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The Discovery of Spectral Opponency in Visual Systems and its Impact on Understanding the Neurobiology of Color Vision

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The two principal theories of color vision that emerged in the nineteenth century offered alternative ideas about the nature of the biological mechanisms that underlie the percepts of color. One, the Young-Helmholtz theory, proposed that the visual system contained three component mechanisms whose individual activations were linked to the perception of three principal hues; the other, the Hering theory, assumed there were three underlying mechanisms, each comprising a linked opponency that supported contrasting and mutually exclusive color percepts. These competing conceptions remained effectively untested until the middle of the twentieth century when single-unit electrophysiology emerged as a tool allowing a direct examination of links between spectral stimulation of the eye and responses of individual cells in visual systems. This approach revealed that the visual systems of animals known to have color vision contain cells that respond in a spectrally-opponent manner, firing to some wavelengths of stimulation and inhibiting to others. The discovery of spectral opponency, and the research it stimulated, changed irrevocably our understanding of the biology of color vision.

Keywords color vision, color theory, single-unit electrophysiology, spectral opponency, eye, lateral geniculate nucleus, Hering, Young-Helmholtz

Current accounts of the coding of color information in mammalian visual systems are derived from a combination of results obtained from a large body of behavioral and biological measurements (for recent reviews, see Gegenfurtner & Kiper, 2003; Solomon & Lennie, 2007; Conway, 2009; Stockman & Brainard, 2010; Lee, 2011). Fundamental to these is the inclusion of a processing stage in which signals originating from the activation of retinal cones containing different types of photopigment converge onto cells where they are combined in a spectrally-opponent fashion so that the recipient cell is excited when the eye is stimulated by some wavelengths of light and is inhibited by stimulation from other wavelengths. It has been known for some time that the interactions that lead to these spectrally-opponent responses are set up initially within the neural networks of the retina (Dacey, 1999)—in some instances, as for example in the retina of the macaque monkey, apparently right in the photoreceptors themselves as a result of a feedback from second-order cells (Packer et al., 2010). Spectrally-opponent signals also have been detected at multiple locations throughout the central visual system (Lennie & Movshon, 2005; Conway, 2009). The discovery of spectral opponency in cells in the visual pathways and the recognition that it represents a basic feature of the coding process underlying color vision

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came about over a relatively short time period starting around the middle of the last century and that realization triggered a fundamental paradigm shift in the quest to understand the biological basis for color vision. This article provides a retrospective review of research conducted during that time period, showing how it evolved and how results from those efforts came to be incorporated into our current conception of the biological underpinnings of color vision.

Background

From behavioral tests of vision and phenomenological observations, two dominant sets of ideas of how color vision works emerged during the nineteenth century (Wasserman, 1978; Turner, 1994; Crone, 1999; Mollon, 2003). Based largely on data obtained from psychophysical studies involving the use of color matching, an idea associated mainly with the observations and writings of Thomas Young, James Clerk Maxwell, and Hermann von Helmholtz, and now commonly referred to as the Young-Helmholtz theory, assumed that color vision derives from the univariant responses of three distinct sets of nervous fibers, each with its own unique spectral responsivity. As Helmholtz himself put it, "The eye is provided with three distinct sets of nervous fibres. Stimulation of the first excites the sensation of red, stimulation of the second the sensation of green, and stimulation of the third the sensation of violet" (Helmholtz, 1924, p. 143; Helmholtz, 1876). Thus, human color vision is at root trichromatic. On the other hand, starting principally from observations about color appearance, Ewald Hering and others were struck by the basic incompatibility of some color percepts—for instance, that although blueish-greens and reddish-yellows are commonly seen, reddish-greens or blueish-yellows are never perceived—and on this basis devised the competing notion that color vision rests on the operation of three paired, opponent-signed mechanisms in the visual system, each of the three providing support for a pair of mutually exclusive sensations: white-black, red-green, and yellow-blue (Hering, 1878, 1964).

Although there was an extended, at times acrimonious, debate between adherents of these two ideas (Turner, 1993), it eventually became apparent that these two types of theory might be applicable to different stages of the processing underlying color vision. To accommodate that position, so-called *zone theories* were proposed in which these two competing conceptions are assumed to reflect organizations that characterize different levels of processing in the visual system. The arrangement sketched in Fig. 1 is an example of one modern zone concept (Kaiser & Boynton, 1996) in which there are three types of cone photoreceptors (now conventionally identified as S, M, and L to indicate that they have maximum absorption of light in the short, middle, and long wavelengths, respectively). Each cone responds univariantly to light stimulation. The outputs from these receptors are then fed into two classes of spectrally-opponent cells where they are combined in a push-pull fashion (L-M and S-[M+L]), while in other cells the inputs from M and L cones are combined additively (spectrally nonopponent cells). These two types of organizations are most frequently said to relay the neural information required to support, respectively, the color and luminance aspects of vision. However, to account for the full range of color vision phenomena, particularly various features of color appearance—as explained below—it has become usual to assume that the visual system must include at least one additional transformation beyond the two shown in Fig. 1. Early multiple-stage zone theories were offered by Johannes von Kries (1882) and Georg Elias Müller (1930) with a later, more formalized version being proposed by Deane Judd (1949). There are now numerous modern

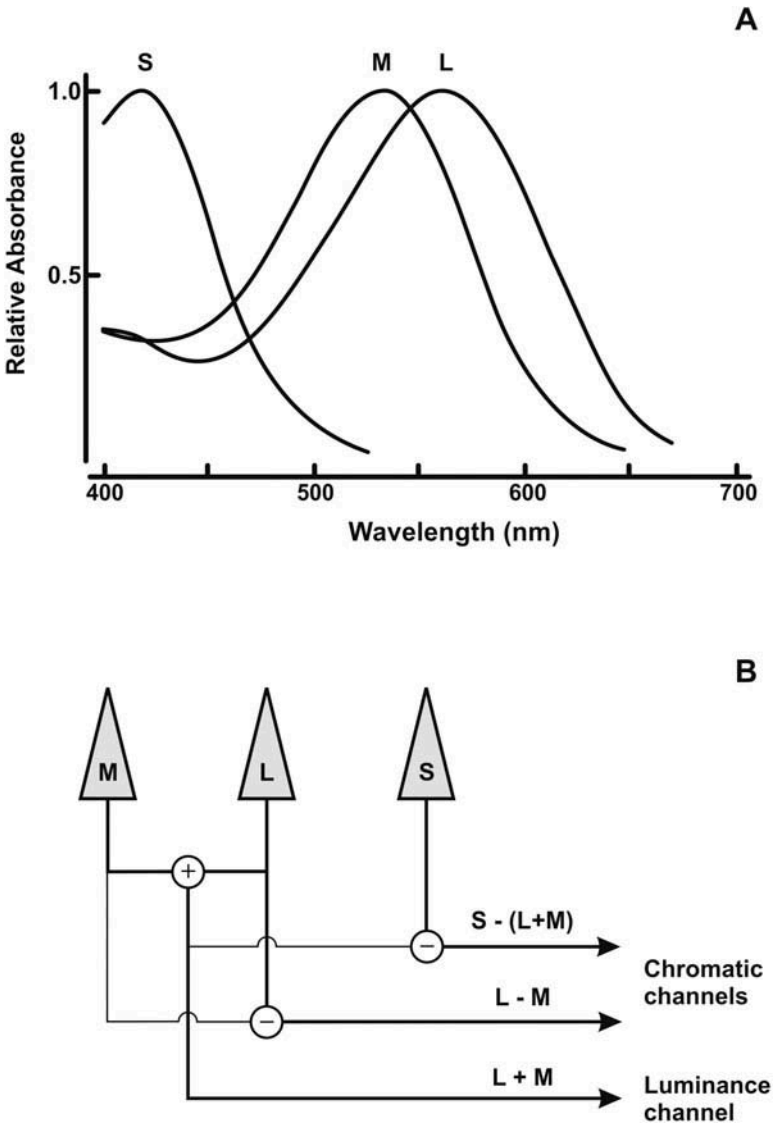

Figure 1. (A) Normalized absorption curves for the three classes of cone photopigments of the human retina (S, M, and L are abbreviations, indicating that the resident pigment has maximum sensitivity to, respectively, short, middle and long wavelengths). (B) One popular modern schema to explain how signals derived from activations of the three cone types are combined in the early stages of the visual system. In the chromatic channels, signals from the cones are combined in two subtractive arrangements (L-M, and S-[L +M]); in the luminance channel, signals derived from the M and L cones are summed.

versions of zone theories that make varying assumptions about both the nature and weighting of inputs at each process stage (e.g., Guth, Donley, & Marrocco, 1969; Ingling & Tsou, 1977; De Valois & De Valois, 1993; Stockman & Brainard, 2010; Neitz & Neitz, 2011).

