

How Do Photoreceptors Work: Counting Photons and Producing Photocurrents

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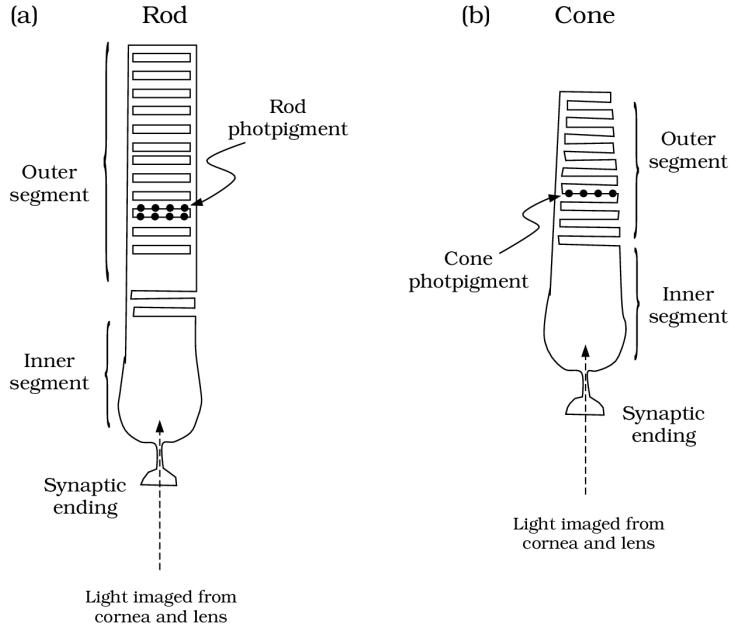


Figure 1: Anatomical structures of rods and cones. The outer segment contains photon-absorbing photopigments, which of which has the capability of absorbing a photon and being excited/isomerized after absorption. From [Wandell \[1995, Fig. 3.2\]](#).

1 Counting Photons: Principle of Univariance

Anatomically, a photoreceptor has two parts: an inner segment and an outer segment. Photons enter from the inner segment, which for the most part can be thought of as a waveguide that funnels the photons to the outer segment. The outer segment contains the photon-absorbing pigments. This is illustrated in Figure 1.

Conceptually, we can think of each photoreceptor as a bucket that collects photons. There are millions of buckets sitting on the retina, having a shower of photons. Many photons entering the eye will not hit any bucket: they are absorbed before they reach the bucket (e.g., by the lens). Any photon that does hit the bucket has certain *probability* of being absorbed. The absorption probability varies with the photoreceptor type and the photon's wavelength.

Fundamentally, a photoreceptor can absorb photons because it contains light-sensitive, photon-absorbing pigments, each of which is able to absorb one photon. Each rod photoreceptor has tens of millions of such pigments [[Nathans, 1992](#), [Milo and Phillips, 2015](#), p. 142-147]. Why is a photon's absorption probability not 100% once it enters a photoreceptor? For one, a photon might not meet a photopigment as it travels through the photoreceptor before the exit. Even if a photon hits a pigment, its absorption is still probabilistic, as absorption is dictated fundamentally by quantum mechanics.

Once a photon is absorbed, it has a certain probability of “exciting” or “isomerizing” the

pigment. A pigment **excitation** or **isomerization** generates a certain level of electrical signal — in the form of a current or voltage change across the cell membrane of the photoreceptor. The excitation probability once a photon is absorbed is called the **quantum efficiency** of the pigment. Quantum efficiency is about two-thirds in the visible spectrum, and is not wavelength sensitive [Dartnall, 1972, Kropf, 1982, Fu, 2010]. A pigment excitation is also called pigment **bleach**, since the pigment after excitation is no longer responsive to light as if it is bleached.

The process of initiating an electrical response upon a photon absorption is called phototransduction. We will study this process in detail shortly in Chapter 4. For now, it is important to know that for a given photoreceptor type the electrical response caused by a photon absorption is constant regardless of the photon's wavelength. This is called the **Principle of Univalence** [Rushton, 1972a,b, Naka and Rushton, 1966]: each photon that generates an electrical response has the same effect as any other photon that does so. In other words, the only effect that wavelength has is to impact the probability a photon gets absorbed; after absorption the wavelength information is lost.

A crucial implication of this principle is that any two lights that are equally absorbed/excited will be seen as the same light by the human vision. *Only* for the purpose of comparing two lights, we can think of each bucket as having a counter; every time a photon is absorbed and excites a pigment, the counter gets incremented by 1. If two lights lead to the same counter value, they are perceptually the same. Crucially, if a bucket's counter is, say, twice as high as another's, it does *not* mean the electrical responses produced by the first photoreceptor is twice as high as that of the second. We will see why this is the case shortly.

2 Spectral Absorbance, Absorptance, and Sensitivity

To understand vision in everyday scenarios, what we care about is not the probability of how a single photon is absorbed and excites a pigment, but the collective behavior of a flux of photons that enter our eyes. Conveniently, when we have a large population of photons, the probability that an individual photon causes an excitation translates to the *percentage* of incident photons that are absorbed and/or cause excitations. In fact, the percentage of absorption is the quantity that we can directly measure.

There are in general two ways to estimate the absorption rate of a flux of photons. The direct way of measurement is using a technique called microspectrophotometry (MSP). The indirect method is to measure the electrical responses using, e.g., suction electrode, and then estimate the absorption. The indirect method gives us only relative absorption across wavelengths, while the MSP approach gives us absolute absorption.

2.1 Absorbance Spectra from Microspectrophotometry

The idea of MSP is to shine a beam of light through a photoreceptor and then measure, at the other side, the percentage of photons that are transmitted, i.e., unabsorbed [Bowmaker,

1984]. Ignoring back-scattering¹, photon absorption by photopigments in a photoreceptor can be modeled using the Beer-Lambert law. The **transmittance** at wavelength λ is defined as the ratio between the amount of transmitted photons $I_d(\lambda)$ and the amount of total incident photons $I_0(\lambda)$:

$$T(\lambda) = \frac{I_d(\lambda)}{I_0(\lambda)} = e^{-\epsilon(\lambda)cl}, \quad (1)$$

where $\epsilon(\lambda)$ is called the absorption coefficient and is wavelength dependent, c is the concentration (the number of pigments per unit volume), and l is the optical length, the length through which a photon has to travel². Both c and l are inherent properties of a photoreceptor and are not dependent on photon wavelength.

Absorptance $a(\lambda)$, the percentage of absorption at λ , is naturally $1 - T(\lambda)$. **Absorbance** $A(\lambda)$ (also called the **optical density**), whose spelling is subtly and annoyingly different from that of absorptance, is defined as:

$$A(\lambda) = -\ln(T(\lambda)) = \epsilon(\lambda)cl. \quad (2)$$

Therefore, absorptance $a(\lambda)$ and absorbance $A(\lambda)$ are related by:

$$a(\lambda) = 1 - e^{-A(\lambda)}. \quad (3)$$

We would repeat this experiment over a frequency range and obtain the axial absorbance at each sampled frequency. The resulting plot is usually called the **absorbance spectrum**. One such example is shown in the right panel in Figure 2, measured by Dartnall et al. [1983] on humans. Many such data have been obtained in the literature, the earliest of which is perhaps work by Marks et al. [1964] and Brown and Wald [1964], which identified three distinct absorbance spectra in cone-mediated vision and, thus, provided physiological evidence for the existence of three types of cone. The three cone types are generally referred to as the **L**, **M**, and **S** cones, since their absorbances peak at, relatively, long, medium, and short wavelengths.

Normalization

Quite often, the absorbance spectrum is normalized to peak at unity, as is the case in Figure 2 (right). According to Equation 2, normalizing absorbance across different wavelengths is equivalent to normalizing ϵ across wavelengths, since c and l are not wavelength specific, whereas

¹The reason we want to ignore back-scattering is so that we can assume any unabsorbed photons will be transmitted through, and measured at the other side of, the photoreceptor. In reality, some photons might be scattered backward toward where they come from and will not be measured either.

² $\epsilon(\lambda)$ so-defined has a unit of m^2 , and c so-defined has a unit of $1/m^3$. In the literature sometimes people define $\epsilon(\lambda)$ to be the **molar absorption coefficient**, which has a unit of m^2/mol , and define c to be the **molar concentration** (the number of moles of pigments per unit volume), which has a unit of mol/m^3 .

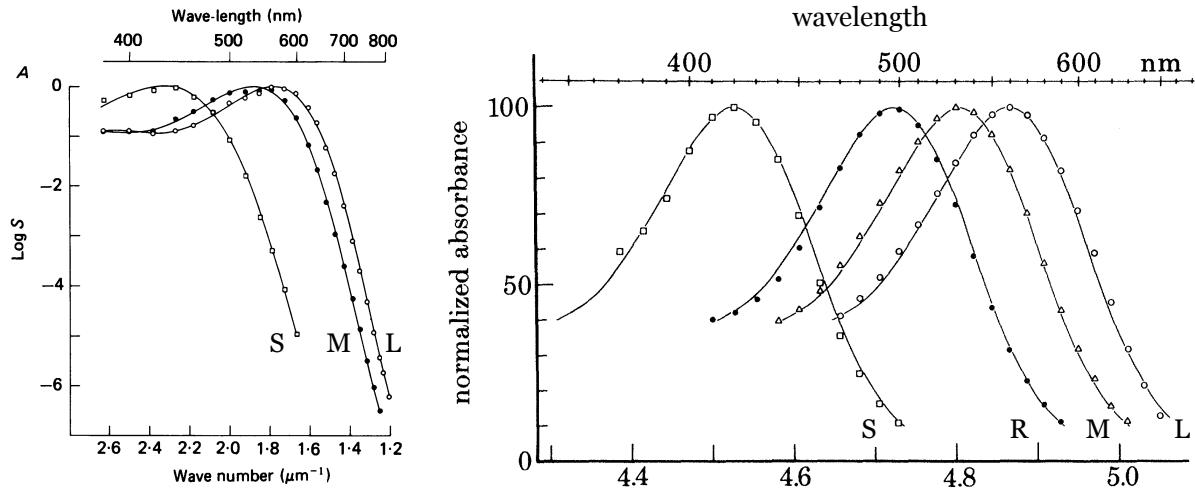


Figure 2: Left: Log-scaled spectral sensitivities of the cones (L, M, S) in a macaque. Adapted from [Baylor et al. \[1987, Fig. 3A\]](#). The spectra are normalized to peak at 1. Right: Absorbance spectra of the three cones (L, M, S) and the rod (R) in a human. The spectra are normalized to peak at 100. Adapted from [Dartnall et al. \[1983, Fig. 2\]](#).

ϵ is. c and l might vary across species and across individuals and might differ between different illumination methods (see below), but ϵ , which is fundamental to the photopigment, does not. Therefore, the normalized absorbance spectrum tells us something fundamental about the wavelength sensitivity of the photopigments.

