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# An Analysis of Rod Outer Segment Adaptation Based on a Simple Equivalent Circuit

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**Abstract.** This model of rod outer segment adaptation is based on the hypothesis that transmitter substance released by bleached rhodopsin closes sodium channels in the outer segment plasma membrane, leading to hyperpolarization of the receptor. The outer segment adaptation processes of the model are associated with the transmitter release, the transmitter background concentration and the plasma membrane leakage. Changes in the three model parameters correspond to the three types of outer segment adaptation processes. According to the model the stimulus-response function is in every adaptational state $U/U_{max} = I/(I + I_H)$. The model predicts how each adaptation process affects $I_H$ and $U_{max}$. Specifically, when the number of liberated transmitter molecules per isomerizing quantum decreases, the amplitude $U_{max}$ remains constant but $I_H$ increases. A short description of this model has been published in a paper reporting experimental results on background adaptation (Hemilä, 1977).

**Key words:** Adaptation – Rod outer segment.

## 1. Introduction

Two general conclusions can be drawn from the recent work on visual adaptation: (1) the main part of adaptation takes place in the receptors themselves, which thus preserve their discriminatory capacity over a wide range of intensities (see e.g. Normann and Werblin, 1974; Dowling and Ripps, 1972; Kleinschmidt, 1973); (2) several mechanisms contribute to the adaptation of the receptors. Therefore, there is a need for a classification of the adaptation mechanisms and for general models of the signal processing in the receptor.

The model presented here includes solely the adaptation processes originating in the rod outer segment (ROS). The basic assumptions of this model are conventional: light liberates from the discs internal transmitter molecules, which close $Na^+$-channels in the plasma membrane of the ROS, thus decreasing the 'dark current' of $Na^+$ ions entering this membrane. The transmitter hypothesis needs further tests, but the decrease of sodium conductance is well demonstrated (basic experiments Toyoda et

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al., 1969; Sillman et al., 1969; Hagins et al., 1970). The decrease of sodium conductance hyperpolarizes both the outer and the inner segment of the cell and gives rise to the late receptor potential. This analysis is not restricted to the hypothesis of $Ca^{2+}$ as a transmitter, although some specific mechanisms presented as examples assume liberation of $Ca^{2+}$ from the discs.

Threshold intensity is a stimulus intensity which elicits a small chosen criterion photoresponse. Threshold measurements alone do not give all aspects of an adaptation mechanism studied. The present analysis refers to experiments, in which *the whole intensity-response function* is measured at different background intensities or during a dark-adaptation process. Complete data of this kind are more difficult to collect than only the threshold values, and relatively few studies of this type have been reported (e.g. Dowling and Ripps, 1972; Pak et al., 1973; Normann and Werblin, 1974; indirect measurements Alpern et al., 1970a, b).

The basic equations of the model include three parameters, and the adaptation processes bring about alterations of these parameters. The effect of each parameter is here analyzed, so that in the framework of the model experimental results on adaptation can give direct information of the changes of these parameters. The model also suggests actual adaptation processes in a molecular level. In an earlier paper (Hemilä, 1977) this model has been described in a condensed form and was used in interpretation of experimental results on background adaptation.

## 2. The Model

Figure 1a shows an equivalent circuit for the sodium currents. It is similar to the equivalent circuit presented by Yoshikami and Hagins (1973), except that the proximal currents of the rod and the outer segment potassium currents have been neglected. The current source $I_0$ (sodium pump) in parallel with the combination of the Nernst potential $E_{Na}$ and the inner segment membrane resistance $R_i$ have been substituted by an equivalent circuit where $-E_i = -I_0R_i + E_{Na}$. Assuming that the Nernst potential $E_j$ across the outer segment plasma membrane is approximately constant along the outer segment, these voltage sources can be combined to $E_i$ resulting in $E = E_i + E_j$. Thus the outer segment is an open-ended leaky cable (Ehrhardt and Baumann, 1975). Such an open-ended cable, with the resistance of the core lead $R = \sum R_j$ (longitudinal cytoplasmic resistance) and the conductance between the core and the mantle $G = \sum G_j$ (total membrane conductance) has an input conductance

$$G_{in} = \sqrt{G/R} \tanh \sqrt{GR} = G(1 - 1/3\ GR + 2/15\ (GR)^2 - \ldots).$$

