

Purpose: There are at least 30 distinct types of mammalian retinal ganglion cells, each sensitive to different features of the visual environment, and these can be grouped according to their morphology. One such group, the gamma cells, was identified more than 40 years ago, but their synaptic inputs have never been described. That was the goal of this study.

Methods: The synaptic inputs to a subtype of gamma cell with dendrites ramifying in the outer sublamina of the inner plexiform layer (IPL) of the rabbit retina were identified in a retinal connectome developed using automated transmission electron microscopy.

Results: Its soma was relatively small and was found in the ganglion cell layer. Because its dendrites in the inner plexiform layer were exclusively postsynaptic, its identity as a ganglion cell was confirmed. Based on its dendritic morphology, this cell was classified as a subtype of gamma cell with higher-order dendrites confined to the outer sublamina of the IPL. The excitatory input to the gamma cell came from 17 OFF cone bipolar cells, 16 making one ribbon synapse each and one making 2. These were tentatively divided into at least 4 types based on their morphology and ultrastructure. The majority of the inputs to the gamma cell were inhibitory synapses from amacrine cells. The presynaptic amacrine cell dendrites did not co-fasciculate with the dendrites of the gamma cell, and each amacrine cell process made only 1 synapse onto the gamma cell. Most amacrine cell processes had ultrastructure typical of GABAergic cells, and some contained large, dense core vesicles. One amacrine cell presynaptic to the gamma cell had ultrastructure characteristic of the bistratified amacrine cell that contains vesicular glutamate transporter 3. Although the gamma cell dendrites co-stratified with the lobular dendrites of Aii amacrine cells, they did not receive any direct synaptic input from them. Taken together, these findings suggest that many types of stimuli in the receptive field surround or outside of the classical receptive field would provide potent inhibition to the gamma cell.

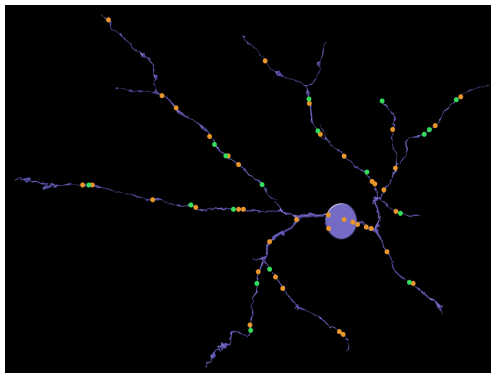


Figure 5. Synaptic inputs to the gamma cell. The gamma cell (purple) was rendered using VikingPlot and displayed in Blender. Amacrine cell inputs at conventional synapses are orange circles; bipolar cell inputs at ribbon synapses are green circles. All symbols were placed manually in Photoshop, using Tulip renders as guides.

Synaptic inputs to a gamma ganglion cell in rabbit retina

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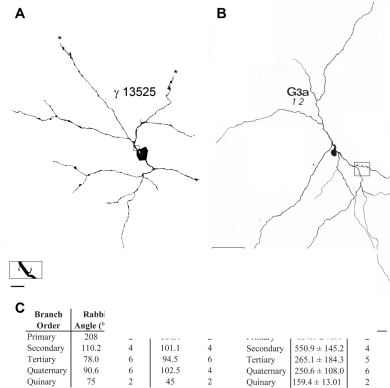


Figure 1. Ganglion cell 13525 is a gamma cell. A. A three-dimensional reconstruction of the gamma cell. The cell has dendritic spines, which have thin stalks and bulbous ends (box = inset at higher magnification). The dendritic tree is sparse and resembles a low tie. Two dendrites (asterisks) exited the volume and could not be fully traced. Scale bar = 10 μm. B. A Golgi stained G3a (gamma-like) cell from human peripheral retina (Kolb et al., 1992) with similar spines (box = inset at higher magnification) and dendritic morphology. Scale bars = 50 μm.

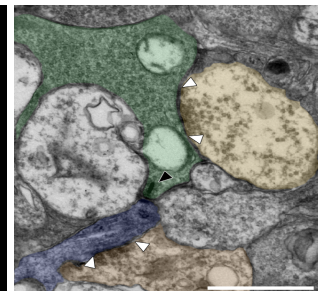


Figure 6. Excitatory and inhibitory synapses onto the gamma cell. A bipolar cell axon terminal (Cba1-2 flex 95020, green) is presynaptic to a dendrite of the gamma cell (blue) at a ribbon synapse (black arrowhead). The ribbon synapse is typical, with a synaptic ribbon and an asymmetric postsynaptic density. An amacrine cell (AC 104726, orange, lower) is presynaptic to the gamma cell at a conventional synapse (white arrowheads). Another amacrine cell (unannotated, yellow, upper) is presynaptic to the bipolar cell axon terminal. Scale bar = 1 μm.

