicuous pupil constriction when a stimulus is turned off. This counterintuitive behaviour does not apply to L-cones. They respond conventionally with a constriction to stimulus onset.
Methods. A four-primary ganzfeld (Diagnosys Colordome) was used to generate selective M- and L-cone stimulation using triple silent substitutions. To test the possibility that the anomalous behaviour of M-cones is linked to the LM ratio, we measured the strength of the effect by injecting a variable amount of positive or negative luminance contamination either side of M-cone isolation. In some cases the balance point at which the pupil responded equally to onset and offset was close to pure cone isolation indicating the paradoxical response was weak or absent. Nineteen individuals with varying LM ratio ranging from 1.0 to 6 were tested.
Results. With most subjects, pupils responded conventionally to L-cone modulation, producing an unambiguous constriction to stimulus onset; this was also seen with luminance modulation. In observers with low LM ratio, the paradoxical effect was weak. There was a significant relationship (r^2 =0.561) between the balance point and LM ratio.
Significance. The effect is likely linked to strong inhibitory signals in L-cone rich retinae associated with cone-opponent pathways.

11.30 Martinovic

Emergence of crowding: the role of contrast and orientation salience

Robert Lee, Cambridge Research Systems, Kent, UK
Josephine Reuther, School of Psychology, University of Aberdeen
Rama Chakravarthi, School of Psychology, University of Aberdeen
Jasna Martinovic, School of Psychology, University of Aberdeen (presenting)

Crowding causes difficulties in judging attributes of an object surrounded by other objects. We investigated crowding for stimuli that isolated either S-cone or luminance mechanisms or combined them. By targeting different retinogeniculate mechanisms, we aim to determine the site at which crowding emerges.

Discrimination was measured in an orientation judgement task where Gabor-targets were presented parafoveally among flankers. In the first experiment, we assessed flanked and unflanked thresholds for S-cone, achromatic and combined stimuli. In the second experiment, we captured individual differences by measuring unflanked detection and orientation sensitivity, and performance under flanker-interference for stimuli containing luminance only or combined with S-cone contrast.

We confirmed that orientation sensitivity was lower for unflanked S-cone stimuli. When flanked, the same signature as for achromatic stimuli was observed when stimuli were set to comparable (i.e. low) contrast levels. We also found that flanker-interference exhibited a genuine signature of crowding only when orientation discrimination threshold was reliably surpassed.

Crowding emerges at a stage that operates on signals representing task-relevant featural (here, orientation) information. Since luminance and S-cone mechanisms have very different spatial tuning properties, it is most parsimonious to conclude that crowding takes place at a neural processing stage after they have been combined.

11.45 Jolly

Inner retinal thickening affects microperimetry thresholds in the presence of photoreceptor thinning in patients with *RPGR* X-linked retinitis pigmentosa

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[2] Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK.

[3] Oxford Centre for Functional MRI of the Brain (FMRIB), Wellcome Centre for Integrative Neuroimaging, University of Oxford, Oxford, United Kingdom

* Presenting author

Background:

Inherited retinal diseases (IRDs) lead to progressive outer retinal degeneration. It was previously thought IRDs would only affect photoreceptor function, increasing evidence now suggests that inner retinal remodelling occurs.

Methods:

A cohort of patients with X-linked retinitis pigmentosa underwent OCT imaging and microperimetry testing of the central 10 degrees of retina. Accurate segmentation of the OCT images was performed using semi-automated software (Orion®, Voxeleron LLC). Eccentricity analysis of 1, 3, 5 and 7 degrees of visual field was performed in MATLAB following centration of the OCT images over the fovea.

Results:

Thickness graphs showed a thinning of the photoreceptor layers with concurrent thickening of the inner retinal layers. Photoreceptor layer thickness differed between patient and control groups across increasing visual field areas ($P < 0.01$), whereas the inner retina thickness significantly differed between groups for the central 1 and 3 degrees only. Microperimetry thresholds were explained by a combination of photoreceptor and inner retinal thickness.

Significance:

Thinning of the photoreceptor layers is associated with thickening of the inner retina. The thickening can mask the thinning in some areas if not measured carefully, possibly as a result of different stages of the retinal remodelling process. Inner retinal changes must be considered when interpreting function.

Variability in gene expression is associated with incomplete penetrance in inherited eye disorders

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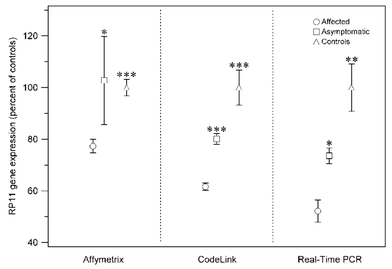
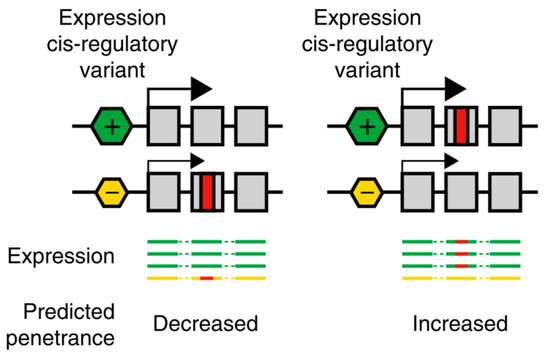
Background

- Inherited eye diseases (IEDs) are a heterogenous group of genetic disorders that are frequently associated with variable expressivity and reduced penetrance (hereafter variable penetrance). These phenomena are thought to be due to environmental, epigenetic, and genetic factors[1]
- Importance of variable penetrance: complicates the relationship between genotype and phenotype and has consequences for genetic counselling[2]



- Example: some previous reports revealed that asymptomatic carriers of heterozygous pathogenic variants in *PRPF31* appear to be protected from disease by increased expression of the wild-type mRNA[3]



- More recently, Castel *et al*.[4] demonstrated that penetrance can be modified by the presence of cis-regulatory variants more generally (not specific to IEDs) through the mechanism outlined below:

- **Aim:** To investigate the scale and potential mechanisms of variable penetrance in IEDs.

Methods

identify genes implicated in IEDs

(green genes in panelApp ophthalmological categories [n=340])

collect disease-implicated variants

(DM variants in HGMD Pro 2019.1: missense, nonsense, small insertion, small deletion, small indel, splicing (n=22,171)

obtain genomic coordinates for all IED-implicated variants using Variant Validator

identify IED-associated variants that are present in unaffected individuals

(determine which variants are present in the gnomAD 2.1 controls-only dataset)

is an IED-implicated gene associated with variable penetrance?

(does an IED-implicated gene have >1 HGMD-listed variants (with CADD score >15) that are present in >1 individuals in the gnomAD controls-only dataset?