If $GR \ll 1$, the resistance $R$ can be omitted. The resulting simple equivalent circuit is presented in Figure 1b. However, estimates on rat rods (Yoshikami and Hagins, 1973; Hagins et al., 1970) suggest, that $R$ is of the same order of magnitude as $G^{-1}$. When $GR \lesssim 1$, an open-ended cable can quite accurately be substituted by a resistance $R/3$ and a conductance $G$ in series (the input conductance of the cable is about 2% larger than the conductance of $R/3$ and $G$ in series, when $GR = 1$). Thus even when $R \approx G^{-1}$, the circuit in Figure 1b is a good approximation, when a third of the

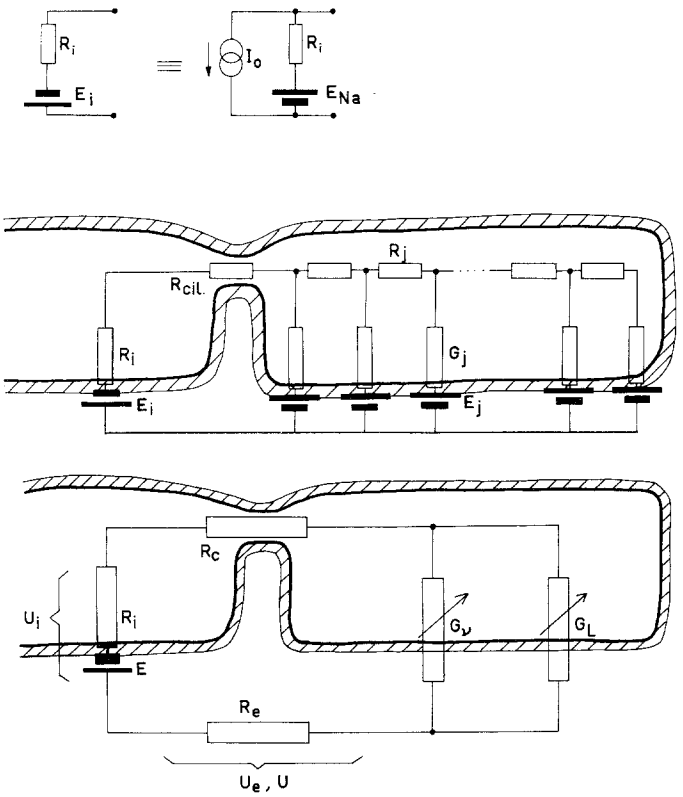


**Fig. 1. a.** An equivalent circuit of the rod. $R_i$ is the resistance of the inner segment plasma membrane, $R_{\text{cil.}}$ is the resistance of the cilium, $\sum R_j$ is the longitudinal cytoplasmic resistance of the outer segment plasma membrane, $\sum G_j$ is the total conductance of the outer segment plasma membrane, $-E_i = -I_0 R_i + E_{\text{Na}}$ is the inner segment source voltage (e.m.f.) caused by the sodium pump current $I_0$ and the Nernst potential $E_{\text{Na}}$ (see inlet), and $E_j$ is the Nernst potential across the outer segment plasma membrane. **b.** The reduced equivalent circuit of the rod used in the model. $G_\nu$ is the conductance of the sodium channels, $G_L$ is the leakage conductance, $R_e$ is the small resistance of the interreceptor space, $R_c = R_{\text{cil.}} + 1/3 \sum R_j$, $E = E_i + E_j$ is the source voltage. Receptor potential is $U = -\Delta U_e$

longitudinal cytoplasmic resistance of the outer segment is added to the resistance of the cilium.

The membrane conductance in Figure 1b is divided in two parts. Stimulus light affects the conductance of the sodium channels, $G_\nu$, while the adapting light may affect both $G_\nu$ and the leakage conductance $G_L$.

*A transmitter background* $c_i$ is the concentration of the internal transmitter in the extradiscal space of the rod before stimulation. A step of light stimulus intensity $I$ elicits a fast increase in the transmitter concentration. Any detailed assumptions concerning the kinetics of transmitter release and reabsorption need not be made, as the analysis is limited to the peak of the photoresponse. Assuming that the final increase is proportional to the stimulus intensity, the transmitter concentration in the stationary state is

