ELSEVIER

Neurocomputing 50 (2003) 407–418

NEUROCOMPUTING

www.elsevier.com/locate/neucom

A competitive model for spectral plasticity in the outer retina

Yu Liu, Jian-Feng Hu, Pei-Ji Liang*

Shanghai Institute of Physiology, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, 320 Yue-Yang Road, Shanghai 200031, China

Received 30 April 2001; accepted 16 February 2002

Abstract

In a previous paper, we reported that repetitive red flashes enhanced the red response of retinal luminosity-type horizontal cell (LHC) and depressed the cell's green response; repetitive green flashes suppressed the cell's red response, but caused trivial changes in its green response. Based on the idea that the spectral plasticity of the horizontal cell may reflect some changes in synaptic efficacy between the horizontal cell and various cones, a simple quantitative model was constructed. The process consists of three components: a linear first-order dynamics, a self-excitatory component within the same kind of synaptic population, and a cross-inhibitory component between different kinds of synaptic populations. It is shown that the model prediction fits reasonably well with the experimental data. The influence of relevant parameters on the model output was further inspected. Our findings suggest that there might be a competitive depression between the red- and green-cone signals that converge onto LHCs.

Keywords: Synaptic plasticity; Competitive model; Retina

1. Introduction

It has been well acknowledged that synaptic strength can be modulated by synaptic or cellular activity [6] in the central nervous system and it has been realized that activity-dependent modification of synaptic efficacy is fundamental to information processing in the nervous system. It was suggested that stimulus pattern generated an activation pattern across the neural structure, and both stimulus pattern and activation pattern were related to the changes in the neurons' response properties. Theoretical work via modeling approaches has been carried out to explain the dynamics of

* Corresponding author. Tel.: +86-21-64370080x170; fax: +86-21-6433-2445.
E-mail address: pjliang@server.shcnc.ac.cn (P.-J. Liang).

0925-2312/03/$ - see front matter
PII: S0925-2312(02)00574-X

synaptic modifications observed from spiking neurons in various parts of the central nervous system [3,8].

Morphological and electrophysiological work has revealed that the synapses between non-spiking retinal neurons were plastic. In teleost fish, retinal luminosity-type horizontal cell (LHC) receives input from both red- and green-sensitive cone photoreceptors. An early study showed that in goldfish retina, the input signals from red- and green-sensitive cones converging onto the postsynaptic LHC were not independent to each other. Regulating the activity of one cone system might influence that of another [5,13]. Evidence on the morphological front further showed that the cone–HC synaptic connection was plastic, which was closely related to the pattern of the conditioning light [12]. Recent experimental observations made from our laboratory demonstrated that the strength of the synapse between cones and horizontal cells was highly stimulus pattern related [4]. The essential findings were that repetitive red flashes enhanced LHC's response to red light, and depressed its response to green light; on the other hand, repetitive green flashes inhibited the cell's response to red stimulus, although it changed the cell's green response little. This work was carried out to investigate the synaptic strength changes that occurred in the outerplexiform layer of carp retina when the neuronal activities were regulated using mono-wavelength lights, via the modeling approach.

2. Model

To describe the process of the stimulus pattern related temporal changes in LHC's light responsiveness, a quantitative model based on the use-dependent synaptic connection in the outer retina was developed, following the factors and assumptions such that: (1) according to the spectral sensitivity curves of various cones of teleost retina [7], the ratio of inputs to red- and green-cone systems was assumed to be 0.9:0.1 for red (703 nm) light stimulus and 0.4:0.6 for green (501 nm) light stimulus; (2) LHC received synaptic inputs from both red- and green-cone systems, and LHC's response consisted of two components, each related to red- and green-cone signals, respectively [13]; (3) cone–LHC synapses have a two-dimensional ($N \times N$) topological arrangement, with each synapse between red cone and LHC being sandwiched by two synapses that connect green cones and LHC, in both abscissa and ordinate directions, and vice versa (Fig. 1); (4) the strength of a certain population of synapses would be increased upon activation at the expense of a corresponding strength decrease of the other synapses. The neural network model constructed can thus be equated as follows:

for red cone–LHC synapses:

$$\begin{aligned}\frac{\mathrm{d}x_{\mathrm{r}}(t,i,j)}{\mathrm{d}t} = &-\frac{1}{\tau_{\mathrm{r}}}(x_{\mathrm{r}}(t,i,j) - x^{*}_{\mathrm{r}0}) \\ &+ \sum_{\substack{m\neq i \\ n\neq j}} (a_{\mathrm{r}} - x_{\mathrm{r}}(t,i,j))x_{\mathrm{r}}(t,m,n)E(i,j,m,n)I_{\mathrm{r}}(t,i,j) \\ &- \sum_{\substack{m\neq i \\ n\neq j}} (x_{\mathrm{r}}(t,i,j) - b_{\mathrm{r}})x_{\mathrm{g}}(t,m,n)S(i,j,m,n)I_{\mathrm{g}}(t,i,j)), \qquad (1a)\end{aligned}$$

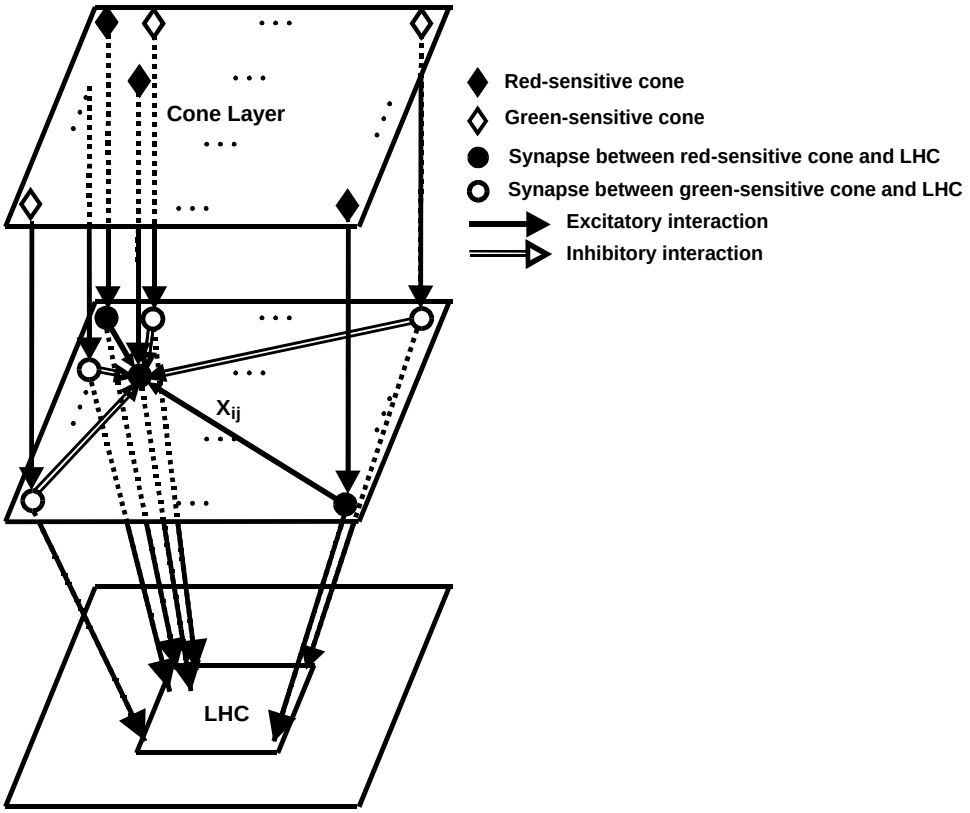


Fig. 1. Model structure for describing the synapses between cones and LHC. Solid and open diamonds represent red- and green-sensitive cones, respectively. Solid and open circles are synapses between LHC and red- and green-sensitive cones, respectively. Solid and open arrows in the synapse layer represent the excitatory interactions within the same synapse population and inhibitory interactions between different synapse populations, respectively.