An Anatomical Hypothesis

The two principal color vision theories that emerged in the nineteenth century were based entirely on behavioral and phenomenological observations. Although at that time knowledge about visual system structure and function was still quite limited, both theories contained clear implications about the nature of the underlying biology. On one side, the Young-Helmholtz approach posited the presence in the eye of three distinct sets of nerve fibers that varied in their spectral responsivity (and thus this idea is sometimes characterized as a component theory); alternatively, Hering's opponent idea required that there must be visual system elements capable of negative as well as positive responses (in his terminology, *dissimilation* and *assimilation*). For a significant portion of the history of this topic, the opponent arrangement was thought to be at odds with the developing understanding of nervous system physiology. Thus, for example, Selig Hecht, a distinguished vision specialist of the early part of the twentieth century, said that Hering's ideas about assimilation and dissimulation "mean nothing in the modern physiology of sense organs and of nerves" (quoted by Leo Hurvich in an evaluation of Hering's many contributions, 1969, p. 506). Based on such perceived incompatibility, many vision scientists of the time rejected the Hering type of approach. Starting in the 1950s, these objections quickly faded, as will be described presently, but in the meantime a possible biological basis for the component approach was proposed that was based on the anatomical organization of a prominent structure in the central visual system, the lateral geniculate nucleus (LGN).

The LGN is the thalamic relay nucleus for the primary visual system, serving as the location where optic nerve fibers departing from the retina synapse on cells whose axons then project onward to the visual cortex. In many mammals, the LGN is a conspicuously laminated structure. In Old World anthropoids, the LGN was conceived classically as being comprised of six such layers. As illustrated schematically in Fig. 2, three of these layers (Layers 1, 4, and 6, as numbered from base-to-apex) receive inputs from the contralateral eye, while the remaining three (Layers 2, 3, and 5) are innervated by optic nerve fibers coming from the ipsilateral eye.

In an early anatomical investigation, Le Gros Clark and Penman (1934) had discovered that small localized lesions made in the retina induced clear degenerative changes in a band of cells resident in each of the three layers connected to that eye with that band radiating in a straight line from the hilum to the convex surface of the LGN. In considering this arrangement, Le Gros Clark was led to propose that the three layers in the LGN that are connected to each eye might receive inputs from one of the three sets of fibers required by the Young-Helmholtz theory—mediating, respectively, the sensations of red (Layers 5, 6), green (Layers 3, 4), and blue (Layers 1, 2)—and providing thereby a potential structural correlate for this popular trichromatic theory (Le Gros Clark, 1940, 1949; Le Gros Clark & Chacko, 1947). In developing his provocative idea, Le Gros Clark drew support from three sources: (1) The differences in LGN lamination patterns between primate species that were believed to differ in their color vision capacities, (2) the differences in lamination patterns for those portions of the LGN that subserved central and peripheral vision, spatial regions that were thought to support characteristically different color vision capacities, and (3) the selective neural degeneration patterns induced in the LGN in animals that had been reared in spectrally-restricted environments.

In reading the various accounts of this idea, one senses that Le Gros Clark offered his anatomical hypothesis only somewhat tentatively, referring to it at one point as, merely, "an interesting speculation" (Le Gros Clark, 1940, p. 559). Nevertheless, some years later Gordon L. Walls, the great comparative vision specialist, was motivated to undertake an

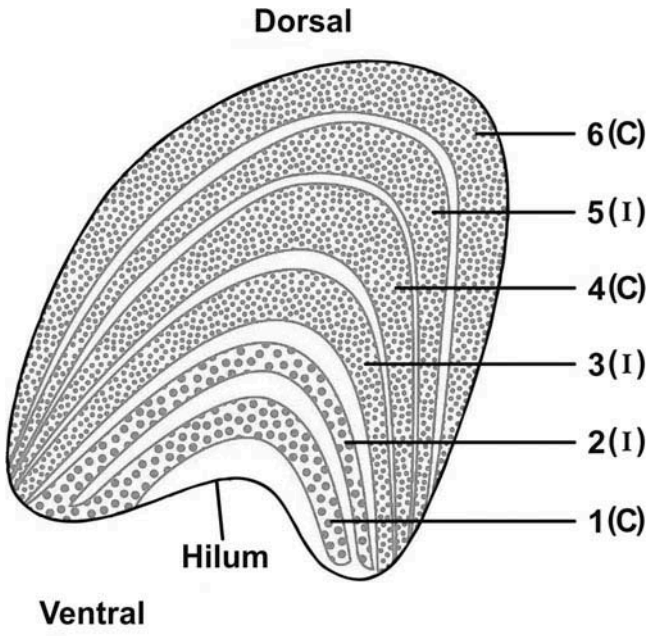

Figure 2. A sketch illustrating a coronal section of the LGN from the visual system of a catarrhine primate. The six laminae are individually innervated by optic nerve fibers coming from the two eyes; Layers 1, 4, and 6 receiving their inputs from the contralateral (C) eye; Layers 2, 3, and 5 from the ipsilateral (I) eye. As described in the text, in the anatomical theory proposed by Le Gros Clark, each adjacent pair of laminae was proposed to mediate one of the three primary sensations of color that had been identified in the Young-Helmholtz theory.

exhaustive examination of the idea (Walls, 1953). Marshalling evidence from comparative neuroanatomy, from behavioral studies of color vision and visual pathology, as well as from visual deprivation experiments, Walls could find no support for Le Gros Clark's idea and drew the confident conclusion that "Each of the group of facts which Clark has ever adduced for his theory has been exhaustively reviewed. None has been found to constitute evidence for the theory" (Walls, 1953, p. 70). Although thus summarily rejected, and perhaps as a result subsequently mostly forgotten, the writings of Le Gros Clark on this topic nonetheless turn out to have had an important influence on future research because in his last publication having to do with his theory, Le Gros Clark concluded with the suggestion that "the geniculate nucleus in monkeys should be carefully explored by electrophysiological methods when the retina is stimulated by light of different wave lengths" (Le Gros Clark, 1949, p. 64). When that happened some years later, the results provided an important forward step in our understanding of color vision.

Granit and the Early Development of Retinal Physiology

> My own opinion, probably shared by most physiologists, is that the subject of colour vision can receive nothing but good from having to adjust itself to new facts obtained by purely physiological experiments on wavelength reception. (Granit, 1947, p. 316)

Electrophysiological studies of the eye in the form of analyses of the electroretinogram (ERG)—a gross electrical potential generated in the outer retina—date from the middle of the nineteenth century (Armington, 1974), but the modern era of retinal electrophysiology was initiated in the 1930s when the first recordings were made from single optic nerve fibers that had been painstakingly dissected from the lateral eye of the horseshoe crab, *Limulus polyphemus* (Hartline & Graham, 1932). Shortly thereafter, it became possible to make microelectrode recordings from the intact eye, an accomplishment that, over time, led to significant progress in understanding the nature of neural messages in the visual system. A pioneer in this enterprise was Ragnar Granit (1900–1991), a Finnish-Swedish physiologist who conducted a long series of investigations exploring the linkages between photic stimulation of the eye and the discharge patterns of single optic nerve fibers in a wide variety of different species. This work, for which Granit received the Nobel Prize in 1967, is summarized in detail in two books (Granit, 1947, 1955), as well as in numerous review papers (e.g., Granit, 1941, 1945a, 1968).

Among his important observations, Granit found that optic nerve fibers have a characteristic ongoing electrical activity that is manifested in the form of an aperiodic discharge of action potentials in the absence of any apparent stimulation of the eye. This feature, termed "spontaneous activity," was detected in all of the types of eyes that he recorded but particularly from cells in mammalian retinas. Granit clearly recognized the implication of this fact for understanding neural codes in sensory systems, noting that this means "normal reception consists in a modulation upon the background of spontaneous activity" (Granit, 1941, p. 572). He also observed, as Hartline had in earlier experiments conducted on both invertebrate and vertebrate optic nerves (Hartline & Graham, 1932; Hartline, 1938), that different fibers may respond in characteristically different ways to illumination of the eye: some firing to the onset of stimulation—either in a transient burst of action potentials or in a more sustained fashion—and some to the offset of stimulation, and still others at both the onset and offset of stimulation. All of these effects have been verified fully in subsequent investigations of the mammalian visual system.

A major goal of Granit's work was to determine the spectral response properties of optic nerve fibers. To accomplish this, he adjusted the intensity of a spectral light illuminating the eye until it produced a noticeable change in the spike discharge rate of a fiber, a point that was established by listening to the discharge patterns of fibers as they were amplified through a loudspeaker. This auditory process of determining response threshold was then repeated for a series of lights having different wavelength composition, thus allowing the eventual determination of a spectral sensitivity curve. Characterized in this fashion, the responses from optic nerve fibers fell into two large groups that Granit designated as being either *dominators* or *modulators*.

