Berkeley Herbert Wertheim School of Optometry & Vision Science

BayArea Vision Research Day 2022

Abstract Book

September 9th, 2022

Speakers

Dr. Daisy Shu, (Speaker 8:15-8:40)

Instructor | Harvard Medical School

"Dimethyl fumarate suppresses inflammation and metabolic rewiring of the retinal pigment epithelium"

Dr. Jay Stewart, (Speaker 8:45-9:10)

Professor | UC San Francisco, Department of Ophthalmology

"Aqueous transcriptome analysis in the conversion from dry to wet age-related macular degeneration"

Dr. Sunwoo Kwon, (Speaker 9:15 - 9:40)

Postdoctoral Scholar | UC Berkeley, Optometry and Vision Science

"Dissociation between perception and action: unilateral V1-stroke and its impact on predictive eye movements"

Dr. Aparna Lakkaraju, (Speaker 9:45 - 10:10)

Professor | UC San Francisco, Department of Ophthalmology

"Ceramide as a novel therapeutic target for macular degenerations"

Dr. Jacob Yates, (Speaker 11:05 - 11:55

Assistant Professor | UC Berkeley, Optometry and Vision Science

"Neural mechanisms of active visual processing"

Dr. Xiaomo Chen, (Speaker 12:00 - 12:25)

Assistant Professor | UC Davis, Center for Neuroscience

"Neural Circuits for Cognitive Control in the Primate Brain."

Dr. Yubei Chen, (Speaker 12:30 - 12:55)

Postdoctoral Scholar | Meta AI

"Seeking for the principles of unsupervised representation learning"

Lightning Talks and Posters

Dr. Manoj Mohan Kulkarni (Lighting Talk: 10:15 - 10:25 | Poster 3:30)

Postdoctoral Scholar | UC Berkeley, Optometry and Vision Science

"The Rod Pathway Drives aberrant Ganglion Cell Activity in the RD10 Retina"

A hallmark of inherited photoreceptor degenerations is the development of aberrant spontaneous activity in retinal ganglion cells (RGCs). This activity may degrade the signal-to-noise ratio of residual visual signals and reduce the effectiveness of treatments to restore vision. AII amacrine cells (AII-ACs) play a central role in propagating aberrant activity to RGCs. AII-ACs receive excitatory input from rod bipolar cells (through CP-AMPA receptors) and ON-cone bipolar cells (through gap junctions). However, the relative contributions of these pathways to the generation of aberrant activity remain unclear. Here, we tested the hypothesis that the rod pathway drives aberrant activity in AII-ACs and RGCs during early and late stages of degeneration in the rd10 mouse. Our results suggest that the rod pathway contributes to aberrant RGC activity in the degenerating retina. Blocking the rod bipolar to AII-AC synapse may improve detection of residual cone signals in the degenerating retina by reducing spontaneous activity.

Dr. Ananya Datta (Lighting Talk: 10:25 - 10:35 | Poster 3:30)

Postdoctoral Scholar | UC Berkeley, Optometry and Vision Science

"Contact lens induced corneal parainflammation involving Ly6G+ cell infiltration requires IL-17A and γδ T cells"