for green cone–LHC synapses:

$$\frac{\mathrm{d}x_{\mathrm{g}}(t,i,j)}{\mathrm{d}t} = -\frac{1}{\tau_{\mathrm{g}}}(x_{\mathrm{g}}(t,i,j) - x^{*}_{\mathrm{g}0}) + \sum_{\substack{m\neq i\\ n\neq j}}(a_{\mathrm{g}} - x_{\mathrm{g}}(t,i,j))x_{\mathrm{g}}(t,m,n)E(i,j,m,n)I_{\mathrm{g}}(t,i,j) - \sum_{\substack{m\neq i\\ n\neq j}}(x_{\mathrm{g}}(t,i,j) - b_{\mathrm{g}})x_{\mathrm{r}}(t,m,n)S(i,j,m,n)I_{\mathrm{r}}(t,i,j), \tag{1b}$$

where $x^{*}_{\mathrm{r}0}=x_{\mathrm{r}0}+\beta\varepsilon(t,i,j)$, $x^{*}_{\mathrm{g}0}=x_{\mathrm{g}0}+\beta\varepsilon(t,i,j)$, $t=1,2,\ldots,40$, $i=1,2,\ldots,N$, $j=1,2,\ldots,N$, $m=1,2,\ldots,N$, $n=1,2,\ldots,N$,

$$i+j=\begin{cases}\text{even}, & \text{for red synapses},\\ \text{odd}, & \text{for green synapses}.\end{cases}$$

In Eq. (1), $x_k(t,i,j)$ $(k = \mathrm{r},\mathrm{g})$ represents the strength of the synapse (i,j) at time t, with x_{k0} being the static value when no stimulation is applied. Constants a_k and b_k denote, respectively, the maximum and minimum possible strength of the relevant synapses. Therefore, non-negative terms $(a_k - x_k(t,i,j))$ and $(x_k(t,i,j) - b_k)$ form non-linear compressions for both self-excitatory and cross-inhibitory processes between the synapse populations, respectively. τ_k reflects the passive decay time constant of the synaptic strength. $I_k(t)$ is the input to the relevant signal pathway at time t. $\varepsilon(t,i,j)$ is a white noise process following the standard normal distribution:

$$\varepsilon \sim N(0,1). \tag{2}$$

The non-negative terms $E(i,j,m,n)$ and $S(i,j,m,n)$ are excitatory and inhibitory interaction functions within and between the synapse populations, respectively [2], with their spatial decay being

$$E(i,j,m,n) = E \times \mathrm{e}^{-((i-m)^2+(j-n)^2)/\sigma_E^2}, \tag{3a}$$

$$S(i,j,m,n) = S \times \mathrm{e}^{-((i-m)^2+(j-n)^2)/\sigma_S^2}. \tag{3b}$$

The model thus has the following properties: (1) the synaptic strength has a static state value x_{k0} when no stimulation is applied, and if any synaptic strength change is driven by an excitatory/inhibitory stimulus, a recovery to the static value will be reached following a first-order dynamics with a time constant τ_k, after the stimulation has ceased; (2) self-excitation within the same kind of population is weighted, as well as restricted, by the term $(a_k - x_k(t,i,j))$; (3) cross-inhibition between different kinds of populations is weighted and restricted by $(x_k(t,i,j) - b_k)$.

The output signal of each synapse population is decided by both the input signal $I(t)$ and the synaptic activity $x_k(t,i,j)$ following a sigmoid function:

$$f(u) = (1 - \mathrm{e}^{-u/\alpha}). \tag{4}$$

The postsynaptic activity, i.e., the response amplitude of LHC at time t, is therefore determined by a simple summation of the output of the two signal pathways:

$$Y(t) = \sum_{i,j} f(x_k(t,i,j) I_k(t,i,j)), \tag{5}$$

where the synaptic weight $x_k(t,i,j)$ varies between 0 and 1, with the initial weight following a normal distribution, both spatially and temporally:

$$x_{k0}^* \sim N(x_{k0}, \beta^2). \tag{6}$$

All the parameters used for the simulation were carefully selected, as listed in Table 1.

3. Result

In the carp retina, LHC receives inputs from both red- and green-cone pathways. The synaptic strength between LHC and each cone system is plastic, which is dependent on both the history and activity of the signal pathway. The experimentally observed auto-enhancement and mutual-depression effects caused by repetitive mono-wavelength

Table 1
Values of the parameters used for the model

Parameters	Values	Parameters	Values
a	0.92	x_{k0}	0.5
b	0.04	α	5.0
E	0.02	σ_E	5.0
S	0.02	σ_S	5.0
N	10	σ_ε	1.0
τ_r	5.0 s	β	0.05
τ_g	5.0 s		