$$c = c_i + Q\,I\,. \tag{1}$$

*The transmitter coefficient* $Q$ is proportional to three factors $\eta$, $q$, and $\tau$. The absorption factor $\eta$ is the fraction of incident quantum flux absorbed by rhodopsin and causing photopigment isomerization. It is constant at weak and moderate background intensities ($\eta$ is roughly proportional to the fraction of rhodopsin still unbleached). If the stimulus $I$ is expressed in quanta *absorbed* per cm$^2$ in s, the factor $\eta$ is constant and may be omitted. *The transmitter release factor* $q$ is the average number of transmitter molecules liberated by each isomerizing quantum. *The life time* $\tau$ is the average life time of the transmitter molecules before they are reabsorbed or otherwise inactivated. During the step of light stimulation transmitter is released at a constant rate and the final concentration is proportional to $\tau$. All the factors $\eta$, $q$, and $\tau$ may depend on the adaptational state of the rod outer segment. In the fully dark adapted state $Q = Q_0$.

Equation 1 refers to a step of light stimulus. The analysis can also be used for stimulation with short flashes of light. The flash creates a transient increase of transmitter concentration, and at the peak of the response this increase is proportional to the intensity $I$ multiplied by flash duration $\Delta t$. Thus in the case of flash stimulation $Q$ in Equation 1 is to be multiplied by $\Delta t/\tau_i$ where $\tau_i$ is an integrating time of the step of light response (see Baylor et al., 1974). As the transmitter life time $\tau$ should be equal to the integrating time $\tau_i$, the comparison of threshold intensities corresponding to step of light and flash stimuli offers a method to study the contribution of the changes in $\tau$ in the adaptation processes.

Let there be $N$ sodium channels in the rod outer segment plasma membrane, each with an electric conductance $g$. The transmitter molecules are assumed to bind rapidly and reversibly to these channels, closing a fraction $B$ of the channels. Thus the total conductance $G_v$ of the $Na^+$ channels is $Ng(1 - B)$. The rate of closing the channels is proportional to the product $(1 - B)c$, while the rate of channel opening is proportional to $B$. In kinetic equilibrium these rates are equal. Thus $B = c/(c + c_H)$, where the constant $c_H$ is the transmitter concentration which reduces $G_v$ to one half. The sodium channel conductance is then

$$G_v = \frac{G_0}{1 + c/c_H}, \quad G_0 = Ng. \tag{2}$$

Baylor et al. (1974), Baylor and Hodgkin (1974), and Schwartz (1976) have analyzed the time courses of the turtle photoreceptor responses succesfully by detailed receptor models. The adaptation model outlined here is in accord with those models. However, both the kinetics and the electric circuit are simpler because this model is not intended for an analysis of the photoresponse time courses.

The stimulation $I$ causes a decrease of the sodium current by decreasing $G_v$ in the equivalent circuit. The decrease of sodium current brings about a receptor potential $U$, i.e. a decrease of voltage across the resistance $R_e$ of the interreceptor space. Denoting $R_s = R_i + R_c + R_e$,

$$U = \frac{E R_e}{R_s + \dfrac{1}{\dfrac{G_0}{1 + \dfrac{c_i}{c_H}} + G_L}} - \frac{E R_e}{R_s + \dfrac{1}{\dfrac{G_0}{1 + \dfrac{c_i + QI}{c_H}} + G_L}} \tag{3}$$

Trivial but lengthy algebraic reductions of this expression give the response

$$U = U_{\max} \frac{I}{I + I_H} \tag{4}$$

$$I_H = \frac{c_1 + c_i}{Q}, \quad U_{\max} = E R_e \frac{C_a}{c_1 + c_i} \tag{5}$$

$$\left.\begin{aligned} c_1 &= c_H \left(1 + \frac{R_s G_0}{1 + R_s G_L}\right) \\ C_a &= \frac{c_H G_0}{(1 + R_s G_L)^2} \end{aligned}\right\}. \tag{6}$$

$U_{\max}$ is the maximum photoresponse and $I_H$ is the intensity producing half of the maximum photoresponse in the prevailing state of adaptation. According to Equation 4 the model predicts a Michaelis stimulus-response function in every adaptational state.