The dominators were fibers that had relatively broad spectral sensitivity. Fig. 3 shows examples of spectral sensitivity curves for dominator elements recorded from the cat optic nerve. As recorded from the dark-adapted eye (left panel) these units had a peak sensitivity at around 500 nm. Because that is also roughly the peak location for the standard scotopic spectral sensitivity function, Granit referred to these as *scotopic dominators*. At the time these recordings were made, there already had been a number of measurements of the absorption spectra of photopigments found in rods and, drawing on these, Granit was able to show that there was sufficiently good correspondence between the spectral absorption curves for rod photopigments and the spectral sensitivity of the scotopic dominators to make it clear that the predominant input to these optic nerve fibers must originate in the rods. When the eye was subsequently light adapted, the peak spectral sensitivity of these dominator elements sometimes shifted to longer wavelengths, achieving a new spectral

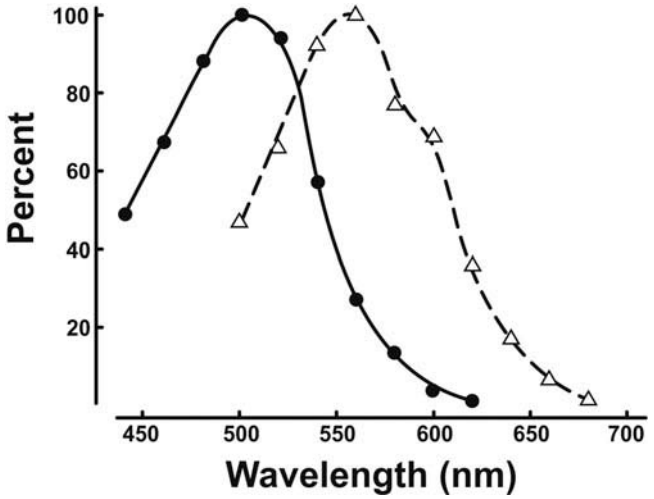

Figure 3. Mean spectral sensitivity curves measured for scotopic (solid circles, left) and photopic (open triangles, right) dominator elements recorded from optic nerve fibers of the cat by Granit. These were recorded as the eye was dark and light adapted, respectively. (Redrawn from Granit, 1955.)

peak at ~560 nm (and now referred to as a *photopic dominator*). The curve to the right in Fig. 3 shows the mean spectral sensitivity for 10 such measurements obtained from optic nerve fibers of the cat. The spectral transition seen here is analogous to that long known to index the spectral sensitivity changes detected by psychophysical measurements made as ambient lighting is progressively changed from dimmer to brighter, the Purkinje shift. To Granit, the obvious implication was that these photopic dominators must reflect those signals that originate in cones.

At the time Granit discovered the dominator elements, there were only a few direct measurements of cone photopigments, and none from mammalian eyes, so it was not possible for him to make direct comparisons between the spectral properties of the photopic dominator elements and cone photopigments in those species, but it seemed apparent that cone signals must be reflected in these photopic dominator recordings. Interestingly, not all the elements Granit studied showed this shift in spectral sensitivity; for example, only about one third of the optic nerve fibers in the eyes of cats shifted in this fashion, and in some species he tested (e.g., guinea pigs and rats), no photopic dominators could be detected. At this time, the eyes of rats and guinea pigs were often assumed to lack cones or to contain only a very sparse representation of such photoreceptors (Walls, 1942), and, thus, the failure to find photopic dominators in these species was not thought to be surprising. In any case, an important implication emerging from the study of these dominator elements was that both rod and cone signals can be communicated to the central visual system along the very same fibers with the nature of the information being transmitted dependent on the adaptation state of the eye.

A second type of signal that Granit detected in his recordings from optic nerve fibers was what he termed *modulators*. These had narrower spectral sensitivity functions than the dominators. In many cases (perhaps most, Granit does not make this clear), the modulator curves were derived indirectly by comparing the spectral sensitivity of optic nerve fibers before and after concurrent chromatic adaptation produced by exposing the eye to lights passed through blue, green, or red filters and thus the spectra obtained for these modulators effectively index the difference in spectral sensitivity between conditions of

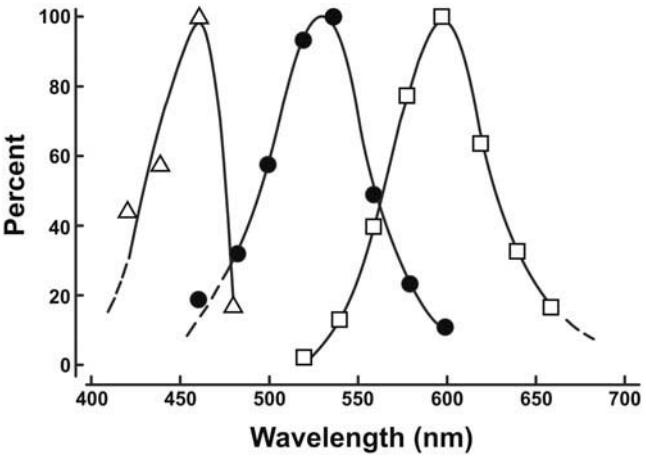

Figure 4. Mean spectral sensitivity curves obtained from the three classes of cat optic nerve fibers having modulator characteristics. The measurement methods are described in the text. (Redrawn from Granit, 1968.)

neutral and chromatic adaptation. Fig. 4 shows modulator spectral sensitivities that were obtained using this procedure from observations he made on cats. There was a good deal of individual variability in the spectral sensitivity of these elements, and, in various publications over the years, Granit vacillated somewhat in how many types he thought there might be. Also, there was some uncertainty about their relative spectral positioning, but taken as a group—and perhaps under the influence of ideas about human trichromacy—Granit eventually concluded that these modulators preferentially peak at three positions: 580–600 nm, 520–540 nm, and 450–470 nm (Granit, 1945a). The modulator spectral sensitivities were distinctly narrower than any known photopigments absorption curves and, as was later pointed out by Brindley (1970), it is not obvious from Granit's descriptions and discussions in what way he thought these elements should be considered as being fundamental. In any case, Granit makes the claim that the modulator elements were responsible for supporting wavelength discrimination. The presence of three such classes of modulator elements seemed to Granit to be consistent with classical thinking and led him to conclude that

> the mechanism of colour reception is organized by the peripheral visual apparatus, the number of colour sensitive elements is relatively limited, and these elements represent widely different regions in the spectrum. These were [Thomas] Young's three fundamental assumptions. . . . The electrophysiological work may indeed be said to confirm the view he gave of the framework of the mechanism of colour reception. (Granit, 1945b, pp. 462–463)

In short, Granit interpreted his work as providing evidence for the Young-Helmholtz idea of component coding of color information in the visual system.

Even though he reached the conclusion that his dominator/modulator results provided support for the biology predicted by a Young-Helmholtz type of theory, Granit did make some observations that might have suggested otherwise. For instance, he showed in recordings made from on-off cells that if test conditions are arranged such that both on- and

off-discharges impinge on a cell at the same time these two can cancel each other. At one point, this led him to note that such evidence provides a "belated vindication of the essential truth of Hering's contention that there are two fundamental process of opposite character in the retina" (Granit, 1955, p. 78). Perhaps even more intriguing, in one paper, he summarized results from an experiment in which he had examined the on/off response ratios of cat optic nerve fibers (Granit, 1948). In the cases of some such units, these ratios were found to vary as a function of the wavelength of the stimulus light, implying that these fibers must reflect the convergence of excitatory and inhibitory signals from afferent elements that differ in their spectral sensitivity. Granit apparently did not think this fact had importance for understanding color coding, as he seems to have made little more of it. In light of subsequent results, perhaps he should have. A modern interpretation of the modulator elements is offered below.

The Discovery of Spectral Opponency in Visual Systems

Around 1950, with the advent of high-impedance microelectrodes, it became possible to extend intracellular recording techniques from the larger nerve cells from which such recordings first had been made (e.g., large motor neurons) to much smaller nerve cells. Gunnar Svaetichin (1915–1981; Fig. 5), at the time working in Granit's laboratory at the Karolinska Institute in Stockholm, used such electrodes to make recordings from the outer portions of the retinas of fish. In so doing, he detected some nonspiking units that gave unusual responses to photic stimulation, generating signals that were, specifically, (1) large in amplitude, (2) graded with the intensity of the light, and (3) sustained throughout the time the eye was illuminated. Even more surprising, he found that, instead of being depolarizing, and thus linked to excitation as might be expected from the classical understanding of nerve impulse generation, these responses were often in the hyperpolarizing direction. In Svaetichin's honor, these electrical signals later became known as *S potentials* (Kaneko, 1987). Initially, based on estimates of the depth in the retina from which the recordings were believed to have been made, Svaetichin concluded these responses reflected the activity of single-cone photoreceptors (Svaetichin, 1953, 1956). The responses to spectral lights were of two qualitatively different kinds. In both cases, they started from a relatively low resting potential of ∼-30 mV when the eye was maintained in darkness. In one type, the response to illumination was a hyperpolarization that was graded in amplitude with the response magnitude and varying as a function of the wavelength of the test light. The other type was especially interesting in the current context because the direction of the response to light depended on stimulus wavelength with the cell hyperpolarizing in response to some wavelengths while depolarizing to other test wavelengths. Over time, these two types of response became designated, respectively, as L-responses (L = "luminosity") and C-responses (C = "chromatic"). Examples are shown in Fig. 6.

As has been noted, Svaetichin initially concluded that S potentials were generated by the photoreceptors themselves, but a few years later Tomita (1957) used an ingenious technique involving a comparison of the electrical signals recorded from two closely spaced electrodes to show convincingly in recordings made from the carp (*Cyprinus auratus*) retina that S potentials could not be generated by cones directly but rather must have their origins in a region of the retina located proximal to the photoreceptors. In subsequent years, it eventually became possible to inject marker dyes from recording electrodes directly into the cytoplasm of cells from which recordings were being made. Application of this dye-injection technique revealed that S potentials are in fact postsynaptic potentials.

