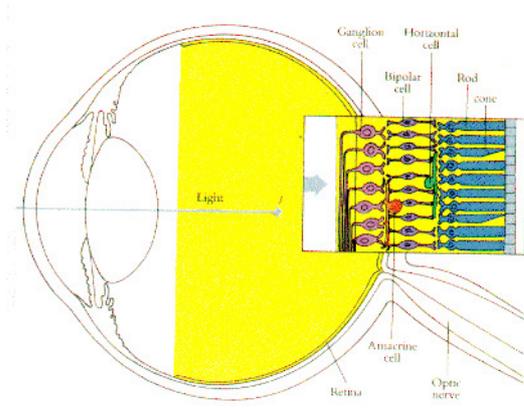# An Adaptive Model for Retinal Horizontal Cell Syncytia

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Theory

The horizontal cells in the vertebrate retina are the first cell-layer after the photoreceptors.

Horizontal cells can be divided into different types. All cells of one type are coupled electrically through gap-junctions. They form a tight layer which can be modelled as a syncytium .

The simplest approximation is to model the lateral interactions between the horizontal cells as a regular triangular, square or hexagonal resistor network . The sheet-resistance between the cells (R_s [Ω]), is due to ionic transport in the cytoplasma and through the gap-junctions. The extracellular resistance has been assumed to be zero. The cell membrane contains channels for various types (N_{Ch}) of ions. Each of these ions i has a constant equilibrium potential E_{Ch_i} [V]. The resistances $R_{Ch_i}(\vec{x}, t)$ [Ω] of the ion-channels are modulated by synaptic inputs from the photoreceptors. The membrane capacity C_m [F] is considered to be constant.
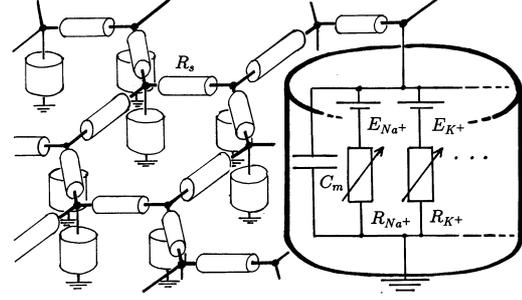
By performing a continuum limit on the circuit equations, one obtains a time t and space $\vec{x}$ -dependent differential equation. This describes correctly the dynamics of the network at large distances and time intervals.

After defining the differential resistances as r_s [$\Omega \mathrm{m}^2$], r_{Ch_i} [Ω] and capacitance c_m [F] one can write

the membrane resistance
$$\frac{1}{r_m} = \sum_{i=1}^{N_{Ch}} \frac{1}{r_{Ch_i}}$$

the length constant
$$\lambda(\vec{x}, t) = \sqrt{\frac{r_m}{r_s}} = \sqrt{\frac{1}{r_s \sum_{i=1}^{N_{Ch}} \frac{1}{r_{Ch_i}}}}$$

the time-constant
$$\tau(\vec{x}, t) = c_m r_m = \frac{c_m}{\sum_{i=1}^{N_{Ch}} \frac{1}{r_{Ch_i}}}$$

and the full-field potential
$$E(\vec{x}, t) = \frac{\sum_{i=1}^{N_{Ch}} \frac{E_i}{r_{Ch_i}}}{\sum_{i=1}^{N_{Ch}} \frac{1}{r_{Ch_i}}}$$

Our equation follows as

$$\tau(\vec{x}, t) \frac{\partial V(\vec{x}, t)}{\partial t} = \lambda(\vec{x}, t)^2 \Delta V(\vec{x}, t) - V(\vec{x}, t) + E(\vec{x}, t)$$

Here λ, τ and E represent averages over areas with similar electrical properties .

Our equation is a generalization of T. D. LAMB's equation published 1976 (Spatial properties of horizontal cell responses in the turtle retina. *J. Physiol.* 263, 239-255), where it is assumed that the length constant λ is independent of time, position and illumination.

For further applications and for standard evaluation of intracellular recording experiments we derive

first the steady state solutions for simple illumination stimuli like a slit or spot. Steady state means that the potential $V(\vec{x}, t)$ does not depend on time, so $V = V(\vec{x})$ and $\frac{\partial V(\vec{x})}{\partial t} = 0$. For simple illumination conditions we assume one constant lenght constant λ^+ and one constant full field potential E^+ inside the illuminated area. Another constant length constant λ^0 and constant full field potential E^0 is valid outside the illuminated area. This implies that the photoreceptors do only influence the horizontal cells directly and not laterally .
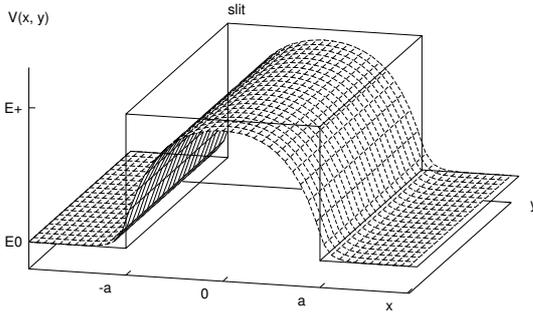
For illumination with a slit ($-a < x < a, -\infty < y < \infty$) the steady state solution for the potential V does not depend on the y-direction:

$$V_{Slit}(x, y; a) = \begin{cases} c_1 \cosh\left(\frac{x}{\lambda^+}\right) + E^+ & ; \quad |x| < a \\ c_2 e^{-\frac{|x|}{\lambda^o}} + E^o & ; \quad |x| \geq a \end{cases}$$

with

$$c_1 = -\frac{E^+ - E^o}{\cosh\left(\frac{a}{\lambda^+}\right) + \frac{\lambda^o}{\lambda^+}\sinh\left(\frac{a}{\lambda^+}\right)}$$

$$c_2 = \frac{(E^+ - E^o)e^{\frac{a}{\lambda^o}}}{\frac{\lambda^+}{\lambda^o}\coth\left(\frac{a}{\lambda^+}\right) + 1}$$

For ilumination with a spot of radius a the solution depends only on the distance $r = \sqrt{x^2 + y^2}$ measured from the center of the spot with radius a:
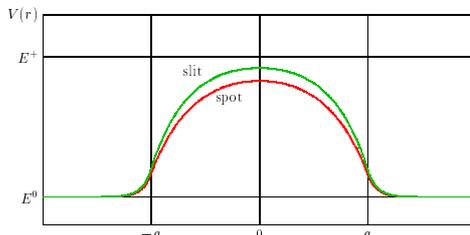
$$V_{Spot}(r; a) = \begin{cases} c_1 I_0\left(\frac{r}{\lambda^+}\right) + E^+ & ; \quad r < a \\ c_2 K_0\left(\frac{r}{\lambda^o}\right) + E^o & ; \quad r \geq a \end{cases}$$

with

$$c_1 = -\frac{(E^+ - E^o)K_1\left(\frac{a}{\lambda^o}\right)}{K_1\left(\frac{a}{\lambda^o}\right)I_0\left(\frac{a}{\lambda^+}\right) + \frac{\lambda^o}{\lambda^+}K_0\left(\frac{a}{\lambda^o}\right)I_1\left(\frac{a}{\lambda^+}\right)}$$

$$c_2 = \frac{(E^+ - E^o)I_1\left(\frac{a}{\lambda^+}\right)}{\frac{\lambda^+}{\lambda^o}K_1\left(\frac{a}{\lambda^o}\right)I_0\left(\frac{a}{\lambda^+}\right) + K_0\left(\frac{a}{\lambda^o}\right)I_1\left(\frac{a}{\lambda^+}\right)}$$

where I_n and K_n denote the usual modified Bessel functions.

Experiments

The length constant λ is a suitable measure of the receptive -field size. I. PERLMAN and J. AMMERMÜLLER considered the effects of dopamine and background light on the receptive-field size of L1 horizontal cells (1994, *Journal of Neurophysiology* 72, 2786-2795). Intracellular recordings were done in the everted eyecup preparation of the red eared swamp turtle *(Pseudemys scripta elegans)*. Receptive field properties were determined in control Ringer solution (NaCl 110mM, KCl 2.5 mM, CaCl$_2$ 2mM, MgCl$_2$ 2mM, NaHCO$_3$ 20mM, D-glucose 10mM, ascorbic acid 0.5mM; bubbled with 95% O$_2$ and 5% CO$_2$; pH 7.4). Photoresponses were elicited in the dark-adapted state with light stimuli of fixed intensity and different diameter. The relationships between the relative response amplitude (normalized to the full field response) $V(0; a)/E^+$ and the spot-radius a were fitted with a theoretical function by OWEN & HARE (1989, Signal Transfer from Photoreceptors to Bipolar Cells in the Retina of the Tiger Salamander. *Neuroscience Research* 10, 77-88) in order to derive the length constants. OWEN & HAREs function is an approximation based on LAMBs theory. We used the data of this measurements to test our theory.

Response of a Horizontal Cell
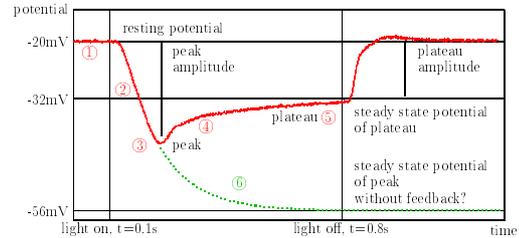
The figure shows a typical response of a horizontal cell. First the cell is on its resting potential E^0 (1). When the light has been switched on the cell hyperpolarizes very quickly (2) to a peak potential (3). Then it depolarizes more slowly (4) to a plateau potential (5).