The parameters $c_1$ and $C_a$ depend only on $G_L$. The values of $c_1$, $C_a$, and $c_i$ in the dark-adapted rod are denoted $c_{10}$, $C_{a0}$, and $c_{i0}$. They correspond to the minimum values of $c_i$ and $G_L$. Thus in the most sensitive (dark-adapted) state of the rod the half-maximum intensity $I_h$ and the absolute maximum response $U_m$ are according to Equation 5

$$I_h = \frac{c_{10} + c_{i0}}{Q_0}, \quad U_m = E R_e \frac{C_{a0}}{c_{10} + c_{i0}}. \tag{7}$$

Let $U_c$ be a small chosen criterion response in threshold measurements, and $I_t$ the corresponding threshold intensity of the stimulating light. The absolute threshold intensity is denoted $I_0$. According to Equation 4

$$\frac{I_0}{I_h} = \frac{U_c}{U_m - U_c}, \quad \frac{I_t}{I_H} = \frac{U_c}{U_{\max} - U_c}.$$

Thus the log threshold increase is

$$\log \frac{I_t}{I_0} = \underbrace{\log \frac{I_H}{I_h}}_{\text{AI}} + \underbrace{\log \frac{U_m}{U_{\max}}}_{\text{AII}} + \underbrace{\log \frac{1 - U_c/U_m}{1 - U_c/U_{\max}}}_{\text{AIII}}. \tag{8}$$

In general, when the responses corresponding to Equation 4 are described by *the operating curve* in a log $I$, log $U$ diagram (Fig. 2a) the threshold $I_t$ may increase either because an increase of $I_H$ moves the curve to the right (AI) or because a decrease of $U_{\max}$ moves the curve downwards (AII). In addition, if the decreasing amplitude $U_{\max}$ approaches the chosen criterion, $U_c$, the sensitivity decreases rapidly towards zero: saturation (AIII). The role of these three factors is less clearly seen in the lin.-log. stimulus-response diagram customarily used (Fig. 2b). The ratios determining the movements of the operating curve are according to Equations 5 and 7

$$\frac{I_H}{I_h} = \frac{c_1 + c_i}{I_h Q} = \frac{Q_0}{Q} \cdot \frac{c_1 + c_i}{c_{10} + c_{i0}} \tag{9}$$

$$\frac{U_m}{U_{\max}} = U_m \frac{c_1 + c_i}{C_a} = \frac{C_{a0}}{C_a} \frac{c_1 + c_i}{c_{10} + c_{i0}} \,. \tag{10}$$

The relative photoresponse $U/U_m$ applies both to the receptor potential (across the resistance $R_e$) and to the hyperpolarization of the inner segment, $\Delta U_i = (R_i/R_e)U$, which gives rise to the synaptic response.

*The direct effect of the background light.* Let the background intensity be $I_B$. A summation of stimulus and background without any adaptation processes means, that $Q = Q_0$, $c_1 = c_{10}$, and $c_i = c_{i0} + Q_0 I_B$. Equations 9 and 10 give

$$I_H/I_h = U_m/U_{\max} = 1 + I_B/I_h \,.$$

The log threshold is then according to Equation 8

$$\log \frac{I_t}{I_0} = \log\left(1 + \frac{I_B}{I_h}\right)^2 + \log \frac{1 - U_c/U_m}{1 - U_c/U_{\max}} \,. \tag{11}$$

The operating curve moves equally downwards and to the right. Half of the threshold increase is thus caused by the amplitude decrease, another half by the movement of the curve to the right (Fig. 3a). When $I_B \gg I_h$ the threshold is proportional to the square of the background light intensity (Fig. 3b). This relation $I_t \propto I_B^2$ disagrees with the Weber's law $I_t \propto I_B$. Therefore, in addition to the mere superposition of the background light actual adaptation mechanisms are functioning in background adaptation.

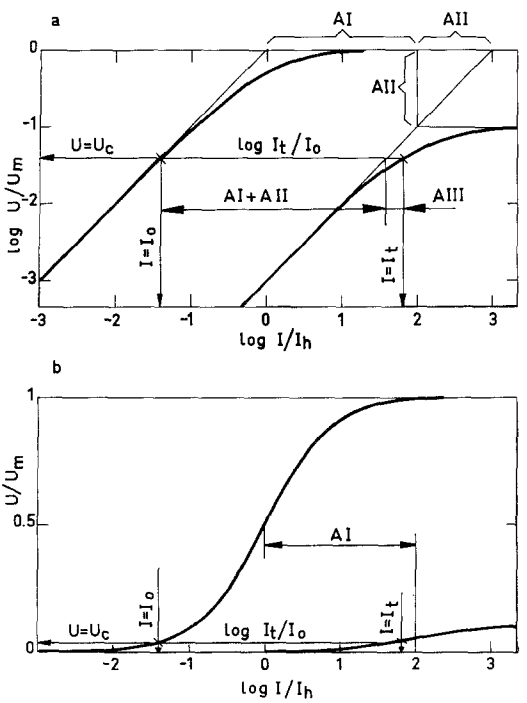


**Fig. 2. a.** Movements of the stimulus-response curve in the log.-log. diagram: the three components of the threshold increase caused by light-adaptation. AI: a movement of the operating curve to the right, AII: a downward movement, AIII: a saturating factor when $U_{\max}$ approaches $U_c$. **b.** The lin.-log. diagram of the same stimulus-response functions

