Structural motifs of excitatory synapses in the mammalian retina

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Background
Connectivity within the nervous system is precise and dysfunctions lead to degraded performance and disease, yet the rules that govern connectivity remain unknown. Recent efforts reveal that different types of cone bipolar cells in the mammalian retina show preferences in the selection and frequency of presynaptic structure types used for signal transmission (Yu et al., 2023). However, it is not yet known how these differences are related to the quantity or type of postsynaptic partner in rabbit retina.

Methods
Retinal Connectome 1 (RC1) N2O Rabbit, Female, 13 months

Figure 1: Anatomical view of the eye and layers of the retina. Rod (R) and cone (C) photoreceptors, located in the outer retina, are the light sensing cells. Ganglion cells (G), located in the inner retina, send visual information through the optic nerve to various parts of the brain for both image and non-image functions. Cone bipolar (CB) amacrine cells (A) reside in between these two cell types and transmit information from the photoreceptor layers to G cells. Horizontal (H) and amacrine (A) cells modulate this signal transfer in the outer and inner synaptic layers, respectively. The inner synaptic layer where CB and RB cells synapse with A and G cells was the region of focus in this study.

Figure 2: Creating a connectome. Retinal Connectome 1 (RC1) contains all synaptic connections of the inner synaptic layer of healthy adult rabbit retina. The dataset was constructed from transmission electron microscopy (TEM) images of serially sectioned mid-peripheral retina tissue captured at 2 nm/voxel. Together with light microscopy images of sections stained and imaged for small molecules, sections are mosaicked and aligned into a volume. Annotation performed using the Viking Viewer for Connectomics to mark morphology and synapses.

Figure 3: Rabbit ON cone bipolar CBb6 cells use 3 excitatory presynaptic structures. A) Transmission electron micrographs of single ribbon (A), multiribbon (B), and ribbonless (C) structures formed by CBb6 ON cone bipolar cells. Single ribbons have 1 ribbon, multiribbons have >1 ribbon, and ribbonless structures lack a ribbon but have ≥2 synaptic vesicles tethered to the presynaptic membrane. Abbreviation: A: ribbon; PSD, postsynaptic density; SV, synaptic vesicle.

Conclusions & Future Directions
It is hypothesized that presynaptic structure types may differ in the strength of neurotransmitter release (ribbonless < single ribbon < multiribbon), but the findings here are inconsistent with such scaling of output to the number of postsynaptic targets. The data suggests that partner type relationships may be more important than the number of targets in determining presynaptic structure type in CBb6 cells. Future efforts will incorporate size differences of presynaptic structures and presynaptic ribbon size, as well as compare across bipolar cell classes, in order to provide further insight into the connectivity rules underlying excitatory synapses in retina.

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