Previously, using a contact lens (CL) wearing murine model, we discovered that lens wear was associated with corneal parainflammation involving CD11c+ cells after 24 h and Ly6G+ cells (neutrophils) after 5-6 days. Here, we investigated the role of IL-17 and γ/δ T cells in CL associated Ly6G+ cell-mediated parainflammation. CL-wearing C57BL/6 wild-type (WT) mice were compared to lens-wearing IL-17A/F single and double gene knock-out mice, or mice depleted of γ/δ T cells. Corneas were assessed to quantify Ly6G+ and γ/δ T cell responses and corneal expression of genes encoding pro-inflammatory cytokines IL-17A, IL-17F, IL-β and IL-18. After 6 days lens wear, WT corneas showed Ly6G+ cell infiltration while remaining free of visible pathology. In contrast, lens-wearing corneas of IL-17A-/- mice and γ/δ T cell-depleted mice showed little or no Ly6G+ cell infiltration. Non-lens wearing controls showed no Ly6G+ cell infiltration. CL-wearing WT corneas also showed a significant increase in γ/δ T cells after 24 h that was maintained up to 6 days of wear, and a significant increase in cytokine gene expression after 6 days versus no lens controls: IL-18 & IL-17A (~3.9 fold) and IL-23 (~6.5-fold). Depletion of γδ T cells also abrogated these lens-induced changes in cytokine gene expression after 6 days. Together, these data show that contact lens-induced parainflammation of the murine cornea involving Ly6G+ (neutrophil) cell infiltration after 6 days of wear requires IL-17A and γδ T cells

Dr. Timothy Day (Lighting Talk: 10:35 - 10:45 | Poster 3:30)

DnaLITE Inc.

"Science to Entrepreneurship in the Gene Therapy Field"

Hannah Doyle (Lighting Talk: 1:00 - 1:10 | Poster 3:30)

PhD Student | UC Berkeley, Electrical Engineering & Computer Sciences

The 2-photon (2P) effect in vision occurs by direct photoisomerization of photoreceptor pigments involving two photons at a given wavelength, creating a percept of light corresponding to a 1-photon (1P) process at half that wavelength. Thus, a 2P effect elicited by 940-nm light may appear similar to 470-nm light. With adaptive optics (AO), we can compress photons in space, increasing the likelihood of 2P photoisomerization.

We scanned a focused spot of 940-nm light in a 0.9° x 0.9° raster pattern using an AO scanning laser ophthalmoscope. A supercontinuum light source was used with a ~20-ps pulse and an average power of 198.2 μW. We varied the focusing depth of the raster in and out of the plane of best focus and carried out color matching experiments.

Subjects' matching data showed a clear increase in luminance and blue hue when the AO-corrected raster was focused on their photoreceptors. Their matches can be interpreted as having a relatively constant red component corresponding to 1P isomerizations at 940 nm superimposed with blue and green components that increase greatly as the raster comes into focus.

2P vision was greatly enhanced by AO. As AO was used to focus a faintly-visible 940-nm scanning raster onto the retina, the raster appearance changed from red to blue, as if it were a mixture of 940- and 470-nm light. Our results are consistent with the hypothesis that this is a 2P isomerization process by the color appearance and by the strong focus dependency.

Dr. So Goto (Lighting Talk: 1:10 - 1:20 | Poster 3:30)

Postdoctoral Scholar | UC Berkeley, Optometry and Vision Science

"Gene expression signatures of contact lens-induced myopia in guinea pig retinal pigment epithelium"

Purpose: To identify key retinal pigment epithelium (RPE) genes linked to the induction of myopia in guinea pigs.

Methods: To induce myopia, two-week-old pigmented guinea pigs (New Zealand strain, n = 5) wore -10 diopter (D) rigid gas-permeable contact lenses (RGPCLs), for one day; fellow eyes were left without CLs and served as controls. Spherical equivalent refractive errors (SE) and axial length (AL) were measured at baseline and 1 day after initiation of CL wear. RNA sequencing was applied to RPE collected from both treated and fellow (control) eyes after 1 day of CL-wear to identify related gene expression changes. Additional RPE-RNA samples from treated and fellow eyes were subjected to quantitative real-time PCR (qRT-PCR) analysis for validation purposes.

Results: The CLs induced myopia. The change from baseline values in SE was significantly different ($P = 0.016$), whereas there was no significant difference in the change in AL ($P = 0.10$). RNA sequencing revealed significant interocular differences in the expression in RPE of 13 genes: 8 genes were significantly upregulated in treated eyes relative to their fellows, and 5 genes, including bone morphogenetic protein 2 (Bmp2), were significantly downregulated. The latter result was also confirmed by qRT-PCR.

