

Evolution of color vision

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Color vision is achieved by comparing the inputs from retinal photoreceptor neurons that differ in their wavelength sensitivity. Recent studies have elucidated the distribution and phylogeny of opsins, the family of light-sensitive molecules involved in this process. Interesting new findings suggest that animals have evolved a strategy to achieve specific sensitivity through the mutually exclusive expression of different opsin genes in photoreceptors.

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Abbreviations

L cone	red-light-sensitive cone
LCR	luciferase control region
M cone	green-light-sensitive cone
R	photoreceptor cell
Rh	rhodopsin
Rh1	blue/green-sensitive opsin
S cone	blue-light-sensitive cone
UV	ultraviolet (light)

Introduction

The compound eyes of insects have a totally different structure from the camera-like, single-lens eyes of vertebrates or cephalopods. Despite their structural differences, both types of eyes perform similar functions and use similar principles for discriminating color. Color perception can be regarded as the particular sensation produced by different light vibrations. Color vision is rooted in the discrimination of color contrast, independent of color intensity, with hue and brightness processed as independent variables.

The origin of color vision is still speculative. Why did primitive organisms need to discriminate among the wavelength contents of light? Common light sources contain a high proportion of short wavelengths (< 450 nm), whereas light reflected from objects lacks UV and is composed predominantly of green/yellow middle-energy wavelengths. Therefore, a high UV content would be equated with an ‘open space’, whereas a low UV content would be interpreted as the habitat or a zone rich in food. Thus, a primitive color vision system could have been composed of two pigments, one UV-sensitive pigment and one sensitive to middle/long wavelengths. This hypothesis is consistent with the distribution of pigments in primitive arthropods

(e.g. Chelicerata), which are sensitive to UV and green wavelengths [1]. This two-pigment system may have evolved into a broader range of wavelength sensitivities through diversification of opsins and the addition of other pigments. Although the presence of different pigments with specific wavelength sensitivity is a pre-requisite for color vision, the subsequent neural wiring determines whether the organism has simply wavelength-specific behavior or true color vision. Direct synapsis between photoreceptor axons, or through interneurons, is a strong indication of color discrimination, which is generally tested by associative learning. By contrast, the wavelength-specific behavior response refers to the lack of flexibility in the color-association task that cannot be altered by training (for reviews, see [2,3]).

Here, we focus on the opsin phylogeny, and we discuss how the compound eye has evolved a system for color discrimination.

Opsin phylogeny

Because most animal species use the same opsin protein (a G-protein-coupled receptor linked to a retinal chromophore) as their photosensitive molecule, the phylogeny of opsins is very informative. The spectral sensitivity of photopigments is determined largely by the opsin moiety, so much work has focused on identifying the amino-acid residues critical for the spectral tuning of each molecule [4–6]. Both physiological and molecular data have led to the classification of opsins into four groups on the basis of their absorption spectra: UV, blue, green and red. Within vertebrates, opsins can be further subdivided into either ‘cone opsins’ or ‘rod-specific opsins’ (which are called rhodopsins). Cone pigments evolved first and diversified into several spectral classes. The rod pigment, rhodopsin, evolved subsequently from a green cone pigment ancestor [7].

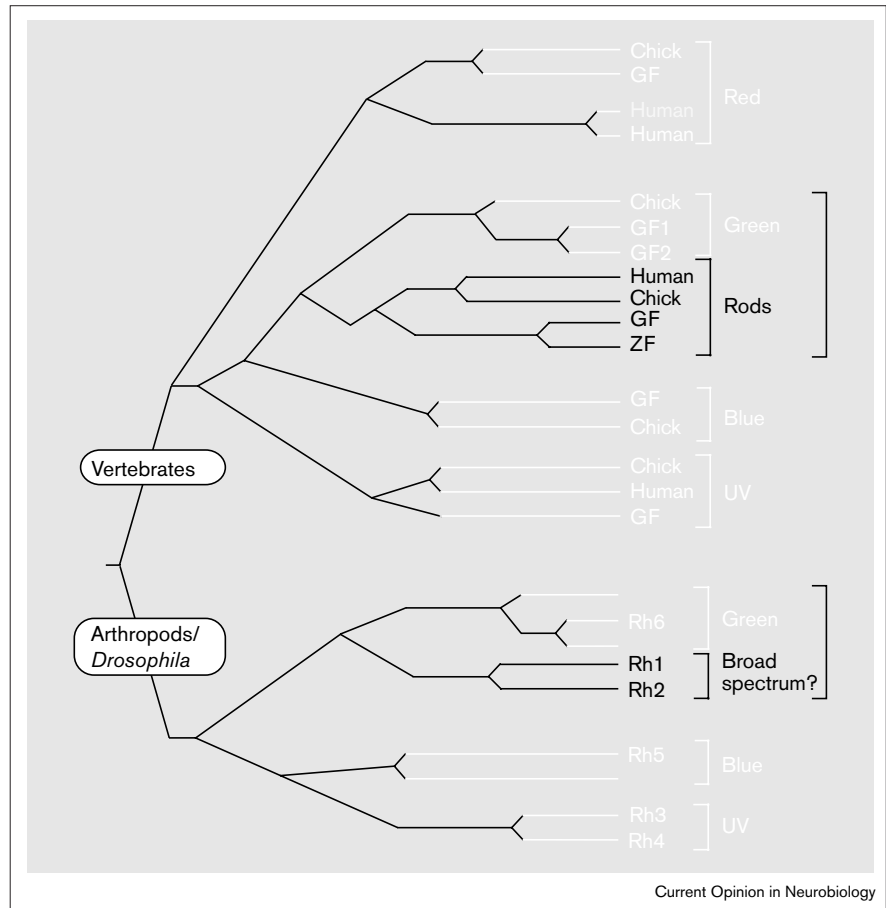
Although the opsins diversified independently after the separation between invertebrates and vertebrates, the two lineages display striking similarities (Figure 1).