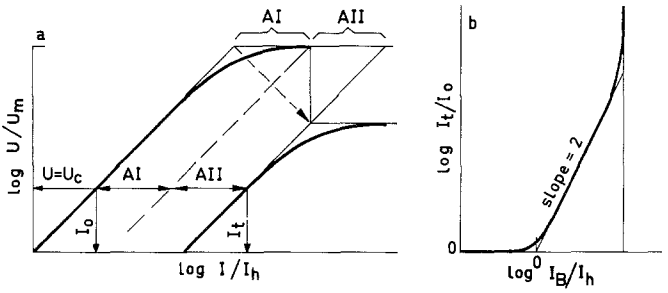


**Fig. 3.** A summation of the background and stimulus lights. **a.** A movement of the operating curve. Contributions AI and AII in the log. threshold increase are equal. **b.** log $I_t$ versus log $I_B$ plot

## *Effects of Parameters*

Considering the transmitter hypothesis of excitation we may assume that the parameters $Q$ and $c_t$, and possibly also $G_L$, are involved in light adaptation: the transmitter coefficient $Q$ decreases and the transmitter background $c_t$ increases, and further the leakage conductance $G_L$ may increase. Three characteristic types of displacements of the operating curve are then obtained.

*a) Transmitter Coefficient Q.* According to Equation 5 the decrease of $Q$ moves the operating curve *to the right* without decreasing $U_{max}$. The increase of log threshold is log $Q_0/Q$ according to Equations 8 and 9. Because the $Q$-decrease does not decrease the amplitude, this process acts like a simple attenuator in front of the detector. In maintaining the dynamic range of the receptor, the $Q$-decrease is a valuable tool from a functional point of view.

Let us consider the case where the background light merely decreases $Q$ and produces the unavoidable transmitter background increase $\Delta c_t = QI_B$. This may be the case when weak or moderate background illuminations are used. Equations 9 and 10 give

$$\frac{I_H}{I_h} = \left(1 + \frac{I_B Q}{I_h Q_0}\right) \frac{Q_0}{Q} = \frac{Q_0}{Q} + \frac{I_B}{I_h} \tag{12}$$

$$\frac{U_m}{U_{max}} = 1 + \frac{I_B Q}{I_h Q_0}. \tag{13}$$

Weber's law is obtained if $Q$ is inversely proportional to $I_B$ at moderate backgrounds,

$$Q_0/Q = 1 + I_B/I_D. \tag{14}$$

If the constant $I_D$ is considerably smaller than $I_h$, $U_{max}$ does not decrease considerably at moderate backgrounds. Increasing $I_B$ moves the operating curve to the right and Equations 12, 13, and 8 give

$$I_t/I_0 \approx I_H/I_h \approx 1 + I_B/I_D.$$

If $Q$ decreases less effectively with increasing $I_B$, the operating curve moves somewhat down beside the displacement to the right, because in that case $QI_B$ increases with increasing $I_B$.

*b) The Transmitter Background $c_i$.* In the direct superposition of the stimulus and background lights the background $I_B$ produces the transmitter background increase $\Delta c_i = Q_0 I_B$, moving the operating curve down along the 45°-line (Fig. 3a). According to Equation 5 any other mechanism increasing the transmitter background also moves the operating curve down along the 45°-line.

*c) The Leakage Conductance $G_L$.* According to Equations 5 and 6 the increase of $G_L$ moves the operating curve predominantly down (the decrease of $C_a$ decreases the amplitude) but also somewhat to the left (smaller decrease of $c_1$ moves the curve up and to the left along the 45°-line).