Conclusion: The results of this RPE gene expression study provide further supporting evidence for an important role of BMP2 in eye growth regulation, here from a guinea pig myopia model.

Chris Kymn (Lighting Talk: 1:20 - 01:30 | Poster 3:30)

PhD Student | UC Berkeley, Redwood Center for Theoretical Neuroscience

"Learning Embeddings for Sparse Visual Features"

Sparse coding provides a mathematical framework for understanding how neurons in the visual system can efficiently represent natural scenes. It has been shown that the basis functions learned by a sparse coding algorithm resemble the localized, oriented, bandpass receptive fields observed in primary visual cortex (V1). Moreover, it has been hypothesized that these basis functions tile a low-dimensional manifold, thus tiling the manifold of natural scenes. We present an unsupervised method for discovering this manifold structure, adapting an algorithm previously used for learning semantic word embeddings for text documents. In our method, the embeddings are high-dimensional vectors, where basis functions nearby on the manifold have highly correlated embedding vectors. Next, we show how these embeddings can be integrated into the inference procedure for sparse coding, extending previous topographic models. Finally, we show how to leverage these embeddings to generate compositional models of images, building off techniques from hyperdimensional computing.

Dr. John Flannery (Poster 3:30)

Professor | UC Berkeley, Optometry and Vision Science

Targeting ON-bipolar cells by AAV gene therapy stably reverses LRIT3-congenital stationary night blindness

Adeno-associated virus–based gene therapies aimed at curing inherited retinal

diseases to date have typically focused on photoreceptors and retinal pigmented epithelia within the relatively accessible outer retina. However, therapeutic targeting in diseases such as congenital stationary night blindness (CSNB) that involve defects in ON-bipolar cells (ON-BCs) within the midretina has been challenged by the relative inaccessibility of the target cell in intact retinas, the limited transduction efficiency of these cells by existing AAV serotypes, poor availability of established ON-BC–specific promoters, and the absence of appropriate patient-relevant large animal models. Here, we demonstrate safe and effective ON-BC targeting by AAV gene therapy in a recently characterized naturally occurring canine model of CSNB: leucine-rich repeat, immunoglobulin-like and transmembrane domain 3 (LRIT3)–CSNB. To effectively target ON-BCs, AAV capsid variants with ON-BC tropism and ON-BC–specific modified GRM6 promoters were adopted to ensure cell-specific transgene expression. Sub-retinal injection of one vector, AAVK9#4-shGRM6-cLRIT3-WPRE, significantly recovered rod-derived b-wave in all treated eyes (six of six) of adult dogs injected at 1 to 3 y of age.

Christian Shewmake (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

Bispectral Neural Networks

We present a novel machine learning architecture, Bispectral Neural Networks (BNNs), for learning representations of data that are invariant to the actions of groups on the space over which a signal is defined. The model incorporates the ansatz of the bispectrum, an analytically defined group invariant that is

complete—that is, it preserves all signal structure while removing only the variation due to group actions. Here, we demonstrate that BNNs are able to discover arbitrary commutative group structure in data, with the trained models learning the irreducible representations of the groups. Remarkably, trained networks learn to approximate bispectra on these groups, recover their Cayley tables, and thus possess the robustness, completeness, and generality of the analytical object.

Dr. Charlotte Wang (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

"Multimodal, Longitudinal Assessment of Retinal Structure and Function Following Laser Retinal Injury"

We present a laser retinal injury case in which an adaptive optics scanning laser ophthalmoscope (AOSLO), AO-based microperimetry (AOMP), and AO-corrected visual acuity (AOVA) were used to examine and monitor the retinal structure and function after accidental exposure to a 1 watt 852 nm continuous-wave laser beam.