Perhaps a subtlety but quite confusing when perusing the literature, the maximum absolute absorbance across all wavelengths (i.e., the peak of an absorbance spectrum) is usually simply called the “optical density”; “peak optical density” would have been more accurate, as optical density is wavelength specific. Using the peak optical density and the normalized absorbance spectrum, we can reconstruct the absolute absorbance spectrum, from there we can get the absolute absorptance spectrum.

While not shown here, the peak absorbance between rods and cones are not that different. The peak absorbance of rods is about 0.475, and the value is about 0.375 for foveal S cones and 0.525 for foveal L/M cones [[Bowmaker et al., 1978](#), [Bowmaker and Dartnall, 1980](#)]. The large sensitivity difference between rod vision and cone vision is not primarily attributed to the difference in their ability to absorb photons.

Correcting for Transverse Illuminations

There is one complication. With MSP, we illuminate a photoreceptor *transversely*, i.e., the light passes from one side of the photoreceptor to the other side. In reality when a photon enters a photoreceptor, it travels *axially* from the inner segment through the outer segment. The main difference between these two scenarios is the optical length that a photon has to travel. A photoreceptor is tall and skinny, so its width is much smaller than its length, about $2.5 \mu\text{m}$ wide

and $35 \mu\text{m}$ long for a fovea L/M cone [Polyak, 1941].

Therefore, we need to first calculate the absorbance per unit length, called the **specific absorbance**, and then scale the specific absorbance by the axial length of the photoreceptor to obtain the axial absorbance, from which we can estimate the axial absorptance using Equation 3. This is shown below (omitting λ for simplicity):

$$A_{\text{transverse}} = -\ln(p_{\text{transverse}}) = \epsilon l_{\text{transverse}} \quad (4a)$$

$$A_{\text{specific}} = \frac{A_{\text{transverse}}}{l_{\text{transverse}}} = \epsilon c \quad (4b)$$

$$A_{\text{axial}} = A_{\text{specific}} l_{\text{axial}} \quad (4c)$$

$$p_{\text{axial}} = e^{-A_{\text{axial}}} \quad (4d)$$

2.2 Relative Absorptance Spectra from Electrical Responses

Another method is by measuring the photoreceptor's electrical responses across different wavelengths using techniques such as suction electrode, which records the electrical responses of an isolated photoreceptor sucked into a micropipette. Spectra so-estimated are usually called the spectral sensitivity of the photoreceptors in the literature, but as we will see, they are equivalent to the *normalized* absorptance spectra.

Figure 3 illustrates the idea, where Baylor and Hodgkin [1973] measured the peak electrical response of a turtle cone (in photovoltage; y -axis) as a function of light intensity (x -axis) at two wavelengths: 644 nm and 539 nm . We see that the curves are almost parallel to each other: we can laterally move the 644 nm curve to coincide that of 539 nm . In this case, we have to shift the former by 1.27 log unit.

Think for a second what this means. When we increase the intensity at 644 nm by a factor of $10^{1.27}$, the sheer number of photons absorbed at 644 nm is increased by a factor of $10^{1.27}$, too. That means without scaling the number of incident photons at 644 nm is $10^{-1.27}$ (about 5.4%) of that at 539 nm . Even with just 5.4% of incident photons, 644 nm light is able to produce the same level of electrical response, i.e., cause the same amount of photon absorption (given the Principle of Univarience), as the light at 539 nm . Therefore, we can say the absorption rate (absorptance) at 644 nm is $10^{1.27}$ higher than of that at 539 nm .

We repeat this experiment across other wavelengths and obtain the relatively spectral sensitivity/absorptance spectra. The left panel in Figure 2 shows one such example obtained by Baylor et al. [1987] on macaque cones. Critically, the absorptance so-obtained is relative: we do not know the absolute absorptance at either wavelength. The y -axis is necessarily normalized to peak at unity. Similar data have been collected on humans as well [Schnapf et al., 1987, Kraft et al., 1993].

Normalized Spectra From the Two Methods Match Well

It is worth noting that suction electrode also uses transversely illuminated lights. Since the absorptance obtained here is relative, we cannot easily use the method in Equation 4 to obtain

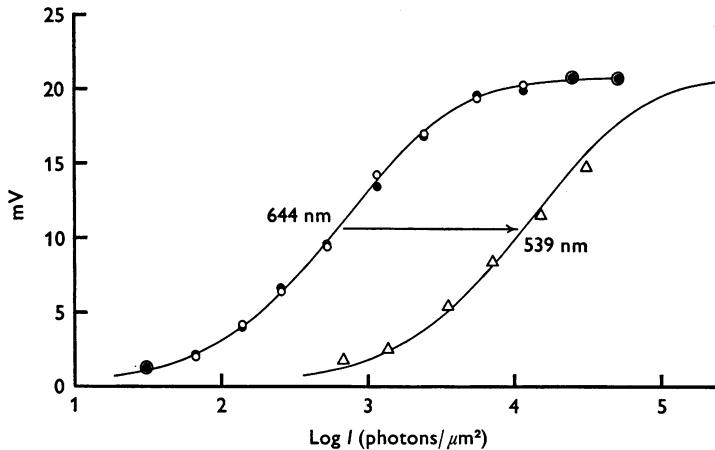


Figure 3: Each curve shows the electrical response (in photovoltage; y -axis) as a function of light intensity (x -axis) at a given wavelength. To estimate the relative sensitivity/absorptance between two wavelengths, we laterally shift one curve so that it coincides with the other. Given the Principle of Univariance, the amount of shift is proportional to the relative absorptance. From [Baylor and Hodgkin \[1973, Fig. 8\]](#).

the absorptance spectra for the axial illumination.

Here is the catch. Numerically, $1 - e^{-A} \approx A$ when A is small. When we illuminate a photoreceptor transversely, the optical length l is the photoreceptor width, which is short, which means A is small [[Wyszecki and Stiles, 1982](#), p. 588, p. 594]. Therefore, the transverse absorbanse and transverse absorptance are approximately equal. So the normalized absorptance spectrum given by the suction electrode method *is* approximately the normalized absorbanse spectrum, as is shown experimentally [[Schnapf et al., 1987](#)] [[Stockman and Sharpe, 2000](#), Fig. 11].

The normalized absorbanse spectra are still not sufficient, since to use the method in Equation 4 we need to know the absolute absorbanse spectra. People usually have to resort to another data source that provides absolute peak absorbanse or fit the data against, e.g., psychophysical measurements that provide some form of absolute measures [[Kraft et al., 1993](#), [Baylor et al., 1984, 1987](#)].

3 Cone Fundamentals: Cornea-Referred Spectral Sensitivities

Our discussions so far have focused on absorption by the photoreceptors, but for a flux of photons arriving at the cornea about to enter our eye, they are also absorbed even before reaching the photoreceptors. Accounting for these **pre-receptoral** filters is important to model human vision. Spectral sensitivities that account for these pre-receptoral filters is what I call cornea-referred spectral sensitivities.

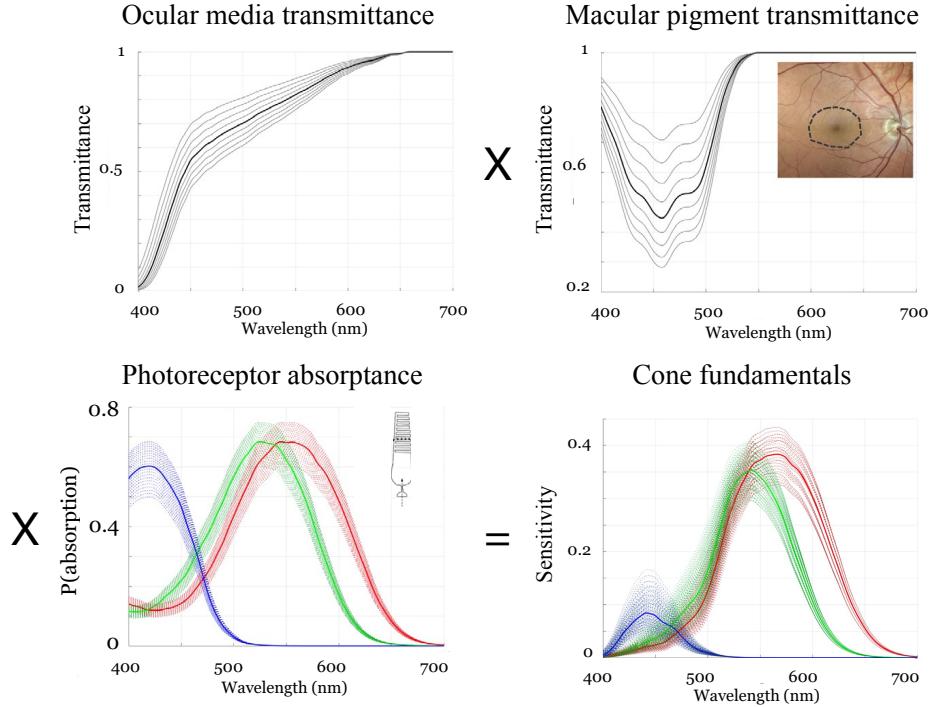


Figure 4: Cornea-referred spectral sensitivity measures the percentage of photons arriving at the cornea (about to enter the eye) that are absorbed by each photoreceptor type at each wavelength. The cone versions of this are called the cone fundamentals and what are visualized here. The sensitivity metric relates to the rate of pigment excitation only by a constant scaling factor (i.e., the photoreceptor quantum efficiency, which is about two-thirds). It is a product of ocular transmittance, macular transmittance, and photoreceptor absorptance. Solid lines represent average values, and light lines represent variations among individuals. Adapted from [Wandell et al. \[2022, Fig. 9, Fig. 10\]](#).

3.1 Cone Fundamentals From Physiology

There are two such pre-receptoral filters: the ocular media (as we have discussed before in the class) and the macular pigments, which are located at a small area in the fovea. Macular pigments absorb lights presumably to counter some of the aberrations from the ocular media and to protect the retina from light damage [[Snodderly et al., 1984](#)]. Both ocular media and macular pigments absorb lights selectively over the spectrum, just like photoreceptors do.

We can model $E(\lambda)$, the fraction of photons arriving at the cornea that are absorbed by the photoreceptors:

$$E(\lambda) = l(\lambda)m(\lambda)a(\lambda) \quad (5)$$

where $a(\lambda)$ represents the photoreceptor absorptance at wavelength λ , $l(\lambda)$ and $m(\lambda)$ represent

ocular and macular transmittance, respectively, i.e., the fraction of photons at λ *unabsorbed* by the ocular media (e.g., lens) [Boettner and Wolter, 1962, Norren and Vos, 1974] and the macular pigments. Figure 4 illustrates this process.

I call these spectra cornea-referred spectral sensitivity functions, since they are calculated with respect to the incident lights at the cornea surface. The cone versions of these sensitivity functions are more commonly called **cone fundamentals**. While based on the same underlying data, the visualizations of the cone fundamentals sometimes differ in at least two ways.