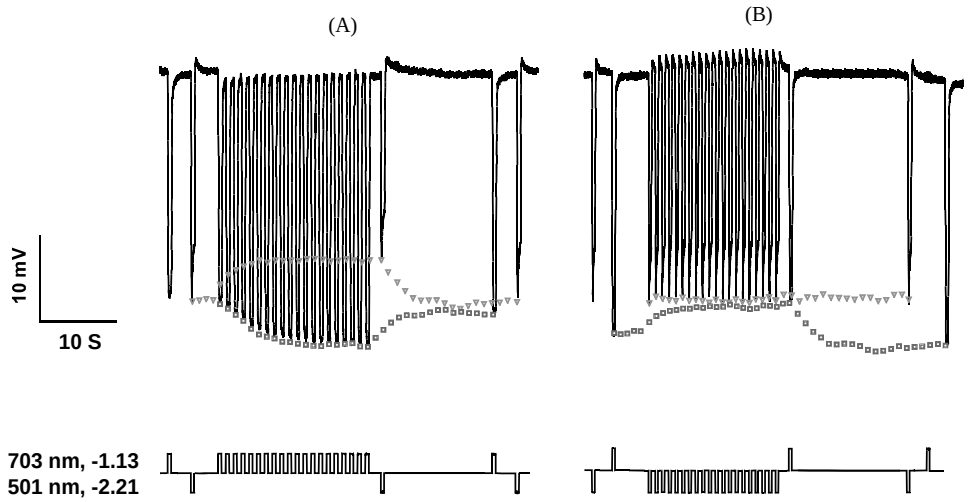


Fig. 2. The comparison between experimental recordings and model prediction. The solid lines in both panels A and B illustrate a typical LHC's response to red and green flashes before, during, and after the 20 s red flickering (upper panel: LHC's response; lower panel: light flash). The model predictions of the cell's response amplitudes to red and green test light during each condition are represented by squares and triangles, respectively.

light flashes are plotted in Fig. 2. It is demonstrated that during the 20 s exposure to red flickering, the repetitive red flashes increased the cell's red response but depressed its green response. Similarly, the cell's response to red test flash was remarkably reduced during exposure to the 20 s green flickering, although repetitive green flashes caused little change in the cell's green response. Such asymmetry in the cell's response changes during relevant stimulus patterns might be related to the spectral behavior of the red- and green-cones. Since LHC received inputs from both red- and green-cones, and green-cones are around 2 log units less sensitive than red-cones to 703 nm stimulus [7], 703 nm flashes at intermediate intensity selectively activate red-cones. The repetitive red flashes actually form simultaneous stimuli on red cones and LHC via the red-cone–LHC pathway, which might result in a strengthened synaptic connection between the red-cone and LHC, and at the mean time depress the green-cone signal pathway. On the other hand, since the sensitivity of red-cones is only 0.5 log units lower than that

of green-cones at 501 nm, the green flashes activate not only green-cones, but also red-cones to some extent. The mixed effects of homo-wavelength-signal enhancement and competitive depression induced a modest enhancement of the LHC's green response during green flickering and an accompanying inhibition of the LHC's red response [4]. The cell's response changes caused by either repetitive red or green flashes were reversible.

To describe the use-dependent synaptic plasticity that occurred in the outer plexiform layer of carp retina, a non-linear model was developed. In this model, the activity of the neural circuitry was represented by synaptic weight, which was highly dependent on the history and activity of relevant neurons. The synaptic connection was strengthened when the particular signal pathway was activated, with the synaptic weight of the unstimulated pathway decreased. Using carefully selected parameters, the model was applied to simulate the LHC's response behavior during various patterns of stimulus.

The model output, i.e., the response amplitude of LHC at each moment, was compared to the experimental data as illustrated in Fig. 2. In both panels A and B, the model output of the cell's responses to red test light during the development of flickering caused response change and recovery are represented by squares, whereas the predicted cell's responses to green test flash during each condition are represented by triangles. The cell's behavior was well simulated by the model that during repetitive red flashes, the cell's response to red light was gradually enhanced while its response to green test light was correspondingly decreased, and such changes could be recovered within 20 s after the red flickering had ceased. Similarly, the cell's response behavior during green flickering light changed little, while the cell's response amplitude to red flash was reduced. The cell's response amplitude was recovered to its initial values within a short period after the green flickering stimulation had ceased.