YES

(56 genes with evidence of variable penetrance)

NO

(284 genes with no evidence of variable penetrance)

comparison of gene expression variability at the population level

using data from the GTEx and EyeGEx datasets and the local coefficient of variation metric of expression variability[5]

Results

1 in 6 genes associated with IEDs show evidence of variable penetrance

- 56 genes had evidence for variable penetrance: 31 of these were labeled as monoallelic, 11 as biallelic, 11 as both monoallelic and biallelic, and 3 as X-linked in panelApp
- In total, 1.3% (285/22,171) of IED-associated variants were present in >1 individuals in the gnomAD controls-only cohort in a disease-causing state; 86% (244/285) of these had a CADD score >15.

panelApp gene set	expression dataset	LCV for IP/VE genes	LCV for other genes	p-value
all ophthalmological	GTEx all tissues	83.7	48.85	0.00002
all ophthalmological	GTEx brain tissues	80.4	49.25	0.0001
all ophthalmological	GTEx whole blood	66.2	40.2	0.04
retinal genes	EyeGEx	83.8	67.8	0.0021

- A potential confounder in these analyses was gene constraint – could the two groups differ in terms of metrics of coding constraint?
- There was no correlation between any of the common coding constraint metrics and LCV
- There were no significant differences in coding constraint between the two groups (IP/VE and others) after adjusting p-values for multiple testing

Conclusions

- Several IED-implicated genes associated with variable penetrance exhibit variability in gene expression at the population level. Previous studies have suggested gene regulatory variants as a potential mechanism of reduced penetrance; this study represents the first effort to assess the extent of this phenomenon
- The results suggest the potential role of variants in cis-regulatory regions in modulating disease risk by altering gene expression levels[6]

Future work

- Elucidate the gene regulatory networks controlling the expression of key IED genes associated with variable penetrance *(CRX, BEST1, PRPF31, TYR, OCA2 etc.)* by linking enhancers to genes using latest methods (activity-by-contact)
- Attempt to assess eQTL status for these genes in individuals at either end of the penetrance spectrum (utilize large datasets of phenotyped individuals, such as UK Biobank)

References

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Lysozyme and lactoferrin modulate virulence in keratitis-causing *Pseudomonas aeruginosa*

Victoria Rimmer, Carole Maldonado-Codina, Philip Morgan, Curtis Dobson and Andrew J McBain

The University of Manchester

Introduction

Pseudomonas aeruginosa (P. aeruginosa) is a Gram negative bacterium often associated with **keratitis** in contact lens wearers. At the ocular surface, the **tear** film is a key part of the eye's innate immune system and contains a number of **antimicrobial proteins**. **Lysozyme** and **lactoferrin** are two of the most abundant **antimicrobials** in tears, accounting for up to **60%** of total protein[1]. This study aimed to characterise the effect of these proteins on ***P. aeruginosa* growth**, **motility**, **virulence** and **biofilm** formation on the surface of **contact lens materials**.

Methods

- **Five clinical isolates** (1-5) of *P. aeruginosa* were used alongside two laboratory strains, PA01 and PA9027, for controls. **Lysozyme and lactoferrin** were used at **physiological concentrations.**
- **Growth dynamics** where monitored by growing cultures for 16 hours in a chemically defined medium (**CDM**), with or without proteins (**CDMP**).
- **Protease secretion and haemolytic activity** were quantified by exposing cultures to proteins for two hours and then assaying with **azocasein erythrocytes** respectively.
- **Motility** was assessed by inoculating **swim** and **swarm** agars.
- To establish **biofilm** growth, contact lenses were incubated with bacterial culture for **24, 48** and **72 hours**. Biofilms were stained for nucleic acids (**DAPI**) and **metabolic activity** and imaged using **confocal** microscopy.

Results – Proteases and haemolysis

Haemolytic activity was significantly increased for all isolates ($P<0.0001$) in the presence of **lysozyme and lactoferrin**, apart from isolate 4 for which there was a significant decrease ($P<0.05$) (Figure 1). No significant change in **protease activity** was observed for any isolate.

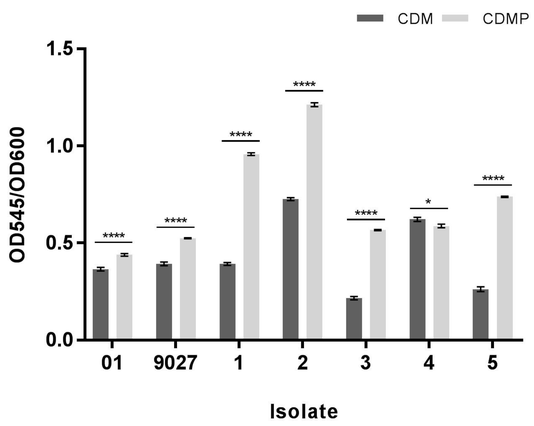

Figure 1. Haemolysis activity for isolates under control conditions (CDM) and in the presence of lysozyme and lactoferrin (CDMP). *, **, *** and **** represent $P<0.05$, $P<0.01$, $P<0.001$ and $P<0.0001$ respectively. Results were analysed with one-way ANOVA and post-hoc Tukey's test.

Growth

In the presence of **lysozyme and lactoferrin, growth rate** was attenuated and **generation time** increased in all strains, with significant differences found for both laboratory strains and isolates 1, 2, 3 and 5 (Figure 2).

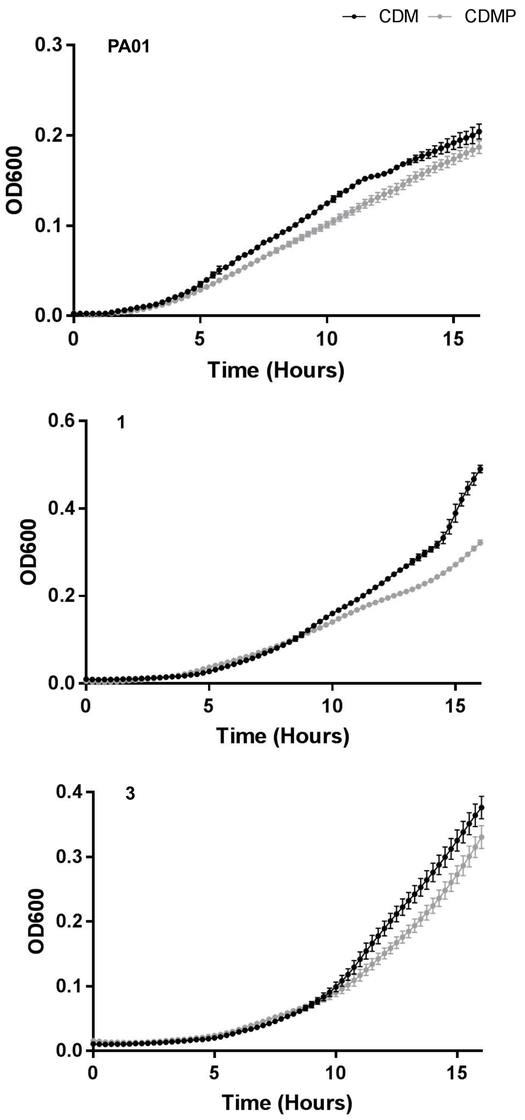

Figure 2. 16 hour growth curves of *P. aeruginosa* laboratory strain PA01 and clinical isolates 1 and 3 in CDM or CDM with the addition of lysozyme and lactoferrin (CDMP).

