Neuron, Vol. 36, 781–786, December 5, 2002, Copyright ©2002 by Cell Press

Multiple Mechanisms for Contrast Adaptation in the Retina

The retina adapts to average light intensity but also to the *range* of light intensities (contrast). A study by Baccus and Meister, in this issue of *Neuron*, identifies three ways that ganglion cells and interneurons adapt to high contrast: shorten integration time, reduce gain, and depolarize. Only the depolarization decays, over tens of seconds.

The retina adapts to the visual environment so that the huge range in light intensity ($\sim 10^8$) over the diurnal cycle can be encoded, at the retinal output, by a ganglion cell's narrow range of spike rates ($\sim 10^2$). Adaptation to the *mean* intensity, termed "light adaptation," involves many processes: intrinsic mechanisms of rods and cones, switching between rods and cones, and switching postreceptoral circuits (Walraven et al., 1990). But another type of adaptation is needed, because, as the eye scans a visual scene, the retina is exposed to different ranges of intensities around the mean (i.e., different contrasts). All retinas from amphibian to primate adapt to the range of intensity, a process termed "contrast adaptation" (Shapley and Victor, 1978; Smirnakis et al., 1997; Benardete and Kaplan, 1999; Brown and Masland, 2001; Kim and Rieke, 2001; Chander and Chichilnisky, 2001). The mechanisms for contrast adaptation are not well understood, but we know that it does not occur in photoreceptors, and thus it must arise in the retinal circuit (Shapley and Victor, 1978; Sakai et al., 1995; Smirnakis et al., 1997; Rieke, 2001).

After the switch from a low- to high-contrast environment, a ganglion cell's spiking response soon reflects reduced sensitivity to contrast (i.e., reduced contrast "gain"). If high contrast persists, some studies suggest that the gain change also persists (Victor, 1987), whereas others suggest that gain continues to decline, over 10–20 s (Smirnakis et al., 1997; Brown and Masland, 2001). In this issue of *Neuron*, Baccus and Meister (2002) clarify the time course of contrast adaptation in ganglion cell spiking responses and show, by intracellular recordings from all major cell classes, where specific adaptive properties first appear in the retinal circuit.

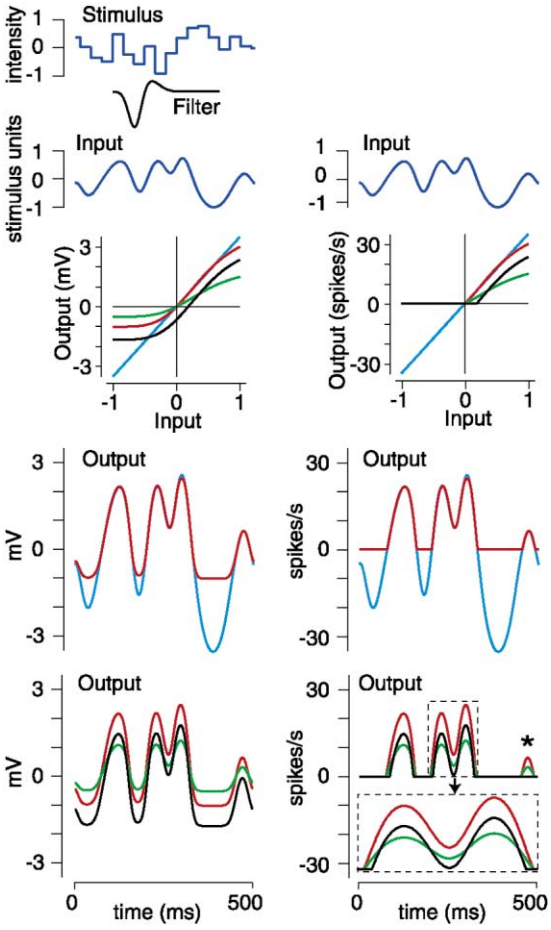
Baccus and Meister (2002) stimulated an in vitro salamander retina with a spatially uniform stimulus whose intensity was drawn anew every 30 ms from a Gaussian distribution with constant mean; this "white-noise" stimulus is useful because it probes a wide range of temporal frequencies. For fixed periods (30 s), contrast was alternately low (Gaussian SD = 0.05 times the mean) or high (SD = 0.35 times the mean). They quantified the intracellular voltage response in all neurons and the spiking response in ganglion cells, using a linear-nonlinear analysis (Victor, 1987; Chander and Chichilnisky, 2001; Kim and Rieke, 2001; Rieke, 2001).

