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Effect of membrane nonlinearity on retinal LHC's light response

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ABSRACT

In the fish retinas, it was found that a dim red background light could enhance the luminosity-type cone-driven horizontal cell's (LHC) light response to green stimulus and *vise versa* (Kamermans *et al.*, 1989; Luo & Liang, 2003). Some presynaptic mechanisms have been reported to be involved in these phenomena (Luo & Liang, 2003) and other research results show that postsynaptic signals interaction may also contribute to the enhancement (Kamermans *et al.*, 1989). Another possibility is that these changes in HC response are related to postsynaptic membrane properties of the HC. The purpose of this study is to characterize the effect of HC's membrane nonlinearity underlying the background induced changes in the HC response amplitude by a cone-HC model analysis.

1. INTORDUCTION

Intracellular recordings made from retinal LHCs indicated that the LHCs' response can be modified when multichromatic cone signals are converted into the LHC. In the fish retinas, it was found that a dim red background could enhance LHC's light response to green stimulus (see Figure 1) and *vise versa* (Kamermans *et al.*, 1989; Luo & Liang, 2003).

However, it is still not clear whether such mutual color enhancement in LHC response is mediated by modification of the presynaptic light response in the photoreceptors or by changes in efficacy of the photoreceptor-LHC synapse. In this study, we proposed a cone-LHC model to characterize the effect of LHC's membrane nonlinearity underlying the background-illumination-induced changes in the LHC response amplitude, and tried to get a quantitative computational analysis.

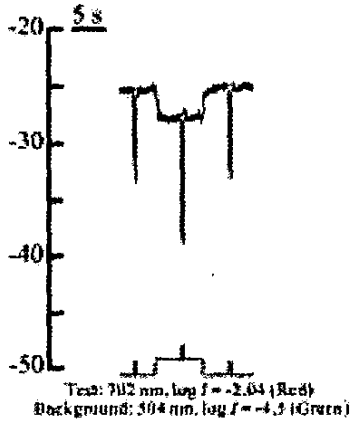

Figure 1. The interaction of red- and green-cone signals in LHC. LHC's response to red test light (701 nm, log I = -2.23) before, during, and after the presence of a dim green background illumination (518 nm, log I = -2.03). The dim green background hyperpolarized LHC and greatly enhanced the cell's response to the red flash, and vise versa (data not shown).

2. METHODS

In this study, we employed a model including the LHC and the relevant cone inputs to simulate the signal transmission between the cones and LHC. The model included the ionic current representation of retinal LHC's membrane potential. The input to LHC was defined as glutamate, which reflects the light stimulus on the cones.

Usui *et al.* (1991; 1996) have modeled the retinal HC's ionic currents using equations similar to that forwarded by Hodgkin and Huxley (1952). In the model, each current can be equated as follows:

$$I_i(V,t) = \overline{g_i} \cdot m^p(V,t) \cdot h^q(V,t) \cdot V_i(V)$$

where $\overline{g_i}$ is the maximal conductance of

the *i*th channel, m and h represent the activation and inactivation variables respectively, V_i denotes the driving force for the ion channel, p and q are positive integers. The membrane potential can thus be computed as a function of the currents and the membrane capacitance using the following differential equation (see Figure 2):

$$C_s \frac{dV}{dt} - (I_{Na} + I_{Ca} + I_{Kv} + I_A + I_{Ka} + I_{glu} + I_l) = 0$$

where C_s is the LHC membrane capacitance, and V is the membrane potential.

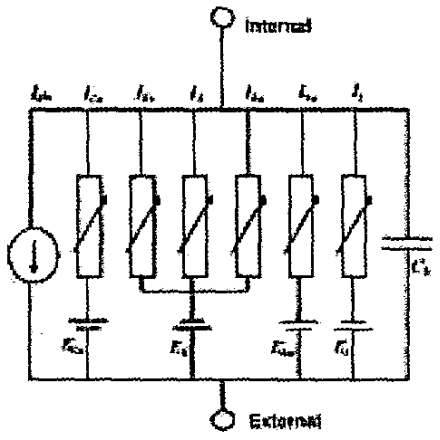

Figure 2. LHC ionic channel model.

The detailed descriptions for each ionic current are given in Table 1; the basic parameters were fitted from voltage and current clamp results (Usui *et al.* 1991, 1996).