Motility

Lysozyme and lactoferrin significantly affected **swimming and swarming** ability depending on the isolate (Figure 3). **Swim zone area** (cm^2) was significantly increased for isolates 1 , 2 and 4 ($P<0.5$). **Swarm zone area** (cm^2) was significantly increased for PA01 ($P<0.001$) and significantly decreased for isolate 5 ($P<0.5$).

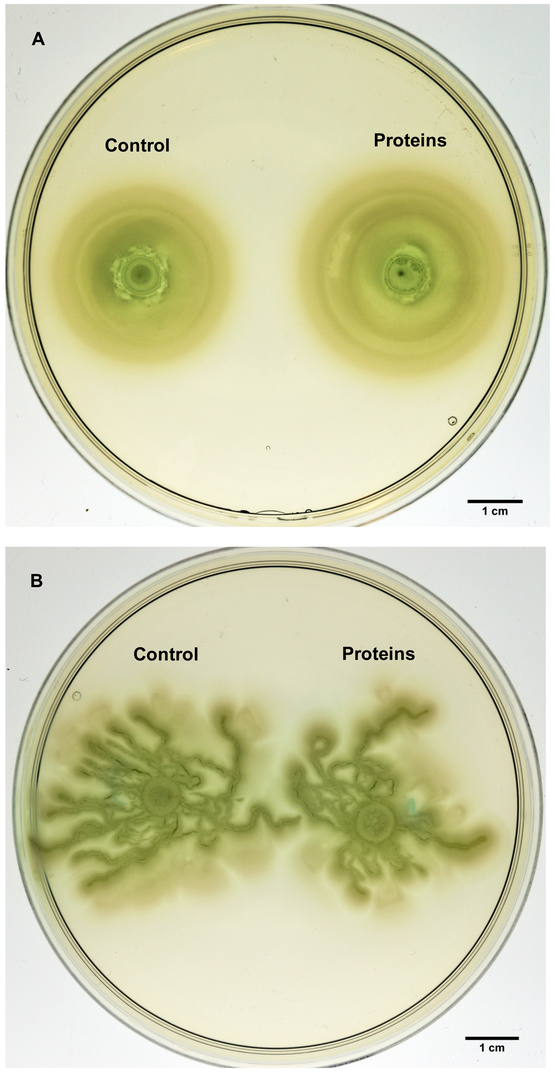

Figure 3. Representative swim (A) and swarm (B) zones of clinical isolates 1 and 5 respectively when grown with or without proteins

Biofilm formation

Of the isolates tested, all formed biofilms on the surface of both Biofinity and Proclear lenses at 24, 48 and 72 hours. Bacteria were metabolically active at all time points and showed even distribution on the lens surface (Figure 4).

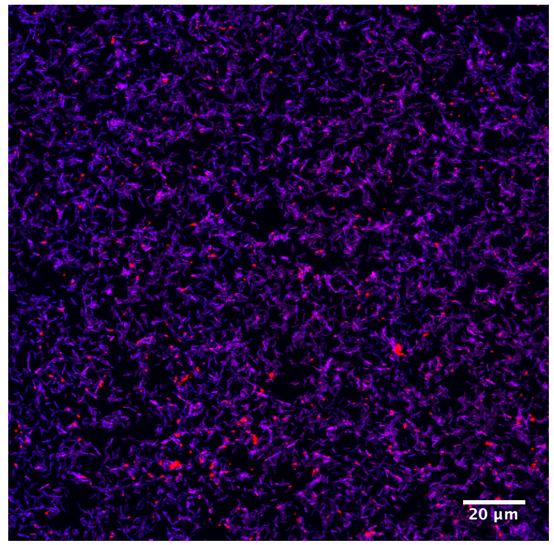

Figure 4. 48 hour biofilm on the surface of a Biofinity lens, Data is representative of a single clinical isolate. DAPI staining is shown in blue, with red staining indicating metabolic activity.

Conclusions

Modulation of **growth dynamics** suggests that **lysozyme and lactoferrin** likely reduce bacterial viability and fitness at the ocular surface. **Motility, protease activity and haemolytic activity** are important **virulence** phenotypes and may facilitate **adherence to and invasion of the corneal epithelium**[2]. The modulation of motility and haemolytic activity reported here provide insight into interactions between *P. aeruginosa* and immune factors. The ability of clinical *P. aeruginosa* isolates to form robust biofilms on contact lens materials highlights the challenges of managing keratitis in lens wearers. Future work will investigate the effect of antimicrobial tear proteins on the ability of isolates to grow as biofilms on lens surfaces.

References

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Contact

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Keynote Lecture

Paul McGraw, University of Nottingham

Changes in visual sensitivity during fixation

In many investigations of spatial vision, fixation is held constant in order to control the retinal eccentricity of stimulation and limit the unwanted effects of eye movements on perception. However, even when we attempt to fixate our eyes are never completely still. Instead, microsaccades incessantly jitter visual input. How does this affect visual sensitivity? To address this, we systematically varied the spatial frequency of a visual target during a detection task and tracked contrast sensitivity as a function of time relative to microsaccades. We found two distinct modulations of sensitivity: suppression during the eye movement itself and facilitation after the eye has stopped moving. Both effects were selective to the spatial content of the stimulus. Next, we asked whether microsaccadic suppression could be modified by training? Using a standard contrast detection in noise task, we found that over the course of training saccadic suppression is gradually eliminated. The change in sensitivity is highly selective to the time that a target is expected to appear. This suggests that the visual system can learn to temporarily silence saccadic suppression when it's advantageous to do so. This flexibility may be particularly useful in the acquisition of learned behaviours.

The problem of shadows: real-world scene matching by merging superpixels

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Introduction

The movement of the sun in the absence of cloud causes variations in the spectrum and geometry of scene illumination [1]. The same surface can have a different appearance at different times of the day, as shown in Fig. 1. Changes in the distribution of shadows are particularly difficult to predict, even over short intervals, leading to errors in matching scenes over time.