How can this be explained qualitatively?
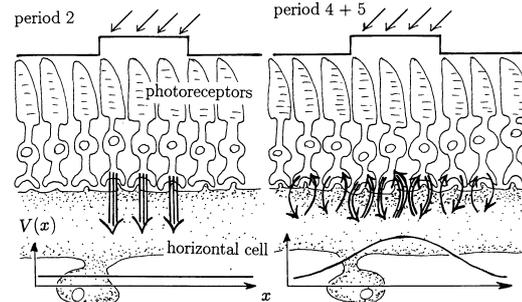
When the light is switched on, the photoreceptors do hyperpolarize. Via synapses they do directly drive the horizontal cells (2) to the peak. Later on the feedback mechanisms between horizontal cells

and photoreceptors become active and brings them back to the plateau (4, 5).

In darkness the horizontal cell syncytium is described by the 'dark' length constant λ^0 and by the resting potential E^0 (1). When light is switched on, the activity of the photoreceptor synapses decreases and the Glutamate driven membrane channels change their resistances. Therefore the syncytium has now a new length constant λ^{peak} and the full field potential E becomes E^{peak} during period (2). In absence of feedback effects, none of the ion channel resistances would change and the potential would follow the dotted line (6). However, due to the GABA feedback mechanism, membrane channels **do** change their resistances, leading to a lenght constant $\lambda^{plateau}$ and full field potential $E^{plateau}$ - see period (4).

Lenght Constant Determination

I. PERLMAN & J. AMMERMÜLLER and others used the peak amplitude in the same way as T. D. LAMB and determined indirectly the length constant by using the theoretical steady state functions. We used our result, namely

$$\frac{V_{Spot}(0;a)}{E^+} = 1 - \frac{1}{I_0\left(\frac{a}{\lambda^+}\right) + \frac{\lambda^o}{\lambda^+}\frac{K_0\left(\frac{a}{\lambda^o}\right)}{K_1\left(\frac{a}{\lambda^o}\right)}I_1\left(\frac{a}{\lambda^+}\right)} \quad ,$$

in the same way. However, we feel that this method has two basic problems, which will be discussed in more detail below.

1. A very elegant indirect method is to derive the length constant by measuring the potential in the center of light-spots with different diameter $2a$. Hence, the length constant is not determined directly from the spatial exponential decay of the potential. Instead, a theoretical function for the potential $V(0;a)$ is used in order to obtain the length constant. The fact is, the length constants has never been measured directly inside and outside the iluminated area ! Therefore, LAMB's basic assumption on the equality of both areas' length constants, has never been checked.

On these grounds, it is not possible to decide which theory is right .
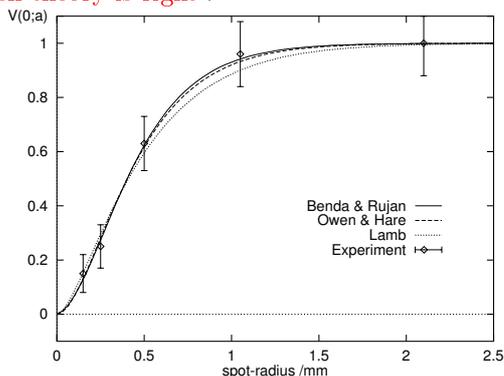
The figure shows a set of experimental results (diamonds). The lines are theoretical functions fitted to the data. Each of them describes the data

very well, but they each provide a different length constant! The blue line is the function based on LAMB's theory ($\lambda_{Lamb} = 326\mu m$). The green line uses the function of OWEN & HARE, which is an approximation of LAMB's function. It fits the experimental data better with a different value for the length constant ($\lambda_{Owen} = 240\mu m$). The fit using our theory (red) is the closest to the data ($\lambda^+ = 243\mu m, \lambda^0 = 41\mu m$). Since we use two length constants instead of one, this is not surprising. Note that for the special case $\lambda^+ \equiv \lambda^0 \equiv \lambda$ one recovers the LAMB function.

2. All the theoretical functions used for evaluating the measurements require steady state conditions. However, distinct peaks are NOT at all in steady state ! Most of our data and LAMB's data are such peak data.

As an alternative, one could use the steady state plateau. Because of the lateral interaction with/between the photoreceptors, the theory itself must be modified in order to account for the continous transition of the length constant and the full field potential between the dark (λ^0, E^0) and the illuminated area (λ^+, E^+). At present, neither the plateau nor the peak should be used for the steady state functions.

What do we plan to do next?

1. Test the theories through a direct measurement of length constants using ilumination with an edge (we have just done the experiments but have not evaluated them yet).

2. Calculate the time dependent solution when switching light on.

3. Try to extrapolate the peak-hyperpolarization (period 2) to its steady state potential and use this to determine the length constants with the above described indirect method.

4. Find out the length constant distribution for the plateau from the edge illumination measurements.

5. Describe the interaction of the photoreceptors with the horizontal cells with two coupled differential equations and derive a solution for the whole response behaviour of the horizontal cell up to the plateau.