

Rayleigh matches in carriers of inherited color vision defects: The contribution from the third L/M photopigment

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Abstract

The mother or daughter of a male with an X-chromosome-linked red/green color defect is an obligate carrier of the color deficient gene array. According to the Lyonization hypothesis, a female carrier's defective gene is expressed and thus carriers may have more than two types of pigments in the L/M photopigment range. An open question is how a carrier's third cone pigment in the L/M range affects the postreceptoral neural signals encoding color. Here, a model considered how the signal from the third pigment pools with signals from the normal's two pigments in the L/M range. Three alternative assumptions were considered for the signal from the third cone pigment: it pools with the signal from (1) L cones, (2) M cones, or (3) both types of cones. Spectral-sensitivity peak, optical density, and the relative number of each cone type were factors in the model. The model showed that differences in Rayleigh matches among carriers can be due to individual differences in the number of the third type of L/M cone, and the spectral sensitivity peak and optical density of the third L/M pigment; surprisingly, however, individual differences in the cone ratio of the other two cone types (one L and the other M) did not affect the match. The predicted matches were compared to Schmidt's (1934/1955) report of carriers' Rayleigh matches. For carriers of either protanomaly or deuteranomaly, these matches were not consistent with the signal from the third L/M pigment combining with only the signal from M cones. The matches could be accounted for by pooling the third-pigment's response with L-cone signals, either exclusively or randomly with M-cone responses as well.

Keywords: Protanomaly, Deuteranomaly, Retinal cone mosaic, Color matching, individual differences

Introduction

Anomalous trichromats need three primaries to match all spectral wavelengths but do not use the same proportions of the primaries as do most trichromats. Their color vision is classified as defective. Anomalous trichromats are subdivided into two groups (Rayleigh, 1881): protanomalous and deuteranomalous.

Visual pigment genes can be isolated with modern genetic techniques (Nathans et al., 1986). Two classes of genes, L- and M-cone pigment genes, are arranged in a head-to-tail tandem array on the X chromosome in individuals with normal color vision. The most common arrangement of this array is a single L gene followed by 2 M genes (Nathans et al., 1986; Drummond-Borg et al., 1989; Neitz & Neitz, 1995; Neitz et al., 1995), though there can be variation in the number and identity of the downstream genes (Sjoberg et al., 1998). Protanomalous trichromats are missing the L-pigment gene and deuteranomalous trichromats are missing the M-pigment gene (Merbs & Nathans, 1992). Anomalous trichromats, however, have at least two of the other type of L/M pigment

gene, which usually result in a small difference in the photopigments' spectral sensitivity peaks (Deeb et al., 1992).

The mother or daughter of a male with an X-chromosome-linked color defect is an obligate carrier of the gene array for that color defect. Carriers have various degrees of deviant color vision from normal (Pickford, 1967). The Rayleigh match is a color-matching test to detect and diagnose red-green color defects. In the test, the observer matches a spectral light of 589 nm to a mixture of spectral 545 plus 670 nm lights. Carriers show a normal (Crone, 1959) to slightly displaced Rayleigh-match midpoint (Verriest, 1972; Jordan & Mollon, 1993) and some carriers have an increased match range compared to normals (Crone, 1959; Verriest, 1972; Jordan & Mollon, 1993). Of the 35 carriers examined by Schmidt (1934, 1955), most protan carriers had their match midpoint between the normal mean and the normal (upper) limit toward protanomaly; most deutan carriers had their match midpoint between the normal mean and the normal (lower) limit toward deuteranomaly.

Carriers' variant color vision may be explained by X-chromosome inactivation, referred to as Lyonization (Lyon, 1961). In embryonic life, one of the two X chromosomes in each female cell is proposed to be randomly inactivated; descendants of a given cell have the same active X chromosome as the parent cell. Female carriers of anomalous trichromacy possess two X chromo-

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somes and thus have genes encoding at least four types of cone photopigments. In addition to the normal's S, M, and L pigments, an additional L/M pigment may be present in the retina.

Women who have more than three types of cones are found to accept trichromatic matches (Nagy et al., 1981; Jordan & Mollon, 1993). In this study, the extra type of cone is assumed to transmit its response within normal trichromatic neural pathways.

The model

Signal pooling assumptions

An open question is how the signal from the extra cone pigment pools with the signals from M and L cones of normals. Three alternative hypotheses are considered: it pools with (1) the signal from a normal's L cones, (2) the signal from a normal's M cones, or (3) signals from both cone types.

For a carrier with two photopigments very similar to a normal's M [L] pigment, the "normal" M [L] pigment is defined as the one that is the same from both the normal and anomalous chromosomes. The additional (third) L/M pigment for protanomaly is denoted here as M^* (for deuteranomaly, L^*). M^* [L^*] is defined as the M [L] pigment from the anomalous X chromosome that is different from the normal M [L] pigment. This definition of M^* [L^*] provides notation to distinguish between two M [L] pigments but does not suggest that the M^* [L^*] pigment itself is genetically anomalous or abnormal.

Consider the assumptions for carriers of protanomaly who have L, M and the additional M^* photopigment (Fig. 1, top row; similar assumptions hold for carriers of deuteranomaly).