For simplicity, the glutamate released from R-cones and G-cones in darkness are set to be 0.5 for each and the quantity of glutamate decrease is equally related to the intensity of light stimulus. In this study, when a dim background illumination is given, the glutamate release from the relevant cone system will be reduced from 0.5 to 0.3 and a test light will change the glutamate release from 0.5 to 0.2. Based on this, we can simulate the LHC background illumination response and analyze the effect of LHC membrane nonlinearity.

3. RESULTS

In carp retina, it was found that a dim green background hyperpolarized LHC and greatly enhanced the cell's response to the red flash (Figure 1), and *vise versa* (data not shown).

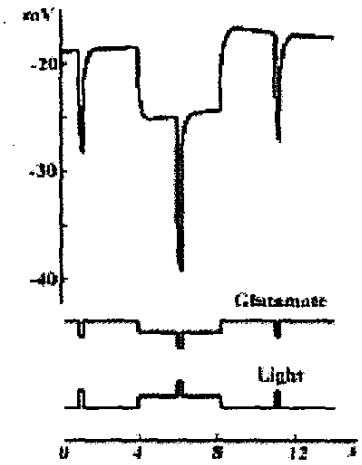

Figure 3. A dim green background illumination enhanced the model cell's response to red test light.

In our model, as shown in Figure 3, the amplitude of LHC's response to a moderate red test flash (glutamate decrease = 0.3) was 9.5 mV in the dark. In the presence of a dim green background light (glutamate decrease = 0.2), the cell's membrane potential was hyperpolarized by 6.5 mV, and its response to the same red stimulus was conspicuously increased to 14.2 mV. The relative response amplitude (response amplitude under the background *vs.* response amplitude during the dark) was 149.5%, which is very similar to electrophysiological result (amplitude increase 158% in Figure 1).

In the same way, we can simulate a dim green background increasing the cell's response to red flash, which is also consistent with experiment (data not shown).

Moreover, the curve of LHC membrane potential to the decrement of glutamate concentration can be drawn as figure 4. When the total glutamate quantity change from 1 to 0.2 with the enhancement of light intensity, the stable LHC membrane potential changed from rested –20 mV to strongly hyperpolarized –65 mV. As shown

Table 1: A representation of ionic currents in LHC based on Hodgkin-Huxley type equations.