First, sometimes the spectra are normalized so that each function peaks at 1. This normalization eliminates the differences at peak across photoreceptor types, but retains the relative spectral sensitivity within a particular type. Thus, this normalization is useful when we care only about comparing the sensitivity of different wavelengths of a particular type of photoreceptor, but not across different types of photoreceptor. We will see both normalized and unnormalized forms. When unnormalized, be careful whether the data shows the absorption or excitation — their normalized forms are the same, since quantum efficiency is a constant at about two-thirds in the wavelength range that we care about.

Second, the cone fundamentals here are given “equal-quantal”: the absorption rates at different wavelengths are given assuming each wavelength has the same amount of photons. Sometimes, especially in CIE standards, the cone fundamentals (and other functions related to cone fundamentals such as luminous efficiency function and color matching functions, both of which we will discuss later) are given based on “equal-energy”, assuming each wavelength has the same energy/power not the same amount. The equal-energy definition is practically useful since the spectrum of a light is defined as power/energy distribution, rather than quantal distribution, over wavelength.

We can make a few general observations about the cone fundamentals. First, the cone sensitivity generally drops to 0 generally beyond the 380 nm and 780 nm range, a range we usually call the visible spectrum, since there will be no pigment excitation beyond that range: lights beyond that range are invisible.

Second, S cones are generally the least sensitive of the three cone types, but it is not because of the photoreceptors, but because of the pre-receptoral filters, which absorb mostly low-wavelength lights.

Finally, the sensitivity peaks of the L cones and M cones are very similar (off by about 20 nm), but both are rather far from the peak of the S cones. This suggests that S cones are quite different from L and M cones. Mammals have only two cone types, a short-wavelength sensitive cone type and a long-wavelength sensitive cone type; the former is evolved into S cones, and the latter separated fairly recently into L cones and M cones [Jacobs, 2008]. The fascinating history of human vision evolution, much of which is understood by comparative studies of our vision with other vertebrates and primates and from individuals with color vision deficiencies, is nicely reviewed by Bowmaker [1998], Jacobs [2008], and Neitz and Neitz [2011]. We will have more to say about this when we discuss color vision later in the class.

3.2 Cone Fundamentals From Psychophysics

The spectral sensitivities discussed above are measured physiologically. We can also measure such functions through psychophysics using what is called the *increment threshold* method. A typical set up is one where there is a uniform background illumination and a spot light superimposed at the center of the background. We ask a participant to adjust a knob to control the intensity of the spot light so that it is just noticeable from the background. The sensitivity is then defined as the reciprocal of the threshold intensity. We repeat this experiment for each sampled wavelength across the spectrum to obtain a sensitivity curve. This method is first used in the pioneering work done by W.S. Stiles [Stiles, 1939, 1959, 1964], and is adopted in virtually all later work [Wald, 1964, Smith and Pokorny, 1975, Stockman et al., 1999, Stockman and Sharpe, 2000].

A curious question is how we can separate the sensitivity of different photoreceptor types, given that the spectral sensitivities of the four types photoreceptor overlap. There are two methods to isolate rods from cones. We can either use very dim lights, to which cone responses are too small to contribute to vision [Crawford, 1949], or we could measure from people with rod monochromacy — individuals who have only rods. When measuring cone sensitivities, we will use intense lights that almost completely saturate rods.

Isolating the three cone types from each other is generally challenging with individuals with normal vision. W.S. Stiles' initial work [Stiles, 1939, 1959] designed special conditions of background illumination to suppress the sensitivity of two unwanted cone types while sparing the one under study. Modern studies usually turn to color-deficient individuals who lack one or two cone types. Isolating S cones is done by measuring from S-cone monochromats [Stockman et al., 1999]. Isolating L and M cones is challenging because individuals with only L or M cones are very rare and the spectral sensitivities of the L and M cones overlap substantially. Instead, a common approach is to resort to Protanopes and Deuteranopes; the former has only M and S cones and the latter has only L and S cones. To isolate M (L) cones from the S cones, we measure from Protanopes (Deuteranopes) using lights that have high spatial and/or temporal frequencies, to which S cones are known to be insensitive [Stockman and Sharpe, 2000, Smith and Pokorny, 1975].

3.3 Physiological and Psychophysical Sensitivities Match Well

We can then compare the spectral sensitivity data from physiology and from psychophysics. This is shown in Figure 5. See the Figure caption for details. Overall it is fair to say that the two sets of data match well.

Think about what this comparison means. What we measure in psychophysics is the threshold intensity (at each wavelength) needed to evoke a criterion level of human *behavioral response* (i.e., just noticeability). The threshold intensity in the physiological measurement represents how much light is needed (at each wavelength) to cause the same amount of pigment absorption and, by the Principle of Univarience, the amount of *electrical responses*. The fact that the two sets of data match suggest that the amount of electrical response we need to evoke a just-noticeable level of perception is a constant regardless of wavelength, a perhaps unsurprising

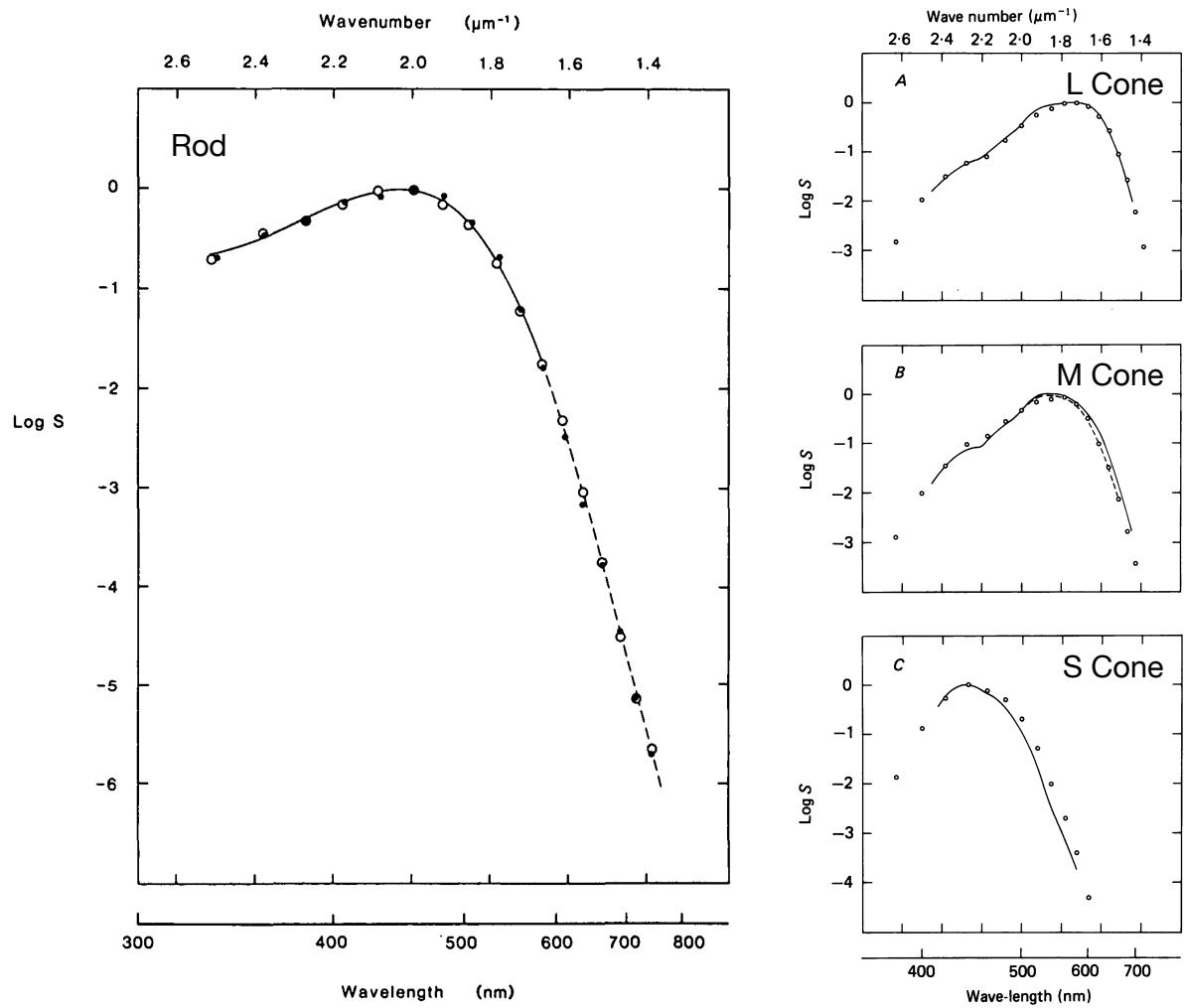


Figure 5: Left: comparison of the physiologically-obtained rod spectral sensitivity from macaques (open circles) and the rod spectral sensitivity from human psychophysics (filled circles); adapted from [Baylor \[1987, Fig. 14\]](#), which is after [Baylor et al. \[1984, Fig. 5\]](#) Right: comparison of the spectral sensitivity of the three cone types between physiology data (open circles; from macaques) and psychophysics data (curves; from humans); adapted from [Baylor et al. \[1987, Fig. 5\]](#). The human psychophysics data is from [Stiles \[1959\]](#) for cones and from [Crawford \[1949\]](#) for rods.

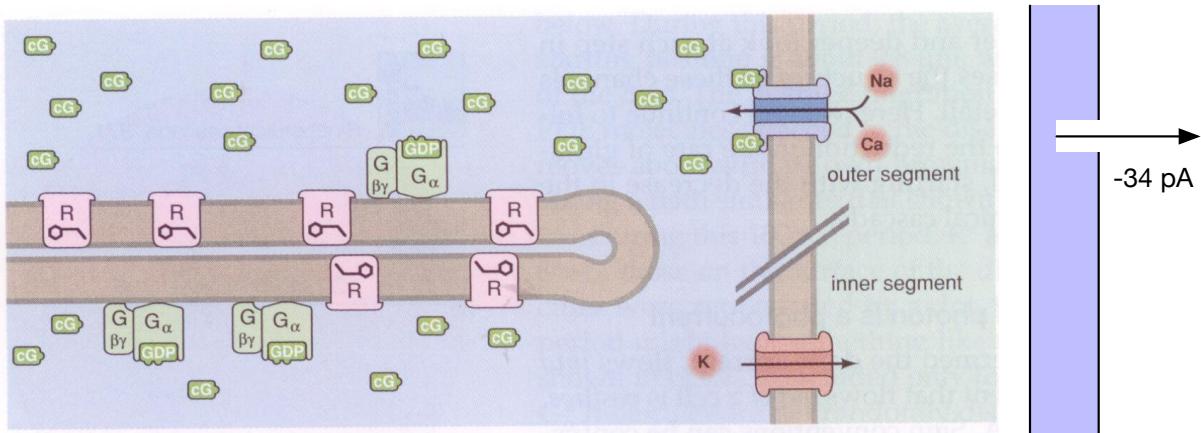


Figure 6: cGMP-gated ion channels keep a transmembrane current of about -34 pA for each photoreceptor in the dark. The current is called the dark current, and its negative sign indicates that the direction of the current is inward). Adapted from [Rodieck \[1998, p. 172\]](#)

inference.