Fig. 1. Illumination changes across different times. The images were captured in October 2003 in Sete Fontes in Portugal [2].

Methods

In the first step, the images were segmented by generating “superpixels” [3], which were then merged by an edge detection algorithm. In the second step, correlation coefficients were obtained in each region for the ratio maps of the quotient of saturation by lightness RM_s and the yellow-blue b_C chromatic component [4]. These correlation coefficients were segmented by minimizing cross-entropy, and the results used to merge regions acquired in the first step. Fig. 2 shows the method applied to the scene in Fig. 1 between 12:25 and 13:21.

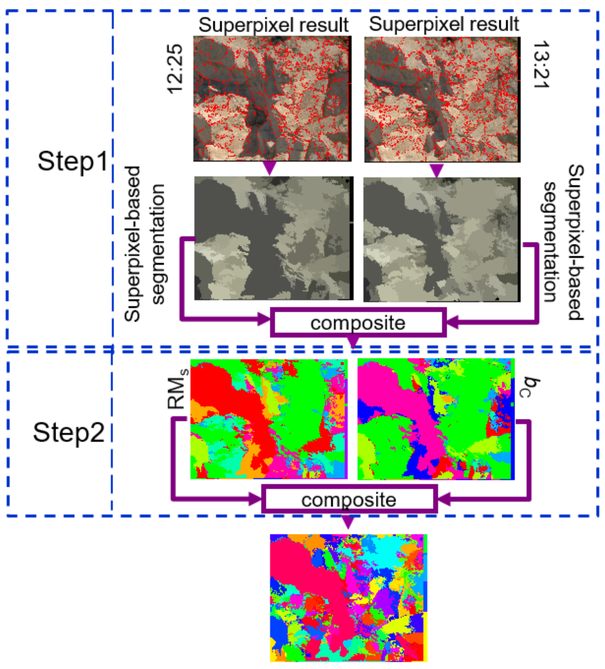

Fig. 2. Segmenting and combining time-lapse images at 12:25 and 13:21 for the Sete Fontes scene.

Results

Pearson correlation coefficient values for Sete Fontes scene are compared in Table 1. The percentage of the whole number of pixels each region contains (PP) are also shown in this table. The Corr_RM_S and Corr_b_C columns show the actual values of the correlation coefficients and PP when RM_S and b_C are combined.

Table 1. Correlation coefficient and PP values for quotient of saturation by lightness and yellow-blue local features for each of 9 regions in final segmentation result.

RM_S and b_C		
Corr_RM_S	**Corr_b_C**	**PP**
0.354	0.367	0.428
0.620	0.137	8.21
0.065	0.726	0.002
0.925	0.742	6.44
0.673	0.779	22.9
0.957	0.419	2.16
0.606	0.248	7.10
0.940	0.936	43.7
0.711	0.873	9.09

The data points in Table 1 are plotted in Fig.3 for the Sete Fontes scene. The correlation coefficients are plotted against the corresponding PP.

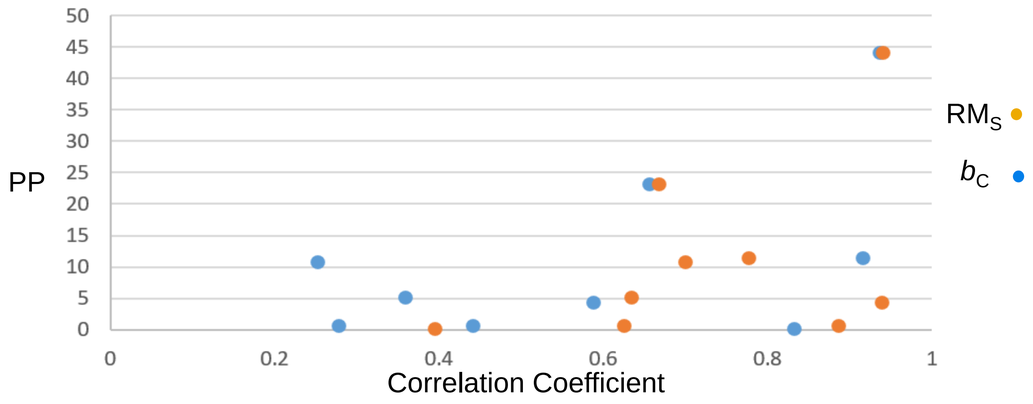

Fig. 3. Correlation coefficient values against PP for the Sete Fontes scene.

The larger correlation coefficients correspond to larger segmented regions, presumably because changes in illumination have less impact.

To test if partitioning into superpixels can be determined automatically, empirical estimates of superpixel numbers were compared with patchiness indices [5]. Results are shown in Table 2. The patchiness indices included standard deviation, skewness and kurtosis of lightness J, red-green a_C and yellow-blue b_C chromatic components.

Table 2. The goodness of fit of patchiness indices with different statistics against the number of superpixels.

	Kurtosis			**Skewness**			**Standard deviation**		
	R^2	Corr	CI	R^2	Corr	CI	R^2	Corr	CI
J	0.745	0.863	0.674 0.949	0.633	0.796	0.447 0.915	0.168	-0.409	-0.660 -0.040
a_C	0.574	0.757	0.338 0.906	0.413	0.642	0.251 0.832	0.231	-0.481	-0.742 -0.154
b_C	0.212	0.461	-0.017 0.794	0.084	0.290	-0.198 0.626	0.041	-0.203	-0.398 -0.016

The correlation coefficient and R^2 values were highest for kurtosis of the lightness values. The linear regression is shown in Fig. 4.

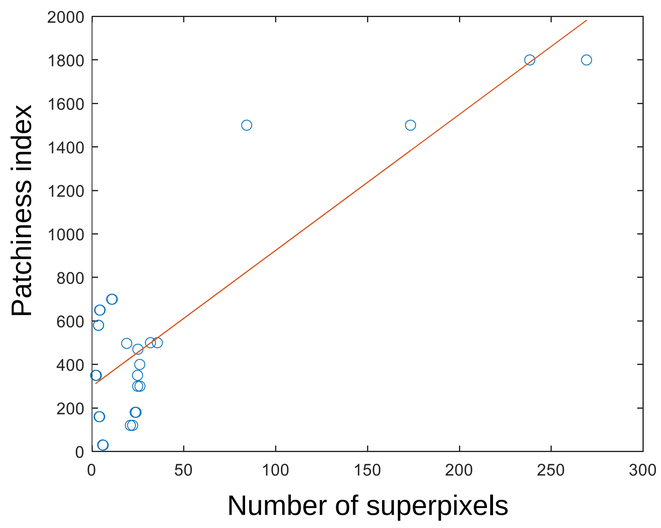

Fig. 4. Patchiness index predicted by number of the superpixels.