First, the main opsins (i.e. rod rhodopsin in vertebrates and the outer photoreceptor pigment Rh1 in flies) have evolved from the green wavelength branch. This may reflect the need for a broad spectrum pigment dedicated to the middle-range wavelengths. Insects other than flies achieve a broad spectrum of detection by accumulating several opsins within single photoreceptors.

Second, insects and vertebrates share the same classes of UV, blue and green pigments. The ‘red’ branch is missing in insects, but there are a few scattered occurrences of red pigment in several genera, suggesting, as for humans, independent duplication events of the green pigment [8–10].

Figure 1

Schematic phylogenetic tree of arthropod and vertebrate opsins. A few representative species are indicated for vertebrates, whereas only *Drosophila* opsins are presented for the arthropod lineage. This representation is purely qualitative and emphasizes the common evolutionary features of opsins in the two lineages. The vertebrate 'red' branch includes both human red and green pigments.



The butterfly *Papilio* has at least five spectral types of photoreceptors [11], as a result of as many as six opsins [12*,13*], which may have evolved for enhanced discrimination within the long wavelengths. The most diverse retina known is that of the mantis shrimp, which has ten types of spectral receptors [14].

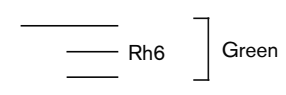
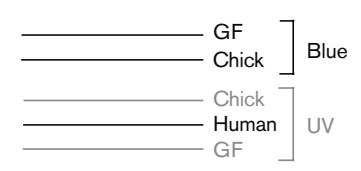
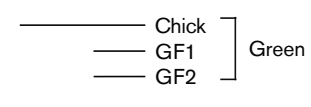
Dual visual system in vertebrates

Most species have two different, overlapping visual systems that are designed for different functions: one that is 'scotopic' and is responsible for dim light vision, and the other that is 'photopic' and is responsible for color vision. In vertebrates, these systems are represented by the two types of photosensitive cells, rods and cones.

Rods support night vision, whereas cones detect colors in bright light. At night, color vision is totally absent [15] and motion perception is impaired (compared to daylight vision) [16*]. Rods and cones are not distributed evenly across the retina. In humans, the fovea, which is at the center of a rod-dominated retina, is composed almost exclusively of cones, whereas the rest of the retina contains 4 million cones and 120 million rods, with the concentration of cones decreasing as the distance from the fovea increases.

Rod and cone photoreceptors are incorporated into very different circuit diagrams. Impulses from individual rods first pass nerve centers, where information from adjacent cells is compared. From these nerve centers, the impulses proceed to the visual cortex for further processing. Signals from the cones travel to the brain through various routes. In most mammalian eyes, bipolar cells combine signals from neighboring cones (i.e. a convergent system); however, in primates, a one-to-one connection has evolved between cones and midget bipolar cells in the center of retina. These cells subsequently contact one midget ganglion cell. Such differences are of great importance in understanding how evolution led to primate trichromatic color vision. The persistence of a convergent neural system would have disabled any selection of new chromatic input.