Assumption 1: The signal from M^ cones pools with only the signal from M cones*

The absorption spectra for M^* and M cones are most similar because M and M^* are actually subtypes of the middle-wavelength-sensitive photopigment. If the most similar responses are pooled then responses from M and M^* cones are combined. The assumption implies that retinal ganglion cells "recognize" both M^* and M as typical middle-wavelength-sensitive pigments, no specific cone-arrangement assumption is required.

Assumption 2: The signal from M^ cones pools with only the signal from L cones*

This assumption may be justified by cone mosaicism if it exists in carriers. Lyon (1961) hypothesized that one of the two X chromo-

somes in females becomes genetically inactivated early in a female embryo's development. When two populations of cells are present with different genotypes (one genotype from each of the X chromosomes), mosaicism follows. A calico cat with black and orange areas of fur is an example of skin mosaicism. For cone mosaicism, each time one X chromosome is activated the cone-pigment genes in that chromosome are expressed. If cells expressing cone pigment genes from one X chromosome form small patches (mosaicism patches), each patch consists of either (1) L and M cones (normal mosaicism patch) if the X chromosome is normal or (2) M^* and M cones (anomalous mosaicism patch) if the X chromosome is anomalous. Assume the proportion of cones in normal mosaicism patches is p and the proportion of cones in anomalous mosaicism patches is $1-p$. If luminance and chromatic pathways pool signals from both normal and anomalous mosaicism patches, then the spatially averaged luminance-pathway signal is

$$\begin{aligned} p(k_1 L + M) + (1-p)(k_2 M^* + M) \\ = pk_1 L + (1-p)k_2 M^* + M \end{aligned}$$

where k_1 is the L:M cone ratio in normal mosaicism patches and k_2 is the M^* :M ratio in anomalous mosaicism patches.

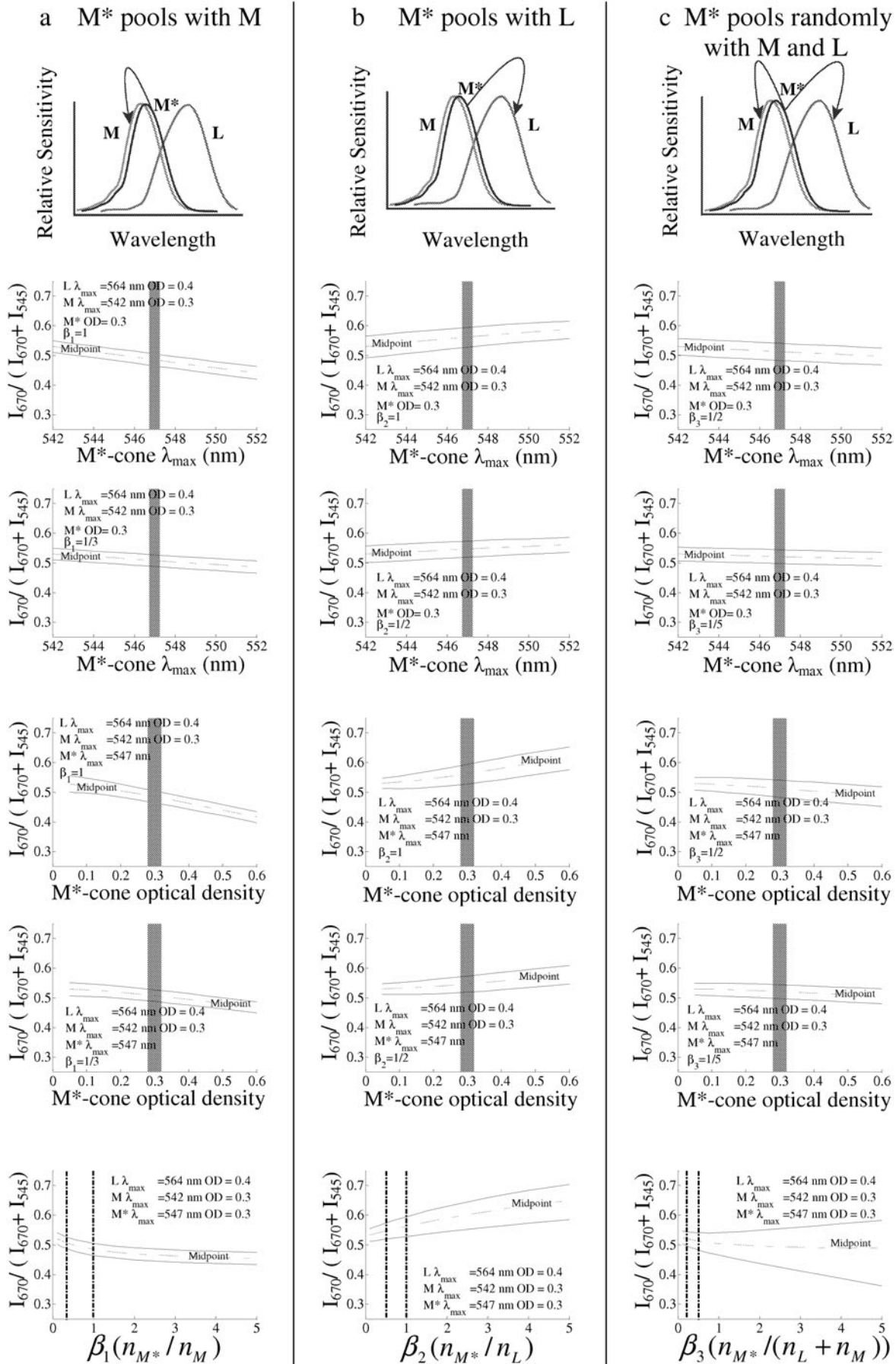
The analogous chromatic-pathway L-M signal under mosaicism is