Interestingly, the physiological data in Figure 5 is obtained from macaques and the psychophysical data is from humans. The fact that they match well suggests the similarities of the visual system among primates — we have come a long way since the monkey days but our photoreceptors have not changed much. Other studies obtaining the physiological sensitivity data from humans show similarly good matches with human psychophysical data [[Crescitelli and Dartnall, 1953](#), [Kraft et al., 1993](#), [Bowmaker and Dartnall, 1980](#), [Mollon, 1982](#)].

4 Beyond Counting Photons: Phototransduction and Recovery

The discussion so far about (spectral) sensitivity has focused on the ability of different types of photoreceptor to absorb (“count”) photons at different wavelengths, and by that measure, rods and cones are not that different: their peak absorbances differ by less than 10% (Chapter 2.1). So then why do we say rod vision is more sensitive than cone vision? What we have ignored is the absolute *strength* of the electrical response once photons are absorbed. To understand the absolute response strength, we need to understand the cellular and molecular processes underlying how electrical responses are actually produced from pigment excitations. These processes constitute the so-called **phototransduction cascade**, and is the focus of this section. George Wald, who won the Nobel Prize in 1967, is largely credited for elucidating these processes [[Wald, 1933, 1968](#)].

4.1 Phototransduction Cascade

The phototransduction cascades in rods and (different types of) cones are exactly the same. The differences appear to be quantitatively rather than qualitatively, and are dictated by the genes

expressing the isoforms of the molecules participating in phototransduction [Ingram et al., 2016, Yau, 1994]. We will mainly use rods as an example to drive the discussion here.

Photoreceptor Has a Stable Transmembrane Current in Dark

A visual pigment in a rod is a special molecule called a rhodopsin, which has two parts: a long strand of protein called opsin (which is insensitive to light) and the light-sensitive ***11-cis* retinal**, a form of Vitamin A as discovered by Wald [1933], that is attached to the opsin and acts as a chromophore. Hofmann and Lamb [2023] present a comprehensive survey of what is known about rhodopsin to date.

In dark, there is a stable current of -34 pA that flows *into* the outer segment called the **dark current**. By convention, inward current is defined as negative. This is illustrated in Figure 6. The dark current is a result of a particular kind of cation-selective ion channels that are permeable to both Na^+ and Ca^{2+} flowing into the outer segment. Critically, these channels are ligand-gated channel — gated by cyclic guanosine monophosphate (cGMP) molecules [Fesenko et al., 1985, Yau and Baylor, 1989]. Think of cGMPs as the guards of the channels; on average each channel needs three cGMPs to remain open [Rodieck, 1998, p. 169]. In a rod outer segment in darkness, there are ample amount (3-4 micromole) of cGMPs, which bind to a large amount of channels and keep them open.

As a result of the dark current, the membrane potential of a photoreceptor in dark is about -35 mV. If you are familiar with basic neuroscience, you would notice that the photoreceptor in dark is depolarized, since the membrane potential is higher than that of the resting potential of a typical neuron. The depolarization is exactly caused by the inward flow of cations through the cGMP-gated channels.

Closing Ion Channels Produces Electrical Responses

Once a photon is absorbed and, with a two-third chance of exciting a pigment (dictated by quantum efficiency, as discussed in Chapter 1), the ***11-cis* retinal** of the pigment changes to its isomer called ***all-trans* retinal** (which will later be separated from the pigment). This is why a pigment excitation is often called a **photoisomerizaton**. This all takes place remarkably fast: the absorption takes about 3 fs and the photoisomerization takes about 200 fs [Gruhl et al., 2023] [Rodieck, 1998, p. 162].

The isomerization changes the conformation of a rhodopsin pigment, which becomes “activated”: it diffuses randomly and activates a transducin (a form of G protein) whenever they meet. This is illustrated by step ① in Figure 7. On average, an activated pigment activates about 700-800 transducins [Purves et al., 2017, p. 243] [Rodieck, 1998, p. 170]. Each activated G protein then meets and binds to a molecule called “cGMP-specific phosphodiesterase” (PDE), activating the PDE. This is step ② in Figure 7. Each activated PDE has the ability to catalyze the hydrolysis of several dozen cGMPs [Rieke and Baylor, 1998], reducing the cGMP concentrations. This is step ③ in Figure 7.

We know that the ion channels that induce dark current are gated by cGMPs. A reduction in cGMP concentration will close some of these channels, *reducing* the dark current and

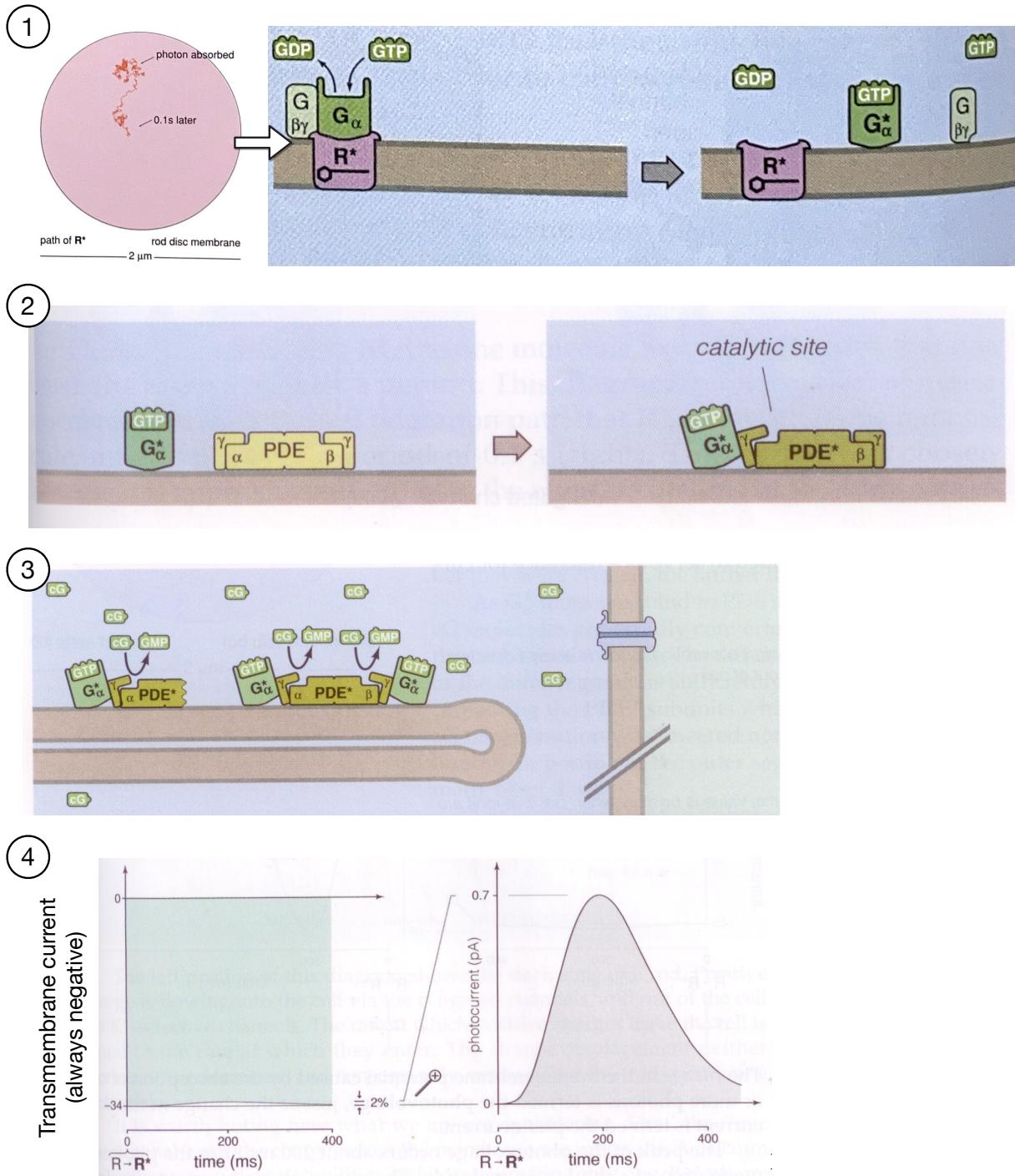


Figure 7: Steps involved in phototransduction. A single excited rhodopsin pigment can close about 2% of the cGMP-gated ion channels, introducing a photocurrent (change in the transmembrane current) of about 0.7 pA; photocurrent is always positive whereas the actual transmembrane current is always negative. Adapted from Rodieck [1998, p. 166–172]

increasing the membrane potential (i.e., the photoreceptor hyperpolarizes). This membrane current/potential change *is* the electrical response of photon absorptions, and *is* the signal that will be delivered to the rest of the visual system to eventually give rise to vision.

At the peak of this transduction process, a single activated rhodopsin in a rod can reduce the number of cGMPs by about 1,400, which translates to about 2% closure of the cGMP-gated channels [Rodieck, 1998, p. 170]. Since each cGMP-gated channel carry the same amount of current, this means the total membrane current is reduced by about 2%. This is step ④ in Figure 7. In the literature, the *change* of membrane current and voltage potential is usually termed **photocurrent** and **photovoltage**, respectively. Since the change in the membrane current is positive and the change in the membrane voltage is negative, the photocurrent is positive and the photovoltage is negative. The actual transmembrane current and voltage are always negative. Some electrophysiological techniques measure the total membrane current/voltage while other measure the photocurrent/photovoltage. Be careful of what quantify is being reported when perusing the literature.

4.2 Deactivation of Phototransduction and Pigment Regeneration

If phototransduction continues without any hindrance, eventually 1) all pigments will be bleached (isomerized), and 2) all the ion channels will be open. If so, the photoreceptor and, ultimately, our visual system will not be able to respond to further lights: additional photons cannot be absorbed and, even if they are absorbed and excite pigments, there are no ion channels to close and so no electrical response will be produced; at that point, our visual system *saturates*.

In order for our visual system to continue responding to lights, two things must take place. First, there must be mechanisms to terminate the phototransduction and re-open the ion channels [Burns and Arshavsky, 2005, Burns and Baylor, 2001]. Second, new pigments must be continuously regenerated. This is the job of the **retinoid cycle** or the **visual cycle**.

Phototransductions are Continuously Being Deactivated

There are activities *constantly* at work attempting to terminate the phototransduction. This can be seen by observing the response kinetics of a photoreceptor to lights. The left panel in Figure 8 shows the photocurrent kinetics of macaque rods in response to a flash light [Baylor et al., 1984]; the right panel shows the photocurrent kinetics of macaque M cones when presented with a step light, i.e., a constant background illumination [Schnapf et al., 1990]. Without the deactivation activities, the responses to the flash light would not have been eliminated after the flash light is removed and the responses to the step light would not have reached an equilibrium.