The linear-nonlinear analysis separates the measurements of interest (i.e., temporal sensitivity, contrast sensitivity) from nonlinear response components (e.g., the spike threshold) that would otherwise seriously distort these measurements. First, a cell's response is described as a filtered version of the stimulus (i.e., the filter emphasizes certain temporal frequencies) that then passes through a nonlinear input-output function. This function takes into account reduced responsiveness at hyperpolarized potentials and zeroing of spike rate below spike threshold (see First Figure). Three response properties are quantified independently: *integration time* is measured in the filter (i.e., time-to-peak); *gain* is measured as the slope of the input-output function; *membrane potential* is measured from the y intercept of the input-output function. To track the time course of adaptation, Baccus and Meister (2002) analyzed the response immediately after the switch to high contrast and later after prolonged stimulation.

Within 1 s following the switch to high contrast, a ganglion cell's intracellular response changed in three ways: integration time shortened (the filter peaked $\sim$20% earlier); gain reduced by $\sim$25%–75%; and the membrane steadily depolarized by $\sim$4mV (Second Figure; Baccus and Meister, 2002). The shortened integration time and the reduced gain persisted as long as contrast remained high (30 s). However, the initial membrane depolarization was followed by a slow hyperpolarization (over 10–20 s) that restored the membrane potential toward baseline by $\sim$50% (their Figure 9B). The cell's spiking response adapted similarly to high contrast: integration time shortened, gain reduced, and the spike rate rose. Changes in integration time and gain persisted as long as contrast remained high, but the initial rise in spike rate slowly declined (Second Figure). Here, the important insight is that changes in gain and average spike rate are separable and follow different time courses. Thus, previous studies that measured the decline in spike rate, without using the linear-nonlinear analysis, would not have accurately tracked changes in gain (Smirnakis et al., 1997; Brown and Masland, 2001).

Cones and one of their postsynaptic targets (horizontal cells) did not express contrast adaptation, suggesting that neither cone voltage nor cone glutamate release adapt (Third Figure; Sakai et al., 1995; Rieke, 2001; Baccus and Meister, 2002). Certain bipolar cells (excitatory interneurons) adapted on one or two of the three properties (integration time, gain, membrane polarization), although typically the adaptations of integration time and gain were small ($<\sim$40%) relative to adaptations in ganglion cells (Baccus and Meister, 2002; their Figure 9). The magnitude of bipolar cell adaptation was consistent with a previous study (Rieke, 2001). Certain amacrine cells (inhibitory interneurons) showed modest adaptations on some of the three properties, similar to bipolar cells, whereas others showed large adaptations on all three properties, similar to ganglion cells (Baccus and Meister, 2002).

There is some controversy regarding gain reduction in ganglion cells. Baccus and Meister (2002) report that gain reduces rapidly ($\sim$1 s) and that the change persists

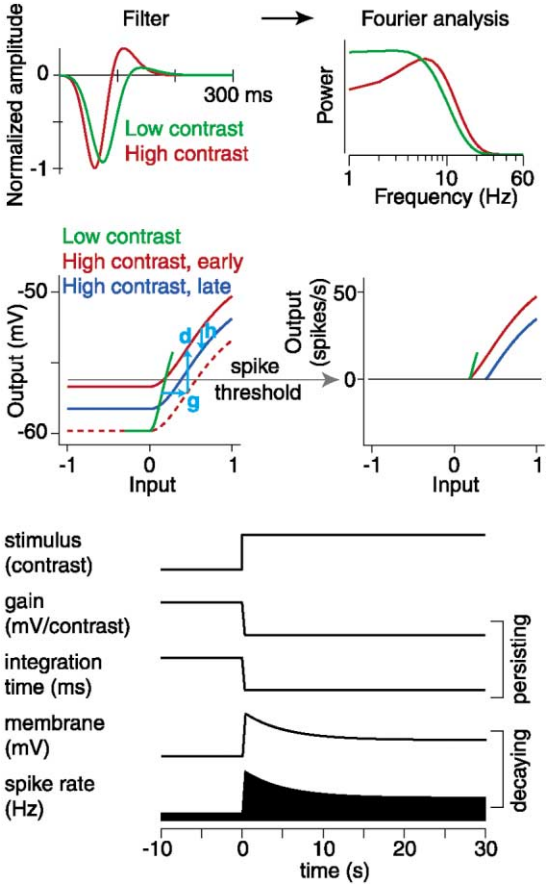


Linear-Nonlinear Model of Intracellular and Spiking Responses

(Left column) Linear-nonlinear model of intracellular response. The stimulus is filtered to generate the linear prediction of response (Input). Input is passed through the Input-Output function; Output closely resembles the measured intracellular response (Kim and Rieke, 2001; Rieke, 2001; Baccus and Meister, 2002). Four Input-Output functions and four Output traces are presented: cyan is a linear transformation of Input (Input × 3.5); red is a rectifying transformation (reduced responsiveness at hyperpolarized potentials and mild saturation at large depolarized potentials); green is identical to red with half the gain; black is identical to red with a 0.7mV hyperpolarization. (For Output, 0 = resting potential.)