$$\begin{aligned} p(k_1 L - q_1 M) + (1-p)(k_2 M^* - q_2 M) \\ = pk_1 L + (1-p)k_2 M^* - [pq_1 + (1-p)q_2]M, \end{aligned}$$

where q_1 [q_2] is the normalization factor for normal [anomalous] mosaicism patches. Normalization establishes a null opponent response to an equal-energy-spectrum (EES) "white" stimulus: $k_1 L - q_1 M = 0$ and $k_2 M^* - q_2 M = 0$; that is, the factor q_1 [q_2] balances the responses from different cones types in normal [anomalous] mosaicism patches.

The expressions for the luminance-pathway and opponent-pathway signals can be simplified to $c_1 L + c_2 M^* + M$ and $c_1 L + c_2 M^* - c_3 M$, respectively, where $c_1 = pk_1$, $c_2 = (1-p)k_2$ and $c_3 = [pq_1 + (1-p)q_2]$. These expressions show that the L- and M^* -cone signals are identically weighted and pooled in both the luminance and opponent pathways. The M-cone signal is added to or subtracted from the pooled response $c_1 L + c_2 M^*$ for the luminance or chromatically opponent responses. Thus cone mosaicism implies mathematically that the M^* -cone signal is pooled exclusively with the L-cone response.

Fig. 1. Predictions of Rayleigh-match midpoint and range for carriers of protanomaly. Rayleigh-match midpoints are indicated by dashed lines. The upper and lower limits of match ranges are shown by solid lines. *Column a:* the signal from M^* cones is assumed to pool only with the signal from M cones. *Column b:* the signal from M^* cones is assumed to pool only with the signal from L cones. *Column c:* the signal from M^* cones is assumed to pool randomly with the signals from both L and M cones. **(Row 1)** Schematic drawings showing the signal pooling assumptions (not to scale). **(Row 2)** Matches with various wavelengths of the M^* -cone spectral sensitivity peak and the M^* :M ratio from the anomalous X chromosome at 2:1. **(Row 3)** As Row 2 but with the M^* :M ratio from the anomalous X chromosome at 1:2. Gray vertical bars in Rows 2 and 3 mark the M^* sensitivity peak at 547 nm (as in Table 1). **(Row 4)** Matches with various M^* -cone optical densities and the M^* :M ratio from the anomalous X chromosome at 2:1. **(Row 5)** As Row 4 but with the M^* :M ratio from the anomalous X chromosome at 1:2. Gray vertical bars in Rows 4 and 5 mark the M^* optical density of 0.3 (as in Table 1). **(Row 6)** Matches with various ratios of the number of M^* cones to the number of M and/or L cones (matches with the M^* : M ratio from the anomalous X chromosome of either 2:1 or 1:2 is marked by vertical dashed lines).



Assumption 3: The signal from M cones pools with signals from both L and M cones*

If these three types of cones are randomly distributed, the signals may be pooled non-selectively. This assumption is consistent with a random cone mosaic (Roorda & Williams, 1999; Hofer et al., 2005).

It is important to distinguish mosaicism (patches of cones from the anomalous or normal X chromosome, Assumption 2) from retinal areas of a single cone-type (“clumps”), which are expected by chance. Mosaicism refers to areas of one or the other X-chromosome expression; mosaicism patches are different from clumps of cones with the identical photopigment. Clumps of cones of a single type are expected to occur with any of the three assumptions discussed above. While observed clumps in retina may or may not be caused by randomness, if randomness holds then some clumps will occur (Roorda et al., 2001). Carriers’ Rayleigh matches were modeled based on each of these three assumptions.

Theoretical modeling of the Rayleigh match

Normal and anomalous trichromats’ Rayleigh matches have been modeled previously (Burns & Elsner, 1985; Pokorny & Smith, 1990; He & Shevell, 1995; Thomas & Mollon, 2004). In this study, the Rayleigh match midpoint and range were determined using the method of He & Shevell (1995). Their model allows each pigment’s wavelength of peak sensitivity and optical density to be varied. In the current paper, the relative number of M* or L* cones also was varied to determine the influence on carriers’ Rayleigh matches.

Receptoral quantal absorption

The fraction of incident light absorbed by any cone type i ($i = L, M, M^*, L^*$) at wavelength λ depends on the extinction function $\varepsilon(i, \lambda)$ and the optical density (d) for the pigment. According to the Beer-Lambert law (Wysecki & Stiles, 1967), the fraction of light at wavelength λ absorbed by cone type i is

$$S_{i,\lambda} = T_\lambda [1 - 10^{-d\varepsilon(i,\lambda)}], \quad (1)$$

where T_λ is the transmittance of prereceptoral filters. Following DeMarco et al. (1992), optical density for the L [M] cones was assumed to be 0.4 [0.3] and the standard spectral sensitivity peak for L [M] cones was 564 nm [542 nm], energy based at the cornea (Table 1). Prereceptoral filtering was taken from Wysecki and Stiles (1967) and interpolated from 10 nm to 1 nm intervals.