## 3. Discussion

The above analysis is based on the operating curve corresponding to the log.-log. diagram of the Michaelis equation (Eq. 4), which in turn is derived from the model circuit in Figure 1b. Recorded receptor photoresponses agree with the Michaelis equation at low intensities (response proportional to the stimulus, see e.g. Baylor and Hodgkin, 1974) and at high intensities (saturation). Often the Michaelis equation fits also the responses around the turning point $I_H$ (e.g. Baylor and Fuortes, 1970; Dowling and Ripps, 1972; Kleinschmidt, 1973; Normann and Werblin, 1974). In other cases a more general formula $I^n/(I^n + I_H^n)$ with $n = 0.7$–$0.9$ have been used (Boynton and Whitten, 1970; Ernst and Kemp, 1972; Pak et al., 1973; Normann and Werblin, 1974). This formula fits the responses $U > 0.05\ U_{max}$ quite well, but fails in the range of small stimuli as it predicts that the sensitivity $U/I$ approaches infinity when $I$ decreases towards zero.

The inhomogenities in the retina provide an explanation for the deviation from Michaelis equation. When measuring mass receptor potentials, the photoresponse is a sum of individual rod signals. As different rods may receive somewhat different light intensities and their $I_H$ and $U_{max}$ values vary, the resulting potential is of the form

$$U = \sum_i U_i \frac{I}{I + I_{Hi}}.$$

When $U \gtrsim 0.1\ U_{max}$, this kind of sum may be very similar to the power law photoresponse $n < 1$. However, the deviation from Michaelis equation is observed also in single cell recordings (e.g. Pak et al., 1973; Copenhagen and Owen, 1976). A possible mechanism acting on the receptor level and causing a deviation is the fast decrease of $Q$ brought about by the stimulus light, as suggested by L. Kramer (personal communication). As weak stimuli do not decrease $Q$, the linear range of the operating curve remains unchanged. Furthermore, $U_{max}$ is not affected by $Q$. Thus the upper part of the operating curve moves to the right, but the *crossing point* of the linear asymptotes of the operating curve (45°-line and horizontal line) is not affected.

The response-disenhancement caused by the non-ohmic couplings between the rods (Schwartz, 1975, 1976) may also contribute observed deviations. Anyway, as the purpose of the model is to predict the displacements of the operating curve due to various adaptation processes, the model is useful as long as the shape of the operating curve is reasonably constant during adaptation. Even the changes in the shape of the operating curve during adaptation period are allowed, if they do not affect the crossing point, and the displacements of the operating curve are based on the displacements of the crossing point. If a deviation from Michaelis equation occurs, the half maximum intensity is *not* equal to the intensity corresponding to the crossing point.

The derivation of the model equations was based on a rod type receptor. The discussion of the cone type receptors was omitted, because the formulation of the transmitter hypothesis for the cones is still somewhat ambigious. However, fairly similar mechanisms seem to function in rods and cones, and according to the experimental evidence the rods and the cones behave qualitatively very similarly. Thus the results of the model seem to be useful also for the analysis of cone adaptation.

In the analysis it was assumed, that the parameters $Q$, $c_i$ and $G_L$ are constant *during the photoresponse.* This assumption is well grounded in the conventional adaptation measurements, including the light-adapted steady states and the slow dark-adaptation periods. The parameters are not constant during the first few seconds after onset or offset of the adapting light (the receptor potential is a superposition of the photoresponses to the stimulus light and the adapting light). Neither does the model take into account the changes in the model parameters brought about by the stimulus light (e.g. a fast decrease of $Q$ brought about by a strong step of light stimulus).

### *Possible Molecular Mechanisms Affecting the Parameters*

A background light or a short bleach may decrease each of the three factors of $Q$. Adapting light may decrease the stores of the transmitter or reduce the capacity of the photoactivated rhodopsin to release or to produce transmitter. In such case the transmitter release factor $q$ decreases. A visual pigment photoproduct or a side product of bleaching could absorb or otherwise inactivate transmitter molecules, thus shortening the life time $\tau$. A strong exposure decreases the fraction of unbleached photopigment and thus decreases the absorption factor $\eta$. The contributions of these three factors in the decrease of $Q$ may be estimated. The decrease of $\eta$ can be calculated on the basis of the amount of rhodopsin bleached. The comparison of the thresholds measured when stimulating with step of light and flash stimuli reveals the changes in $\tau$.

