Neurons show their true colours

How do we tell red from green? Work on the primate retina shows how neural circuitry combines signals from individual cone photoreceptors to provide the basic building blocks for colour vision. See Article p.673

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The processing of visual information begins in the retina, where specialized neurons called photoreceptors absorb light and stimulate multiple neural circuits. Each circuit generates specific patterns of electrical activity and converges on one of about 20 types of retinal ganglion cell. These cells’ axons — the optic nerve fibres — then convey signals to various brain targets. For colour vision, specific retinal circuits compare the activity levels of different types of cone photoreceptor cells that have different spectral sensitivities. On page 673 of this issue, Field et al. describe simultaneous recordings from hundreds of ganglion cells, and a new method to map the inputs that these cells receive from individual cones. The results provide insight into the initial stages of colour vision.

Old World primates, including humans, have three types of cone photoreceptors that are maximally sensitive to long (L), middle (M) or short (S) wavelengths of light. In isolation, however, each cone is colour-blind because its activity depends on both the wavelength and intensity of incident light. For example, an M cone’s activity would be the same for a dim green light and a bright red light. Neural circuits derive a colour signal by comparing the activity of different cone types — cone opponency. In primate retinas, there are two broad classes of opponency: S–(L+M) opponency contrasts the activity of S cones with the combined activity of L and M cones, whereas L–M opponency contrasts the activity of L and M cones.

Primate cones are arranged in a mosaic, presenting several challenges to implementing cone opponency (Box 1). First, only a single cone exists at each location in the mosaic, so comparing cone signals confounds spatial and spectral information. Second, S cones are sparse, limiting the spatial resolution of S–(L+M) opponency. Third, the M/L cone arrangement is random or nearly random, leading to ‘clumps’ of either cell type. This limits the spatial resolution of L–M opponent signals. For example, L–M resolution must be coarser at the centre of a clump of L cones than in a region where L and M cones alternate.

S–(L+M) opponency is an ancient and well-developed subsystem of colour vision. The genes encoding the S and M/L cone opsins — proteins that determine spectral sensitivity — diverged more than 500 million years ago. Moreover, the primate retina contains specialized ganglion cells for computing S–(L+M) opponent signals. The small bistratified ganglion cells, for example, receive excitatory inputs from S cones through S–cone bipolar cells, and (L+M) cone signals oppose the S-cone signals by means of two distinct retinal pathways. Similar cone opponency is mediated by ganglion cells in other mammals.

As for L–M opponency, this depends on a third opsins that arose in Old World primates less than 40 million years ago. The neural mechanisms underlying L–M opponency have remained elusive. It could be that a specialized ganglion-cell type analogous to the small bistratified cells collects pure antagonistic signals from L and M cones. So far, however, there has been no definitive identification of such cells.

Alternatively, L–M opponency might arise in other cells that existed before the emergence of the third cone opsin. A favourite candidate is the midget ganglion cell, named for its small size in the fovea — the central part of the retina. In the fovea, each of these cells connects through a midget bipolar cell to a single cone, and thus receives an excitatory ‘centre’ signal that is selective for L or M. The centre signal is opposed by a ‘surround’ signal that is driven by the surrounding cones. Consequently, even if the surround draws randomly on L and M cones, most foveal midgets will exhibit a degree of L–M opponency because the centre signal is always pure (Box 1).

Each ganglion-cell type tiles the retina completely, but is larger in the retinal periphery than in the fovea. The centre signals of the larger midget cells in the periphery therefore connect to a dozen or more cones, and analysis of these connections should provide information about the M/L selectivity of peripheral midget cells. The selective-wiring hypothesis predicts selective connections between each midget cell and either M or L cones; the random-wiring hypothesis, by contrast, predicts random connections. Evidence has been reported in favour of both hypotheses, making it difficult to rule either out definitively. To date, one roadblock has been that inputs to
Cone opponency in the primate retina

A schematic representation of the mosaic arrangement of cones in the monkey retina that are sensitive to long (L, red), middle (M, green) and short (S, blue) wavelengths of light. S cones are rare, constituting 5–10% of the mosaic, and L cones outnumber M cones by about 2 to 1. L and M cones are arranged near randomly. For simplicity, the cone mosaic is shown as rectangular in arrangement. The actual mosaics are more hexagonal and also less regular: in the central all-cone fovea, cones are tightly packed, whereas in the retinal periphery they are separated by the more numerous rod photoreceptors, which are used for seeing in dim light.

a. In the central fovea, a midget ganglion cell combines an excitatory centre-region signal driven by a single cone — outlined in white — with an opposing signal from the surrounding region driven by surrounding cones (outlined in black). This cell would have M–L opponency.

b. A midget ganglion cell that aligns with a clump of L cones, however, would lack opponency, because the centre and surround are driven by the same class of cones. c. In contrast to foveal midget ganglion cells, a peripheral midget cell may receive excitatory input from a dozen cones. There is a bias, measurable across the population of cells, in which the centre region of the receptive field is wired to favour one cone type, tending towards cone purity. In this case, for example, the midget cell avoids some M cones near those that comprise the centre (marked with a yellow asterisk) in favour of the L cones that make up the majority. This cell will have L–M opponency. In this example, the S cones are skipped, but a subgroup of midget cells is connected with S cones.

d. For S–(L+M) opponency, a small bistriated ganglion cell receives an S-cone input that is opposed by M/L cone inputs. Because of the irregular layout of S cones and other features of the underlying neural circuitry, these cells lack the canonical centre-surround structure found in many other ganglion-cell types, including midget cells.1,5,8, J.B.D. & D.H.B.

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