Table 1. Assumptions about cone pigments for the Rayleigh-match predictions (assumptions about the normal’s L and M are from DeMarco, Pokorny, and Smith, 1992; the peak of L* [M*] is shifted -5 nm [+5nm] from the normal’s L [M])

Cone Pigment	Normal’s L	L*	Normal’s M	M*
Sensitivity Peak (nm)	564	559	542	547
Optical Density	0.4	0.4	0.3	0.3

The spectral sensitivity peak of an L* or M* cone was shifted from the L or M peak by 5 nm. The optical density for the L* [M*] cones was assumed to be 0.4 [0.3]. M*- and L*-cone absorption spectra are denoted by $S_{M^*,\lambda}$ and $S_{L^*,\lambda}$. They can be approximated closely by shifting the peak of the quantal absorption function of the normal’s L or M spectral sensitivity along a log-wave number axis (Wald, 1965; He & Shevell, 1995).

Postreceptoral non-quantal sensitivity

The Rayleigh match of a normal or anomalous trichromat involves two types of cones. A quantal match occurs when each type of cone absorbs the same number of photons from the two hemifields. A carrier’s Rayleigh match involves three types of cones. Her match cannot be quantal because the match depends on two postreceptoral neural signals for each hemifield. For simplicity, “neural L” for protanomaly is defined as a postreceptoral response with a spectral sensitivity that is a weighted sum of the absorption functions of the L cone and M* cone (L and L* cones for deuteranomaly). “Neural M” for protanomaly is a postreceptoral response with a spectral sensitivity that is a weighted sum of the absorption functions of the M and M* cones (M and L* cones for deuteranomaly). The case of the protanomalous carrier is given here. (The derivation for carriers of deuteranomaly is similar except that each occurrence of M* is replaced by L*.)

Assumption 1: M-cone signal pools with only the M-cone signal*

Let

$$\alpha = \frac{n_L}{n_M} \text{ and } \beta_1 = \frac{n_{M^*}}{n_M}, \quad (2)$$

where n_L , n_M and n_{M^*} are the number of L, M, and M* cones, respectively. Then the proportion of L cones among all cones is

$$P_L = \frac{n_L}{n_L + n_M + n_{M^*}} = \frac{\alpha n_M}{\alpha n_M + n_M + \beta_1 n_M} = \frac{\alpha}{\alpha + 1 + \beta_1}. \quad (3)$$

The proportion of M cones is

$$P_M = \frac{n_M}{n_L + n_M + n_{M^*}} = \frac{n_M}{\alpha n_M + n_M + \beta_1 n_M} = \frac{1}{\alpha + 1 + \beta_1}, \quad (4)$$

and the proportion of M* cones is

$$P_{M^*} = 1 - P_L - P_M = \frac{\beta_1}{\alpha + 1 + \beta_1}. \quad (5)$$

The weighted sensitivity function for the “neural L” response under this assumption is just the sensitivity for L alone:

$$S_{L_{\text{neural}},\lambda} = 1 \cdot S_{L,\lambda} + 0 \cdot S_{M^*,\lambda} = S_{L,\lambda}. \quad (6)$$

The sensitivity function of the “neural M” response is

$$\begin{aligned} S_{M_{\text{neural}},\lambda} &= \frac{P_M}{P_M + P_{M^*}} S_{M,\lambda} + \frac{P_{M^*}}{P_M + P_{M^*}} S_{M^*,\lambda} \\ &= \frac{1}{1 + \beta_1} (S_{M,\lambda} + \beta_1 S_{M^*,\lambda}). \end{aligned} \quad (7)$$

Note that α ($= n_L/n_M$) does not appear in Eqs. (6) or (7). Thus, the relative number of L to M cones does not affect the Rayleigh match.

Assumption 2: M^ -cone signal pools with only the L-cone signal*

Let

$$\alpha = \frac{n_L}{n_M} \text{ and } \beta_2 = \frac{n_{M^*}}{n_L}. \quad (8)$$

The sensitivity functions of the “neural L” and “neural M” responses are

$$\begin{aligned} S_{L_{neural},\lambda} &= \frac{P_L}{P_L + P_{M^*}} S_{L,\lambda} + \frac{P_{M^*}}{P_L + P_{M^*}} S_{M^*,\lambda} \\ &= \frac{1}{1 + \beta_2} (S_{L,\lambda} + \beta_2 S_{M^*,\lambda}) \end{aligned} \quad (9)$$

and

$$S_{M_{neural},\lambda} = 1 \cdot S_{M,\lambda} + 0 \cdot S_{M^*,\lambda} = S_{M,\lambda}. \quad (10)$$

Again, the relative number of L to M cones (α) does not affect the Rayleigh match.