Because discs arise as invaginations of the plasma membrane of the rod outer segment it is natural to think that also the plasma membrane contains rhodopsin. Several experiments with rhodopsin antibodies (Dewey et al., 1969) and with early receptor potential responses (Rüppel and Hagins, 1973; Govardovskii, 1975) give direct evidence for the presence of rhodopsin in the ROS plasma membrane. This rhodopsin probably experiences the same conformational changes on bleaching as rhodopsin in the discs. Thus plasma membrane rhodopsin may cause adaptation. If bleached rhodopsin in the plasma membrane were a $Ca^{2+}$ channel, it would cause an

increased $c_i$ as long as it is in the bleached state. An intermediate photoproduct or an opsin molecule in the plasma membrane could also act as a sodium leak, increasing a leakage conductance $G_L$. Because of cooperative phenomena $G_L$ could increase faster than the fraction of rhodopsin bleached.

One more mechanism of rod outer segment adaptation can be included in the model. The conformational changes in the plasma membrane rhodopsin could in the case of a strong bleach incapacitate (close) a fraction $e$ of the sodium channels independently of the transmitter blockade. The increase of $e$ moves the operating curve down and to the left:

$$c_1 = c_H \left(1 + \frac{(1-e)R_s G_0}{1 + R_s G_L}\right), \quad C_a = \frac{(1-e)c_H G_0}{(1 + R_s G_L)^2}. \tag{15}$$

As the effects of $G_L$ and $e$ are qualitatively similar, a common term plasma membrane adaptation may be used to include both the increases of $G_L$ and $e$.

*Background Adaptation.* The fast adaptation processes in the receptor constitute background adaptation. The displacements of the operating curve in the steady states corresponding to different background light intensities can be measured, and furthermore the time courses of the displacements of the operating curve after onset or offset of the background light may be determined (excluding the first few seconds). Such measurements in frog rods have been reported in an experimental paper (Hemilä, 1977). The analysis of those experimental results according to the model indicate the central importance of the transmitter coefficient $Q$. The other published studies on background adaptation in several species also point to the importance of the decrease of $Q$. This is not surprising considering that the decrease of $Q$ acts as an attenuator in front of the defector, maintaining the dynamic range of the receptors at different background intensities. The published works on background adaptation have been discussed in Hemilä (1977).

*Dark Adaptation.* When the intensity of the background is increased to the range where the exposure bleaches a noticeable fraction of visual pigment, the sensitivity during the bleach is usually completely lost because of saturation, $U_{\max} < U_c$. However, the mechanisms of adaptation can be studied after strong bleaches during the dark adaptation period. In the frog, after an exposure bleaching several per cents of rhodopsin, the fast background adaptation is succeeded by two distinct adaptation periods (Donner and Reuter, 1968; Hood et al., 1973; Baumann and Scheibner, 1968). The first sequence, intermediate adaptation, occurs both in the isolated retina and in the opened eye; its time constant is less than 10 min at 14° C. The magnitude of this adaptation depends strongly on the duration of the bleach, even when the total amount bleached is constant (Hemilä and Donner, 1975). In the opened eye this period is succeeded by a still slower 'opsin adaptation', so called because it may be connected with the rhodopsin regeneration. In the isolated frog retina without pigment epithelium and with a very limited regeneration capacity there is correspondingly a permanent threshold rise which increases with the amount of rhodopsin bleached. The intermediate adaptation during the decay of long-lived rhodopsin photoproducts have also been observed in several other species (axolotl: Grabowski and

Pak, 1975; crucian carp: Donner, 1973; rat: Ernst and Kemp, 1972; man: Rushton and Powell, 1972a, b).

The two slow adaptation sequences may refer to combined actions of different mechanisms. If the leakage $G_L$, the incapacitation $e$, or the transmitter background $c_i$ *in dark* cause adaptation, that is expected to be important after considerable bleaches. The dark-adaptation would then describe the returns of $Q$, $c_i$, $G_L$, and $e$ to their values in the dark adapted state.

There are not much data on *the operating curves* concerning these slow adaptations in different animals. According to Normann and Werblin (1974) the operating curve in *Necturus* cones moves during dark-adaptation essentially *to the left,* pointing to an increase in the parameter $Q$. Moreover, Pak et al. (1973) observed in the isolated retina of the axolotl a considerable permanent increase of log $I_H$ proportional to the amount bleached, suggesting that the opsin adaptation is in the main also caused by the decrease of $Q$. The same holds for the indirect results obtained in man (Alpern et al., 1970b). On the other hand, the permeability studies of isolated rod outer segments have revealed a long-lasting decrease of sodium conductance (Korenbrot and Cone, 1972; Paulsen et al., 1975), suggesting an increase of $c_i$ in the dark or an increase of the fraction $e$ of the sodium channels temporarily incapacitated (Eq. 15).

