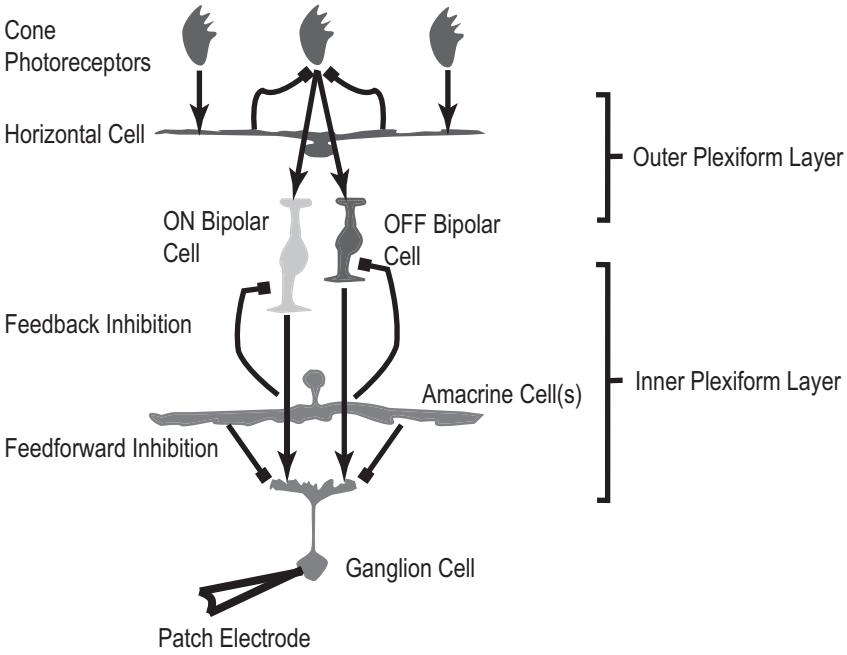
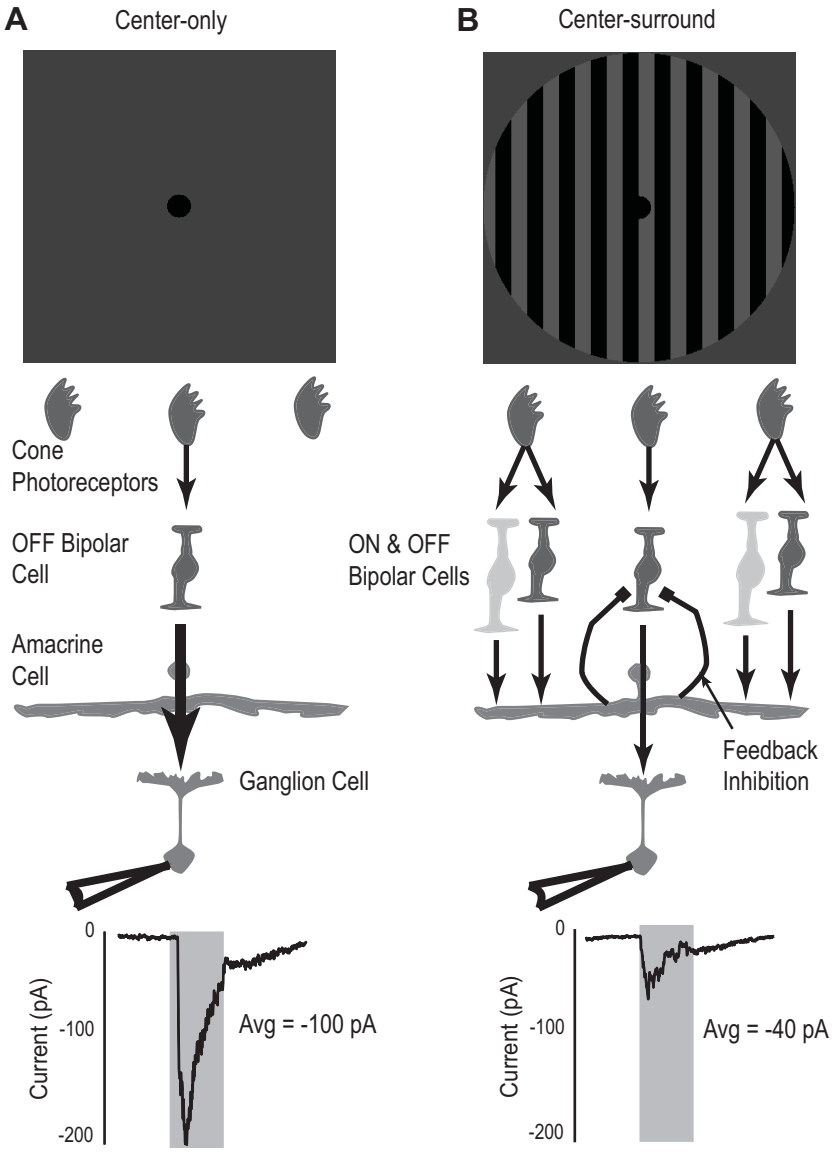
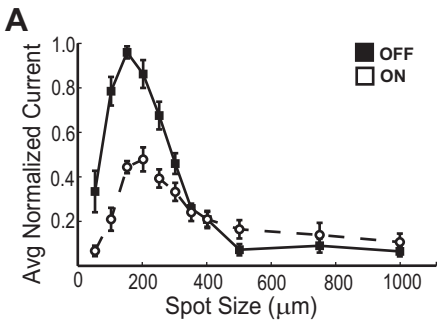
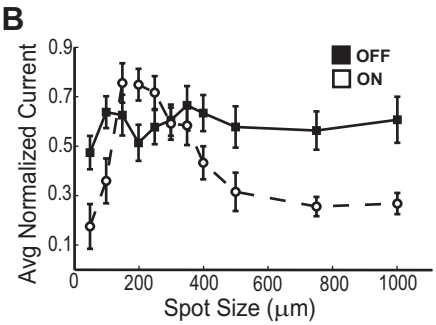
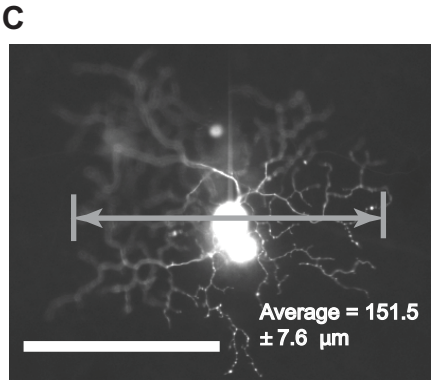