Figure 5. Gunnar Svaetichin. © Webvision. Reproduced by permission of Webvision. Permission to reuse must be obtained from the rightsholder.

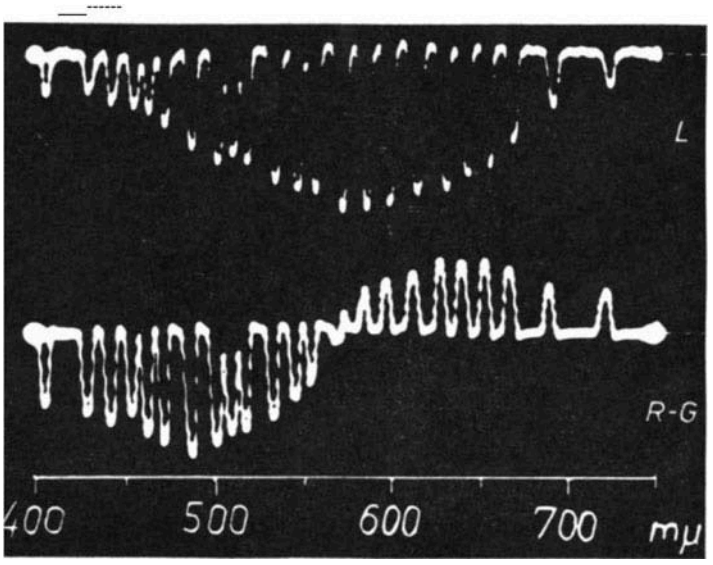

Figure 6. S-potentials recorded from the retinas of fish in the mid-1950s by Svaetichin and MacNichol. The stimuli were brief flashes of light of constant energy that were varied in wavelength. In this depiction, hyperpolarizing responses are indicated by downward defections of the oscilloscopic trace; depolarizing responses are indicated by upward deflections. The upper trace is an L-type potential; the lower trace shows an S-type potential. © Elsevier. Reproduced by permission of Elsevier. Permission to reuse must be obtained from the rightsholder.

At one point, it was suggested that the C-potentials were produced by Müller cells, a large, transretinal glial cell common to vertebrates (Svaetichin et al., 1961), but it later became clear that all S potentials are in fact generated by horizontal cells (Kaneko, 1970). Since their initial discovery, S potentials have been detected in a wide variety of different vertebrate species. It is noteworthy, however, that, although both L-type and C-type responses have been recorded from most vertebrates, only L-type responses are produced by horizontal cells in mammalian retinas (Twig, Levy, & Perlman, 2003).

In the mid-1950s, following a move from Sweden to the Instituto Venezolano de investigaciones cientificas (IVIC) in Caracas, Venezuela, Svaetichin continued his examination of the nature of fish S potentials. There he teamed up with an American physiologist, Edward F. MacNichol, Jr., to explore in detail the spectral response properties of both L and C-type elements; the recordings illustrated in Fig. 6 are in fact taken from their joint

endeavor (Svaetichin & MacNichol, 1958). In C-type recordings obtained from different species of fish, they discovered that, although many show only a single type of biphasic response (similar to that of Fig. 6), in some species they detected two qualitatively distinct types of biphasic responses, the two differing with respect to the spectral peak locations of hyper- and depolarization. Svaetichin and MacNichol designated these different types of C responses as Y-B (yellow-blue) and R-G (red-green) according to the spectral properties of the lights that produced the maximal responses. Interestingly, they further observed that the nature of the spectral responses recorded from various species correlated with their photic habitats—those fishes inhabiting shallow depths yielding both Y-B and R-G elements, while species native to greater depths, and thus exposed to different ambient lighting environments, had only a single type of C response. Apparently, the use of human hue terms (blue-yellow, etc.) to describe these responses were only intended to describe the portion the spectrum that produced the maximal responses, but the clear implication drawn by Svaetichin and MacNichol, as well as by others at the time, is that these C elements provided direct codes for perceived colors.

Further examination of the C-type responses made it clear that they must arise from combinations of two separate potentials that are, effectively, subtracted from one another. The evidence for this was, first, that the hyperpolarizing and depolarizing components of the response had different latencies and, even more compelling, that chromatic adaptation could be used to influence selectively one of the response phases; for example, adapting the eye to a bright blue light led to significantly greater diminution of the G response in an R-G cell than of the R response (Svaetichin & MacNichol, 1958). Finally, Svaetichin and MacNichol drew attention to the several points of apparent resemblance between the recording results they obtained from fish retinas and the opponent-color scheme proposed by Hering to account for human color vision.

This demonstration of spectrally-opponent mechanisms in vertebrate retinas provided at once a potential physiological justification for opponent-type theories of color vision, something that had been missing to that point. In retrospect, it seems clear that Svaetichin's discovery ranks as one of the signal events in the long history of vision science. Dorothea Jameson and Leo M. Hurvich, in an appreciation written following his death in 1981, refer to Gunnar Svaetichin, most fittingly, as "a man of vision" (Jameson & Hurvich, 1982, p. 307).

Spectral Opponency in the Primate Visual System

Although Svaetichin's work on fish retinas demonstrated that spectrally-opponent mechanisms are physiologically realistic, it left open the possibility that such arrangements might be not be universal. We know, for instance, that present-day teleost fishes and mammals have occupied generally different ecological niches and have evolved independently for millions of years and that, reflective of these facts, the respective visual systems of modern representatives of these two groups show many striking structural differences. Such differences raise the possibility that the spectral opponency detected in fish might be absent in humans, or it might exist in both lineages but differ in fundamental ways. What seemed clearly required to resolve these possibilities was a thorough examination of primate visual systems, and that is exactly what Russell L. De Valois (1926–2003; Fig. 7) and his colleagues at the University of Michigan set out to do in the mid-1950s (De Valois et al., 1957). Specifically, they made extracellular recordings from cells located in the LGN of macaque monkeys as the eye was stimulated with lights varying in wavelength and in intensity, much

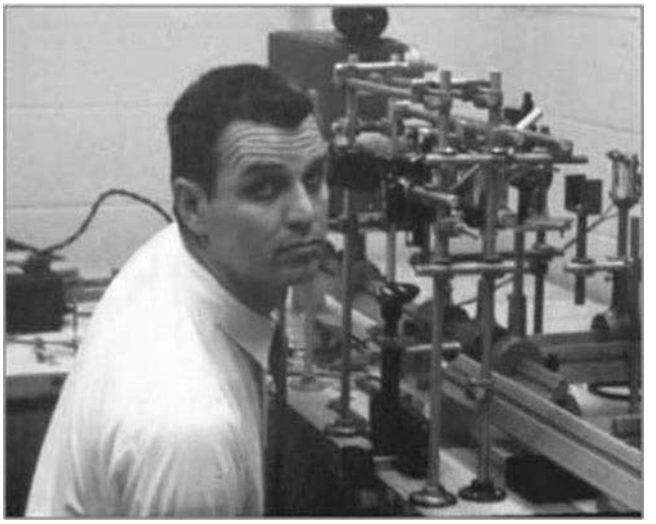

Figure 7. Russell L. De Valois. Reproduced by permission of Israel Abramov.

in the fashion that Le Gros Clark had suggested earlier. Macaque monkeys (catarrhine species) seemed good choices as subjects for such experiments because it long has been known that, although the visual systems of these monkeys are by no means identical with those of humans, they are generally quite similar (for a modern discussion of this issue, see Preuss, 2000). In particular, for purposes of understanding the coding of color information in humans, perhaps the most attractive feature of macaque monkeys was that it had been established early on that these species do have a trichromatic color vision capacity that is virtually identical to that characteristic of normal humans (Trendelenburg & Schmidt, 1930; Grether, 1939).

The first experiments conducted by De Valois and colleagues had a twofold motivation: first, to provide a direct test of Le Gros Clark's hypothesis that each of the three pairs of LGN laminae are related to one of the three fundamentals of classical trichromatic theory and, second, to examine the nature of the neural message linked to color vision in this structure, to ask, in the words of these investigators, whether "the systems operate independently, as Helmholtz maintained, or in opposing, complementary pairs, as suggested first by Hering" (De Valois et al., 1958, p. 238). The earliest results of their investigation showed that the laminar segregation of primaries suggested by Le Gros Clark did not exist; rather, cells recorded from each layer of the LGN blanketed the entire visible spectrum and thus that "the results are incompatible with the Le Gros Clark theory" (De Valois et al., 1959, p. 667). Some years later, when better methods for pinpointing the anatomical locations of electrophysiological recordings became available, an investigation of the electrophysiology of cells in different layers of the macaque LGN documented that, although there are indeed some clear laminar differences in the response properties of cells found therein, the conclusions of De Valois and his colleagues were correct, the information is not segregated in the component fashion proposed by Le Gros Clark (Schiller & Malpeli, 1978). For a contemporary interpretation of functional specialization in the layers of the LGN, see Kaplan (2014).