Assumption 3: M^ -cone signal pools with both the L- and M-cone signals*

Let

$$\alpha = \frac{n_L}{n_M} \text{ and } \beta_3 = \frac{n_{M^*}}{n_L + n_M}. \quad (11)$$

If the signal from an M^* cone is randomly pooled with either an L or M cone, the relative number of L to M cones ($n_L/(n_L + n_M)$) determines the proportion of M^* cones contributing to the “neural L” and “neural M” responses. The proportion of M^* cones contributing to the “neural L” response is

$$\begin{aligned} P_{M^*(L)} &= \frac{n_L}{n_L + n_M} P_{M^*} = \frac{n_L}{n_L + n_M} \cdot \frac{n_{M^*}}{n_L + n_M + n_{M^*}} \\ &= \frac{\alpha}{\alpha + 1} \cdot \frac{(\alpha + 1)\beta_3}{\alpha + 1 + (\alpha + 1)\beta_3} = \frac{\alpha\beta_3}{(\alpha + 1)(\beta_3 + 1)} \end{aligned} \quad (12)$$

and the proportion of M^* cones contributing to the “neural M” response is

$$\begin{aligned} P_{M^*(M)} &= \frac{n_M}{n_L + n_M} P_{M^*} = \frac{n_M}{n_L + n_M} \cdot \frac{n_{M^*}}{n_L + n_M + n_{M^*}} \\ &= \frac{\beta_3}{(\alpha + 1)(\beta_3 + 1)}. \end{aligned} \quad (13)$$

Note that

$$P_L = \frac{\alpha}{(\alpha + 1)(\beta_3 + 1)} \text{ and } P_M = \frac{1}{(\alpha + 1)(\beta_3 + 1)}.$$

Thus, the sensitivity function of the “neural L” response is

$$\begin{aligned} S_{L_{neural},\lambda} &= \frac{P_L}{P_L + P_{M^*(L)}} S_{L,\lambda} + \frac{P_{M^*(L)}}{P_L + P_{M^*(L)}} S_{M^*,\lambda} \\ &= \frac{1}{\beta_3 + 1} (S_{L,\lambda} + \beta_3 S_{M^*,\lambda}). \end{aligned} \quad (14)$$

The sensitivity function of the “neural M” response is

$$\begin{aligned} S_{M_{neural},\lambda} &= \frac{P_M}{P_M + P_{M^*(M)}} S_{M,\lambda} + \frac{P_{M^*(M)}}{P_M + P_{M^*(M)}} S_{M^*,\lambda} \\ &= \frac{1}{\beta_3 + 1} (S_{M,\lambda} + \beta_3 S_{M^*,\lambda}). \end{aligned} \quad (15)$$

Modeling non-quantal matches and chromatic discrimination

The discrimination model for the Rayleigh match is taken from He and Shevell (1995):

$$\frac{I_{670}}{I_{545}} = \frac{U(S_{L_{neural},545} + S_{M_{neural},545}) - S_{L_{neural},545}(S_{L_{neural},589} + S_{M_{neural},589})}{S_{L_{neural},670}(S_{L_{neural},589} + S_{M_{neural},589}) - U(S_{L_{neural},670} + S_{M_{neural},670})}, \quad (16a)$$

where

$$\begin{aligned} U &= S_{L_{neural},589} \pm a\{(S_{L_{neural},589} + S_{M_{neural},589}) \\ &\quad + b[S_{L_{neural},589} - qS_{M_{neural},589}]\}. \end{aligned} \quad (16b)$$

It was applied to the sensitivity functions of the “neural L” and “neural M” responses. In Eq. (16a), I_λ is the radiance at wavelength λ ; a , b , and q are constants (see He & Shevell, 1995). When a is zero, Eq. (16a) gives the midpoint of the match; when a is negative, it specifies the lower end-point of the match; when a is positive, it specifies the upper end-point of the match. Mixture proportions of the Rayleigh match, $I_{670}/(I_{670} + I_{545}) = (I_{670}/I_{545})/(I_{670}/I_{545} + 1)$, were calculated for the usual “deutan mode” of anomaloscopic calibration in which the maximal level (100%) of the 670 nm light equals the maximal level of the 545 nm light with respect to quantal absorption by the L cone.

Results

Carriers of protanomaly and deuteranomaly

Rayleigh matches were predicted with Eq. (16), expressed as the proportion of 670 nm in the mixture, $I_{670}/(I_{670} + I_{545})$. Based on the characteristics of the normal's pigments (Table 1, from DeMarco et al., 1992), the match range for a normal trichromat is 0.51–0.55. The spectral sensitivity peaks of M^* and L^* pigments were assumed to be 547 nm and 559 nm, respectively (Table 1). These are 5 nm shifts toward long wavelengths and short wavelengths from the sensitivity peaks of the M and L pigments,