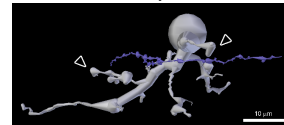


Figure 2. The gamma cell stratifies in the OFF sublamina of the IPL. Distal dendrites of the reconstructed gamma cell (purple) co-stratified with lobular appendages (hollow arrowheads) of a nearby Aii amacrine cell (GAC Aii 7225, white) and are therefore in sublamina a of the IPL. Scale bar = 10 μm.

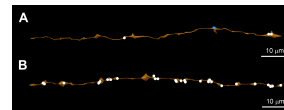


Figure 3. Two kinds of amacrine cell processes provide inhibitory input to the gamma cell. A. Dendrite of an amacrine cell (AC 130239) which made 3 conventional synapses (white circles) and received 1 conventional synapse (blue circle) from an unannotated amacrine cell. B. The amacrine cell AC 104740 made 27 inhibitory conventional synapses (white circles) along its length but did not receive any synapses. It was therefore classified as an axon. Scale bar = 10 μm.

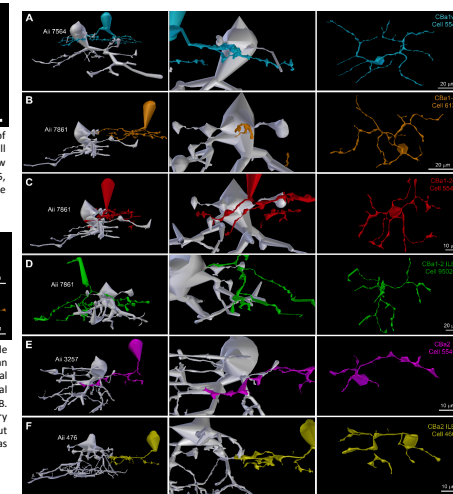


Figure 4. Classification of bipolar cells presynaptic to the gamma cell. Each well-annotated cell is shown in a vertical section alongside a nearby Aii amacrine cell (left), at higher magnification (middle), and in a flatmount view (right). There were 2 non-flex Cba2 cells presynaptic to the gamma cell: 5545 and 7362; only cell 5545 is illustrated here. The axonal arbor sizes differed between cells, as illustrated by the scale bars for each figure (right). Note that all the bipolar cell axons co-stratified with the lobular dendrites of the Aii amacrine cells.

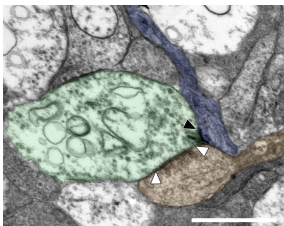


Figure 7. Bipolar cell input to the gamma retinal ganglion cell (blue) in S2 of the IPL. Bipolar cell Cba2 7362 (green) was presynaptic to the gamma cell at a ribbon synapse (black arrowhead). An amacrine cell (orange) in this dyad synapse made a reciprocal synapse onto the bipolar cell (white arrowheads). Scale bar = 1 μm.

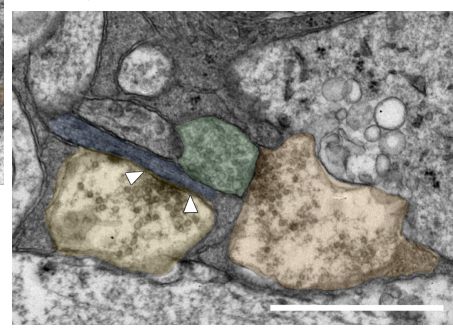


Figure 8. Amacrine cell input to the gamma cell. An amacrine cell (AC 122073, yellow) was presynaptic to the gamma cell (blue) at a conventional synapse (arrowheads). A nearby amacrine cell (C 123061, orange) was presynaptic to a bipolar cell (Cbx 64830, green), which was, in turn, presynaptic to both the gamma cell and AC 122073 later in the series. Scale bar = 1 μm.

Conclusions

- The local synaptic interactions described here would be expected to generate relatively weak OFF responses to stimuli confined to the center of the receptive field.
- The gamma cell received a small input from each of 4 types of OFF bipolar cells. Because the bipolar cells vary in their response kinetics and contrast sensitivity, each type would provide a small, asynchronous excitatory drive to the gamma cell during decrements in light intensity.
- The amacrine cells that make up the second member of the dyad synapses with the gamma cell dendrites are expected to provide only a small amount presynaptic inhibition; reciprocal synapses were observed in only 3 of the 18 ribbon synapses.
- Local postsynaptic inhibition was somewhat more common; in 6 instances, the bipolar cells presynaptic to the gamma cell or their electrically coupled neighbors also provided input to an amacrine cell that inhibited the gamma cell.
- The other inhibitory synaptic inputs to the gamma cell are likely to have a much greater impact on the light responses because they are more numerous. These are from axons and long dendrites of GABAergic amacrine cells, and they provide 86% of the amacrine cell input or 60% of all the input.
- This finding suggests that many types of stimuli in the receptive field surround or outside of the classical receptive field would provide potent inhibition to the gamma cell under a wide range of stimulus conditions.
- Thus, the synaptic inputs reported here suggest that the light responses of gamma cells in rabbit retina would be suppressed by large stimuli, like their homologs in mouse retina.

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