The early results from the investigations of De Valois and colleagues seemed to show that there were two distinct types of neural responses in the LGN as wavelength was varied. On the one hand, many cells gave on-responses to a relatively narrow band of wavelengths.

The spectral locations of peak responsivity of such units were believed to fall into four or (perhaps) five classes, one of which was considered to possibly be linked to contributions from rod photoreceptors (De Valois, Smith, & Kitai, 1959; De Valois, 1960). The averaged spectral response curves for a sample of such on-cells are illustrated in Fig. 8A. Additionally, some cells in the monkey LGN gave an excitatory response either at the onset of stimulation or at its offset, the direction of change being dependent on the wavelength of stimulation. The averaged responses of such units are shown in Fig. 8B. To interpret these two variant types of cells, De Valois suggested that the primate visual system jointly supports a spectrally-opponent organization similar to that postulated by Hering and detected in fish retinas by Svaetichin along with a parallel organization similar to that postulated by Helmholtz and later detected by Granit in the recordings he made from other mammalian retinas. De Valois further proposed that the two types of organization might underlie different aspects of color perception (De Valois, 1960).

Around 1960, as recording from LGN cells in macaque monkeys was pursued further in the De Valois laboratory, by now relocated to Indiana University, in Bloomington, it became clear that the cells earlier believed to possess only narrow spectral tuning were, in fact, of the spectrally-opponent variety.[1] Thus, in a paper published in 1963, it was stated explicitly that some 50% of all cells lying in the foveal projection belong to what was then termed a "red-green" system—cells that either increase their firing rate to green lights and decrease them to red lights (dubbed "+G-R") or cells that show mirror-image behavior ("+R-G")—and, of these, "no cells are found which respond only to red or only to green: the two components are *always* linked in an opponent relationship" (De Valois, Jacobs, & Jones, 1963, p. 91, emphasis added). Reasons for this change in categorization are revealed below. The averaged responses of those cells plotted in Fig. 8B would be considered +R-G cells in this new terminology. The macaque LGN was also shown to contain other spectrally-opponent units that seemed to differ from these red-green cells in their spectral locations of peak excitation and inhibition. And, although not documented with regard to their spectral response properties, the earliest reports of macaque monkey LGN recordings also had made passing note of the presence of some cells that responded with the same direction of response (either excitation or inhibition) across a broad range of spectral wavelengths (De Valois et al., 1959). Shortly thereafter, LGN cells of this unidirectional type were found in a New World monkey (Jacobs, 1964). In various publications, this latter group of cells was referred to as broad band or nonopponent. In sum, by the early 1960s, the spectrally narrowly tuned cells had disappeared from the list of cells believed to exist in the primate LGN and it now seemed clear that, with regard to their responses to spectrally variant lights, all monkey LGN units were either spectrally opponent or broadly sensitive and spectrally nonopponent.

Resolutions of the Claims for Narrow-Band Spectral Tuning in Mammalian Visual Systems

Both in Granit's research on optic nerve fibers in the cat and in the early work done on the monkey LGN by De Valois and colleagues, results were obtained that appeared to support the idea that some neurons in the mammalian visual system possess narrow spectral tuning, much in the fashion predicted by the Young-Helmholtz theory. How are those claims to be

[1] Starting in January, 1960, the author was a student in the laboratory of R. L. De Valois. At least from that time forward, it had become abundantly clear that *all* of the LGN cells previously identified as having narrow-band spectral responsivity were actually of the spectrally-opponent variety.

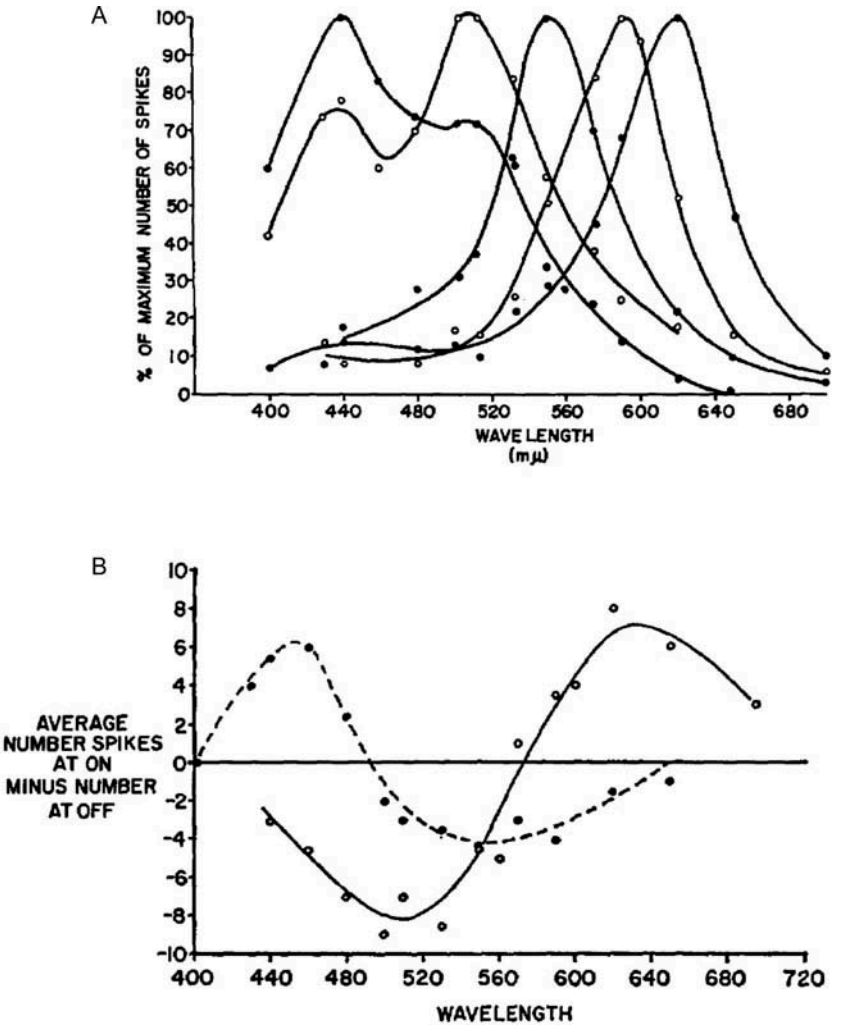

Figure 8. Spectral response curves obtained in recordings made from cells in the LGN of macaque monkeys in the middle-to-late 1950s. It was initially believed that there were two types of cells: (A) those that gave on-responses to a relatively narrow band of wavelengths and (B) those that gave spectrally-opponent responses like those of the averaged response of the cells whose on- (solid line) and off- (dashed line) response properties are plotted. As described in the text, it was later established that all of the apparently narrowly tuned units were in fact of the type shown at the bottom, that is, spectrally opponent.

understood in light of our present understanding of the electrophysiology of mammalian visual systems?

For the monkey LGN, the answer emerged quickly. The early recordings had been made from barbiturate-anesthetized animals in which the spontaneous activity rates of nerve cells were depressed significantly, and, although excitatory responses were clearly apparent in such preparations, it was difficult to detect any inhibitory responses (De Valois, Abramov, & Mead, 1967). Accordingly, when the spectral response properties of these

cells were plotted as a percentage of their maximum response rates (as, for example, in Fig. 8A, and as was common at the time), potential inhibitory responses were often obscured. As the recording preparations were improved, inhibitory responses became more obvious, the evidence for spectrally narrowly tuned cells evaporated, and the widespread presence of spectrally-opponent responses in the monkey visual system became apparent.

It is somewhat less clear how to square the evidence for the modulators found in Granit's research program with our modern understanding of visual physiology. There are at least three different explanations. First, it seems likely that at least some of optic-nerve fibers Granit studied were in fact of the spectrally-opponent variety. As noted above, in one paper Granit (1948) described some units whose on-/off-response ratios varied as a function of wavelength, a feature that would imply spectral opponency. Second, most modulator curves were determined by effectively taking the difference between the spectral sensitivity curves measured under neutral adaptation (apparently, mostly from the dark-adapted eye) and from spectral sensitivity curves subsequently measured during chromatic adaptation. The modulator curves so obtained thus would seem to have reflected the difference in spectral sensitivity between a mostly rod-driven signal and one that principally reflects the activity of single-cone types. The significant individual variations in spectral sensitivity that Granit found among the modulator units would be consistent with the likelihood that the effectiveness of the two adaptation states varied from experiment-to-experiment. Third, the curves derived for at least some of the modulator elements may have been due to features that are unique to the structure of some eyes. Thus, a modulator with a peak at about 610 nm had been detected in the eyes of albino rats (Granit, 1968). Modern measurements show that this species has only two photopigments absorbing light over the middle to long wavelengths, a typical rod pigment with a ~500 nm peak and a very slightly long-shifted cone pigment with a peak of 510 nm (Jacobs, Fenwick, & Williams, 2001). It is difficult to see how the differences in the absorption spectra of these two could yield an element with a distinct peak at 610 nm. However, the choroidal blood supply in the eyes of albino animals, such as the rats that Granit studied, produces prominent intraocular scattering of long-wavelength lights, and that scatter enhances the effectiveness of such lights, leading to a significant elevation of the spectral sensitivity curves of albinos in the longer wavelengths (Dodt, Copenhaver, & Gunkel, 1959). It seems likely that this same explanation could account for the erroneous detection of a "red" modulator in the eye of the albino rat.