Table 2. Cone ratios implied by model

	Carriers of protanomaly		Carriers of deuteranomaly	
Normal X chromosome	$\frac{n_L}{n_M} = \frac{2}{1}$	$\frac{n_L}{n_M} = \frac{2}{1}$	$\frac{n_L}{n_M} = \frac{2}{1}$	$\frac{n_L}{n_M} = \frac{2}{1}$
Anomalous X chromosome	$\frac{n_{M^*}}{n_M} = \frac{2}{1}$	$\frac{n_{M^*}}{n_M} = \frac{1}{2}$	$\frac{n_{L^*}}{n_L} = \frac{2}{1}$	$\frac{n_{L^*}}{n_L} = \frac{1}{2}$
$\beta_1 = \frac{n_{M^*}}{n_M}$ or $\frac{n_{L^*}}{n_M}$	1	$\frac{1}{3}$	2	1
$\beta_2 = \frac{n_{M^*}}{n_L}$ or $\frac{n_{L^*}}{n_L}$	1	$\frac{1}{2}$	$\frac{2}{3}$	$\frac{1}{4}$
$\beta_3 = \frac{n_{M^*}}{n_L + n_M}$ or $\frac{n_{L^*}}{n_L + n_M}$	$\frac{1}{2}$	$\frac{1}{5}$	$\frac{1}{2}$	$\frac{1}{5}$

correspondingly. The moderate shifts of 5 nm were based on the studies of hybrid pigments by Merbs and Nathans (1992), Asenjo et al. (1994), Neitz et al. (1995) and Sharpe et al. (1998). Compared to the normal trichromat, a protanomalous trichromat needs more 670 nm light in the mixture to match 589 nm (0.81–0.94); a deuteranomalous trichromat requires less 670 nm light in the mixture (0.18–0.30). Both types of anomalous trichromats have a broader match range than the normal.

Assumptions about the relative number of the various cone types are needed to predict the Rayleigh matches of carriers. As described in the previous section, two cone ratios (α and β_i) are necessary to describe the relative cone numbers for a fovea with three types of L/M cones (L, M, and M* or L* cones). The ratio of L to M cones ($\alpha = n_L/n_M$), however, has no effect on the sensitivity functions “neural L” and “neural M”, and thus no effect on the Rayleigh match. For a carrier of protanomaly, the M*: M ratio from the defective X chromosome is assumed to be either 1:2 or 2:1, depending on whether M or M* is the first gene in the head to tail array; for a carrier of deuteranomaly, the L*: L ratio from the defective X chromosome is assumed to be 1:2 or 2:1, depending on whether L or L* is the first gene. Initial values of β_i assume (1) a carrier’s two X chromosomes (one normal and the other anomalous) are equally expressed and (2) the L: M ratio from the normal X-chromosome is 2:1 (note that this ratio is not α because it is not the ratio of the total number of L to M cones in the retina from the two X chromosomes). Cone ratios β_1 , β_2 and β_3 so calculated are shown in Table 2.

Under the assumption that the signal from the M* cones pools with only the signal from M cones, the predicted matches for a carrier of protanomaly shift toward less 670 nm in the mixture than the normal 0.51–0.55 (Table 3, second and third columns). This is particularly clear for an M*:M ratio from the anomalous X chromosome of 2:1. The protanomalous carrier’s matches shift in the opposite direction under the assumption that the signal from the M* cones pools with only the signal from L cones. In this case, the match overlaps part of the normal range whether M*:M is either 2:1 or 1:2. If the M* signal combines randomly with M and L, there can be slightly less 670 nm than normal in the match but still a region of substantial overlap with the normal range.

Schmidt (1934, 1955) reported that most protan carriers’ match midpoint was between the normal mean and the normal (upper) limit toward protanomaly. Those measurements are not expected if a carrier’s M*-cone signal pools with only the M cones because such pooling shifts matches toward the lower rather than upper normal limit. For example, with an M*:M ratio of 2:1, the predicted match midpoint is about 0.48. The other two assumptions, with M*-cone signals combining with signals from L cones, either exclusively or not, are viable and cannot be differentiated by the reported Rayleigh matches.

The predications for the Rayleigh-match range of a carrier of deuteranomaly are in the two rightmost columns of Table 3. Under the assumption that the signal from the L*-cone pools with only the signal from M cones, the predicted matches shift completely out of the normal range toward less 670 nm light in the mixture than

Table 3. Predications of Rayleigh-match ranges and midpoints (in parentheses) of $[I_{670}/(I_{670} + I_{545})]$ for carriers of protanomaly and deuteranomaly based on pigment assumptions in Table 1 and cone ratio assumptions in Table 2

M* - or L* -cone signal assumed to pool with:	Carriers of protanomaly (L, M and M*)		Carriers of deuteranomaly (L, M and L*)	
	M*:M ratio		L*:L ratio	
	$\frac{n_{M^*}}{n_M} = \frac{2}{1}$	$\frac{n_{M^*}}{n_M} = \frac{1}{2}$	$\frac{n_{L^*}}{n_L} = \frac{2}{1}$	$\frac{n_{L^*}}{n_L} = \frac{1}{1}$
Only M	0.46–0.50 (0.484)	0.49–0.53 (0.507)	0.35–0.43 (0.392)	0.41–0.47 (0.439)
Only L	0.53–0.59 (0.562)	0.52–0.57 (0.546)	0.53–0.57 (0.553)	0.52–0.56 (0.540)
Both L and M	0.48–0.54 (0.512)	0.50–0.54 (0.521)	0.48–0.53 (0.505)	0.49–0.54 (0.517)

normal. The predicted matches under the other two assumptions overlap with part of the normal range. Schmidt reported that deutan carriers' had a match midpoint between the normal mean and the normal (lower) limit toward deuteranomaly. Comparison of Schmidt's report to the model's results suggests that the signal from the L* cones does not pool exclusively with the M-cone signal.