Color vision is possible because the retina contains cones that differ in their spectral sensitivity. In humans, light of normal intensity differentially activates the three cones — blue (S), green (M) and red (L) — in a ratio that depends on the wavelength composition of the light. Subsequently, opponent interaction (i.e. differential summation or subtraction) occurs between the input from the M/L and



____ Chick
____ GF
____ Human
____ Human

Red

____ Chick
____ GF
____ GF

Green

____ GF
____ Chick

Blue

____ Chick
____ Human
____ GF

UV

____ Rh5
____ Rh3
____ Rh4

Green

____ Rh5
____ Rh5

Blue

____ Rh3
____ Rh4

UV

—— Chick
—— GF
—— Human
—— Human] Red

—— Chick
—— GF1
—— GF2] Green

——
—— Rh6
——] Green

S cones [17,18*]. Recent technological advances have permitted direct imaging of the cone cell mosaic in living human retina. Roorda and Williams [19**] found that whereas the S cones form a regular mosaic and represent 5–10% of all cones, the relative distribution (i.e. number and arrangement) of the M and L cones varies from one retina to another. Thus, it appears that human evolution did not select a specific or optimal ratio of M and L cones, either because the L pigment is a relatively recent acquisition or because the sub-retinal neural network is plastic enough to perform optimal color vision using any distribution and/or ratio of M and L cones.

Dual organization of the insect retina

The insect retina is composed of photoreceptors organized in optical units called ommatidia, which also exhibit a dual system of photoreceptor projections. Although the functional significance of these two systems is not fully understood, it can be inferred from work on the organization of the fly retina. All insects have short visual fibers projecting to the lamina part of the optic lobe. They may correspond to the rods of vertebrates, as they represent a scotopic, high-sensitivity system involved in dim light vision and motion detection [20,21]. The other system is represented by the long visual fibers that project to the medulla and may enable color vision, similar to vertebrate cones. In flies, input from the long fibers appears to be processed in the medulla. Flies are able to discriminate colored and polarized light; however, color vision has not yet been formally demonstrated. It is notable that long visual fibers in lower diptera and bees have synaptic connections in the lamina (the part of the optic lobe that is involved in image formation) [22,23], suggesting its involvement in color discrimination.

The rhabdomeres are the light-gathering membrane structures that contain opsins. In *Drosophila*, the distinction between short- and long-fiber systems is clear: the short-fiber photoreceptors R1–R6 are optically and physiologically independent from one another [24], whereas the long-fiber photoreceptors R7 and R8, which are in the center of the ommatidium, are in the same optical path, one on top of the other [25,26]. Rhabdomeres R1–R6 contain a blue/green-sensitive opsin (Rh1) as well as a photostable pigment that absorbs UV light and transfers its energy to Rh1 [27,28]. This system provides the short visual fibers with a broad spectral sensitivity (i.e. UV to green wavelengths) [29]. These cells project to large monopolar cells in the lamina (for reviews, see [30,31]). A very sophisticated array of projections (called ‘neural superposition’) allows for dim light vision, as well as increased resolution [32,33].

Although the distinction between the systems for dim light and color vision is clear in flies (in which photoreceptors are independent within each ommatidium, an ‘open rhabdom’ structure), it is less clear in other insects (e.g. bees and butterflies), which have a ‘fused rhabdom’ structure. In this case, all the photoreceptors within an ommatidium

share the same light gathering structure by merging their rhabdomeres (although they remain physiologically independent), which makes it possible to absorb many photons. It is likely that, contrary to vertebrates or flies, several opsins are expressed in the same photoreceptor in these animals [13*,34,35]. Alternatively, some of the photoreceptors may be coupled electrically, thereby broadening the absorption spectrum. Although both short- and long-fiber photoreceptors exist in insects with fused rhabdoms, it is difficult to correlate, for example, long-fiber projections to the medulla with a specific type of opsin, the morphology or the size of the rhabdomere, the position in the retina, or the axonal connectivity.

Drosophila ‘color’ vision

Color vision in flies has not been studied in great detail. However, the organization of the fly retina and recent studies on the expression of opsin genes strongly suggest that color vision is supported by the long visual fibers of R7 and R8, which contain different opsins. Two types of ommatidia are stochastically distributed in the *Drosophila* retina: y-type ommatidia, which represent 70% of the ommatidia and are composed of R7 cells expressing exclusively Rh4 and R8 cells expressing Rh6, and 30% of p-type ommatidia, which are composed of R7 cells expressing Rh3 and R8 cells expressing Rh5 [36,37]. Although the UV opsins (Rh3 and Rh4) are expressed by two, non-overlapping subsets of R7 cells, they have only slightly different spectra of absorption. A blue-absorbing photostable filtering pigment is present in y-type R7 cells [38]. It is possible that the lamina (and thus R1–R6) is also involved in color processing because R1–R6 cells synapse in the lamina on the L3 mononuclear cell that enters the medulla together with the two long visual fibers (R7 and R8) [39]. However, the most probable current model of *Drosophila* color vision has the long visual fibers R7 and R8 as the only color opponent system [40,41].