Much of Granit's work on the mammalian optic nerve focused on the visual system of the domestic cat. For the prospects of detecting spectral opponency, this turns out to have been an unfortunate choice, for it since has become clear that spectrally-opponent units are only sparsely represented in the feline visual system. Two separate estimates suggest that such units comprise no more than something on the order of 1% to 11% of all cells in the LGN of the cat (Daw & Pearlman, 1970; Buzas et al., 2013). One can but wonder what alternative insights Granit might have been led to if, instead of the cat, he had made his recordings from Old World monkeys, animals whose visual systems are rich in spectrally-opponent cells.

Ubiquity of Spectral Opponency in Mammals

In the years following the discovery of spectrally-opponent cells in macaque monkeys, a series of technical advances made it much easier to record from single nerve cells in mammalian visual systems, and as a result electrophysiological investigations of the visual system expanded greatly. As this happened, a range of other mammalian species became

targets for study and over time it became clear that spectral opponency is a common theme across mammalian visual systems. Presently, spectrally-opponent cells have been recorded from, and characterized in, visual systems of representative species drawn from at least six mammalian orders. A few examples of these are the following:

1. Primates: Old World monkeys. For example, various species of macaque monkeys (references cited above and many dozens of studies on these animals in the years since then); vervet monkeys (Bertulis, Guld, & Lennox-Bucthal, 1977); baboons (Diller et al., 2004). New World monkeys. For example, squirrel monkeys (Jacobs & De Valois, 1965); spider monkeys (Hubel & Wiesel, 1960); marmosets (Blessing et al., 2004); Cebus monkeys (Lee et al., 2000); and howler monkeys (Silveira et al., 2004).
2. Rodentia: Ground squirrels (Michael, 1966; Jacobs & Tootell, 1981); tree squirrels (Blakeslee, Jacobs, & Neitz, 1988; Van Hooser, Hemel, & Nelson, 2003); guinea pigs (Yin et al., 2009); mice (Ekesten & Gouras, 2005).
3. Lagomorpha: Rabbits (De Monasterio, 1978).
4. Carnivora: Domestic cats (Daw & Pearlman, 1970; Buzas et al., 2013).
5. Scandentia: Tree shrews (Johnson, Van Hooser, & Fitzpatrick, 2010).
6. Diprodonta: Tammar wallabies (Hemmi, James, & Taylor, 2002).

Although there are dramatic differences in the incidence of spectrally-opponent cells in these different mammals, the observation that such cells are present in all these diverse species implies that the basic neural organizations requisite for producing spectral opponency—multiple types of photopigment and appropriate neural wiring—are likely shared features that must have been present in early mammals; indeed, it seems likely that these arrangements date to at least the time of the earliest vertebrates (Jacobs, 2009; Lamb, 2013).

In considering how this first came about, one suggestion is that the evolution of a capacity for color vision may have been nearly inevitable (Jacobs, 2004). The argument for this contention rests on the fact that the absorption of half-band widths of photopigments are fixed in size (some 50–70 nm) and thus to enlarge the spectral window through which an animal can sample the photic environment necessarily involves the addition of new photopigment types, an event that can occur as a result of discrete mutational changes in the resident opsin genes (Neitz & Neitz, 2011). With multiple photopigments in place, what is additionally required to allow color vision is the presence of spectral opponency, that is, the convergence of excitatory and inhibitory inputs onto recipient cells. Just such an arrangement is at the heart of the analysis of spatial information where excitatory and inhibitory influences contrast the effects of stimulation at neighboring locations on the photoreceptor mosaic. Thus, a visual system that has evolved to analyze spatial information, a capacity already characteristic of many quite primitive organisms (Nilsson, 2013), has the basic organization to set up spectral as well as spatial comparisons. In that sense, the addition of a new photopigment type may be expected to lead, perhaps almost inevitably, to the evolution of novel color vision.

Nature of Mammalian Spectrally-Opponent Cells

The discovery of spectrally-opponent cells in the mammalian visual system raised several obvious questions; for instance, (1) how can their response properties be best characterized, (2) what are the identities of the peripheral mechanisms linked to these spectrally-opponent

responses and, more generally, (3) in what ways might the activation of these cells contribute to the production of color vision? In this section, I address the first two of these concerns.

The spectral response profiles of individual spectrally-opponent cells (Figs. 7 and 8) are quite variable, being jointly dependent on both the wavelength and the intensity of the stimulus light as well as being dramatically influenced by the adaptation state of the eye. Given that, one of the initial questions was whether these cells fall into some natural groupings. From a consideration of the spectral response properties of ~100 spectrally-opponent cells recorded from the LGN of the macaque monkey, De Valois and colleagues concluded that the least variable properties of the response patterns of these cells might be the spectral locations where the responses transitioned from being excitatory to being inhibitory (the so-called *crosspoint*; De Valois, Abramov, & Jacobs, 1966). From an analysis of the distribution of wavelengths of these spectral crosspoints in the available sample of spectrally-opponent cells, it seemed justified to divide these spectrally-opponent cells into four classes. The averaged responses obtained from cells from the four classes so defined are plotted in Fig. 9. As can be seen, this analysis yields two pairs of cells, each member of a pair being an effective mirror image of the other with the spectral locations of excitation and inhibition reversed. As noted previously, these spectrally-opponent cells were denoted with hue names (red/green; blue/yellow) to reflect the appearances of the lights that led to maximum responses. From their spectral response profiles, it was concluded that the R/G cells must receive contrasting inputs from two cone types, while the B/Y cells probably involve signals from one cone type that is contrasted to the summed signal from the other cone types, most likely in the fashion illustrated in the model of Fig. 1.

Subsequent investigations showed that the actual locations of the crosspoints in the spectrally-opponent cells are highly dependent on both the adaptation state of the eye *and* the luminance of the test stimulus relative to that of the background light to which the eye has been adapted. Thus, for example, if the test light is brighter than that of the background light (as they were in the original De Valois et al. experiments), the spectral locations of the crosspoints are shifted toward longer wavelengths for the R/G cells relative to where they are located when the two lights involve no net luminance change (Marrocco & De Valois, 1977). Furthermore, some cells that do not appear to be overtly spectrally opponent when tested under conditions of neutral adaptation may show spectral opponency when subsequently tested in the presence of intense chromatic adaptation (De Monasterio, Gouras, & Tolhurst, 1975a). All these factors suggest that both the relative numbers of cells categorized as being spectrally opponent versus spectrally nonopponent, as well as the relative representation of the four types of spectrally-opponent cells, may well have been misestimated in the early experiments. Despite these possible complications, it turned out, as will be described below, that the identities of the four classes of spectrally-opponent cells first described in the LGN of the macaque monkey accord pretty well with results from most subsequent investigations.

In the early 1950s, it became clear that individual nerve cells in the mammalian visual system are highly selective for the spatial location of the stimulus relative to the position of the eye (Kuffler, 1953). The spatial region over which any given cell responds is designated as the receptive field of that cell. It was discovered that, in many cases, the receptive field of the cell contains separable regions that when individually stimulated produce either excitatory or inhibitory responses. For retinal ganglion cells, these two regions are most often concentrically organized into center and surround regions with the two being mutually antagonistic, the result being to render these cells sensitive to the spatial properties of the stimulating light (Kuffler, 1953).

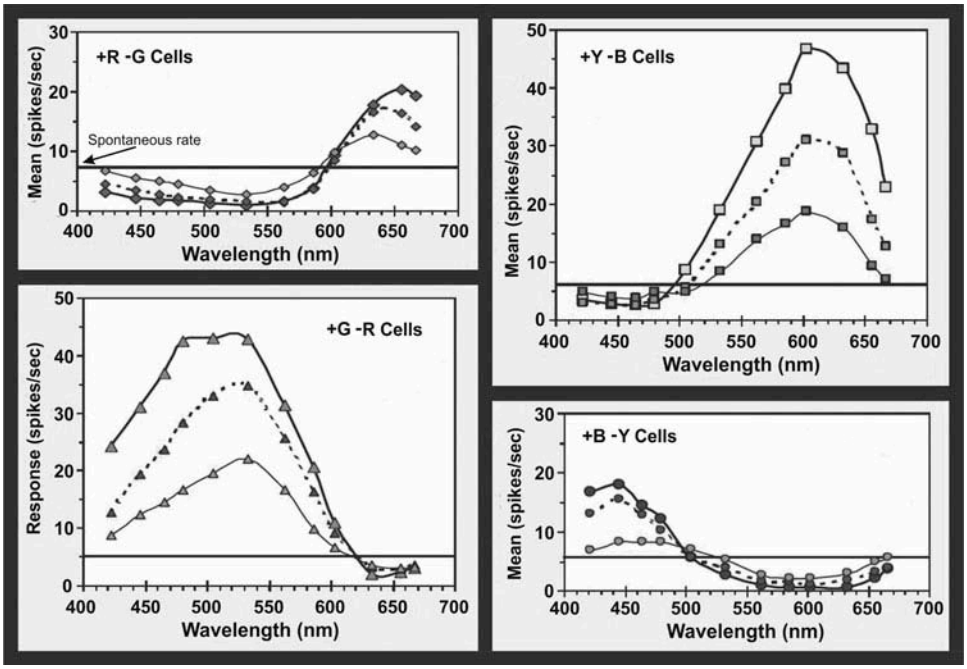

Figure 9. Mean response curves for four types of spectrally-opponent cells recorded in the LGN of the macaque monkey. Each data point represents the average response obtained for a single wavelength and intensity setting. For the four classes (depicted as +R-G, +G-R, +Y-B, +B-Y), responses are shown for three different equal-energy intensities. (Replotted from De Valois, Abramov, & Jacobs, 1966.)