Possible causes of protanomalous carriers' individual differences in Rayleigh matches

The Rayleigh matches of carriers of protanomaly are affected by three features of cones with M* photopigment: wavelength-of-peak-sensitivity, optical density, and the relative number of M* cones. The influence of these factors is shown in Fig. 1.

Spectral location of M-cone sensitivity peak*

The spectral peak sensitivity (λ_{\max}) of M* photopigment changes the Rayleigh-match midpoint but has little effect on the match width (rows 2 and 3, Figs. 1a, 1b, 1c). The predicted Rayleigh match shifts toward less 670 nm light in the mixture as the λ_{\max} difference between M and M* increases, under the assumption that the signal from M* cones pools with responses from only M cones (rows 2 and 3, Fig. 1a; when M* and M have the identical peak at the vertical axis, the match is identical to the normal match). The predicted match shifts in the same direction, but to a lesser extent, under the assumption that the M*-cone signal pools with both cone types (rows 2 and 3, Fig. 1c). The predicted match shifts in the opposite direction under the assumption that the M*-cone signal pools with only L cones (rows 2 and 3, Fig. 1b). These relations might help to differentiate the three assumptions with knowledge of the Rayleigh matches from a large number of carriers with various cone-pigment spectral sensitivity peaks, inferred for example from genetics (Carroll et al., 2002). Note that varying the λ_{\max} difference alters the magnitude but not direction of shift from normal. For example, the direction of shift is always contrary to Schmidt's matches when M* pools with only M.

Optical density of M cones*

The optical density of the M* cones changes the Rayleigh-match midpoint but has limited effect on the range (rows 4 and 5, Figs. 1a, 1b, 1c). The predicted Rayleigh match changes as the M*-cone optical density increases, in a manner similar to the increase in λ_{\max} difference between M and M* (rows 2 and 3). These relations also might help to differentiate the three assumptions with Rayleigh matches from a large number of carriers by, for example, comparing Rayleigh matches before and after optical density reduction by photopigment bleaching. Varying optical density changes the magnitude but not direction of shift from normal so for all densities the direction of shift is not in accord with Schmidt's measurements when M* pools with only M.

Relative number of M cones*

The relative number of M* cones in the retinal area responsible for the color match strongly alters carriers' Rayleigh-match midpoint and/or range (bottom row, Figs. 1a, 1b, 1c). As shown in Eqs. (7), (9), (14), and (15), the ratio α of the number of L to M cones (n_L/n_M) does not contribute to the relative spectral sensitivities of "neural L" and "neural M" and thus does not change the match.

The relative number of M* cones, however, does influence these spectral sensitivities. Cone ratios β_1 , β_2 and β_3 in Eqs. (2), (8), and (11) have different definitions for the three different signal-pooling assumptions. In each case, the relative number of M* cones substantially alters carriers' Rayleigh matches (bottom row, Fig. 1) but, again, not the direction of shift from normal.

Under the assumption that the signal from the M* cones pools with only M cones (bottom panel, Fig. 1a), the predicted match range changes very little but the midpoint shifts toward less 670 nm light with increases in the ratio $\beta_1 (= n_{M^*}/n_M)$. Under the assumption that the signal from the M* cones pools with only L cones (bottom panel, Fig. 1b), the range enlarges and the midpoint shifts rapidly toward more 670 nm light in the mixture as the ratio increases ($\beta_2 = n_{M^*}/n_L$). Finally, under the assumption that the signal from the M* cones pools with responses from both cone types (bottom panel, Fig. 1c), if the ratio β_3 is 1.0 or less the predicted Rayleigh-match range changes little; if the ratio is greater than 1.0, the predicted Rayleigh-match range increases rapidly with increases in the ratio $\beta_3 (= n_{M^*}/(n_L + n_M))$.

Normal or anomalous trichromats have two types of cones in the L/M range. The relative number of the two cone types does not affect the quantal match. In carriers of anomaly, however, three types of cones are involved. If the three types of cones feed only two distinct neural pathways then the relative number of M* or L* cones alters the two weighted-sum neural responses and thus the Rayleigh match.

Conclusions

The model shows that the M*- and L*-cone pigments may cause carriers to make normal to shifted Rayleigh matches. The comparisons between Schmidt's classical measurements and the model predictions for carriers of both protanomaly and deuteranomaly indicate that the signal from M* or L* cones is unlikely to pool with only the response from the M cones. Instead, M* or L* cones appear to pool their signal with the L-cone signal, either exclusively (as implied by mosaicism) or randomly with both M and L. Individual differences in the spectral sensitivity peak, optical density and the relative number of the cones can cause individual differences in carriers' Rayleigh matches, though individual differences in the ratio of L to M cones does not affect carriers' matches.