The stimulus pattern related LHC's spectral sensitivity changes are essentially attributed to the balance of synaptic weight changes during each condition, i.e., a red flash sequence strengthened the synapses between red-cones and LHC, while it weakened that between green-cones and LHC, and vice versa. Relevant synaptic weight changes as calculated by the model are plotted in Fig. 3.

Since the behavior of the model is entirely determined by the values of its parameters once the model structure is decided, we next inspected the influence of relevant parameters on the model prediction of the cell's response amplitude during repetitive red stimulus. Basically, the excitatory and inhibitory interaction coefficients E and S, as well as the non-linear compressive coefficients for the enhancement and depression processes a and b, were investigated.

Fig. 4A illustrates the influence of the excitatory coefficient E on the model output. In this set of calculation, the value of E was changed from 0.0 to 0.05, with steps being 0.01, whereas the values of other parameters were kept constant as given in Table 1. It is shown that at an extremely low value of E, the model prediction of LHC's response to red and green flash both decreased along the 20 s period; when the E value exceeded 0.03, the calculated green responses showed a brief enhancement before it was decreased; only when E was set at a value around 0.02, the model output was able to simulate the experimental observations reasonably that the cell's response to red flash increased while that to green flash decreased.

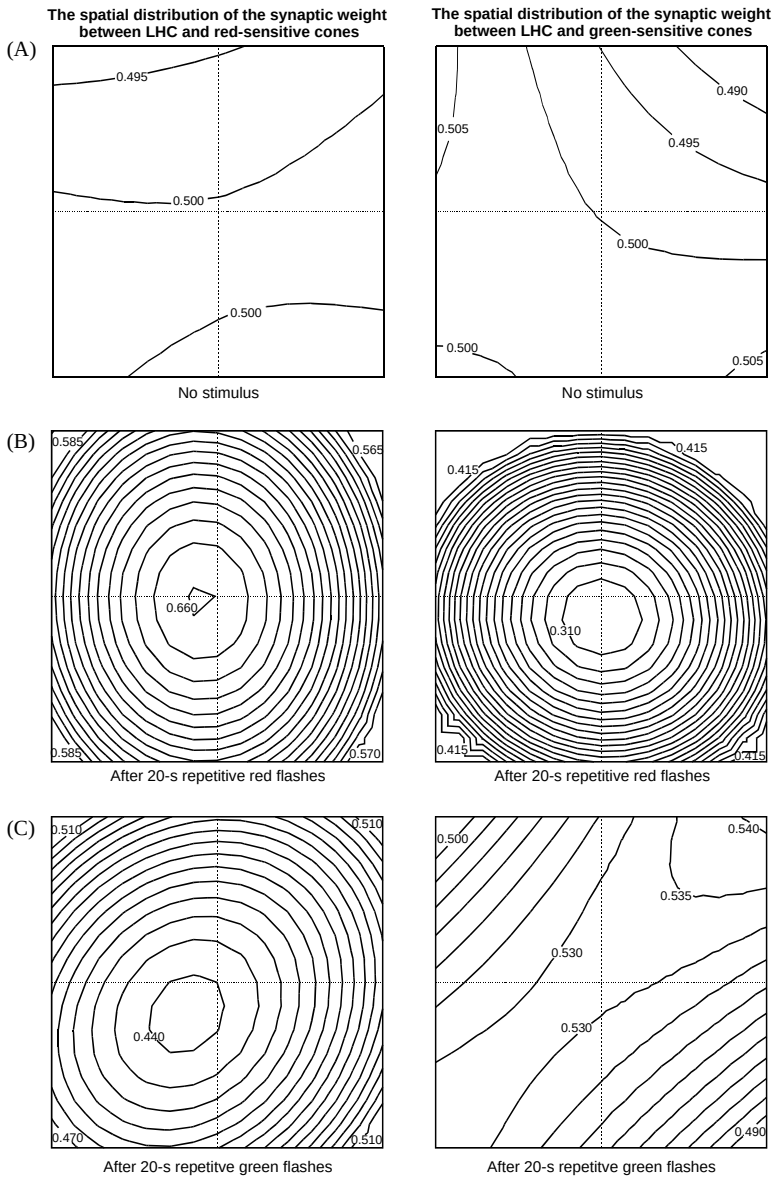


Fig. 3. The spatial distribution of synaptic weights during various conditions. Left and right panels represent the spatial distribution of synapses between LHC and red- and green-cones, respectively. (A) When no stimulation was applied, the spatial distributions of weights of synapses between red/green-sensitive cones and LHC were kept near their static values, only a random fluctuation occurs, due to the intrinsic noise. (B) 20-s repetitive red flashes remarkably strengthened the synaptic connection between red-cone and LHC, but weakened that between green-cone and LHC. (C) 20-s repetitive green flashes moderately inhibited the red-cone synapses, and slightly enhanced the green-cone synapses. The difference in synaptic weight between adjacent lines is 0.005.