In recordings made from the LGN of the macaque monkey, Wiesel and Hubel (1966) examined both the spatial and spectral response properties of single cells. They found that the vast majority of the LGN cells they recorded had both spatial and spectral opponency (some 70%, designated by them as being Type 1). Thus, for example, a cell that was excited when stimulated with a red light falling into the center of its receptive field would be inhibited by green light positioned in the surround region of its receptive field; others behaved similarly with the responses to red and green light reversed. A smaller number of cells (called Type 2) showed spectral opponency but no spatial opponency, for example, firing red light positioned throughout the receptive field while inhibiting green light similarly varied. From the description of the spectral-response properties, it seems likely that nearly all the Type 1 and Type 2 cells are the same as those designated +R-G and +G-R in the De Valois et al. (1966) study, but Wiesel and Hubel also reported finding a small number of cells showing spectral opponency that may be similar to the Y/B types earlier identified—although that conclusion is a bit uncertain from the published records—and they detected a number of cells showing no spectral antagonism but having a spatial antagonism (their Type 3). The latter would appear identical to those cells identified by De Valois et al. as being spectrally nonopponent. In sum, with regard to the issue of spectral opponency, the studies by Wiesel and Hubel (1966) and De Valois, Abramov, and Jacobs (1966) appear to have been in substantial agreement.

A subsequent study that examined both the spectral and spatial properties of ganglion cells in the macaque monkey retina produced slightly different results (De Monasterio &

Gouras, 1975). Although the vast majority (276 out of 288) of spectrally-opponent cells they recorded from appear identical to the R/G and Y/B subtypes seen in the earlier studies, the remainder were believed to have spectral properties that were more complex, that is, involving inputs from all three cone types in a variety of different combinations.

It seemed obvious from all of these studies that the responses of spectrally-opponent cells in the macaque monkey reflected excitatory/inhibitory combinations of signals derived from the activation of the three different cone types, but it proved difficult to be certain exactly what combinations of cone types were involved in providing inputs to the various types of spectrally-opponent cell. One reason for this was that, although it long had been clear that trichromatic color vision must derive from the activations of three types of cone photoreceptors, the spectral properties of these had not been accurately measured. That issue was finally resolved when the human cone spectra were derived from high-precision psychophysical measurements (Smith & Pokorny, 1975) and when direct measurements of the cone spectra of macaque monkeys revealed that their cone pigments were very similar to human cone pigments (Bowmaker, Dartnall, & Mollon, 1980). These cone spectra are the ones sketched in Fig. 1 and knowing their spectral properties provided a rational basis for attempting to link more precisely cone signals to opponent-cell responses. A second aspect of this problem arises from the considerable overlap of the absorption spectra of the cone photopigments. In particular, note in Fig. 1 that the M and L pigments are so closely similar in their absorption properties that it is not possible to stimulate the eye with any monochromatic light and selectively activate only one of the two cone types or in fact to differentially adapt one or the other. That fact makes it very difficult to separate the relative contributions made by the M and L pigments in response to illumination of the eye with monochromatic stimuli (as was the case in all of the early experiments). A similar, albeit somewhat less severe, problem arises if one tries to activate differentially the S versus the M or L pigments with simple spectral stimuli.

An essential solution to this second problem came from the development of the so-called "silent substitution" techniques (Estevez & Spekreijse, 1982) and from the advent of color monitors and light-emitting diodes (LEDs), devices that made it is possible to gain independent control of the red, green, and blue primaries thus allowing the production of complex color stimulus patterns. These technical advances permitted the construction of chromatic stimuli calculated to produce an equal effect on all but one of the underlying mechanisms; any residual response then reflects the contributions of that mechanism. A significant fraction of modern research on color vision, both psychophysics and physiology, exploits some adaptation of these silent-substitution paradigms. The term silent substitution alludes to the fact that for cells that combine linearly the signals from different types of cones there will be a restricted set of lights for which the cell will be equally sensitive such that lights in this set can be exchanged rapidly one for another without evoking a response from the cell—a silent substitution.

In what turned out to be a trend-setting study, Derrington, Krauskopf, and Lennie (1984) employed an adaptation of the silent-substitution technique to characterize the responses of macaque monkey LGN cells. In this case, they represented their stimuli in a spherical color space in which an axis representing luminance varies in elevation without any change in chromaticity. Chromaticity is then indexed by variations in azimuth with two orthogonal axes, one representing those chromaticity changes that do not alter excitation of the S cones and the other being a constant M and L axis in which chromaticity varies without changing the relative excitation of the M and L cones. For any cell then, there is a null plane passing through the white point at the center of the color sphere that will encompass all the lights that can be exchanged without changing the response of the cell. They

determined the azimuths of the null planes for a sample of 101 cells located in the top four layers of the monkey LGN. These azimuth values clustered tightly in two locations that correspond closely to those cells previously identified as antagonistically combining inputs from M and L cones (R/G cells) and a much smaller number of cells that correspond to the B/Y grouping that combine inputs from the S cones versus a (variably) weighted sum of the signals from the M and L cones.

The early studies of the retina and LGN of trichromatic primates were in reasonable agreement that there were essentially two classes of spectrally-opponent neurons—a majority group that reflected the antagonistic combination of signals originating in the M and L cones (R/G cells) and a much smaller group of cells that combine signals from S cones with some summative combination of signals from M and L cones (B/Y cells). All subsequent research seemed to provide a validation of this conclusion. However, it later became clear that there are also some other cells, arguably only a small population, that reflect different combinations of cone signals, as had in fact been suggested in a pair of earlier studies (De Monasterio & Gouras, 1975; De Monasterio, Gouras, & Tolhurst, 1975b). For instance, in a recent investigation that employed the improved stimulus-control techniques (i.e., silent substitution), it was discovered that there are cells in the macaque monkey LGN whose responses reflect a summative combination of signals from S and M cones that have been subtracted from signals originating in L-cone class, that is, L – (S +M) (Tailby, Solomon, & Lennie, 2008). The functional role(s) that opponent cells like these that involve combinations of three cone inputs may play remains, at present, a matter under active investigation. Whether, as it has been suggested, these combinations of cone signals are critical for understanding the links between cell physiology and color appearance (Schmidt, Neitz, & Neitz, 2014) or whether they may arise simply as "a consequence of imprecision in the wiring of known cell types" (Lee, 2014) remains to be resolved.

Linking Spectrally-Opponent Cells to Color Vision

The spectrally-opponent cells found in the early recordings from visual systems of macaque monkeys, particularly those characterized as having R/G and B/Y response profiles, bore obvious resemblances to the characteristics of the spectrally-opponent response processes hypothesized by opponent-color theory (Hurvich & Jameson, 1957); however, to establish that these spectrally-opponent neurons are actually relevant to understanding color vision required evidence beyond mere superficial resemblance. Subsequently, several kinds of observations were made that strengthened the case for that linkage.

Color vision is defined formally as a capacity that allows one to discriminate among objects or lights of different wavelength composition irrespective of their relative intensities, and thus tests for the presence of color vision are designed to eliminate, or to make irrelevant, luminance differences among the stimuli to be discriminated (Wyszecki & Stiles, 1982). A first question, then, was whether spectrally-opponent cells satisfy this formal criterion. In fact, they do. Early experiments showed clearly that the spectrally-opponent cells in the LGN of macaque monkeys generate discharge patterns that vary continuously in magnitude as a function of the wavelength of monochromatic lights that have been equated to be of equal luminance (De Valois et al., 1963). This means that, as judged by their responses, such cells do at least transmit information toward the cortex that would be required to support this fundamental criterion for the presence of color vision. Analogous experiments later run on spectrally-opponent optic-nerve fibers in the ground squirrel, a rodent known to have dichromatic color vision, yielded a similar outcome (Jacobs, Blakeslee, & Tootell, 1981).