For the phototransduction cascade to terminate, there are mechanisms to deactivate every step in the transduction: activated rhodopsin must be deactivated so that they cannot activate more G proteins, activated G protein must come off the PDE so that the PDE cannot hydrolyze more cGMPs, the cGMPs must be replenished, and the cGMP-gated ion channels must reopen. Every step must be deactivated; for instance, it is not sufficient to just deactivate the pigments: that just means the inactivated pigments will not activate more G proteins, but

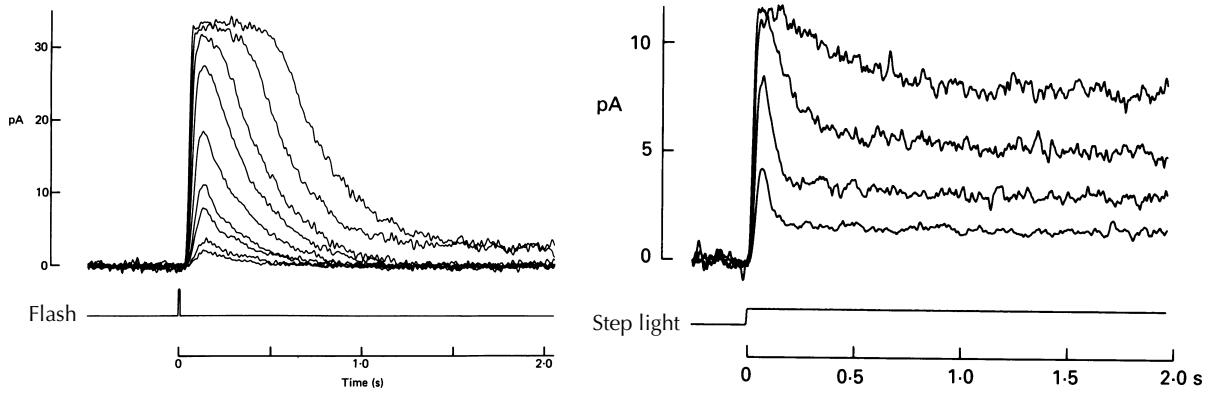


Figure 8: There are activities constantly at work to deactivate the phototransduction. This can be seen by observing the response kinetics to a flash light (left) and to a step light (right). Without the deactivation activities, the responses to the flash light would not have been eliminated and the responses to the step light would not have reached an equilibrium. Left: macaque rods; adapted from Baylor et al. [1984, Fig. 1]; Right: macaque M cones; adapted from Schnapf et al. [1990, Fig. 7A].

existing G proteins that are still activated will continue activating PDEs and the rest of the phototransduction.

The deactivation also involves a set of biochemical reactions that we will not detail here, but just to give you a flavor, here is how the pigments are deactivated, and the process is illustrated in Figure 9. An enzyme, rhodopsin kinase (RK), binds to and phosphorylates an activated pigment. Another protein called arrestin (A) then binds to phosphorylated pigment, which inhibits the pigment's ability to activate G proteins, essentially deactivating the pigment.

Deactivation is Accelerated by Negative Feedbacks

Interestingly, some of the deactivation steps are *accelerated* by *negative feedback* mechanisms mediated by Ca^{2+} concentration. One such mechanism is shown in Figure 10. Let's briefly take a look at this, not only because it is a classical example of the dynamics common in visual neuroscience (and many dynamical systems) but also because we will come back to this negative feedback when we discuss light adaptation later in the class.

The closing of cGMP-gated channels from phototransduction reduces the inward flows of Ca^{2+} and Na^+ to the outer segment. Importantly, Ca^{2+} inhibits guanylate cyclase (GC), which inherently re-synthesizes cGMPs. As the Ca^{2+} level reduces, the cGMP re-synthesis rate increases, which replenishes cGMPs and re-opens ion channels. That is, phototransduction initially reduces the cGMP concentration, and the very reduction of concentration serves to replenish the cGMPs — the feedback is negative. Without this negative feedback, the response still would have stabilized. For instance, soon after we move the flash light the cGMP concentration will stop falling while the GC-induced resynthesis is steadily going on. Eventually, the cGMP con-

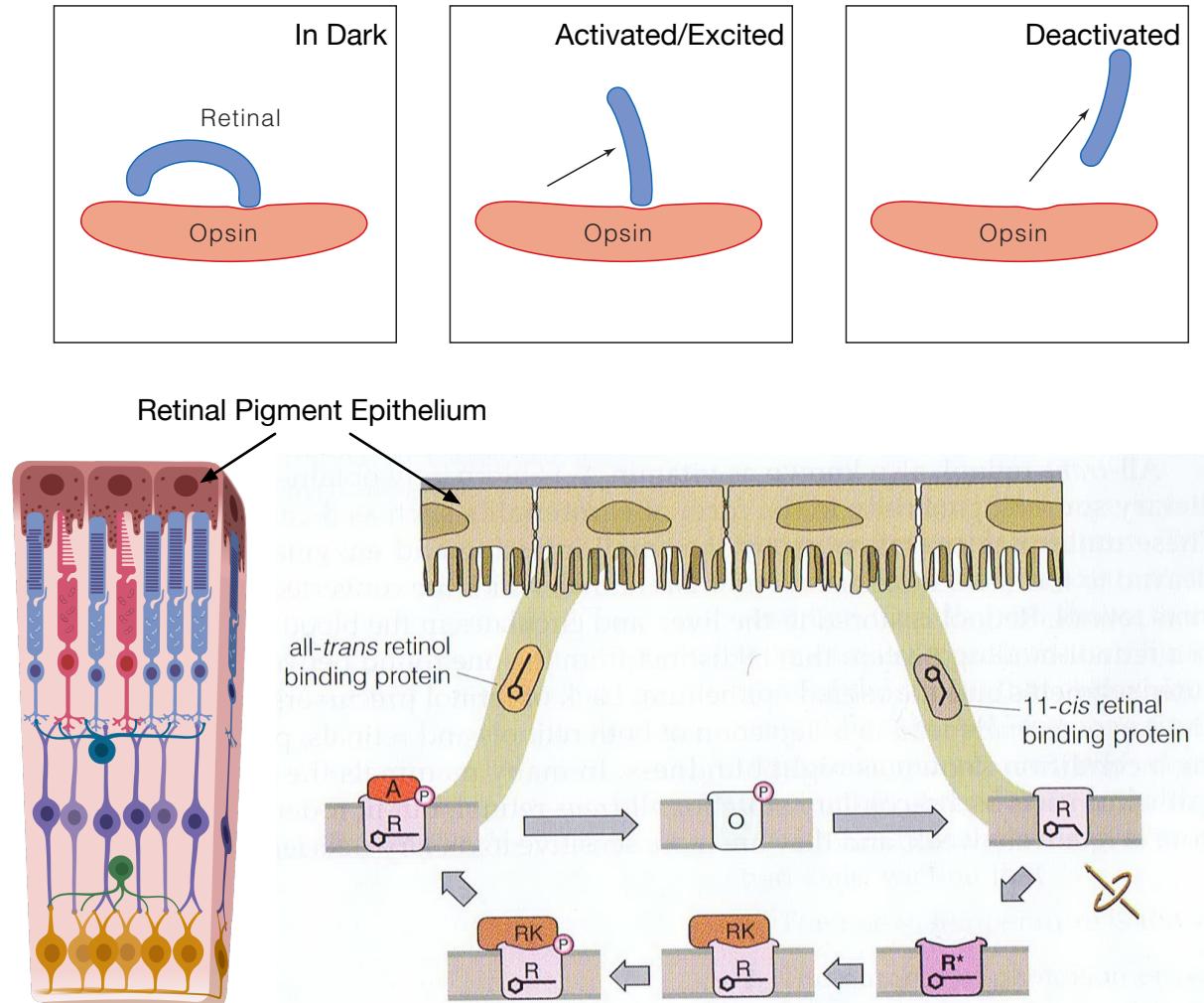


Figure 9: Steps involved in pigment deactivation and regeneration. An activated pigment is first deactivated, at which point the *11-cis* retinal falls off the opsin and is transported to the RPE to be re-synthesized back to *all-trans* retinal. Top: adapted from Goldstein [2009, Fig. 3.20]; Bottom right: from Rodieck [1998, p. 511]; R* denotes activated pigments, RK denotes rhodopsin kinase, and A denotes arrestin.

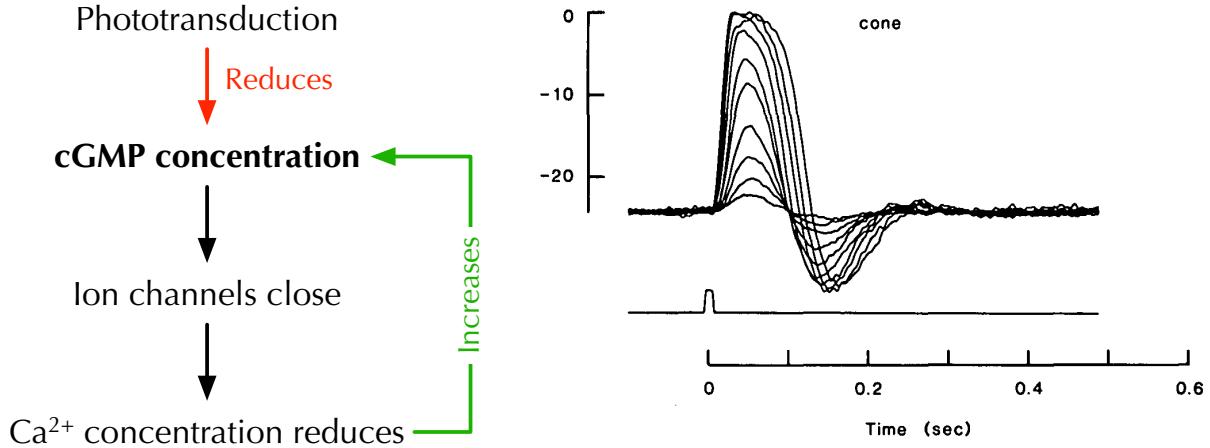


Figure 10: The deactivation is accelerated by the negative feedback from Ca^{2+} . The negative feedback is so strong in cones that the response kinetics have undershoots. Right: macaque L cones; from [Baylor \[1987, Fig. 11\]](#).

centration will be restored to the original level³. The negative feedback simply accelerates this process.

The strength of the negative feedback is much stronger in cones than in rods [[Yau and Hardie, 2009](#), [Burns and Baylor, 2001](#)]. The stronger negative feedback is the reason why cone responses recover much faster than do rods: compare the kinetics of macaque rods under flash lights of varying intensities in Figure 8 (left) and the macaque L cone kinetics under the same set of lights in Figure 10 (right), and pay attention to the timescale on the *x*-axis. In cones, the negative feedback is so strong that there is actually a temporary over-provision of cGMPs during the deactivation phase, leading to an undershoot in the current (right panel in Figure 10).