(Right column) Linear-nonlinear model of spiking response. The stimulus and Filter (not shown) and Input are identical to the Left column. The Input-Output functions are the same as the membrane functions, multiplied by 10 and completely rectified at 0 spikes/s (i.e., red, green, and black do not go negative). Average spike rate is ~5 Hz for red and ~2.5 Hz following gain reduction (green) or hyperpolarization (black). Despite the fact that green and black have similar average spike rates, the timing of individual spike bursts differs. Black shows narrower bursts of larger amplitude, whereas green shows wider bursts of lower amplitude (see expanded trace, dashed box). The smallest bursts (*) are eliminated by hyperpolarization (black) but not by gain reduction (green).

This simulation, performed in Matlab (Mathworks, Natick, MA), is representative of the ganglion cell responses in the study by Baccus and Meister (2002).



Three Mechanisms of Contrast Adaptation in Ganglion Cells

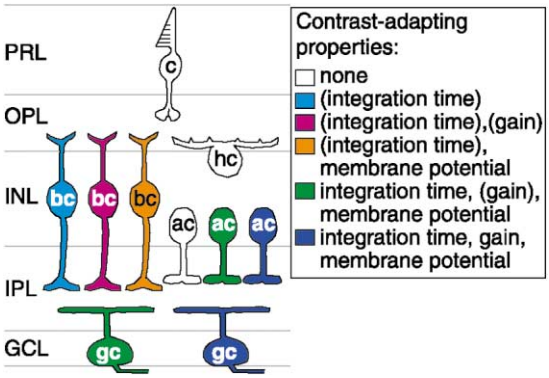
(Top row) Left, The filter (for both intracellular and spiking responses) peaked earlier and became narrower during high contrast (i.e., shorter integration time). The change in the spike filter was apparent ~100 ms after the switch to high contrast (Baccus and Meister, 2002). Right, Fourier analysis of the two filters. After the switch to high contrast, the tuning goes from low-pass (about equal sensitivity to ~1–4 Hz) to bandpass (peak sensitivity at ~6 Hz).

(Middle row) Left side shows input-output function for membrane potential. After the switch to high contrast, the cell's gain (g) reduces (green line stretches to red dashed line), and the cell depolarizes (d; red line). Following prolonged exposure to high contrast (blue), the cell slowly hyperpolarizes (h) back toward green by ~50%. Right side shows input-output function for spikes (a rectified, scaled version of the membrane function). After the switch to high contrast, the gain reduces (slope changes from green to red); prolonged exposure to high contrast causes an apparent rightward shift (red to blue).

(Bottom row) Time course of contrast adaptations.

for the duration of high contrast (Second Figure); Kim and Rieke (2001) agree that gain reduces rapidly (~1 s) but find it then to continue declining slowly (~10–20 s). The discrepancy may relate to the different recording conditions: current clamp (Baccus and Meister, 2002) versus voltage clamp (Kim and Rieke, 2001). In current clamp, prolonged contrast evoked a slow hyperpolarization, and this should increase driving force on depolarizing inputs (i.e., whose reversal potential is positive to the resting potential). This increased driving force would slowly *increase* responsiveness, which might cancel the slow *decrease* in gain that was evident in voltage clamp (Kim and Rieke, 2001); the net effect, in current clamp, might be no slow reduction in gain (i.e., which is what Baccus and Meister report).

Why should the retina adapt to high contrast in three



Contrast Adaptations in Retinal Circuitry

Different cell types showed unique patterns of contrast adaptation on the three properties. The properties in () indicate adaptations that were <~40% of the largest adaptations observed in ganglion cells. c, cone; hc, horizontal cell; bc, bipolar cell; ac, amacrine cell; gc, ganglion cell; PRL, photoreceptor layer; OPL, outer plexiform layer; INL, inner nuclear layer; IPL, inner plexiform layer; GCL, ganglion cell layer.

ways? Shortening integration time reduces sensitivity to low temporal frequencies, which are partially redundant components of the stimulus that can be safely eliminated when the signal is strong (Second Figure). Reducing gain protects against response saturation. The rapid depolarization (and consequent increase in ganglion cell spiking) might usefully signal that the scene has changed, but prolonging the high spike rate would be expensive metabolically (Attwell and Laughlin, 2001). Thus, the subsequent slow hyperpolarization (and reduction in spike rate) might conserve energy. Of course, a ganglion cell could reduce spike rate by reducing gain, instead of hyperpolarizing. However, hyperpolarizing might be advantageous for preserving spike timing (i.e., sharp bursts) and for removing the smallest, least significant bursts (First Figure).