It appears that the kurtosis of lightness values can aid in the automatic determination of superpixel size in scene matching.

Conclusion

Reliable surface colour comparisons are possible despite changes in illumination and the distribution of shadows. With the aid of superpixel segmentation, scene regions can be broadly labelled according to whether they remain in direct light, in shadow, or in a mixture of the two, offering the possibility of improved surface matching overall.

References

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Differences in Perception of Emotion from Dynamic and Static Faces
Testing a Novel Methodology

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Background

- Facial emotion recognition (FER) is an essential element of interpersonal communication and socialisation (1). It is reported to be impaired in several patient populations (2, 3, 4).
- Dynamic facial stimuli are arguably more ecologically valid than static stimuli. Motion may aid emotion recognition, particularly when stimuli are subtle or degraded (5, 6).
- While several widely used tests of FER exist, such as the Ekman 60 faces test and the JACFEE, these do not use dynamic stimuli (7, 8).
- This study aims to test and establish a novel methodology to assess FER using dynamic stimuli.

Ethics approval from University of Manchester SPS Ethics Committee ref: 2018-2381-4759.

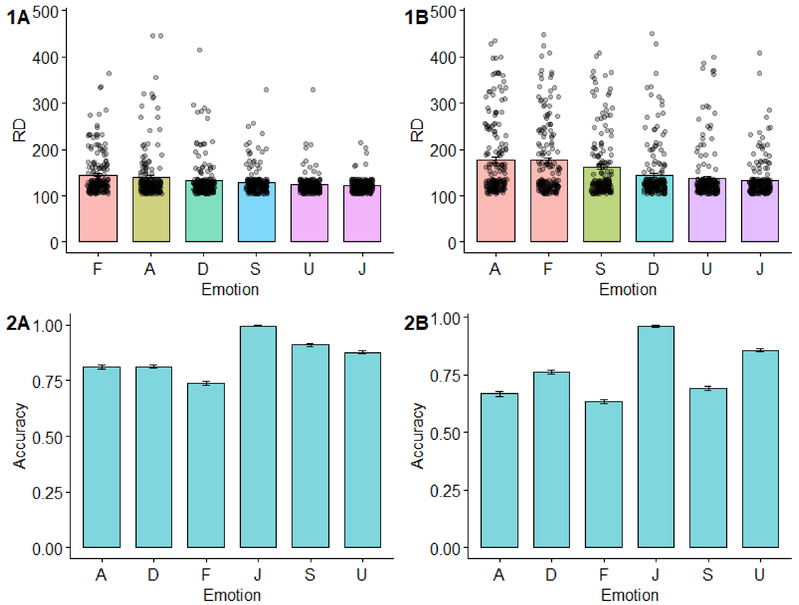
Materials and methods

- 19 healthy control participants were recruited for this study.
- The six 'basic' emotions of anger, disgust, fear, joy, sadness, and surprise were included. Stimuli were adapted from the Amsterdam Dynamic Facial Expression Set (ADFES) (9).
- Stimuli were grouped based on condition (static or dynamic), with the order of condition and stimuli randomised.
- A fixation cross was shown on screen for 500ms before every stimulus presentation.
- A Stimulus was initially presented for 120ms, and participants were asked to identify the emotion from a list of options. The same stimulus was then shown again for gradually increasing durations, until the longest duration (480ms, total of 10 durations), with participants responding each time.
- If a participant responded correctly to two consecutive stimulus presentations, the earlier of these durations is recorded as their response duration (RD) for that stimulus.
- Mean RD was assessed using Honest Significant Difference (HSD) tests and ANOVA; Pearson's Chi-squared tests for assessing accuracy differences.
- Eye tracking was performed, and analysis is ongoing (*figure 3*).

Hypotheses

- There will be a significant difference in mean response duration (RD) depending on emotion for both static and dynamic conditions. [1]
- There will be a significant difference in accuracy between emotions for both the static and dynamic conditions.[1]
- Mean RD for each emotion will be lower in the static condition than the dynamic condition.[2]
- Accuracy will be lower in the dynamic condition than the static condition.[2]

1. *Other FER tests report certain emotions are easier to recognise than others (7, 8). If differences in mean RD or accuracy were not found it might suggest an issue with the methodology of this test.*
2. *In the dynamic condition stimuli begin with a neutral expression, while in the static condition stimuli are at the apex emotion for the full duration. Therefore, it is predicted that mean RD will be lower and accuracy higher in the static condition.*



1A. Mean RD for each emotion (static) with added jitter. HSD groups are: Fear (a), Anger (ab), Disgust (bc), Sadness (cd), Surprise (d), Joy (d).
1B. Mean RD for each emotion (dynamic) with added jitter. HSD groups are: Anger (a), Fear (a), Sadness (ab), Disgust (bc), Surprise (c), Joy (c).
2A. Accuracy for each emotion (static) with standard error bars.
2B. Accuracy for each emotion (dynamic) with standard error bars.

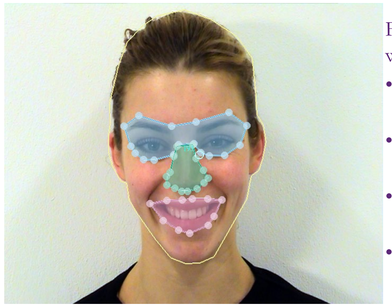


Figure 3 – An example stimulus (F01 Joy static), with the manually delineated areas of interest.

- AoIs are eyes (blue), nose (green), mouth (pink) and face (yellow outline).
- Eye AoIs included both eyes, eyebrows, and the glabella for all stimuli.
- In the dynamic condition AoIs were adjusted as required for each frame.
- All stimuli were displayed to participants without visible AoIs.

Results

- There was a significant difference in mean RD between emotions in both the static ($p < 0.01$, *1A*) and dynamic ($p < 0.01$, *1B*) conditions.
- Joy had the lowest mean RD in both conditions (static = 122ms, dynamic = 132ms). The highest mean RD was fear in the static (145ms) and anger in the dynamic condition (177ms).
- There was a significant difference in accuracy between emotions in both the static ($p < 0.01$, *2A*) and dynamic ($p < 0.01$, *2B*) conditions.
- In both conditions joy had the highest mean accuracy (static = 99.6%, dynamic = 96.1%) and fear had the lowest (static = 83.8%, dynamic = 63.4%).
- Mean RD was lower, and accuracy was higher, in the static condition than the static condition for all emotions.

Discussion

- As was hypothesised, there was a significant difference in mean RD between emotions. This fits with previous research suggesting some emotions are recognised more easily than others (7, 8).
- The emotion with the lowest mean RD and highest accuracy was joy in both conditions, similar to other FER tests (7, 8).
- Lower accuracy and higher mean RD for the dynamic condition does not fit with some past research suggesting motion aids recognition (5, 6). This may be because in the static condition the apex emotion is visible throughout, while dynamic stimuli gradually change from a neutral to an emotional expression.