The negative feedback through Ca^{2+} concentration also accelerates other steps in deactivation, including accelerating pigment deactivation (although with a much less potent effect than that on the GC [[Nikonov et al., 2000](#), [Pugh Jr et al., 1999](#)]) and increasing the sensitivity of cGMP-gated channels to cGMPs (so that the channels can be open even at lower cGMP levels) [[Hsu and Molday, 1993](#)].

Pigments are Continuously Being Regenerated

Deactivating phototransduction is not enough; it re-opens ion channels and replenish all the materials involved in phototransduction — except the pigments themselves. Pigments must somehow be restored so that they are available for phototransduction again, and this is the

³You might be wondering: if the GC-induced re-synthesis is always going on, wouldn't the outer segment of a photoreceptor be packed with cGMP molecules? It turns out that in dark even unactivated PDEs can hydrolyze cGMPs — at a much lower rate than activated PDEs do. These two forces counter each other and maintain a steady cGMP level in dark [[Rodieck, 1998](#), p. 373].

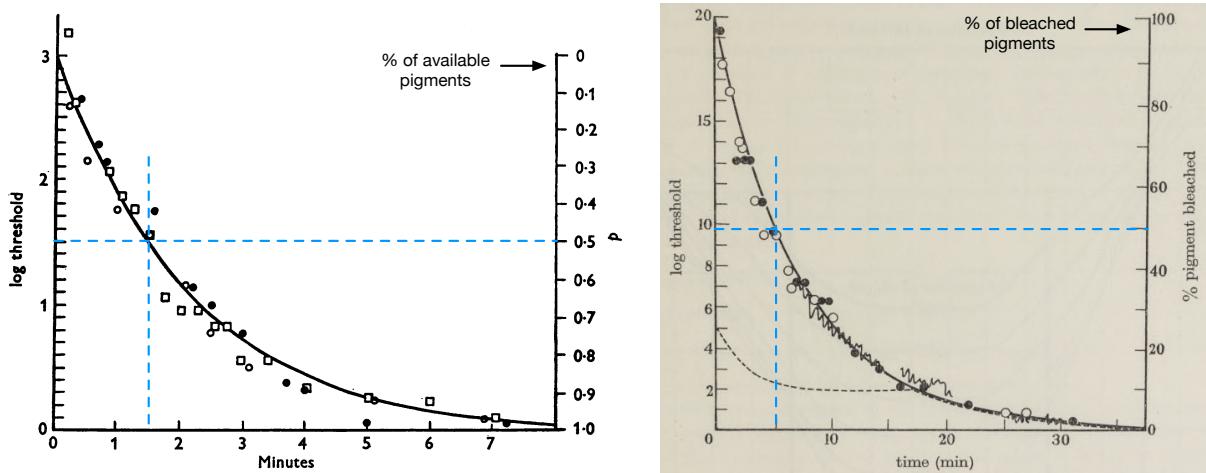


Figure 11: Bleach all pigments using intense light, then remove light and measure the fraction of available/bleached pigments vs. time in dark. Left: human rod kinetics; adapted from Rushton [1963, Fig. 3]; Right: human cone kinetics; adapted from Rushton [1965, Fig. 3].

job of the retinoid cycle. An activated pigment roams about randomly and gets deactivated when it meets rhodopsin kinase and arrestin. When an activated pigment is deactivated, the *all-trans* retinal falls off the pigment. This is shown in the top panel in Figure 9. The *all-trans* retinals then leave the photoreceptor and are transported to the Retinal Pigment Epithelium (RPE), which is a layer of special skin cells just outside the retina and is where *all-trans* retinals are converted back to *11-cis* retinals, which are then transported back to the outer segment, recombining with the opsin portion of the pigment, at which point the pigment is re-constituted to its original form and is sensitive to photons again. This is shown in the bottom panel in Figure 9.

Rushton used retinal densitometry to measure the pigment regeneration of both cones and rods in the living eye. The kinetics of the rod and cone pigment regenerations are shown in Figure 11. The half-life of cone pigments regeneration is about 3 times shorter than that of rod pigments [Rushton, 1961, 1963, 1965]. The fast regeneration of cone pigments means it is unlikely that the steady-state cone pigment bleaching level exceeds about 90% under the normal range of illumination levels throughout a day [Burns and Lamb, 2014, p. 15]. In contrast, under normal daylight rod pigments are almost all bleached.

Compared to the speed of pigment generation, the deactivation of phototransduction takes place much more rapidly. On average, a cone pigment is regenerated in about 2 minutes [Rodieck, 1998, p. 184-185], and phototransduction deactivation (and activation for that matter) happens in millisecond scale. Imagine in your visual field there is a brief flash. You see the flash as a flash, because the phototransduction initiated by the flash quickly goes away almost immediately as the flash is removed.

Steady Vision Means Equilibrium

Both pigment regeneration and phototransduction deactivation are constantly at work, countering the effect of the phototransduction in light. The more pigments are excited and the more ion channels are open, the stronger the deactivation and pigment regeneration processes are.

Under a modest background illumination, the opposing forces reach an equilibrium where the rate of closing cGMP-gated ion channels matches that of re-opening them. So dynamically a fixed number, not all, of the ion channels are open. If after light exposure we move to a dark room, there is no photons coming in so there is no phototransduction. The countering forces completely dominate and eventually all the materials involved in phototransduction are replenished and all the ion channels are open — another equilibrium. If we flash a light on top of the background, some cGMP channels open for a short period time and then close as the flash goes away; our vision goes back to the steady state.

If we increase the intensity of the steady background a little, again some cGMP channels will open and simultaneously the countering forces are at work trying to close them. Eventually a new equilibrium is reached where more channels are steadily open than before. What if we keep increasing the background light's intensity? Every time we intensify the background light a little, we reach a new equilibrium with fewer channels steadily open. This is readily seen in the right panel in Figure 8, where the steady-state response increases (i.e., fewer channels are open) as the background light intensity increases. Eventually all the channels will close, and our vision is said to be saturated. This is what we will study next.

5 Absolute Sensitivity and Saturation in Rods vs. Cones

Now that we understand phototransduction and its recovery, we can appreciate some fundamental differences between rods and cones in their absolute sensitivity and saturation levels, which shape our daily visual experience.

5.1 Rods Have a Much Higher Signal-to-Noise Ratio Than Cones

Psychophysical experiments show that human can reliably detect a flash when only about 5 to 7 pigments are excited in a field of about 500 rods; in contrast, it takes about 5 pigment excitations *per cone* in a pool of about 10 cones for humans to signal a flash [Hecht et al., 1942, Barlow, 1956, Donner, 1992, Angueyra-Aristizábal, 2014]. Assuming the visual system requires the same level of electrical response to see a flash, the difference suggests that rods are able to produce the same amount electrical response using fewer pigment excitations than cones.

Part of this can be explained by the different levels of neural convergence in the rod and cone pathway, which we have discussed before. But the difference in sensitivity between the photoreceptors themselves also plays a significant role: rod photoreceptors have a higher electrical response and a lower noise floor than cones. This contributes to the lower detection threshold in rod vision. Let's examine the signal and the noise separately.

Single Photon Response is Much Larger in Rods than in Cones

The photocurrent, i.e., the signal part of the SNR, from a single rod pigment excitation is about 20 times higher than that by a cone pigment excitation (34 pA vs. 0.7 pA) [Baylor et al., 1979b, 1984, Baylor, 1987, Schnapf et al., 1990, Ingram et al., 2016, Angueyra-Aristizábal, 2014]. A single rod pigment excitation already closes about 2% of the ion channels in a rod, and about 30 pigment excitations would close half of the ion channels in a rod in dark. In contrast, it requires about 650 pigment excitations in a cone photoreceptor to provide a half-maximal response in dark [Baylor et al., 1984, Schnapf et al., 1990].

Part of the reason why rods have larger responses than cones is because the phototransduction cascade in rods is much more rapid [Ingram et al., 2016]: the rate of PDE activation is higher, the rate of cGMP concentration reduction is higher, etc. As a result, a lot of cGMP-gated ion channels already close before much of the “countering forces” (that are simultaneously trying to deactivate phototransductions) kick in, resulting in higher peak responses in rods than in cones.

Cones are Much Noisier than Rods

Not only do rods produce a higher response per pigment excitation, the inherent noise in a rod is much lower than that in a cone. Photocurrents exist even in dark — because of noise, which comes from two main sources [Baylor et al., 1980, Rieke and Baylor, 2000]: 1) the spontaneous, thermal-induced activations of pigments, which shows up as discrete spikes in photocurrents, and 2) the spontaneous activation of PDEs, which causes the cGMP concentration to fluctuate and shows up as the continuous rumbling of the photocurrent [Rieke and Baylor, 1996]. Photocurrent in dark has the equivalent effect of a background illumination in dark, so it is also termed **dark noise, dark light**, or “eigengrau” (German: one’s own light). As we can imagine, dark noise interferes with light detection when the signal is weak, i.e., illumination is dim [Barlow, 1957], where behaviorally we cannot tell for certain if we are seeing actual light or dark light.

Dark noise is much higher in cones than in rods [Angueyra-Aristizábal, 2014, Donner, 1992]. For instance, the dark light in rods is equivalent to about once pigment excitation every 90 seconds [Baylor et al., 1984] and about 500 – 1,000 times per second in cones [Schnapf et al., 1990, Schneeweis and Schnapf, 1999, Rieke and Baylor, 2000, Burns and Lamb, 2014, Rieke and Baylor, 1998]. The dark light in cones is high enough to allow a rod to reach its half-maximum response [Tamura et al., 1991, Nakatani and Yau, 1988, Matthews et al., 1988]! As a result, the SNR in cones is much lower than that in rods.

5.2 Rods Saturate Much More Easily Than Cones

We know the rod-mediated vision saturate under much lower light levels than does the cone-mediated vision. Because of this, rods are not useful in mediating vision typical daylight illuminations. Cones are much harder to saturate, if ever, under normal daylight [Burns and Lamb, 2014, Barlow, 1972, Shevell, 1977], so they are primarily responsible for daylight vision. But why do the rod-mediated vision saturate more easily, other than the higher degree of neural

convergence? Again, the difference in the photoreceptor themselves plays a role.

First, the photocurrent generated by a pigment excitation is much higher in rods than in cones, as discussed before. Second, the phototransduction kinetics is faster in cones than in rods. As we have seen in Figure 8, the electrical response of a pigment excitation is an event that does not finish instantaneously: it takes time for the photocurrent to rise, reach its peak, and then decay. The rising phase, as discussed in Chapter 5.1, is briefer in rods than on cones, but the decay phase is much longer in rods than in cones [Ingram et al., 2016]. The faster decay is due to the stronger phototransduction deactivation in cones than in rods [Yau and Hardie, 2009, Burns and Baylor, 2001] (which is attributed to the stronger negative feedbacks as discussed in Chapter 4.2), which means ion channels are more rapidly restored. Overall, the duration of a cone phototransduction is about four times shorter than that for a rod (100 ms vs. 400 ms) [Baylor, 1987, Angueyra-Aristizábal, 2014, Nakatani and Yau, 1988, Rodieck, 1998, p. 185].