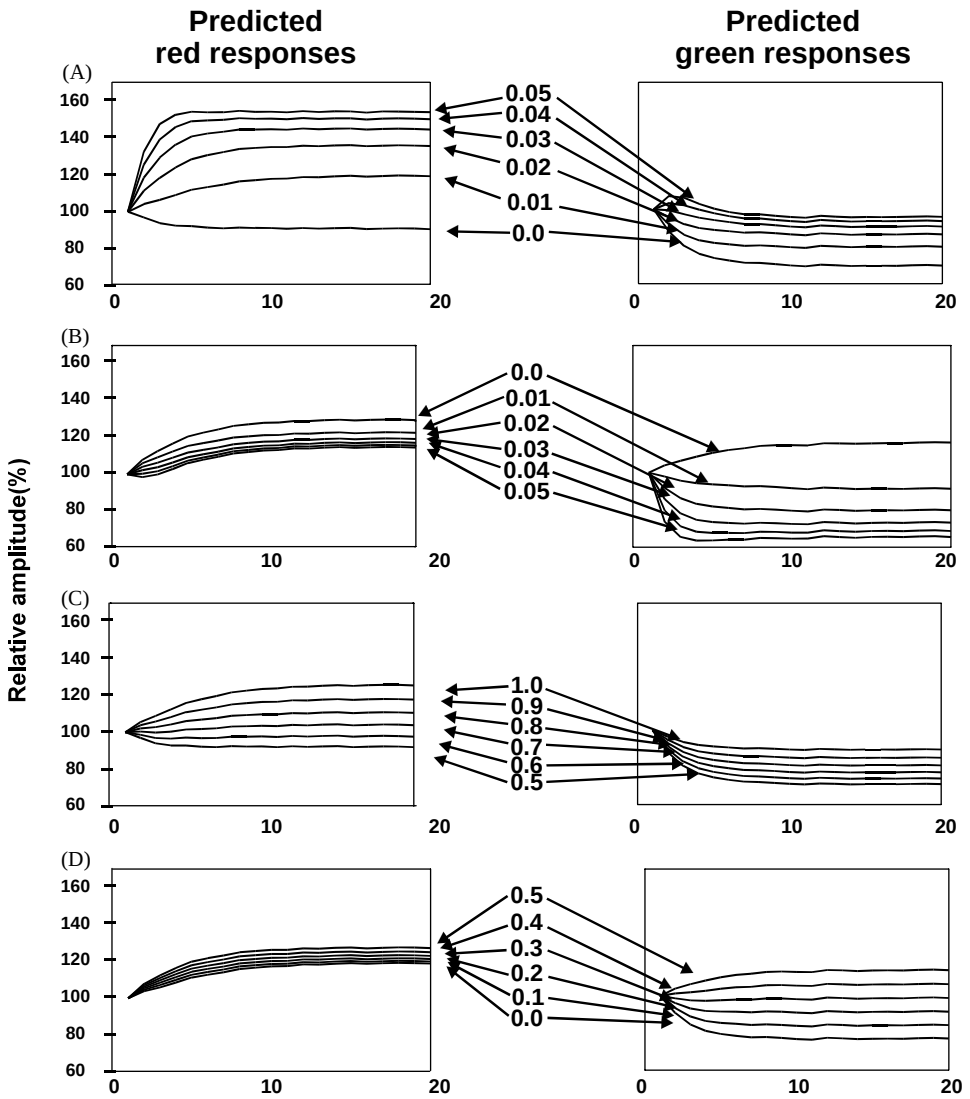


Fig. 4. Effects of relevant parameters on the model output during repetitive red flashes: (A) influence of the excitatory coefficient E on the model output; (B) influence of the inhibitory coefficient S on the model output; (C) influence of maximum strength a on the model output; (D) influence of the minimum strength b on the model output. Left and right panels are for the calculated cells' response amplitude to red and green test flashes, respectively.