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Visual and Auditory Timing in Autistic Adults

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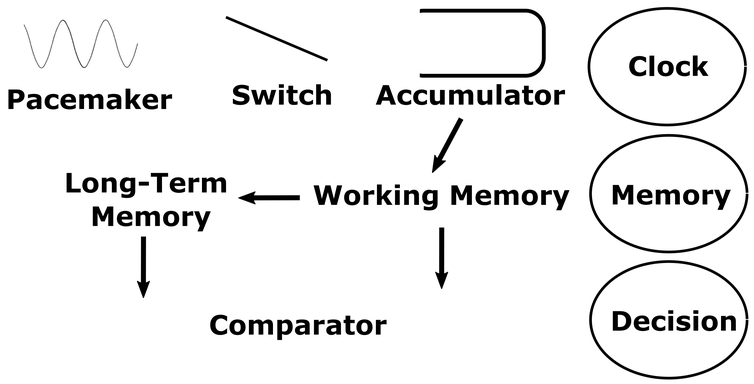
Introduction

- Autism is a lifelong, neurodevelopmental condition which can impact communication, social interaction, sensory processing and motor control
- The temporal deficit hypothesis (Allman, 2011) proposes that timing and time perception is disrupted in the condition. Deficits in sub-second timing are proposed to underly behavioural and cognitive differences which are characteristic of the condition
- In a systematic review (Casassus et al, 2019) we found that the evidence for timing deficits in autism are mixed and dependent on the nature of the task. Work to date has not been well grounded in established models of time perception
- We used a battery of timing tasks derived from Scalar Expectancy Theory and recruited a large sample of participants

Research questions
Is precision in estimates of duration reduced in autistic adults in comparison with non-autistic (neurotypical) controls?
Is there a general timing impairment in autism?

Scalar Expectancy Theory

- Dedicated 'clock' type timing system in the brain



General Method

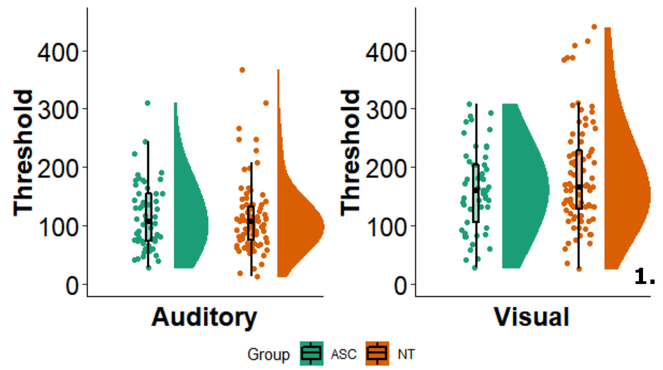
	Autistic (n = 57)	Neurotypical (n = 91)
Age	31.34 ± 8.91	30.38 ± 7.75
FSIQ	115.51 ± 13.21	114.99 ± 11.42

- Participants completed battery of psychophysical tasks involving timing judgements about identical stimuli.
- Visual (grey square presented at fixation) and auditory (tones presented through speakers). Chin rest to control distance from screen
- Study was pre-registered: https://osf.io/pcahj/

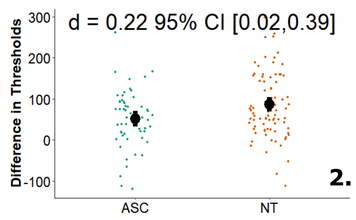
Threshold Task

Which was longer?

- Asked which of two consecutive stimuli was longer. Standard (700ms) or comparion (variable duration)
- Duration of comparison adjusted using an adaptive staircase procedure (3 up 1 down - point at which participant can discriminate ~ 75% accuracy
- Lowest threshold determined after two runs taken as threshold for that condition (lower threshold = more precise)



- Thresholds reduced for auditory durations (see Fig 1)
- No difference in auditory or visual thresholds between groups, but difference between thresholds was smaller for autistic group (see Fig 2)

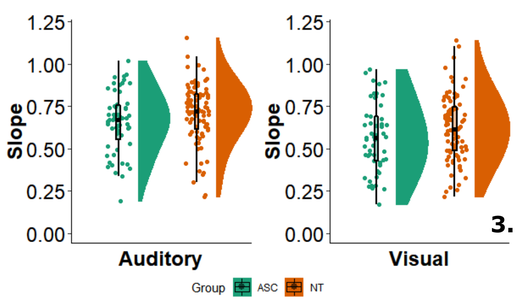


Verbal Estimation Task

How long was that?

Clock

- Participant asked to estimate the duration of a stimulus (in ms) 77 - 1183 ms
- Fit linear regression to mean estimate at each duration.
- Slope used as measure of precision (closer to 1 = more precise)

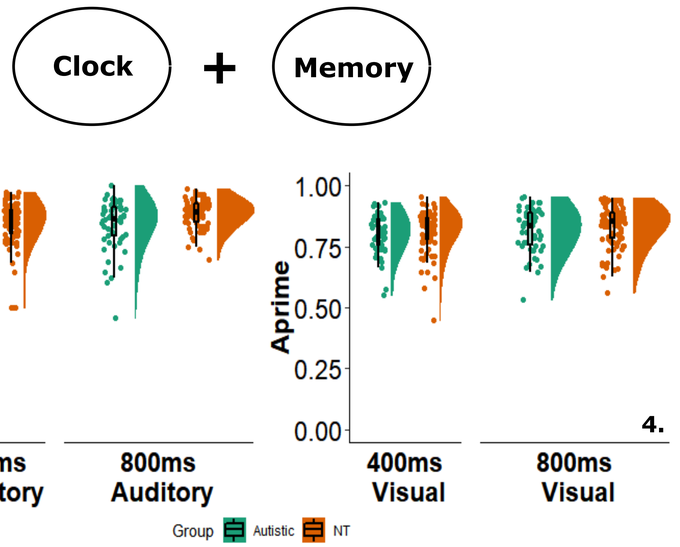


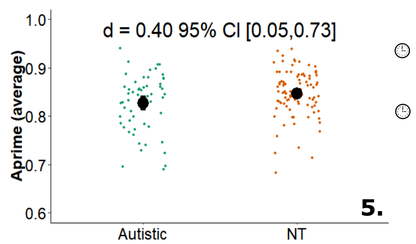
- Slopes increased for auditory durations
- No differences between the groups (see Fig 3)

Temporal Generalisation Task

Was that the same duration as the standard?

