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.

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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-

sus those located at regions where orientation preference changes more gradually. In these technically challenging experiments, orientation maps were first elucidated by imaging the locations in cortex that were activated by visual stimuli of various orientations. These images revealed the locations of the characteristic orientation pinwheels, where neurons tuned for widely disparate orientations converge to a singularity, as well as regions where orientation preference shifts more gradually and neighboring neurons share a common preference (see Figure). These locations were then targeted for intracellular recording and measurements of visually evoked changes in membrane potential and action potential firing. The measurements of membrane potential provided an estimate of the orientation preference of the inputs to each cell, while the spiking provided a measure of the cell's transformation of this input to its orientation-tuned output.

Previous studies have shown that, based on spiking outputs, individual neurons at pinwheel centers are just as well-tuned for orientation as those in constant-orientation regions (e.g., Maldonado et al., 1997). Schummers et al. (2002) obtained the same result based on their measurements of action potentials. But they found that the underlying changes in membrane potential were highly dependent on location within the orientation map. For neurons in constant-orientation regions, changes in membrane potential were just as well-tuned for stimulus orientation as the spiking responses. Schummers et al. found, however, that neurons at orientation pinwheels had subthreshold membrane depolarizations at all stimulus orientations. A further analysis showed that the membrane potential responses of the cells were closely correlated to orientation preferences mapped to regions surrounding the cell. Cells having neighbors with a diversity of orientation preferences had broadly tuned membrane potential changes, while those with similarly tuned neighbors had narrowly tuned changes in membrane potential. But the spiking responses did not show this correlation.

Further studies will be required to better resolve the precise mechanisms underlying the disparate results that Schummers et al. obtained for neurons at pinwheels versus constant-orientation regions. The subthreshold changes in membrane potential measured by Schummers et al. must reflect a combination of both excitation and inhibition. The relative contributions of excitation and inhibition can be revealed by measuring visual responses while injecting hyperpolarizing or depolarizing current. Schummers et al. report results from this manipulation for one neuron located at a pinwheel and show that responses at the nonpreferred orientation reflect both excitation and inhibition. If this observation holds up, it will provide further support for the conclusion that substantially different mechanisms are operating at different cortical locations. We can expect to see a good deal more investigation of this issue in the future.

These new findings imply that the mechanisms that generate orientation selectivity depend on the location of a neuron within the orientation map. The cortex may find multiple solutions to the same problem, depending on the local opportunities and constraints. This interpretation is also consistent with the diversity of models that are able to mimic the orientation selective behavior of
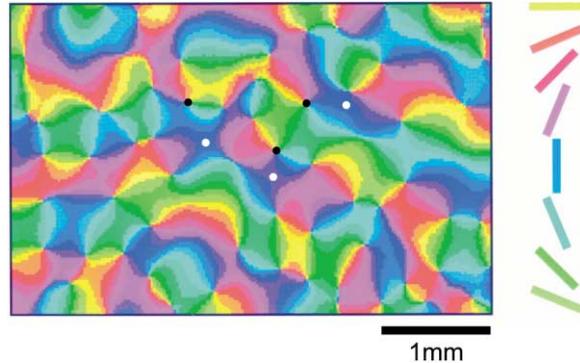
Orientation Preference Map Obtained from Optical Imaging of Cat Cortical Area 17

Regions responding preferentially to visual stimuli of various orientations are color coded according to the scale to the right. Locations of selected orientation "pinwheels" are marked by black circles. Locations of selected "constant-orientation" regions tuned for vertical stimuli are indicated by white circles. Modified from Hubener et al. (1997).

cortical neurons (see Ferster and Miller, 2000, for review). Previous intracellular recording studies showing that inhibitory and excitatory synaptic inputs are tuned to the same orientation as the spiking output have led to the development of a compelling "feedforward" model with "push-pull" inhibition (Ferster and Miller, 2000). The results that Schummers et al. obtain at constant-orientation regions are also consistent with this mechanism. But the broadly tuned synaptic input that Schummers at al. observe at orientation pinwheels suggests that older "feedback" models may also be viable for these neurons. (See Ferster and Miller [2000] for a detailed review of various models and relevant experimental data.)

The decision of Schummers at al. to compare neurons at different locations in the orientation map was undoubtedly influenced by other work in the Sur lab. This work shows that short-term plasticity of orientation preference depends on the location of the neuron within the orientation map (Dragoi et al., 2001), suggesting that the potential for plasticity, like the orientation specificity of synaptic input, depends on the orientation preferences of nearby neurons. Such differences could reflect a difference in the orientation preference of neurons providing local excitatory or inhibitory connections.