In Fig. 4B, the model predictions with changing values of S are compared. It is demonstrated that the model cell's response to red stimulus was kept enhanced when the S values changed from 0.0 to 0.05. Although the amplitude was affected slightly, the dynamics followed a similar process. However, the model cell's response to green stimulus showed an enhancement at an extremely low value of S. When the S value

reached a high value of 0.04, the model predictions showed some undershoot of depression during the first few seconds. The model gave satisfactory simulation when the S values were set around 0.02.

Similar to the excitatory coefficient E, changes in non-linear compressive coefficient a also caused some changes in the model behavior, as plotted in Fig. 4C. When changed from a low value of 0.5 to a high value of 1.0, it did not alter the depressive effect on the cell's response to green light; however, the model cell's response to red stimulus was only enhanced when a reached a value > 0.7.

The influence of coefficient b is illustrated in Fig. 4D, which shows that the change of this parameter between the ranges of 0.0–0.5 did not change the model cell's response to red stimulus very much, apart from some difference in response amplitude. However, its influence on the model cell's green response was dramatic. Response depression only occurred at a low value of b (< 0.3), whereas an enhancement would occur when the b value was set > 0.4.

These results show that during red flickering flashes, parameters a and E are related to the enhancement effect of synaptic weight between LHC and red-cones, while b and S are crucial in describing the depression effect of synaptic weight between LHC and green-cones.

4. Discussion

Synaptic plasticity has long been a topic for neurobiologists and modelers. Numerous works have been reported during the past decades. Among these, an attractive model was formulated by Bienenstock and colleagues [1], in which the ability of synaptic modification varied as a non-linear function of corresponding input signal, as well as postsynaptic activity. The direction and degree of changes in synaptic strength (Δw_i) were both governed by a combination of intensity of input signal and the activity of postsynaptic neuron, which can be termed as $\Delta w_i \propto (x - \theta_x)(y - \theta_y)$ [6], where x and y denote the presynaptic input and the postsynaptic output, respectively; θ_x and θ_y represent pre- and post-synaptic modification thresholds, respectively. In this model, potentiation occurs only when both x and y are above their thresholds; whereas depression should be induced when one is below its threshold and another above. An important additional assumption of Bienenstock's model is that the threshold values are not fixed, but rather fluctuate according to the history and present activity of the pre- and post-synaptic neurons. Such a property of synaptic connection has been termed "meta-plasticity", which means that the modifiability of the synaptic strength is changeable. Thus, as a result of stimulation induced increase, θ may shift to promote synaptic depression, and vice versa. Following Bienenstock's theory, the hetero-synaptic depression which refers to depression of the unstimulated synapses observed in this laboratory might result from $y > \theta_y$ and $x < \theta_x$, and the auto-enhancement of the stimulated synapses could be attributed to the status $y > \theta_y$ and $x > \theta_x$.

Extended from Bienenstock's model which describes the meta-plasticity in a single synapse, our model is somewhat more complicated in the sense that it describes the multi-signal interactions in the outer plexiform layer of carp retina. The strength

change of a certain population of synapses is determined by the combination of two major factors. Basically, the relationship between the presynaptic input intensity and the postsynaptic activity weighted by the excitatory function E, which is similar to the form proposed by Bienenstock, decides the self-excitation within the synapse population; the activation status of the other synapses population, weighted by the inhibitory function S, forms a cross-competition effect between the different populations of synapses. Taking the idea that the spatial profiles of the excitatory- and inhibitory-interactions in forming the retinal ganglion cells' receptive field both follow a Gaussian-like spatial distribution [9,10], E and S are assumed to decay along distance with a Gaussian-like manner. However, since the various cones are randomly distributed in the outer plexiform layer [11], we chose the two functions as with identical decay rate. In this model, the changeability of the synaptic strength (the first derivative of x_k as given by the equations) is not a constant, but rather a function defined by the stimulus pattern and the synaptic status along time, with the synaptic weights confined by the maximum and minimum values a and b, respectively. A continuous second derivative of the synaptic weight is available, and the model is thus endowed with the property of "meta-plasticity" as discussed by previous authors [1,6].