References

- ASENJO, A.B., RIM, J. & OPRIAN, D.D. (1994). Molecular determinants of human red/green color discrimination. *Neuron* **12**, 1131–1138.
- BURNS, S. & ELSNER, A. (1985). Color matching at high illuminance: The color-match-area-effect and photopigment bleaching. *Journal of the Optical Society America A* **2**, 698–704.
- CARROLL, J., NEITZ, J. & NEITZ, M. (2002). Estimates of L:M cone ratio from ERG flicker photometry and genetics. *Journal of Vision* **2**, 531–542.
- CRONE, R.A. (1959). Spectral sensitivity in color-defective subjects and heterozygous carriers. *American Journal of Ophthalmology* **48**, 231–238.
- DEEB, S.S., LINDSEY, D.T., HIBIYA, Y., SANOCKI, E., WINDERICKX, J., TELLER, D.Y. & MOTULSKY, A.G. (1992). Genotype-phenotype relationships in human red/green color-vision defects: Molecular and psychophysical studies. *American Journal of Human Genetics* **51**, 687–700.
- DEMARCO, P., POKORNY, J. & SMITH, V.C. (1992). Full-spectrum cone sensitivity functions for X-chromosome-linked anomalous trichromats. *Journal of the Optical Society of America A* **9**, 1465–1476.
- DRUMMOND-BORG, M., DEEB, S.S. & MOTULSKY, A.G. (1989). Molecular patterns of X chromosome-linked color vision genes among 134 men of

- European Ancestry. *Proceedings of the National Academy of Sciences* **86**, 983–987.
- HE, J.C. & SHEVELL, S.K. (1995). Variation in color matching and discrimination among deuteranomalous trichromats: Theoretical implications of small differences in photopigments. *Vision Research* **35**, 2579–2588.
- HOFER, H., CARROLL, J., NEITZ, J., NEITZ, M. & WILLIAMS, D.R. (2005). Organization of the human trichromatic cone mosaic. *Journal of Neuroscience* **25**, 9669–9679.
- JORDAN, G. & MOLLON, J.D. (1993). A study of women heterozygous for colour deficiencies. *Vision Research* **33**, 1495–1508.
- LYON, M.F. (1961). Gene action in the X-chromosome of the mouse (*Mus musculus* L.). *Nature* **190**, 372–373.
- MERBS, S.L. & NATHANS, J. (1992). Absorption spectra of the hybrid pigments responsible for anomalous color vision. *Science* **258**, 464–466.
- NAGY, A.L., MACLEOD, D.I.A., HEYNEMAN, N.E. & EISNER, A. (1981). Four cone pigments in women heterozygous for color deficiency. *Journal of the Optical Society of America A* **71**, 719–722.
- NATHANS, J., THOMAS, D. & HOGNESS, D.S. (1986). Molecular genetics of human color vision: The genes encoding blue, green, and red pigments. *Science* **232**, 193–202.
- NEITZ, M. & NEITZ, J. (1995). Numbers and ratios of visual pigment genes for normal red-green color vision. *Science* **267**, 1013–1016.
- NEITZ, M., NEITZ, J. & GRISHOK, A. (1995). Polymorphism in the number of genes encoding long-wavelength-sensitive cone pigments among males with normal color vision. *Vision Research* **35**, 2395–2407.
- PICKFORD, R.W. (1967). Variability and consistency in the manifestation of red-green colour vision defects. *Vision Research* **7**, 65–77.
- POKORNY, J. & SMITH, V.C. (1990). Color matching as a clinical tool: Theory of modification by disease. In *International Research Group on Color Vision Deficiencies. Symposium (1990, Tokyo, Japan)*, pp. 255–267. The Netherlands: Kugler & Ghedini.
- RAYLEIGH, L. (1881). Experiments on colour. *Nature* **25**, 64–66.
- ROORDA, A., METHA, A.B., LENNIE, P. & WILLIAMS, D.R. (2001). Packing arrangement of the three cone classes in primate retina. *Vision Research* **41**, 1291–1306.
- ROORDA, A. & WILLIAMS, D.R. (1999). The arrangement of the three cone classes in the living human eye. *Nature* **397**, 520–522.
- SCHMIDT, I. (1934). Über manifeste Heterozygotie bei konduktorinnen für Farbensinnstörungen. *Klinische Monatsblätter für Augenheilkunde* **92**, 456–467.
- SCHMIDT, I. (1955). A sign of manifest heterozygosity in carriers of color deficiency. *American Journal of Optometry* **32**, 404–408.
- SHARPE, L.T., STOCKMAN, A., JÄGLE, H., KNAU, H., KLAUSEN, G., REITNER, A. & NATHANS, J. (1998). Red, green, and red-green hybrid pigments in the human retina: correlations between deduced protein sequences and psychophysically measured spectral sensitivities. *Journal of Neuroscience* **18**, 10053–10069.
- SJOBERG, S.A., NEITZ, M., BALDING, S.D. & NEITZ, J. (1998). L-cone pigment genes expressed in normal colour vision. *Vision Research* **38**, 3213–3219.
- THOMAS, P.B.M. & MOLLON, J.D. (2004). Modelling the Rayleigh match. *Visual Neuroscience* **21**, 477–482.
- VERRIEST, G. (1972). Chromaticity discrimination in protan and deutan heterozygotes. *Die Farbe* **21**, 7–16.
- WALD, G. (1965). Frequency or wavelength. *Science* **150**, 1239–1240.
- WYSZECKI, G., STILES, W.S. (1967). *Color Science: Concepts and Methods, Quantitative Data and Formulae*. New York: John Wiley and Sons.