- Participant asked to remember a standard (400ms or 800ms duration) and is asked if comparison durations are the same as the one they remembered
- Signal detection analysis to extract A'Prime a non-parametric measure of sensitivity (increased APrime = more precise)





- Precision increased for auditory durations (see Fig 4)
- Overall precision reduced in autistic group (see Fig 5)

Discussion

- Smaller modality effect in autistic group observed in threshold experiment, but not replicated across tasks
- Memory for duration may be implicated in autism
- In further analysis we are using unsupervised learning to identify any sub-groups in the autistic and neurotypical groups

There is no generalised timing impairment in autism

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Does the radial speed bias depend on eccentricity?

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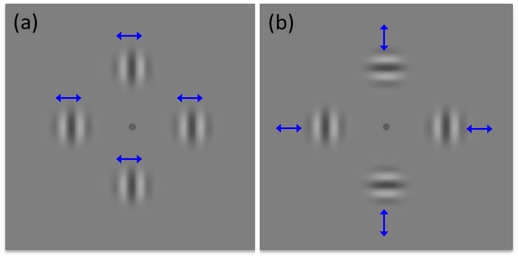
1. Introduction

Background

- Radial motion (Fig.1b) is perceived as 20-60% faster than linear motion (Fig.1a) with identical local spatio-temporal properties [1,2]. Why?
- Bex & colleagues [1,2] suggested bias arises because radial motion is interpreted as motion in depth.

Fig. 1: Stimuli used across experiments – Gabor patches are identical but orientation is changed to give a different global motion configuration



Aims

We test the motion in depth (MID) account by investigating

- The **effects of eccentricity** (Exp 1-3): bias should decrease with eccentricity since same retinal speed at higher eccentricity consistent with slower MID
- The **effects of monocular viewing** (Exp 3): bias should increase when binocular cues conflicting with MID interpretation are removed.

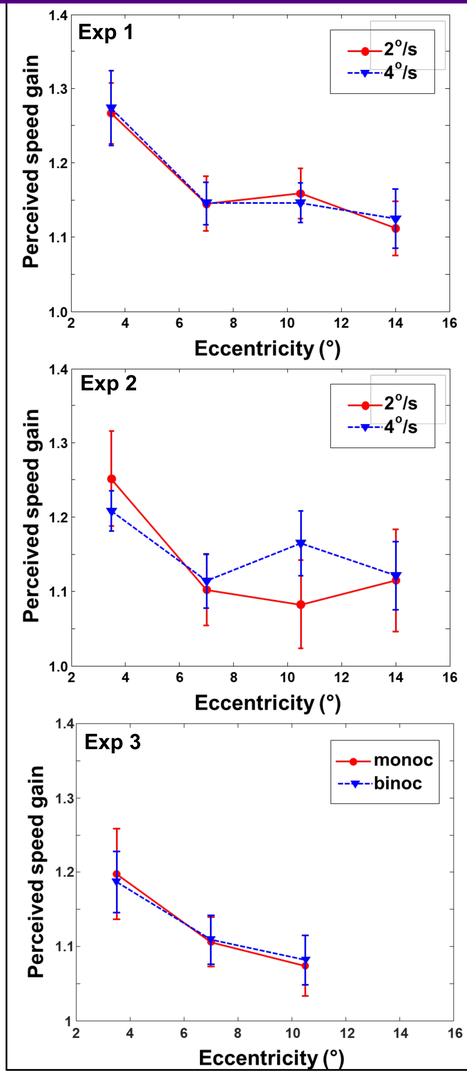
2. Methods

Stimulus & Procedure

- 4 linear Gabor patches (64% contrast) arranged around fixation point (Fig.1)
- Test linear speed controlled by staircase procedure
- 2IFC paradigm: which interval contained the fastest motion?

	Experiment 1	Experiment 2	Experiment 3
N	8	8	14
Eccentricities	3.5, 7, 10.5, 14	3.5, 7, 10.5, 14	3.5, 7, 10.5
Size (SD)	0.67°	0.67°, 0.97°, 1.26°, 1.56°	0.67°
Spatial Frequency (cyc/deg)	1	1, 0.69, 0.53, 0.43	1
Standard speed (deg/s)	2, 4	2, 4	4
Viewing condition	Binocular	Binocular	Monocular & Binocular

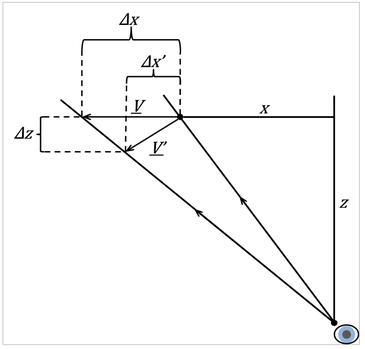
3. Results



- Measured perceived speed gain:

  The increase in speed of the linear stimulus required to perceptually match the speed of the radial stimulus.
- Gain decreased with eccentricity in all experiments, consistent with MID
- This tailed off at ~7°
- ANOVAs showed a significant effect of eccentricity on gain
- But found no effect of spatial scaling with eccentricity
- No effect of monocular viewing
- No effect of stimulus speed

4. Modelling



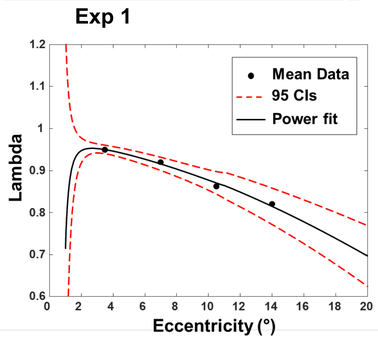
- Clifford et al. [4] propose a model of speed perception based on minimising cost ***H*** with components due to **motion in depth** and **object deformation**:

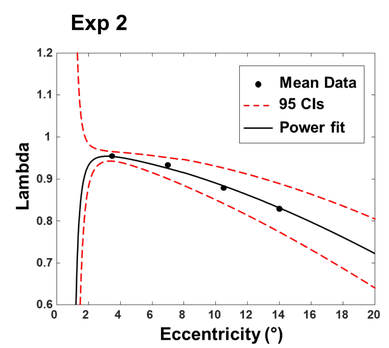
$$H = \lambda\left(\frac{\Delta z}{z}\right)^2 + (1-\lambda)\left(\frac{\Delta x'}{x}\right)^2$$

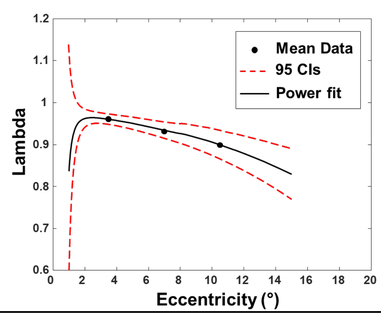
- Parameter λ controls the extent to which motion is perceived in depth:

  λ = 1 => deformation in plane
  λ = 0 => motion in depth

- We implemented this model for each participant in our experiment and solved (in closed form) for parameter λ.
- λ decreases with eccentricity in all experiments







5. Conclusion

- Radial speed bias decreases with eccentricity.
- This was less marked beyond 7.5°.
- Modelling of data shows that parameter λ, which reflects the extent to which motion is perceived in depth, decreases with eccentricity.
- The findings support the motion in depth account but, crucially, they show the tendency to perceive radial motion as motion in depth depends upon eccentricity.