The challenge now is to identify how contrast adaptation arises through synaptic and cellular mechanisms. To study synaptic mechanisms, we need to understand more thoroughly which cells interconnect. However, it is not clear that contrast adaptation depends primarily on inhibitory circuits, involving amacrine cells, rather than intrinsic cellular properties of bipolar and ganglion cells. Rieke (2001) found aspects of bipolar cell contrast adaptations (integration time, gain) that depend on an intrinsic mechanism, insensitive to voltage, and involving Ca^{2+}. Furthermore, some contrast adaptation in ganglion cells (gain) could be explained by effects on spike generation related to Na^{+} channel inactivation (Kim and Rieke, 2001). Thus, some features of retinal contrast adaptation may depend on intrinsic cellular properties.

Jonathan B. Demb
Department of Neuroscience
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania 19104

Selected Reading

Attwell, D., and Laughlin, S.B. (2001). J. Cereb. Blood Flow Metab. *21*, 1133–1145.

Baccus, S.A., and Meister, M. (2002). Neuron *36*, this issue, 909–919.

Benardete, E.A., and Kaplan, E. (1999). Vis. Neurosci. *16*, 355–368.

Brown, S.P., and Masland, R.H. (2001). Nat. Neurosci. *4*, 44–51.

Chander, D., and Chichilnisky, E.J. (2001). J. Neurosci. *21*, 9904–9916.

Kim, K.J., and Rieke, F. (2001). J. Neurosci. *21*, 287–299.

Rieke, F. (2001). J. Neurosci. *21*, 9445–9454.

Sakai, H.M., Wang, J.L., and Naka, K. (1995). J. Gen. Physiol. *105*, 815–835.

Shapley, R.M., and Victor, J.D. (1978). J. Physiol. *285*, 275–298.

Smirnakis, S.M., Berry, M.J., Warland, D.K., Bialek, W., and Meister, M. (1997). Nature *386*, 69–73.

Victor, J.D. (1987). J. Physiol. *386*, 219–246.

Walraven, J., Enroth-Cugell, C., Hood, D.C., MacLeod, D.I.A., and Schnapf, J.L. (1990). In Visual Perception: The Neurophysiological Foundations, L. Spillman and J.Z. Werner, eds. (San Diego: Academic Press), pp. 53–101.

Orientation Tuning—A Crooked Path to the Straight and Narrow

Neurons in visual cortex are selective for the orientation of a visual stimulus, while the receptive fields of their thalamic input are circular. Cortical orientation selectivity arises from the organization of both thalamic input and local cortical circuits. In this issue of *Neuron*, Schummers and colleagues provide evidence that the local circuit mechanisms contributing to orientation selectivity differ depending on the local organization of the orientation map.

Since the first reports of optical mapping of orientation preference in visual cortex (Blasdel and Salama, 1986; Grinvald et al., 1986; Bonhoeffer and Grinvald, 1991), the intrinsic beauty of orientation maps (see Figure) has captured the attention of the vision community. More than a few journal covers have been graced by these images. But the beauty of orientation maps is more than skin deep. A major challenge for neuroscience is to understand the neural mechanisms that lead to perception and behavior. And over the last several decades, studies of the mechanisms that the cortex uses to generate neurons with orientation selectivity from LGN inputs with circular receptive fields have played a central role in this endeavor. A persistent challenge in linking function to mechanisms, however, has been the difficult task of relating the functional properties of neurons to the underlying neural circuits. Orientation maps have proven to be one way to bridge this gap. Another has been the use of intracellular recordings of visual responses, allowing synaptic inputs to be related to output spikes.

In this issue of *Neuron*, Schummers, Mariño, and Sur (2002) combine optical imaging of orientation maps with intracellular recording of visual responses to provide some surprising new insights into how cortical circuits can shape orientation selectivity. The most important difference between this and previous intracellular studies is that Schummers et al. focused on a comparison between neurons at "pinwheel" centers (see Figure) ver-