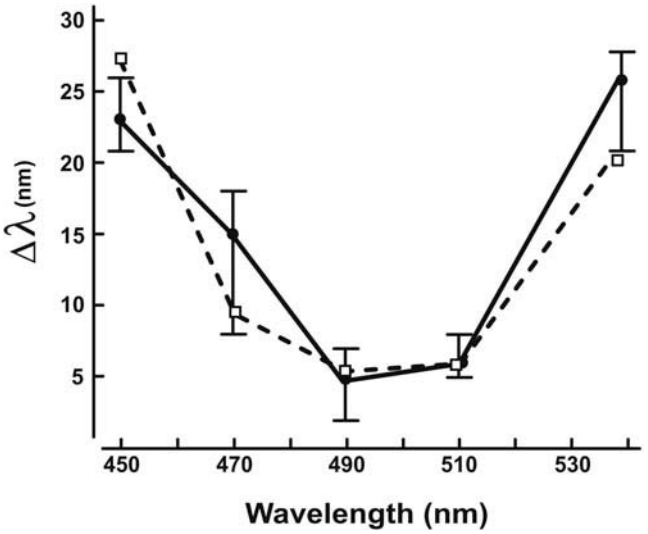

Figure 10. Comparison of wavelength-discrimination functions obtained from behavioral measurements made on three ground squirrels (open squares) and the functions obtained from measurements made on the two classes of spectrally-opponent units in the ground squirrel optic nerve (solid circles). Details of the way in which the latter results were obtained are given in the text. (Replotted from Jacobs, Blakeslee, & Tootell, 1981.)

Another fundamental and long-recognized feature of color vision is that the ability to discriminate differences in wavelength across the spectrum varies, with individuals being acutely sensitive to pure wavelength differences in some parts of the spectrum and less sensitive to such differences in other portions of the spectrum (Wright, 1947). If the spectrally-opponent neurons transmit information required to support color vision, presumably they would be expected to show similar variations. Direct tests of the abilities of spectrally-opponent neurons to discriminate wavelength differences (as indexed by a significant change in their discharge rates to equiluminant lights differing in wavelength) were made on both trichromatic macaque monkeys (De Valois, Abramov, & Mead, 1967) and dichromatic ground squirrels (Jacobs, Blakeslee, & Tootell, 1981). In both cases, the capacities of these cells to discriminate among wavelengths were found to be similar to behaviorally assessed wavelength discrimination. For example, Fig. 10 compares a wavelength-discrimination function measured in behavioral tests conducted on three ground squirrels (solid line) with the average wavelength-discrimination functions obtained from 29 spectrally-opponent, optic-nerve fibers (dashed line). The clear qualitative agreement provides further support for linking this class of cells to the production of color vision.

Another way to evaluate whether spectrally-opponent neurons are in fact linked to color vision rests on the fact that the nature of color vision usually varies across species and, in some cases, among individuals within a species. To the extent that the linkage is solid, these behavioral variations should co-vary with the functional properties of the spectrally-opponent neurons. In this case, the evidence was unambiguous. As described above, trichromatic macaque monkeys whose color vision derives from the operation of three classes of cone photopigments have spectrally-opponent neurons that reflect antagonistic interactions between various combinations of all three cone types. Additionally,

species that have dichromatic color vision feature two classes of cone and spectrally-opponent neurons that compare the activation of these two in a push/pull fashion. Prime examples of this latter group include both ground squirrels (Jacobs & Tootell, 1981) and cats (Buzas et al., 2013). Finally, in recent years a minority of mammalian species have been shown to lack a capacity for color vision (Jacobs, 2013). One such species is the platyrrhine owl monkey (*Aotus*) (Jacobs et al.,1993) and, in accord with the linkage prediction, the visual system of this animal appears to contain no spectrally-opponent neurons (Silveira et al., 2004).

A potentially even stronger test resides within those species that feature clear individual variations in color vision, for example, color vision polymorphisms. In such cases, the nature of spectrally-opponent neurons should vary among individuals whose measured color vision varies. Starting about 30 years ago, it was discovered that most species of New World monkey are highly polymorphic with individual animals having one of several forms of dichromatic or trichromatic color vision (for reviews see Jacobs, 2007, 2008). Recordings made from such animals show clearly that the nature of their spectrally-opponent neurons is exactly as predicted from their color-vision phenotypes; most crucially, M/L spectral opponency is present in those individuals known to have trichromatic color vision and absent in conspecific dichromatic monkeys (Jacobs, 1983; Yeh et al., 1995; Lee et al., 2000; Blessing et al., 2004).

One final bit of evidence about the linkage between spectrally-opponent neurons and color vision comes from experiments in which attempts were made to destroy such cells and then to examine the visual consequences. Experiments that involve lesioning of nervous tissue inevitably have many ambiguities of interpretation, but the general result has been that such cellular loss leads to significant declines in color-vision performance measures. For example, Merigan (1989) sought to destroy selectively the spectrally-opponent retinal ganglion cells in macaque monkeys through the administration of an acrylamide monomer. Subsequent behavioral tests of these animals revealed a profound loss in the ability to make color discriminations paired with relative sparing of (at least some) achromatic discrimination abilities.

Nature of the Linkage Between Spectrally-Opponent Cells and Color Vision

Taken as a whole, the observations reported in the previous section made it abundantly clear that the presence and the characteristics of spectrally-opponent neurons are correlated with various features of color vision. But what exactly is the nature of that linkage?

As noted, those vision scientists who first recorded from spectrally-opponent neurons characterized them using human hue terms (red/green, etc.); indeed, such cells were sometimes—indeed, still are—referred to as "color opponent cells." This led to an initial belief, even today still promoted in some texts, that the discovery of these cells provided a physiological basis for Hering's theory. But Hering's theory was based on phenomenological observations and in the years following these initial physiological discoveries it became increasingly clear that the spectrally-opponent cells are not isomorphic with color perception—most fundamentally, the response properties of R/G and B/Y cells do not correspond to the properties of the red-green and yellow-blue color dimensions postulated by Hering (e.g., Gouras & Eggers, 1984; Mollon, 1995). Among other discrepancies, the wavelengths at which R/G cells transition from excitation to inhibition should correspond to the wavelengths associated with the percept of so-called unique yellow (defined as a color sensation that is neither red nor green). However, that transition point is actually at much shorter wavelengths than the spectral location of unique yellow (Derrington, Krauskopf, &

Lennie, 1984). Similarly, firing of the +R-G cells cannot code uniquely for the percept of "red" because such cells also fire in response to the presentation of a white light (Abramov & Gordon, 1994). In recognition of these facts, and many others, in recent years there has been an increasing tendency to label these early stage spectrally-opponent cells according to their cone inputs (L/M, etc., as is done in Fig. 1) and perhaps if that tack had been followed from the beginning and they had become known as cone-opponent cells instead of color-opponent cells some of the subsequent confusion might have been avoided.[2]

Although the spectrally-opponent neurons of the retina and LGN clearly transmit information requisite for supporting color vision, this lack of correspondence between the properties of the spectrally-opponent cells and color perception underlines the fact that further transformations must occur in the cortex to account for the multiple details of color appearance. That realization, as well as what is by now a long list of psychophysical results, has led to the promulgation of the various zone theories referred to at the beginning of this article. Although much work has been done to try to understand the physiology of these cortical color transformations (for recent reviews, see Conway et al., 2010; Conway, in press; Shapley & Hawken, 2011), that topic lies beyond the scope of this communication. At this point, it suffices to say that the story of how color is represented in the cortical portions of the visual system is still in the form of a rough draft.

Coda

For a period of some 10–15 years, starting in the early 1950s, results emerging from electrophysiological research provided an entirely new view of how information relevant to seeing color is encoded in the visual system. Up to that time, physiological, behavioral, and phenomenological approaches to the study of color vision had provided starkly contrasting views on how color perception is biologically realized. The discovery of spectrally-opponent elements in visual systems and the demonstration of their ubiquitous presence in the visual systems of widely divergent species have proven to be transformative in the sense that all contemporary accounts of the operation of visual systems now necessarily rest on the presence and the elaboration of information from spectrally-opponent mechanisms—for spatial vision as well as for color vision. To the eye of the modern reader, viewing the world from the vantage of current technology, these early experiments may appear crude and, certainly, like all explorers, those involved in the early stages of this research story made their share of mistakes, sometimes misinterpreting observations, sometimes missing relevant facts. Yet, in the end, their work provided the introduction to an entirely new chapter in visual science and for that reason alone it is worth remembering these early efforts.

[2] To be fair to these researchers, at the time of the discovery of spectrally-opponent neurons in the primate visual system, the spectral absorption properties of the primate cone photopigments still had not been accurately determined; indeed, there were continuing arguments as to whether there were three types of cones (e.g., Willmer, 1961), and it was still some years before the cone photoreceptors would be routinely identified as S, M, and L. It is also noteworthy that the tendency to use human hue designations to label biological structures or processes misleadingly has extended well beyond the naming of spectrally-opponent neurons. For example, the three types of cones of the trichromatic retina often have been identified as "blue, green, and red," a practice still followed in some circles, despite the fact that it has long been appreciated that the locations of the peak sensitivity of these cones do not correspond to the spectral locations associated with these percepts and that, in any case, each class of photoreceptor responds univariantly and thus each must be "color blind." And there are even more unforgiveable cases of this kind of label misattribution; for example, the genes that specify the opsin proteins that comprise the three classes of cone photopigments have at times also been labeled using human hue names (e.g., "red genes").

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