A 23-year-old patient was unwittingly exposed to a 1-watt, continuous-wave 852 nm laser at work as they noticed a small central scotoma in the right eye (OD). An initial eye examination was done one-day post exposure and the OD acuity was 20/25-2. Posterior segment evaluation revealed disrupted outer retina and retinal pigment epithelium in the OD fovea. AOSLO imaging 2 weeks after the exposure revealed a 0.50x0.75-degree elliptical area with irregular borders and abnormal cone reflectivity just below the fovea.

Starting one-month follow-up, OCT showed significant retinal structural recovery. Subsequent AOSLO imaging showed significant recovery of cone reflectivity. Importantly, AOMP showed measurable detection thresholds at all affected retinal locations at 6 months, and all locations restored normal sensitivity at 10 months.

Retinal structure and function from laser injury can be visualized and measured with OCT, AOSLO imaging, and AO-based psychophysics. An intact Bruch's membrane on OCT and measurable retinal sensitivity by AOMP may serve as good biomarkers for retinal recovery.

Alexander Belsten (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

"Image Reconstruction from Retinal Ganglion Cell Population Response"

Efficient coding theory (ECT) provides insight into the functional properties of biological information transfer systems. This theory states that sensory systems attempt to reduce the redundancy of their inputs while maximizing information transfer. ECT has been applied to a simple model of retinal processing, which includes a population of linear-nonlinear retinal ganglion cells (RGCs), and input image and output retinal ganglion cell spiking noise. When this model is optimized to maximize information transfer between input images and RGC responses, subject to a firing constraint, the linear filters converge to a population of ON and OFF center-surround receptive fields that tile the input image space. While the emergence of center-surround receptive fields and their tiling properties has provided insight into biological retinal processing, the metric used to evaluate this model in literature to date has been in terms of information (i.e., bits) which does not provide an intuitive metric for retinal coding. In this work, we further develop this model to do Bayesian image reconstruction (i.e., our ability to reconstruct the input image given a set of noisy RGC responses). We analyze image reconstruction for a group of ECT model retinas trained under

various input/output noise levels. We also comment on the biological plausibility of this Bayesian inference and its implications for image decoding in early visual cortex.

Reem Almagati (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

"Effects of Precision of A Peripheral Cue on Ensemble Perception"

Exogenous attention is a fast involuntary attentional mechanism initiated by a salient cue which increases the spatial resolution of peripherally perceived stimuli. Previous work showed the effects of exogenous attention on performance in a crowding and ensemble perception tasks. In these tasks, subjects were first asked to report the orientation of a central gabor surrounded by 9 uniformly spaced flankers arranged in a circular fashion (crowding task) followed by an ensemble task of the same stimuli parameters but subjects reported the average orientation of all the gabor patches (target and flankers). Results suggest that exogenous cueing modulates performance depending on whether the cued gabor patch was congruent or incongruent with the ensemble value. Results also showed significant effects of cue size on performance (big vs small). We followed up on this work in a naive pool of subjects who were only tasked to report the ensemble value of uniformly distributed gabor patches in a 4X4 grid. Effects of exogenous attention on performance were evaluated based on cue size in three different conditions congruent, neutral and and incongruent, with respect to the arithmetic mean of all orientations.

Dr. Raul Rodriguez (Poster 3:30)

Postdoctoral Scholar | UC Berkeley, Optometry and Vision Science

"Measuring torsional optokinetic nystagmus in virtual reality"

A torsional optokinetic stimulus drives torsional nystagmus, and a tilted frame during a rod and frame subjective visual vertical (SVV) task affects SVV and biases torsional eye position. We posit that a visual gravity cue provided by a frame in a torsional optokinetic stimulus would further bias torsional nystagmus. In order to test this theory, we use a FOVE VR headset (FOVE Inc., Tokyo, JP, model FOVEVR) to place the subject in a virtual room with circles forming either a rectangular room or a tubular room (frame/no frame). We placed a fixation point at the center of the room while the room rotates at 0°/s, ±6°/s, or ±12°/s. In addition, we had the subject perform a rod and frame SVV task, 0° ± 12° (upright) with nine equidistant divisions, asked twice per condition set. Preliminary data (N = 3) shows that the virtual reality setup produced the expected relationship between the speed of the rotation of the room and the slow-phase velocity of the induced nystagmus as well as the bias in the perception of upright. With the perceived upright tilted in the direction of the rotation. Additionally, we did not find a difference in torsional slow phase velocity (SPV), ocular torsion position, or perception of upright, between the frame and no frame condition across all rotation velocities and no significant difference in the SVV in intersubject results.