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14.40 Wright

Rhodopsin and altered rhodopsin constructs as a bipolar cell targeted optogenetic therapy

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Background

Optogenetic therapies are promising vision restoration tools with rhodopsin being of particular interest due to its high sensitivity. Within this study we aim to determine whether bipolar cells are a safe target for ectopic rhodopsin expression, and whether or not altered rhodopsin constructs possess better light evoked response properties.

Methods

GRM6Cre mice were intravitreally injected in both eyes with an AAV vector (containing rhodopsin, E122Q or 6103) and electrophysiological recordings conducted using a 256 electrode array. Retina's were immunolabelled for either mCherry or PKCa, and apoptotic cells labelled (TUNEL). mRNA expression of mCherry and PKCa was assessed via qPCR and retinal thickness was measured via ocular coherence tomography.

Results

Treated mice were found to possess widespread transgene expression. This expression was localised to bipolar cells and resulted in light responses to a variety of light intensities. Rhodopsin treated retinas did not display any changes in retinal thickness, or any difference in specific bipolar cell marker expression, nor cause any significant increase in levels of apoptosis within the INL.

Significance

We have shown that bipolar cells are a safe target for ectopic rhodopsin expression, and when transduced with rhodopsin and the other constructs, reproducible light responses can be found.

14.55 Bano-Otalora

Daytime light enhances the amplitude of circadian output in a diurnal mammal

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Abstract

Mammalian circadian rhythms are orchestrated by a pacemaker in the hypothalamic suprachiasmatic nuclei (SCN), which receives information about the 24h light:dark cycle from the retina. The accepted function of this light signal is to reset circadian phase in order to ensure appropriate synchronisation with the celestial day. Here, we ask whether light also impacts another key property of the circadian oscillation, its amplitude. To this end, we measured behavioural and physiological rhythms and SCN electrophysiological activity in the diurnal rodent *Rhabdomys pumilio* following stable entrainment to 12:12 light:dark cycles at 4 different daytime intensities (ranging from 12.77 to 14.80 log melanopsin effective photons/cm^2/s). *Rhabdomys* showed strongly diurnal activity and body-temperature rhythms in all conditions, but measures of rhythm robustness were positively correlated with daytime irradiance. Whole-cell and extracellular recordings of SCN electrical activity *ex vivo* revealed substantial differences in electrophysiological activity between dim and bright conditions. At lower daytime irradiance, daytime peaks in SCN spontaneous firing rate and membrane depolarisation were substantially depressed, leading to an overall marked reduction in the amplitude of circadian rhythms in spontaneous activity. Our data reveal a previously unappreciated impact of daytime light intensity on SCN physiology and the amplitude of circadian rhythms, and highlight the potential importance of daytime light exposure for circadian health.

15.10 Rodgers

USING A BISTABLE ANIMAL OPSIN FOR SWITCHABLE AND SCALABLE OPTOGENETIC INHIBITION OF NEURONS

Jessica Rodgers[1], Beatriz Bano-Otalora[1], Mino DC Belle[2], Sarika Paul[1], Rebecca Hughes[1], Phillip Wright[1], Richard McDowell[1], Nina Milosavljevic[1], Patrycja Orlowska-Feuer[1,3], Franck Martial[1], Jonathan Wynne[1], Edward R Ballister[1,4], Riccardo Storchi[1], Annette E Allen[1], Timothy Brown[1], Robert J Lucas[1]

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Background: Lamprey parapinopsin ('Lamplight') is a Gi/o-coupled bistable animal opsin that can be activated and deactivated by short and long wavelength light, respectively. Since native mechanisms of neuronal inhibition frequently employ Gi/o signalling, we asked whether Lamplight could be used for optogenetic silencing.

Methods: We examined Lamplight driven activity using a live-cell assay of G protein activation in Hek293T cells, whole-cell current clamp electrophysiology of neurons in the hypothalamic suprachiasmatic nucleus and retinal multi-electrode array recordings.

Results: Short (405nm) and long (525nm) wavelength pulses repeatedly switches Lamplight between stable signalling active and inactive states, while combining these wavelengths can be used to achieve intermediate levels of activity. These properties can be applied to produce switchable and scalable neuronal silencing in mouse hypothalamic neurons. Expressing Lamplight in (predominantly) ON bipolar cells can photosensitise retinas following advanced photoreceptor degeneration, with 405 and 525nm stimuli producing responses of opposite sign in retinal output neurons.

Significance: We conclude that Lamplight can co-opt endogenous signalling mechanisms to allow physiological optogenetic inhibition that is scalable, sustained and rapidly reversible. The unique properties of Lamplight make it well suited to basic research of GPCR signalling biology as well as therapeutic applications, including vision restoration.

15.25 Storchi

A high dimensional quantification of the mouse defensive behaviours reveals enhanced diversity and stimulus specificity

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Background: The ability of specific sensory stimuli to evoke spontaneous defensive responses in the mouse represents a powerful approach to study how the mammalian brain processes sensory information and selects appropriate motor actions. For visually and auditory guided behaviours the relevant action has been empirically identified as a change in locomotion state. However, the extent to which locomotion alone captures the diversity of those behaviours and their sensory specificity is unknown.

Methods: To tackle this problem we developed a method to obtain a faithful 3D reconstruction of the mouse body that enabled us to quantify a wide variety of movements and changes in postures.

Results: This higher dimensional description of behaviour revealed that responses to different sensory inputs is more stimulus-specific than indicated by locomotion data alone. Thus, equivalent locomotion patterns evoked by different stimuli (e.g. looming and sound evoking locomotion arrest) could be well separated along other dimensions. The enhanced stimulus-specificity was explained by a surprising diversity of behavioural responses. A clustering analysis revealed that distinct combinations of motor actions and postures, giving rise to at least 7 different behaviours, were required to account for stimulus-specificity. Moreover, each stimulus evoked more than one behaviour revealing a robust one-to-many mapping between sensations and behaviours that could not be detected from locomotion data.

Significance: Our results challenge the current view of visually and auditory driven defensive behaviours as purely locomotion-based actions (e.g. freeze, escape) and indicate that behavioural diversity and sensory specificity unfold in a higher dimensional space spanning multiple motor actions.