Given the model structure, the strength change of a certain synapse predicted by our model is governed by the following factors: (1) the correlation between the two synapse populations ($x_k x_{\bar{k}}$, $k = \mathrm{r}, \mathrm{g}$); (2) the status of the synapse population inspected (x_k) and that of the other population of synapse ($x_{\bar{k}}$); (3) the squared synaptic weight (x_k^2); and (4) a constant value. When applied to the experimental data, various combinations of parameter values were compared, and the set of parameters which yield satisfactory simulation results are listed in Table 1. The results are such that the coefficients related to the correlation between the two populations ($x_k x_{\bar{k}}$) are negative, which implies that the interaction between the different populations is competitive; the x_k terms are weighted by negative coefficients while the coefficients of the $x_{\bar{k}}$ terms are positive, which suggests that the energy supporting the strengthening of a certain synapse population is not provided by the environment, but rather at the expense of the other synapses; x_k^2 terms also have negative coefficients, which implies that the synaptic weight changes are limited by the synaptic status.

5. Conclusion

Taken together, our results suggest that the stimulus pattern related HC spectral plasticity is likely to be attributed to the activity-dependent synaptic strength modification in the outer plexiform of retina, and the activity-dependent processes are conservative, i.e., the strengthening of the stimulated synapses is compensated by the weakening of the others.

Acknowledgements

This research was supported by grants from the State Key Basic Research and Development Plan (No. G1999054000) and the National Foundation of Natural Science of China (No. 30170263).

References

[1] E.L. Bienenstock, L.N. Cooper, P.W. Munro, Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex J. Neurosci. 2 (1982) 32–48.

[2] S.A. Ellias, S. Grossberg, Pattern formation, contrast control, and oscillations in the short-term memory of shunting on-center off-surround networks, Biol. Cybernet. 20 (1975) 69–98.

[3] T. Fukai, Oscillations for rapid selection of neural activities based on spike timing, Neuro Report 29 (1995) 273–277.

[4] J.-F. Hu, Y. Liu, P.-J. Liang, Stimulus pattern related plasticity of synapses between cones and horizontal cells in carp retina, Brain Res. 857 (2000) 321–326.

[5] M. Kamermans, B.W. van Dijk, H. Spekreijse, Lateral feedback from monophasic horizontal cells to cone in carp retina, J. Gen. Physiol. 93 (1989) 681–694.

[6] K.D. Miller, Synaptic economics: competition and cooperation in synaptic plasticity Neuron 17 (1996) 371–374.

[7] A.G. Palacios, F.J. Varela, R. Srivastava, T.H. Goldsmith, Spectral sensitivity of cones in the goldfish, *Carassius auratus*, Vision Res. 38 (1998) 2135–2146.

[8] J.H. Reynolds, L. Chelazzi, R. Desimone, Competitive mechanisms subserve attention in Macaque areas V2 and V4, J. Neurosci. 19 (1999) 1736–1753.

[9] R.W. Rodieck, Quantitative analysis of cat retinal ganglion cell response to visual stimuli, Vision Res. 5 (1965) 583–601.

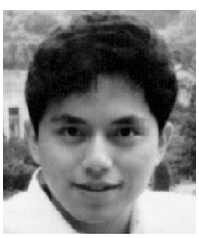
[10] R.W. Rodieck, J. Stone, Response of cat retinal ganglion cells to moving visual patterns, J. Neurophysiol. 28 (1965) 819–832.

[11] A. Roorda, D.R. Williams, The arrangement of the three cone classes in the living human eye, Nature 397 (1999) 520–522.

[12] H.J. Wagner, M.B.A. Djamgoz, Spinules: a case for retinal synaptic plasticity Trends Neurosci. 16 (1993) 201–206.

[13] X.-L. Yang, M. Tauchi, A. Kaneko, Convergence of signals from red-sensitive and green-sensitive cones to external horizontal cells of the goldfish retina, Vision Res. 23 (1983) 371–380.

Yu Liu is currently a Ph.D. student of Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.



Jian-Feng Hu is currently a Ph.D. student of Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

Pei-Ji Liang received her D.Phil. in physiology from the University of Oxford. She is currently an associate professor in Shanghai Insititutes for Biological Sciences, Chinese Academy of Sciences.