Stephanie Reeves (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

"Microsaccade directions are not influenced by the orientation of natural scene tilt during fixation"

When exploring a visual scene, humans make more saccades in the horizontal direction than any other direction. This horizontal saccade bias is well documented despite its unknown origin. While many have

shown that the horizontal saccade bias rotates in response to natural scene tilt, it is unclear whether the direction distribution of microsaccades made while fixating a small target might rotate with background image tilt. Study participants (n=9) viewed tilted scenes at -30, 0, and 30 degrees, and were asked to either fixate a central round dot (0.5 degrees) or free view the image while we recorded eye movements binocularly. Saccade distributions during fixation did not rotate significantly between image tilts (2.1 ±2.01 degrees; $t(8) = 1.05$, $p = 0.32$). In contrast, saccade distributions during free viewing were significantly rotated by a mean angle of 14.6 ±5.41 degrees ($t(8) = 2.69$, $p = 0.03$). We also found that small amplitude saccades during the free viewing task occurred most in the horizontal direction while large amplitude saccades were more closely oriented to the scene tilt. This result appears to indicate at least two reference frames in saccade generation: one egocentric which appears to dominate for small saccades and biases the saccades even in the absence of a visual stimulus and another allocentric one that biases the saccades along the orientation of the image.

Clara Maria Bacmeister (Poster 3:30)

PhD Student | Stanford University

"Uncovering regional differences in glial populations in developing visual cortex."

The microstructural development of human visual cortex is an open question and is intimately associated with functional changes. Therefore, understanding regional differences in cellular processes is key to understanding the biological mechanisms governing the maturation of human visual cortex. To explore the biological underpinnings of human visual cortical development, we conduct immunohistochemical analyses for astrocytes and oligodendrocyte lineage cells in three visual areas: V1 (calcarine sulcus), place-selective (collateral sulcus), and face-selective (fusiform gyrus) regions. Our findings suggest that astrocytes and oligodendrocyte lineage cells display distinct developmental trajectories in gray vs. white matter and further indicate cortical layer-specific glial dynamics in multiple visual areas. Preliminary data suggests astrocytes populate the cortex before oligodendrocyte lineage cells. After birth, oligodendrocyte lineage cells show relatively even distribution across layers while myelin density is inhomogeneous across cortical layers, suggesting oligodendrocyte lineage cells may perform distinct functions depending on cortical layer and stage of development. Together, our findings suggest cell-specific, region-dependent, and cortical layer-driven differences in glial populations across visual cortex development.

Dr. Eline R Kupers (Poster 3:30)

Postdoctoral Scholars | Stanford University, Psychology

"A population receptive field modeling framework of sensory suppression in human visual cortex"

When presenting multiple visual items simultaneously in the receptive field, the neurophysiological response is surprisingly lower than presenting the identical items sequentially. However, the underlying computations of this suppression effect are not well-understood. Here, we leveraged population receptive field (pRF) models to computationally test how linear, compressive spatial, or compressive spatiotemporal summation contributes to suppression at the voxel level. We collected two fMRI experiments in 10 subjects: (i) retinotopy to estimate pRFs and (ii) an experiment with simultaneous or sequential stimuli, both varying in duration and size. In V1, there was no simultaneous suppression and responses were larger for bigger stimuli. This was well- predicted by linear pRFs. However, the linear model failed to capture larger

responses in V1 for brief vs long durations. In V2 and high-level areas, responses were lower for simultaneous vs sequential stimuli, larger for brief vs long durations, and did not increase much with size. Both compressive pRF models predicted simultaneous suppression and the effect of stimulus size, but only the compressive spatiotemporal model predicted the effect of duration. Our results suggest that compressive spatiotemporal pRFs are necessary to predict responses in visual cortex to simultaneous vs sequential stimuli and underscore the power of pRF models for providing new insights into spatiotemporal computations of sensory suppression.

