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INTRODUCTION

Amacrine cells: Seeing the forest *and* the trees

> You only need sit still long enough in some attractive spot in the woods that all its inhabitants may exhibit themselves to you by turns.
> – Henry David Thoreau, *Walden*

The amacrine cell class comprises as many distinct cell subtypes as the rest of the retina combined. Though bewildering in their number and diversity, amacrine cells nonetheless often exhibit common morphological motifs and physiological features, suggesting the alluring possibility that we might someday understand them as a functional collective. Our progress toward that "big picture" goal is frequently sidetracked, however, by the morphological beauty and functional complexity of each individual subtype that appears beneath our objectives or electrodes. In this special issue of *Visual Neuroscience*, a collection of scholarly reviews of amacrine cell research reflects both the field's appreciation for each individual species of amacrine cell and our ongoing efforts to understand the amacrine forest as a whole. In his opening Perspective, **Masland** argues that the remarkable morphological consistency *within* amacrine cell subtypes likely indicates that each performs specific tasks within the retinal circuitry, and that the daunting diversity *between* subtypes reflects the diversity of ganglion cells, the downstream beneficiaries of amacrine cell processing. In other words, behind every great ganglion cell, there is a great amacrine cell (or two).

Although we are far from matching each ganglion cell type with its supporting amacrine cell(s), we do know that behind every directionally selective ganglion cell, there exists a network of starburst amacrine cells (SBACs). Easily distinguished by their spectacular eponymous dendritic arbor, SBACs play a critical role in directional selectivity, one of the most thoroughly studied visual computations performed in the retina. Here, **Taylor and Smith** review the synaptic and biophysical mechanisms underlying directional responses in SBAC dendrites and present a network model that gauges the impact of reciprocal GABAergic inhibition between synaptically coupled SBACs. A role for acetylcholine, the SBAC's other neurotransmitter, in directional selectivity is less clear, but cholinergic transmission does play a critical role in the retinal waves that propagate across the neonatal retina and contribute to the organization of the retinofugal projections to targets downstream in the visual pathway. **Ford and Feller** discuss how this cholinergic circuitry in the retina assembles and dissembles during the first postnatal week.

Although perhaps less handsome than their starburst counterparts, AII amacrine cells hold the distinction as the most numerous amacrine cell in the mammalian retina. Long known for their central role in the rod pathway, AII amacrine cells have recently been shown to mediate "crossover inhibition" between the ON pathway and OFF ganglion cells. **Demb and Singer** describe recent work on how the bidirectional gap junctions between AII amacrine cells and ON cone bipolar cells enable AII amacrine cells to play distinct roles in night and day vision.

Thanks to amacrine cells, bipolar cells are not mere intermediaries that passively relay the conversation between photoreceptors and ganglion cells. Amacrine cells spice up the lives of bipolar cells by shaping and nuancing the outputs of distinct classes of bipolar cells. **Grimes** reveals how amacrine cell synaptic contacts with bipolar cell terminals enliven signaling by contributing to the temporal and spatial processing of visual information. Amacrine cells provide reciprocal feedback inhibition to bipolar cells, to modulate the time course of transmitter release. Other amacrine cells provide lateral inhibition to bipolar cells, shaping spatial properties of the visual signal. Like a good editor, amacrine cells provide feedback to bipolar cells to refine their coarse signals to allow them to elegantly communicate with ganglion cells.

Amacrine cells, the major inhibitory interneurons in the retina, influence bipolar cells, ganglion cells, and other amacrine cells by releasing inhibitory neurotransmitters that activate ionotropic and metabotropic postsynaptic receptors. Roughly, half of the amacrine cells release GABA and the other half release glycine. **Zhang and McCall** focus their review on the ionotropic receptor targets of these two inhibitory neurotransmitters. The diversity of amacrine cells and GABA and glycine receptor subtypes combine to give rise to a rich melange of inhibitory signaling within the inner plexiform layer (IPL). Inhibition is also mediated by metabotropic G protein-coupled receptors (GPCRs), an important yet often overlooked aspect of retinal synaptic transmission. Both conventional and neuropeptide neurotransmitters, released by amacrine cells, modulate visual processing by activating GPCRs. **Gleason** examines the complex unconventional world of GPCR signaling within and between amacrine cells. Her review shows that amacrine cell signaling through GPCRs has both subtle and powerful effects on retinal processing.

The tremendous morphological, chemical, and functional diversity of amacrine cells may overwhelm the pessimists among us. However, through the diligent efforts of anatomists, physiologists, and molecular biologists digging away in the amacrine cell forest, some common amacrine cell motifs are emerging. Work from a number of laboratories suggests that wide-field and narrow-field amacrine cells play fundamentally distinct roles in visual processing. Wide-field amacrine cells signal over long distances, are typically GABAergic, and usually ramify within in a narrow stratum of the IPL. Narrow-field amacrine cells signal over short distances, are

typically glycinergic, and signal between IPL strata. We also know that amacrine cells participate in a number of different forms of inhibition—conventional, serial, and crossover—that, together, contribute to the richness and complexity of visual processing within the IPL. Although there is still much to be learned, we now have a much greater appreciation of this forest and its elegant trees. Like Thoreau, our time in these woods has been well spent.

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