Why does the time duration matter? It is because a longer duration integrates responses of more incoming photons. Consider an example where two excitations are taking place, say, 200 ms apart in a photoreceptor. In a rod, the time durations of these two excitations overlap, so the total electrical response the photoreceptor generates is greater than that if only one excitation takes place. In a cone, however, these two events do not overlap and so their effects do not add up.

As a side, the slow kinetics of rods is the reason we cannot sense object movement very well in low light conditions. If you have ever played basketball at night, you would know that even though you can tell where the ball is when it is still, but you cannot track the movement of the ball well.

It is worth noting that even though cone pigments regenerate much faster than rods (Chapter 4.2), a slower pigment regeneration rate unlikely affects the saturation in rods. There are tens of millions of pigments in a mammalian rod cell [Nathans, 1992, Milo and Phillips, 2015, p. 142-147] but a rod is almost saturated by only several hundreds of pigment excitations, so when a rod is saturated the vast majority of pigments are still available [Lamb, 1980]. It is the fact that almost all cGMP-gated ion channels are closed, rather than all pigments are bleached, that prevent rods to respond further to lights. The slow regeneration rate in rods does affect dark adaptation time, which we will discuss later in the class.

6 Response vs. Light Intensity

The Principle of Univariate tells us that the electrical response from a photon absorption is constant without regard to the photon wavelength, but it does not tell us how the *magnitude* of the electrical response varies with the *number* of photons absorbed. With the basic understanding of phototransduction, we can now turn to this question. You might be tempted to think that the relationship is linear, and you would be wrong!

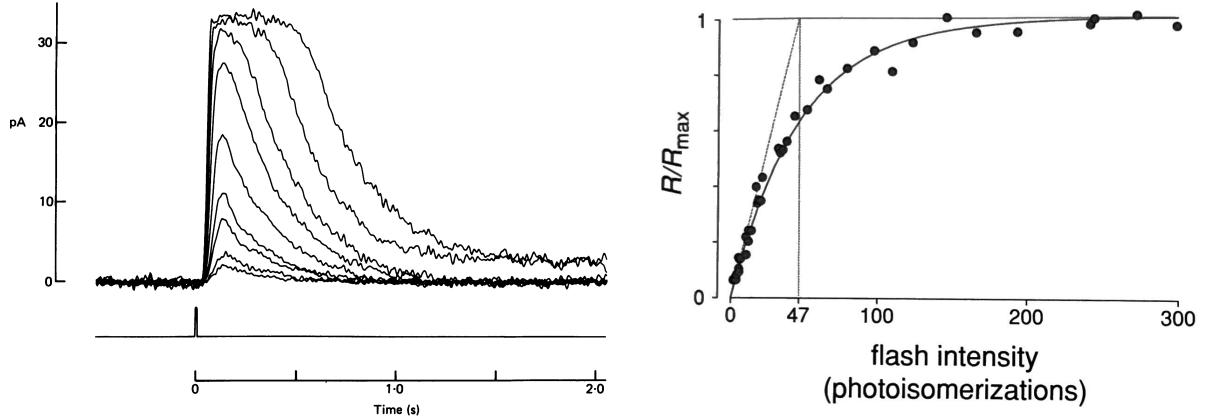


Figure 12: Left: the electrical response (photocurrent) kinetics of macaque rods under varying flash light intensities (quantified by the total number of pigment excitations/isomerizations); from [Baylor et al. \[1984, Fig. 1\]](#). Right: the peak response (normalized to maximum response) as a function of flash intensity; from [Rodieck \[1998, p. 178\]](#), which uses the underlying data in the left plot.

6.1 Peak Response is Not Linearly Proportional to Light Intensity

Figure 12 (left) shows the response (photocurrents) kinetics of macaque rods under flash lights of different intensities. The right plot shows the peak response (normalized to the maximum response) as a function of flash intensity.

If the relationship between the response magnitude and the light intensity were linear, the curve would be a straight line. But in reality, we can see that the response grows quickly initially, but the growth slows down soon. What does the actual relationship tell us about photoreceptors? Let's define the photoreceptor's sensitivity, or its response rate, to flash lights as the additional response per unit increment in light intensity. The sensitivity/response rate is given by the derivative of the curve, i.e., the slope at every point on the curve. Evidently, the response rate slows down as light becomes more intense; in other words, the photoreceptor becomes less sensitive as light becomes more intense. While the discussions here focus on photoreceptor responses to flash lights, the conclusion holds for responses to steady background lights as well.

This non-linear relationship can be used to explain our brightness perception. Our perceived brightness is not linear with respect to the light intensity. Imagine you walk into a dark room and turn one light on; the perceived brightness changes a lot (literally from 0 to 1); then you turn another light on and another light on; every time you turn on an additional light, your perceived brightness increases, but not as much as before. As you continue, the additional brightness you feel from turning one additional light on becomes smaller: you probably would not notice it if someone turns on one more light when there are 1,000 lights on already.

This non-linear relationship between perceived brightness and absolute light power is important when deciding how to effectively allocate digital bits when encoding pixel values. A classic example is the gamma encoding/compression in the popular sRGB color space, a topic we will

turn to when we discuss color.

6.2 Why and How Do Photoreceptors Desensitize?

The reduction of sensitivity under stronger lights is called **desensitization**, and is stereotypical of photoreceptor **light adaptation**. Photoreceptor adaptation plays an important role in our behavioral adaptation, which we will have a lot to talk about later in the class. But a curious question for now is, does desensitization provide us any benefits? Do we not want our photoreceptors to be more sensitive to light? Without desensitization, i.e., if the initial response rate was maintained, the rod would saturate at about 47 pigment excitations, as shown in Figure 12. The desensitization allows the photoreceptors to extend its operating range, which, in turn, allows our vision to operate at higher light levels.

What mechanisms cause photoreceptor desensitization? We will leave a thorough discussion to later in the class when we actually discuss adaptation, but briefly there are two reasons.

The first reason is the natural exponential decay you would observe in pretty much any dynamical system. Recall that the reason a photoreceptor can produce electrical responses is because of the sequence of biochemical reactions, which require a bunch of materials, like the cGMPs, PDEs, etc., to bump into each other. Under stronger lights, the concentration of these materials is lower, which means they are less likely to meet each other. That in turn means the rate of cGMP concentration reduction becomes even slower, and the ion channels close even less frequently.

The second reason, first experimentally shown by [Matthews et al., 1988] and [Nakatani and Yau, 1988], has to do negative feedbacks regulated by Ca^{2+} ions. Interestingly, these negative feedback mechanisms are exactly the same as those that accelerate phototransduction deactivation, as discussed in Chapter 4.2. As we will discuss more quantitatively in the adaptation lecture, this is not a coincidence: desensitization and faster recovery kinetics are two hallmarks of photoreceptor light adaptation.

6.3 Linear Range

If you observe Figure 12 (right) closely, you will see that the response vs. flash intensity is linear when the lights are dim. This linear relationship is used to estimate the single photon response: we cannot easily measure the response of a single photon as it is difficult to precisely deliver just one single photon, but this linear relationship in the dim range allows us to estimate such a response by scaling the response of a dim light by its intensity.

Mathematically, the response vs. intensity relationship is modeled in literature either by a negative exponential function (when negative feedbacks are weak) [Baylor et al., 1984, Lamb et al., 1981, Kraft et al., 1993] or by the Michaelis equation (when negative feedbacks are not negligible) [Baylor and Fuortes, 1970, Baylor et al., 1974, 1979a, Normann and Perlman, 1979]. The negative exponential model would look something like $r/r_{max} = 1 - e^{-ki}$, where r , r_{max} , and i denote the response, maximum response, and flash light intensity, respectively; k is a constant fit to data. The Michaelis equation, which is also called the Naka–Rushton equation (presumably because Naka and Rushton [1966] was the first to use it), looks like $r/r_{max} = \frac{i}{i + \sigma}$,

where σ is a constant fit to data. Sometimes it would fit the data better to use the generalized Michaelis equation, which takes the form $r/r_{max} = \frac{i^n}{i^n + \sigma^n}$, where n is the additional control parameter. Both models can be approximated by a linear function when i is small. This linear region perhaps also explains why the sRGB encoding is a piece-wise function where the encoding is linear when light levels are low.

References

- Juan M Angueyra-Aristizábal. *The Limits Imposed in Primate Vision by Transduction in Cone Photoreceptors*. PhD thesis, University of Washington Libraries, 2014.
- Horace B Barlow. Retinal noise and absolute threshold. *Josa*, 46(8):634–639, 1956.
- Horace B Barlow. Increment thresholds at low intensities considered as signal/noise discriminations. *The Journal of physiology*, 136(3):469, 1957.
- Horace B Barlow. Dark and light adaptation: psychophysics. In Matthew Alpern, editor, *Visual Psychophysics*, pages 1–28. Springer, 1972.
- Denis A Baylor. Photoreceptor signals and vision: The proctor lecture. *Investigative ophthalmology & visual science*, 28(1):34–49, 1987.
- Denis A Baylor and MGF Fuortes. Electrical responses of single cones in the retina of the turtle. *The Journal of physiology*, 207(1):77–92, 1970.
- Denis A Baylor and Alan L Hodgkin. Detection and resolution of visual stimuli by turtle photoreceptors. *The Journal of physiology*, 234(1):163–198, 1973.
- Denis A Baylor, AL Hodgkin, and TD Lamb. The electrical response of turtle cones to flashes and steps of light. *The Journal of Physiology*, 242(3):685–727, 1974.
- Denis A Baylor, TD Lamb, and KW Yau. The membrane current of single rod outer segments. *The Journal of physiology*, 288(1):589–611, 1979a.
- Denis A Baylor, Trevor D Lamb, and KW Yau. Responses of retinal rods to single photons. *The Journal of physiology*, 288(1):613–634, 1979b.
- Denis A Baylor, G Matthews, and KW Yau. Two components of electrical dark noise in toad retinal rod outer segments. *The Journal of physiology*, 309(1):591–621, 1980.
- Denis A Baylor, BJ Nunn, and JL Schnapf. The photocurrent, noise and spectral sensitivity of rods of the monkey macaca fascicularis. *The Journal of physiology*, 357(1):575–607, 1984.
- Denis A Baylor, BJ Nunn, and JL Schnapf. Spectral sensitivity of cones of the monkey macaca fascicularis. *The Journal of Physiology*, 390(1):145–160, 1987.