Calcium current I_{Ca}

$$\alpha_{mCa} = \frac{5\cdot(70-V)}{\exp(\frac{70-V}{28})-1}$$

$$\beta_{mCa} = 2\cdot\exp(-\frac{V}{15})$$

$$\frac{dm_{Ca}}{dt} = \alpha_{mCa}\cdot(1-m_{Ca}) - \beta_{mCa}\cdot m_{Ca}$$

$$\frac{dh_{Ca}}{dt} = -0.25\cdot h_{Ca} + 0.25\cdot h_{Ca\infty}$$

$$h_{Ca\infty} = \frac{0.7}{1+5\cdot(E_{Ca}\cdot m_{Ca}^{4})^{0.5}}$$

$$\bar{g}_{Ca} = 250 \quad [nS]$$

$$E_{Ca} = \frac{1}{1+\exp(\frac{V-20}{8})} \quad [mV]$$

$$I_{Ca} = -\bar{g}_{Ca}\cdot m_{Ca}^{3}\cdot h_{Ca}\cdot E_{Ca} \quad [pA]$$

Transient outward K current I_A

$$\alpha_{mA} = \frac{40\cdot(140-V_K)}{\exp(\frac{140-V_K}{15})-1}$$

$$\beta_{mA} = 8\cdot\exp(-\frac{V_K}{20})$$

$$m_A = \frac{\alpha_{mA}}{\alpha_{mA}+\beta_{mA}}$$

$$\alpha_{hA} = 0.01\cdot\exp(-\frac{V_K}{20})$$

$$\beta_{hA} = \frac{2}{\exp(\frac{30-V_K}{10})+1}$$

$$\frac{dh_A}{dt} = \alpha_{hA}\cdot(1-h_A) - \beta_{hA}\cdot h_A$$

$$\bar{g}_A = 2 \quad [nS]$$

$$E_K = -60 \quad [mV]$$

$$I_A = \bar{g}_A\cdot m_A^{3}\cdot h_A\cdot(V-E_K) \quad [pA]$$

Anomalous rectifying K current I_{Ka}

$$m_{anom} = \frac{1}{1+\exp(\frac{V+60}{30})}$$

$$\bar{g}_{anom} = 50\cdot[1-0.5\cdot Glu(t)] \quad [nS]$$

$$E_K = -60 \quad [mV]$$

$$I_{anom} = \bar{g}_{anom}\cdot m_{anom}^{4}\cdot(V-E_K) \quad [pA]$$

Delayed rectifying K current I_{Kv}

$$\alpha_{mK} = \frac{10\cdot(120-V_K)}{\exp(\frac{120-V_K}{20})-1}$$

$$\beta_{mK} = 5\cdot\exp(-\frac{V_K}{20})$$

$$\frac{dm_K}{dt} = \alpha_{mK}\cdot(1-m_K) - \beta_K\cdot m_K$$

$$\bar{g}_K = 0.25 \quad [nS]$$

$$E_K = -60 \quad [mV]$$

$$I_K = \bar{g}_K\cdot m^{4}\cdot(V-E_K) \quad [pA]$$

Sodium current I_{Na}

$$\alpha_{mNa} = \frac{40\cdot(80-V)}{\exp(\frac{80-V}{15})-1}$$

$$\beta_{mNa} = 10\cdot\exp(-\frac{V}{20})$$

$$\frac{dm_{Na}}{dt} = \alpha_{mNa}\cdot(1-m_{Na}) - \beta_{mNa}\cdot m_{Na}$$

$$\alpha_{hNa} = 0.01\cdot\exp(-\frac{V}{30})$$

$$\beta_{hNa} = \frac{2}{\exp(\frac{70-V}{10})+1}$$

$$\frac{dh_{Na}}{dt} = \alpha_{hNa}\cdot(1-h_{Na}) - \beta_{hNa}\cdot h_{Na}$$

$$\bar{g}_{Na} = 120 \quad [nS]$$

$$E_{Na} = 55 \quad [mV]$$

$$i_{Na} = \bar{g}_{Na}\cdot m_{Na}^{3}\cdot h_{Na}\cdot(V-E_{Na}) \quad [pA]$$

Glutamate sensitive current I_{glu}

$$\overline{I_{glu}} = 600\cdot Glu(t)$$

$$I_{glu} = \overline{I_{glu}}\frac{\exp(\frac{V+3}{125})-1}{\exp(\frac{3-V}{125})+1} \quad [pA]$$

Leakage current I_l

$$\bar{g}_l = 0.5 \quad [nS]$$

$$E_l = -60 \quad [mV]$$

$$I_l = \bar{g}_l\cdot(V-E_l) \quad [pA]$$

in Figure 4, we can explicitly see the nonlinear change of LHC membrane potential to the amount of glutamate stimulus.

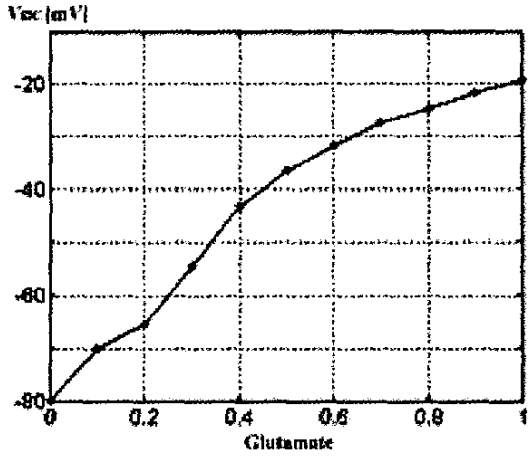

Figure 4. Nonlinearity of the LHC's membrane potential change in response to the decrement of glutamate concentration.

4. DISSCUSSION

In the retinal cone-HC synapse, HC receives glutamatergic input and produces GABAergic feedback to cones. GABA has been certified as not significantly affect the background-induced change in response dynamics and amplitude (Yang & Wu, 1989; Luo & Liang, 2003). It has been reported that the presynaptic metabotropic glutamate receptor mediated hetero-synaptic interaction of red- and green-cone inputs to LHC may be involved in these phenomena (Luo & Liang, 2003). In this study, we constructed a model including the LHC and the relevant cone inputs to simulate the synaptic connection of cone-LHC. Based on this, the model simulates the LHC background illumination induced enhancement response properly.

The results of simulation show the LHC background illumination response can be affected by the nonlinear membrane properties changing with different membrane potential, and the background illumination induced enhancement of cell response is due to, at least partly, the LHC membrane nonlinearity.

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5. REFRENCES

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