Color vision in other insects

The distribution and arrangement of color receptors differ appreciably between different regions of the eye in many insects other than flies.

In the butterfly *Papilio*, a stochastic pattern of ommatidia restricted to the ventral part of the eye displays a UV-screening pigment superimposed onto UV or green-sensitive opsins [42*]. This pigment shifts the spectral sensitivity of some UV opsin-containing photoreceptors into the violet spectrum and sharpens the peak of absorption in cells containing the green opsin. Hence, the *Papilio* retina has at least six spectrally distinguishable classes of photoreceptors (UV, violet, blue, two kinds of green, and red), which are created by different combinations of opsins and filtering pigments.

In some species, the R7/R8 system may have even lost its ability to discriminate between different colors. For instance, the male *Musca* has sacrificed color vision in a

large part of the retina where R7 no longer expresses Rh3 or Rh4 but instead expresses Rh1 and projects to the lamina. This adaptation may reflect the need for an additional outer-like photoreceptor to detect the flying female with the part of the retina called the ‘love spot’ [43].

The jumping spider presents an interesting variation on this theme in that the retina of its principal eye comprises four layers of photoreceptors, each of which appear to have different absorption spectra. This peculiar arrangement, together with the strong chromatic aberration created by the single-lens eye, may allow light of different wavelengths to be differentially processed so that each layer detects only colored light that is in focus [44,45]. In these spiders, the remaining six eyes contain a middle-energy-sensitive opsin, which may be equivalent to fly outer photoreceptors.

Exclusive expression of opsins in photoreceptors

Most animals have developed a color vision system that involves the exclusive expression of a single opsin per photoreceptor. In fact, this is a recurrent phenomenon observed in many sensory systems, where the general rule is ‘one receptor molecule per receptor cell’. This design makes it possible to avoid overlap of sensory inputs that cannot be discriminated within a single receptor. The receptors often belong to large families (e.g. olfactory receptors), and each cell makes a stochastic choice to express a specific receptor molecule and to exclude all others. The photoreceptors of some insects may represent a departure from this general theme, however, as simultaneous expression of two opsins in the same cell [13*] appears to be a strategy for broadening the spectrum of light sensitivity.

The molecular mechanisms involved in the transcriptional exclusion of opsins and the signaling that takes place between retinal cells are not fully understood, although some insight has come from recent molecular studies in humans and flies.

One of the best-characterized examples is the exclusive expression of the red and green opsin genes in Old World monkeys (i.e. apes and humans). Wang *et al.* [46,47**] found that the two genes are present in a cluster, often with several other tandem copies of green, red or green/red chimeric genes, each with its own promoter. A locus control region (LCR) upstream of the cluster appears to be capable of activating one gene at a time. The LCR may ‘choose’ to activate a given gene, to the exclusion of all the other genes in the cluster [46,47**]. As the red/green gene cluster is on the X chromosome, there is no need for allelic exclusion to avoid expression of two different opsin genes from the two chromosomes.

In the *Drosophila* R7 cell, the transcriptional mechanisms that control *rh3* or *rh4* gene expression are not understood. The two genes are not found as a cluster, and their short promoters, which share almost no sequence homology, are

regulated differently [48]. As described above, the stochastic choice to express one opsin in R7 is coordinated with the choice to express the corresponding gene in R8 (e.g. *rh3* in R7 and *rh5* in R8). This coordination requires a contact between R7 and R8 because, in the absence of R7, all R8s take on a ‘default’ state (specifically, they all express *rh6*) [36,37]. Chou *et al.* [49**] report that R7’s choice of opsin does not require the presence of R8, suggesting that the active decision is made in R7 and is communicated to R8. The signal transduction pathway involved is not known, but it is possible that rhodopsin molecules themselves play an active role, similar to the role played by olfactory receptors in directing olfactory neurons projections to specific glomeruli [50,51*].

Conclusions

Color vision probably exists in most vertebrates and invertebrates. It is also probably most highly developed in birds (i.e. tetra/pentachromatic vision) and least developed in mammals, which generally have dichromatic or poor color vision. The extreme diversity in the design of eyes is as striking as the extreme convergence in the ability of these eyes to extract essential light parameters, such as contrast, color, polarization, shapes, motion, and evaluation of distance. Bees and primates demonstrate highly convergent visual strategies, particularly for chromatic discrimination. The recent findings in *Drosophila* and Old World monkeys described above suggest a common theme of exclusive expression of the opsins, as well as a convergent evolution between the broad spectrum vertebrate rhodopsin and its invertebrate equivalent, Rh1.

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