- Edward A Boettner and J Reimer Wolter. Transmission of the ocular media. *Investigative ophthalmology & visual science*, 1(6):776–783, 1962.
- James K Bowmaker. Evolution of colour vision in vertebrates. *Eye*, 12(3):541–547, 1998.
- James K Bowmaker and HJk Dartnall. Visual pigments of rods and cones in a human retina. *The Journal of physiology*, 298(1):501–511, 1980.
- JK Bowmaker. Microspectrophotometry of vertebrate photoreceptors: a brief review. *Vision Research*, 24(11):1641–1650, 1984.
- JK Bowmaker, HJ Dartnall, JN Lythgoe, and JD Mollon. The visual pigments of rods and cones in the rhesus monkey, macaca mulatta. *The Journal of physiology*, 274(1):329–348, 1978.
- Paul K Brown and George Wald. Visual pigments in single rods and cones of the human retina. *Science*, 144(3614):45–52, 1964.
- Marie E Burns and Vadim Y Arshavsky. Beyond counting photons: trials and trends in vertebrate visual transduction. *Neuron*, 48(3):387–401, 2005.
- Marie E Burns and Denis A Baylor. Activation, deactivation, and adaptation in vertebrate photoreceptor cells. *Annual review of neuroscience*, 24(1):779–805, 2001.
- Marie E Burns and Trevor D Lamb. Visual transduction by rod and cone photoreceptors. In *The New Visual Neurosciences*. MIT Press, 2014.
- BH Crawford. The scotopic visibility function. *Proceedings of the Physical Society. Section B*, 62(5):321, 1949.
- Frederick Crescitelli and Herbert JA Dartnall. Human visual purple. *Nature*, 172(4370):195–197, 1953.
- Herbert J.A. Dartnall. Photosensitivity. In Herbert J.A. Dartnall, editor, *Photochemistry of Vision*, pages 122–145. Springer Berlin Heidelberg, 1972.
- Herbert JA Dartnall, James K Bowmaker, and John Dixon Mollon. Human visual pigments: microspectrophotometric results from the eyes of seven persons. *Proceedings of the Royal society of London. Series B. Biological sciences*, 220(1218):115–130, 1983.
- Kristian Donner. Noise and the absolute thresholds of cone and rod vision. *Vision research*, 32(5):853–866, 1992.
- Evgeniy E Fesenko, Stanislav S Kolesnikov, and Arkadiy L Lyubarsky. Induction by cyclic gmp of cationic conductance in plasma membrane of retinal rod outer segment. *Nature*, 313(6000):310–313, 1985.
- Yingbin Fu. Phototransduction in rods and cones. In Helga Kolb, Eduardo Fernandez, and Ralph Nelson, editors, *WebVision: The Organization of the Retina and Visual System*. 2010.

- E. Bruce Goldstein. *Sensation and Perception*. Cengage Learning, 8 edition, 2009.
- Thomas Gruhl, Tobias Weinert, Matthew J Rodrigues, Christopher J Milne, Giorgia Ortolani, Karol Nass, Eriko Nango, Saumik Sen, Philip JM Johnson, Claudio Cirelli, et al. Ultrafast structural changes direct the first molecular events of vision. *Nature*, 615(7954):939–944, 2023.
- Selig Hecht, Simon Shlaer, and Maurice Henri Pirenne. Energy, quanta, and vision. *The Journal of general physiology*, 25(6):819–840, 1942.
- Klaus Peter Hofmann and Trevor D Lamb. Rhodopsin, light-sensor of vision. *Progress in Retinal and Eye Research*, 93:101116, 2023.
- Yi-Te Hsu and Robert S Molday. Modulation of the cgmp-gated channel of rod photoreceptor cells by calmodulin. *Nature*, 361(6407):76–79, 1993.
- Norianne T Ingram, Alapakkam P Sampath, and Gordon L Fain. Why are rods more sensitive than cones? *The Journal of physiology*, 594(19):5415–5426, 2016.
- Gerald H Jacobs. Primate color vision: a comparative perspective. *Visual neuroscience*, 25(5-6): 619–633, 2008.
- TW Kraft, DM Schneeweis, and JL Schnapf. Visual transduction in human rod photoreceptors. *The Journal of physiology*, 464(1):747–765, 1993.
- Allen Kropf. Photosensitivity and quantum efficiency of photoisomerization in rhodopsin and retinal. In *Methods in Enzymology*, volume 81, pages 384–392. Elsevier, 1982.
- TD Lamb. Spontaneous quantal events induced in toad rods by pigment bleaching. *Nature*, 287 (5780):349–351, 1980.
- TD Lamb, PA McNaughton, and K-W Yau. Spatial spread of activation and background desensitization in toad rod outer segments. *The Journal of physiology*, 319(1):463–496, 1981.
- WB Marks, William H Dobelle, and Edward F MacNichol Jr. Visual pigments of single primate cones. *Science*, 143(3611):1181–1183, 1964.
- HR Matthews, RLW Murphy, GL Fain, and TD Lamb. Photoreceptor light adaptation is mediated by cytoplasmic calcium concentration. *Nature*, 334(6177):67–69, 1988.
- Ron Milo and Rob Phillips. *Cell biology by the numbers*. Garland Science, 2015.
- John D Mollon. Colour vision and colour blindness. In Horace B Barlow and John D Mollon, editors, *The Senses*, pages 165–191. Cambridge University Press, 1982.
- KI Naka and William AH Rushton. S-potentials from colour units in the retina of fish (cyprinidae). *The Journal of physiology*, 185(3):536–555, 1966.
- K Nakatani and KW Yau. Calcium and light adaptation in retinal rods and cones. *Nature*, 334 (6177):69–71, 1988.

- Jeremy Nathans. Rhodopsin: structure, function, and genetics. *Biochemistry*, 31(21):4923–4931, 1992.
- Jay Neitz and Maureen Neitz. The genetics of normal and defective color vision. *Vision research*, 51(7):633–651, 2011.
- S Nikonov, TD Lamb, and EN Pugh Jr. The role of steady phosphodiesterase activity in the kinetics and sensitivity of the light-adapted salamander rod photoresponse. *The Journal of general physiology*, 116(6):795, 2000.
- Richard A Normann and I Perlman. The effects of background illumination on the photoreponses of red and green cones. *The Journal of Physiology*, 286(1):491–507, 1979.
- Dirk V Norren and Johannes J Vos. Spectral transmission of the human ocular media. *Vision research*, 14(11):1237–1244, 1974.
- Stephen Lucian Polyak. *The retina*. Univ. Chicago Press, 1941.
- EN Pugh Jr, S Nikonov, and TD Lamb. Molecular mechanisms of vertebrate photoreceptor light adaptation. *Current opinion in neurobiology*, 9(4):410–418, 1999.
- Dale Purves, George J. Augustine, David Fitzpatrick, William Hall, Anthony-Samuel LaMantia, Richard D. Mooney, Michael L. Platt, and Leonard E. White. *Neurosciences*. Oxford University Press, 6 edition, 2017.
- F Rieke and Denis A Baylor. Molecular origin of continuous dark noise in rod photoreceptors. *Biophysical Journal*, 71(5):2553–2572, 1996.
- Foster Rieke and Denis A Baylor. Single-photon detection by rod cells of the retina. *Reviews of Modern Physics*, 70(3):1027, 1998.
- Fred Rieke and Denis A Baylor. Origin and functional impact of dark noise in retinal cones. *Neuron*, 26(1):181–186, 2000.
- Robert W Rodieck. *The first steps in seeing*. Sinauer Associates, 1998.
- William AH Rushton. Visual pigments in man. In Herbert J.A. Dartnall, editor, *Photochemistry of Vision*, pages 364–394. Springer Berlin Heidelberg, 1972a.
- William Albert Hugh Rushton. Rhodopsin measurement and dark-adaptation in a subject deficient in cone vision. *The Journal of physiology*, 156(1):193, 1961.
- William Albert Hugh Rushton. Cone pigment kinetics in the protanope. *The Journal of Physiology*, 168(2):374, 1963.
- William Albert Hugh Rushton. The ferrier lecture, 1962 visual adaptation. *Proceedings of the Royal Society of London. Series B. Biological Sciences*, 162(986):20–46, 1965.

- William A H Rushton. Review lecture. pigments and signals in colour vision. *The Journal of physiology*, 220(3):1P, 1972b.
- JL Schnapf, TW Kraft, and Denis A Baylor. Spectral sensitivity of human cone photoreceptors. *Nature*, 325(6103):439–441, 1987.
- JL Schnapf, BJ Nunn, M Meister, and Denis A Baylor. Visual transduction in cones of the monkey *macaca fascicularis*. *The Journal of physiology*, 427(1):681–713, 1990.
- David M Schneeweis and Julie L Schnapf. The photovoltage of macaque cone photoreceptors: adaptation, noise, and kinetics. *Journal of Neuroscience*, 19(4):1203–1216, 1999.
- Steven K Shevell. Saturation in human cones. *Vision research*, 17(3):427–434, 1977.
- Vivianne C Smith and Joel Pokorny. Spectral sensitivity of the foveal cone photopigments between 400 and 500 nm. *Vision research*, 15(2):161–171, 1975.
- DM Snodderly, PK Brown, FC Delori, and JD Auran. The macular pigment. i. absorbance spectra, localization, and discrimination from other yellow pigments in primate retinas. *Investigative Ophthalmology & Visual Science*, 25(6):660–673, 1984.
- WS Stiles. The directional sensitivity of the retina and the spectral sensitivities of the rods and cones. *Proceedings of the Royal Society of London. Series B-Biological Sciences*, 127(846):64–105, 1939.
- WS Stiles. Color vision: the approach through increment-threshold sensitivity, 1959.
- WS Stiles. Appendix by ws stiles: Foveal threshold sensitivity on fields of different colors. *Science*, 145(3636):1016–1017, 1964.
- Andrew Stockman and Lindsay T Sharpe. The spectral sensitivities of the middle-and long-wavelength-sensitive cones derived from measurements in observers of known genotype. *Vision research*, 40(13):1711–1737, 2000.
- Andrew Stockman, Lindsay T Sharpe, and Clemens Fach. The spectral sensitivity of the human short-wavelength sensitive cones derived from thresholds and color matches. *Vision research*, 39(17):2901–2927, 1999.
- Tarnura Tamura, K Nakatani, and KW Yau. Calcium feedback and sensitivity regulation in primate rods. *The Journal of general physiology*, 98(1):95–130, 1991.
- George Wald. Vitamin a in the retina. *Nature*, 132(3330):316–317, 1933.
- George Wald. The receptors of human color vision: Action spectra of three visual pigments in human cones account for normal color vision and color-blindness. *Science*, 145(3636):1007–1016, 1964.
- George Wald. Molecular basis of visual excitation. *Science*, 162(3850):230–239, 1968.

- Brian A. Wandell. *Foundations of vision*. Sinauer Associates, 1995.
- Brian A Wandell, David H Brainard, and Nicolas P Cottaris. Visual encoding: Principles and software. *Progress in Brain Research*, 273(1):199–229, 2022.
- Günther Wyszecki and WS Stiles. *Color science: concepts and methods, quantitative data and formulae*. 1982.
- KW Yau. Phototransduction mechanism in retinal rods and cones. the friedenthal lecture. *Investigative ophthalmology & visual science*, 35(1):9–32, 1994.
- KW Yau and Denis A Baylor. Cyclic gmp-activated conductance of retinal photoreceptor cells. *Annual review of neuroscience*, 12(1):289–327, 1989.
- KW Yau and Roger C Hardie. Phototransduction motifs and variations. *Cell*, 139(2):246–264, 2009.