Cone
Photoreceptors
Horizontal Cell
Outer Plexiform Layer
ON Bipolar
Cell
OFF Bipolar
Cell
Feedback Inhibition
Amacrine Cell(s)
Inner Plexiform Layer
Feedforward Inhibition
Ganglion Cell
Patch Electrode

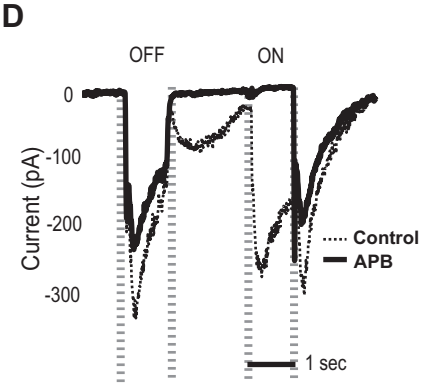


1.0 - (-40 pA / -100 pA) = 60% reduction


A
Avg Normalized Current
1.0
0.8
0.6
0.4
0.2
0
200
400
600
800
1000
Spot Size (μm)
OFF
ON


B
Avg Normalized Current
0.9
0.7
0.5
0.3
0.1
0
200
400
600
800
1000
Spot Size (μm)
OFF
ON


C
Average = 151.5
± 7.6 μm


D
OFF
ON
0
-100
-200
-300
Current (pA)
Control
APB
1 sec

Supplementary Fig 1. General retina circuitry and terminology.

Cones respond to increments and decrements in light with decrease or increase in glutamate release, respectively. All glutamate synapses are represented with arrows. Horizontal cells and bipolar cells are driven by glutamate from cones in the outer plexiform layer. Horizontal cells modulate cone glutamate release (lines with blocks in the outer plexiform layer). In the inner plexiform layer, ON and/or OFF bipolar cells drive ganglion cells via glutamate release. Inhibitory amacrine cells use GABA or glycine (both indicated as lines with blocks) to inhibit bipolar cell terminals (feedback inhibition) or ganglion cells directly (feedforward inhibition).

Supplementary Fig. 2. Measurement of feedback inhibition.

A: LED is whole-cell voltage clamped at -60 mV to record excitatory currents. An OFF spot (-100% luminance, 150 μm), shown above, is flashed for 3 seconds. The reduction in luminance causes an increase in glutamate release (arrows) from OFF bipolar cells, exciting the ganglion cell. The current (below) is set to a zero baseline and averaged over the course of the stimulus (grey square).

B: In addition to the 150-μm center square (A), 2 Hz inverting gratings are presented in the surround (150-2000 μm). OFF and ON bipolar cells in the surround are stimulated, which in turn stimulate amacrine cells. Amacrine cells release inhibitory neurotransmitters onto bipolar cell terminals (feedback inhibition, lines with blocks), causing a suppression of glutamate release to the ganglion cell. The current is set to a zero baseline and averages over the course of the stimulus (grey square). The center-surround average current is divided by the center-only average current and subtracted from 1.0 to derive a percent reduction in excitatory current levels.

Supplementary Fig 3. Basic receptive field measurements and pharmacology for ON and OFF excitation.

A-B: Average excitatory (A) and feedforward inhibitory (B) currents were measured for OFF (-100% luminance) and ON (+300% luminance) spots of varying size and normalized to the maximum measured average current. Error bars = SEM, n=6.

C: Example of an anatomic photomicrograph of an LED filled with Alexa-488 during

electrophysiological recording, with average dendritic field size measurement. Scale bar=100 μm, n=13.

D: Average of responses to OFF and ON spots for control and in the presence of APB, n=9.