Together, these and the present findings strongly suggest that local connections near orientation pinwheels interconnect neurons with disparate orientation preferences, while those at constant orientation regions interconnect neurons with similar orientation preference. Anatomical findings also support this interpretation (Yousef et al., 2001). It remains to be determined why the cortex would choose these different paths to the same result. Perhaps wire-length optimization drives the emergence of the pinwheel configuration in orientation maps (Koulakov and Chklovskii, 2001) and this necessitates a range of mechanisms for generation of orientation selectivity. Alternatively, the neuronal behavior that results from the disparate circuits may not truly be the same. For example, the differences in short-term plastic-

ity that arise from the different solutions may provide an adaptive advantage.

An intriguing implication of the Schummers et al. findings is that the precise mechanisms that generate orientation selectivity could be different at different locations in cortex—there is not just one way in which orientation selectivity is generated. This notion challenges the conventional view of visual cortex as a more-or-less crystalline structure in which the same circuit iterates the same function across the cortical surface, with each module varying only with respect to the portion of the visual field represented. If the relationships between local circuits and function vary across the cortical surface, then the challenge for linking circuits to function becomes even greater than assumed. These findings therefore underscore the need for the development of increasingly sophisticated methods to more directly link neural circuits to function. Rather than extrapolating between one set of studies which reveals circuits and another that reveals function, further progress will likely benefit from more directly correlating the circuitry of single cortical neurons or identified cell types to their functional properties in vivo. These new findings should provide a much-needed push in that direction.

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A Hidden Sensory Function for Motor Cortex

Sensory perception has traditionally been attributed to the activation of sensory cortices. However, by inducing an illusory perception of movement, Naito and colleagues show in this issue of *Neuron* that the illusory perception of movement is related to activation of primary motor cortex.

Which patterns of neuronal activity are related to kinesthesia—that is, with the sense of our own corporal movements? It is not easy to tackle this question, because a number of factors come into play in this perceptual process. When a voluntary movement is made, in addition to the neuronal activity associated with kinesthesia, there is also cortical activity related to the intention of movement (Roland et al., 1980), to the motor commands themselves (Georgopoulos et al., 1982) and to the sensory information fed back into the cortex by proprioceptors (Dietz, 2002). To study kinesthesia, then, what is required is an experimental paradigm that allows the neuronal activity associated with this phenomenon to be isolated from the neuronal activity of other processes that naturally occur simultaneously with it.

By taking advantage of an interesting sensory illusion, Naito and colleagues (2002) inquired into the neural basis of the sense of kinesthesia in human subjects. They were able to produce an illusory perception of movement in either one of the hands through a vibratory stimulus (80 Hz) applied to the tendon of the *carpi ulnaris extensor* muscle of the wrist. The illusion of movement is produced as the vibration in the tendon activates the muscle spindles in a similar way to when the muscle actually stretches.

In principle, this illusion should allow us to study the patterns of neural activity associated with kinesthesia in the absence of movement, but the problem is how to eliminate the cortical activity arising in the muscle spindles activated by the vibratory stimulus? Naito and colleagues resolved this problem elegantly by *transferring* the illusion of movement to the nonstimulated hand. The transference of the illusion occurs when both hands come into skin contact (palm to palm or palm to back of hand). Upon detecting that the vibrated hand is moving and that both hands are in contact, the brain—after an interval of a few seconds (4–12)—interprets this information as if both hands were moving.

Since the subjects were not asked to generate any motor action, the hemisphere controlling the nonstimulated hand was free of any activity related to the intention of movement, to motor commands, and to the sensory information that motion would have been generated. It can be assumed that a pure sensory percept of kinesthesia exists in the hemisphere controlling the hand with the transferred illusion. The perception of the illusion of movement in the nonstimulated hand thus constitutes an ideal phenomenon for studying the neuronal basis of kinesthesia.

What is the pattern of neural activity related to the illusory perception of movement? By recording neuronal activity through fMRI, Naito and colleagues obtained an unexpected and surprising result: when the image of cortical activity during a control condition (stimulus vibration with separated hands) was subtracted from the image of cortical activity during the perception of the illusion (stimulus vibration with hands in contact), the only area that remained active—that can be related exclusively to the perception of the transferred illusion—was the area 4p in the primary motor cortex (MI). This result is surprising because, as the authors themselves mention, the sense of kinesthesia has traditionally been associated with the somatosensory cortex.

Such an extraordinary result required incisive tests,