The most numerous ganglion cell type of the mouse retina is a selective feature detector.

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Background:

What is a feature detector?
2) What is a pixel detector?
3) Does it matter?

Two visions for the eye

Eye as a camera

Faithful camera
• Each photoreceptor is a pixel
• Needs to be high resolution, sharp receptive fields
• E.g. primate retina with P-type ganglion cells: receptors / Ganglion cells = 1:1

Information Processor
• 20 different ganglion cells, covering entire visual field (= 20 channels)
• 8 channels for direction of movement (3 for controlling eye movements), 4-5 types encode light levels for pupil control, or clock setting

Contrasting Views of the Retina
The retina of has over 50 known cell types belonging to the 5 traditional classes (receptors, horizontal, bipolar, amacrine, ganglion) - mostly from rabbit. From Masland (2001) Nature Neuroscience; reprinted in Gollisch and Meister Neuron, Volume 65, Issue 2, 150-164, 28 January 2010.

**5 major cell types**

**Principal Cells:** the Ganglion cells (projection cells) axons go to:

- Supra-chiasmatic nucleus (circadian rhythms)
- Pre-tectal nucleus (control pupil size)
- Superior colliculus (orients eye and head movements)
- Lateral geniculate (form vision and movement)
How are the authors able to visualize only the W3 retinal ganglion cell so that they can create a map of all of the W3 neurons in the retina?

Transgenic mouse lines permits selective labeling of RGC subtypes. Here, RGC W3

Characteristics of W3 RGC

- Numerous
- Small RF
- High spatial resolution
- Candidate pixel detector

Transgenic mice

Mice. The generation of W3 mice has been described previously (12). Briefly, they were generated from a vector in which Thy1 regulatory elements drive the expression of YFP, wheat-germ agglutinin (WGA), and Escherichia coli β-galactosidase (lacZ, Thy1-Iox-YFP-STOP-Iox-WGA-LacZ). In the absence of Cre, YFP was expressed in a distinct subset of RGCs in the W3 retina, presumably due to effects of sequences near the site of transgene integration in the genome (19). All experiments were carried out in accordance with protocols approved by the Harvard University Standing Committee on the Use of Animals in Research and Teaching.

Thy-1 is a surface protein, a thymocyte antigen, used for marking stem cells, including axon processes of neurons.

W3 expressing neurons in a mouse retina whole mount.

Greater density in ventral retina.

Left: vertical section of the inner plexiform layer.
Red: ChAT label of amacrine cells (Choline acetyltransferase)
Green: YFP label of W3 cells
Blue: cell bodies (Nissl)

Note: the dendrites of W3 are sandwiched between two bands of ChAT-positive bands in the IPL.

Density of cells in the central retina
Dashed: randomly spaced
Red: hexagonal array
The diameter of the dendritic arbor of W3 neurons is very small compared to other ganglion cells in the retina. The cell body is also small.

Coverage factor is 4.5 in densest region of retina (i.e. 4 to 5 cells cover each point in space)

W3 neurons are of a single cell type, with a relatively regular distribution.

- The density recovery profile (density of W3 neurons versus their average spacing) indicates repulsion at close range; close fit to hexagonal packing.

"Together, these results provide strong evidence that W3-RGCs are a single cell type that represents the smallest-field and highest density RGCs in the mouse retina.

Hence one expects this population to sample the visual scene at the highest spatial resolution."

By using transgenic lines of mice containing YFP gene inserted into gene Thy1 get yellow fluorescence in subset of W3 RGC.
Whole cell patch electrode records from one cell

Whole cell patch clamp from RGCs, some from W3 (guided by strong fluorescent label) others from non-W3. Response to natural scene movies from “rat-cam”. Non-W3 RGCs respond to rat-cam movie; W3 cells are generally silent.

Natural stimuli

- Recorded via head-mounted video (rat cam)
- Contains significant pan motion due to angular and linear head movement – turning, walking
- Presented to W3 cells – no response
- For mouse in nature, head movements would be compensated by counter eye movement (VOR) but normal stimuli should contain significant optical flow patterns.
- What about when freezing?

The authors conclude that W3 neurons in the retina respond both to lights turning “on” and lights turning “off”. How might this be possible, given that cones all respond to lights turning on with hyperpolarization?
W3 Receptive Fields

A. Shows the receptive field of the RGC overlaps with that of the dendritic area.

Recording from W3, stimulate with light, cell fires spikes on “ON” and on “OFF”.

Average spike rate for on/off responses plotted as a function of time. Note that the on response is delayed compared to the off response.

B. Directionality of a moving bar stimulus. In each direction there are the opposite wings of the bar (on, then off). Restricted receptive field area.

C. Stimulus is a line of light and dark bands each traveling in opposing directions. The spatial frequency is determined (subjected to PCA, and principal component analysis). The light band phase activates the cell. The cell responds with an excitatory post synaptic potential (EPSP). The inhibition is faster and stronger.

D. Model of the W3 ganglion cell is a single neuron with one On bipolar and one Off bipolar, each is a rectifying synapse.

The authors conclude that W3 retinal ganglion cells are “feature detectors” for aerial predators. Make a list of characteristics of stimuli that cause the cells to fire that would lead to this conclusion.
Response of W3 neuron to small dark objects such as a dark outline of a hawk flying overhead on a bright background. Small objects, about the size of the W3 receptive field evoke the strongest response, independent of trace. No directional preference.

Summary

A small, numerous, RGC, W3 is found over the entire retina. It has a small cell body, small, dense thorny dendritic field. W3 cells are a candidate for pixel detector in the retina.

Transgenic lines selectively label W3 neurons with strong YFP signals.

W3 neurons are silent to most stationary, and moving stimuli. W3 respond both to on and off stimuli. Appear to receive both on and off bipolar inputs. Both are rectifying, and do not cancel each other out. In response to natural movie with head movements, cells do not respond. Other RGCs fire significantly.

In response to moving stimuli appear to be strongly inhibited by peripheral movement.

Inhibition is spike-dependent, from Amacrine cells.

W3 neurons act as feature detectors for small dark objects on light background moving slowly.