Shruthi Satheesh

Undergraduate Student | UC Berkeley, Molecular Cell Biology, Neurobiology

Title: Outdoor Activity in Myopic and Non-Myopic Children

Purpose: This preliminary analysis of the Childhood Activity and Myopia (CAM) Study data aims to explore the effect of outdoor activity, measured in a dynamic way, on myopia status and severity in children.

Methods: 13 participants aged 6-11 years wore a Phillips Actiwatch that measured children's habitual lighting intensity, a proxy to record the frequency and duration of their daily outdoor activity for two weeks. We also collected parental survey data inquiring about each child's typical school schedule and extracurricular activities to more comprehensively capture their routine outdoor exposure during the school year.

Results: Preliminary data show that the non-myopes spend more time in a week, on average 24 more minutes, performing far work and outdoor activities than the myopes.

Myopes seem to spend shorter durations of time outdoors each time they go outside, compared to the non-myopes who spend longer stretches of time outdoors even if they go outside less frequently in a day. As a result, myopes constantly seem to experience a decrease (~195 lux) in total outdoor illuminance experienced per day.

Conclusions: The above mentioned results correlate with the hypotheses that being under outdoor conditions for longer and performing less near work are two major protective factors against myopia development. The CAM Study is an ongoing longitudinal study, therefore further work is warranted to further assess these trends and if they relate to future myopia progression in our cohort.

Josephine D'Angelo (Poster 3:30)

PhD Student | UC Berkeley, Optometry and Vision Science

"Measuring Upright Perception and Torsional Eye Position in Virtual Reality"

When viewing the world, we perceive a stable upright image. This upright perception is maintained despite our eyes, head, neck, and body continuously moving. When the head tilts, the eyes roll in the opposite direction of the head tilt and this reflex is called ocular counter-roll (OCR) or torsion. Tilting the head typically increases errors in upright perception which can be measured using the subjective visual vertical (SVV) task. It has been shown that convergence suppresses OCR when looking at near objects. Here we wanted to take advantage of new virtual reality technology to study the interaction between head tilt and convergence on perception of upright and ocular counter-roll. Three subjects were tested using the FOVE VR headset. We used a subjective visual vertical (SVV) task to measure their upright perception while simultaneously recording torsional eye position at three head positions: upright, head roll 30 degrees left,

and head roll 30 degrees right. At each of the head positions we also tested SVV at two vergence distances: near (25 cm) and far (1.5 m). We scaled to maintain constant size in degrees of visual angle at different distances. In the current configuration we did not observe a difference in the amount of ocular counter-roll observed with head tilt during near and far viewing. Perception of upright also did not appear to differ between viewing conditions and head tilts. Our results may suggest that the mechanisms by which near viewing suppresses OCR may not apply under the current VR configuration.

Beatrice Le (Poster 3:30)

Undergraduate Student | Helen Wills Neuroscience Institute

Dr. Antonia Stefanov (Poster 3:30)

Postdoctoral Scholar |Helen Wills Neuroscience Institute

“Pilot or co-pilot? Promoter specificity might be transgene dependent

A shift in promoter specificity upon cytosolic versus membrane bound ectopic expression of GFP in the C57Bl6 and rd1 mouse retina”

Promoter candidates are routinely assessed through screening cytosolic GFP expression in the retina as the preferred method for its enhanced visibility over membrane bound GFP. Here, we report for the first time that promoter specificity may become altered by a downstream gene insert design and that this phenomenon is independent of retinal phenotype.