*Inner Segment Adaptation Processes.* Only the adaptation mechanisms in the receptor outer segment are included in the model. There is, however, experimental evidence that part of the observed receptor adaptation originates in the receptor inner segment:

1. The sodium pump slows down because of background light. Maintaining a constant pumping rate of sodium during hyperpolarization would need an increased energy consumption. Instead, Sickel (1973) observed a considerable decrease of oxygen consumption during the background illumination. A decrease of pumping rate, typically within a minute after the onset of the background light, was also observed by Zuckermann (1973) in his extracellular current distribution studies.

2. Brown and Pinto (1974) first suggested, that the potassium permeability of the inner segment is increased by hyperpolarization. This 'regenerative hyperpolarization', studied in detail by Werblin (1975), intensifies the photoresponse in the synaptic region (see also Arden, 1976).

3. There are contradictory statements about the distribution of Na-K-ATPase producing the dark current. Pump activity concentrated in the inner segment produces two opposite sodium dark current loops (Zuckermann, 1973; Arden, 1976). Pump molecules distributed evenly in the proximal parts of the receptor produce an one-loop current distribution (Penn and Hagins, 1972). There could be a mechanism regulating the activity of the pump molecules and thus changing the current distribution depending on the state of the receptor. That mechanism would also act as an adaptation process.

4. The secondary conductance changes associated with the rod-rod couplings (disenhancement, Schwartz, 1975, 1976) constitute a very fast adaptation process, appearing already during the response to the stimulus. This process could also affect adaptation measurements (e.g. by introducing stationary disenhancements during background illumination).

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*List of Symbols*

| | |
|---|---|
| $B$ | the fraction of sodium channels closed; |
| $c$ | the transmitter concentration in the extradiscal space of the ROS; |
| $c_i$ | the transmitter background, the initial transmitter concentration before stimulation; |
| $c_H$ | the transmitter concentration corresponding to $B = 1/2$; |
| $c_1$, $C_a$ | the parameters of the general photoresponse equation (Eq. 5); |
| $c_{10}$, $C_{a0}$ | the parameters $c_1$ and $C_a$ in the dark-adapted state; |
| $E$ | the source voltage (e.m.f.) in the rod inner segment; |
| $e$ | the fraction of the sodium channels closed temporarily by a strong bleach independently of the transmitter blockade; |
| $G_0$ | $= Ng$; |
| $G_p$ | $= G_0 (1 - B)$, the total conductance of the open sodium channels; |
| $G_L$ | the leakage conductance of the ROS plasma membrane; |
| $g$ | the conductance of one sodium channel; |
| $I$ | the stimulus light intensity; |
| $I_H$ | the stimulus intensity which elicits a response $\frac{1}{2}U_{\max}$; |
| $I_h$ | the value of $I_H$ in the dark adapted state; |
| $I_t$ | the threshold intensity corresponding to the criterion response $U_c$; |
| $I_0$ | the absolute threshold intensity (dark adapted state); |
| $I_B$ | the background light intensity; |
| $N$ | number of sodium channels in the ROS plasma membrane; |
| $Q$ | the transmitter coefficient ($c = c_i + QI$); |
| $Q_0$ | the value of $Q$ in the dark adapted state; |
| $q$ | the transmitter release factor, the average number of transmitter molecules liberated by an isomerizing quantum; |
| $R_e$ | the resistance of the interreceptor space; |
| $R_i$ | the resistance of the inner segment plasma membrane; |
| $R_c$ | the resistance of the cilium (plus a third of the longitudinal cytoplasmic resistance); |
| $R_s$ | $= R_e + R_i + R_c$; |
| $U$ | the receptor potential, the change in voltage across the resistance $R_e$ brough about by the stimulus light; |
| $U_{\max}$ | the maximum receptor potential in the prevailing state of adaptation; |
| $U_m$ | the value of $U_{\max}$ in the dark adapted state; |
| $U_c$ | the criterion photoresponse (threshold measurements); |
| $\Delta U_i$ | the hyperpolarization of the rod inner segment plasma membrane; |
| $\Delta t$ | duration of the flash stimulus; |
| $\eta$ | the absorption factor, the fraction of incident quantum flux absorbed by rhodopsin and causing photopigment isomerization; |
| $\tau$ | the life time of the transmitter molecules; |
| $\tau_i$ | the integrating time in the response to the step of light. |

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