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Brightness change is optimal stimulus for parasol retinal ganglion cells

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Abstract

Magnocellular-projecting retinal ganglion cells show spike response in two cases. Firstly, as a result of presentation of the optimal stimulus. Secondly, rebound excitation when removing the opposite stimulus. Also, there are studies suggesting that rebound excitation meets conditions to participate in visual perception at the same sensitivity and reaction speed as a response to the optimal stimulus. Thus, white noise stimulation creates possibility to catch the form of a smooth transition from one type of response to another. Using freely available data, a spike-triggered behavior map was built that does not show the area of silence between those two types of spike triggers. Moreover, linear filter with biphasic temporal properties which work as the derivative kernel demonstrate that both responses are two sides of the same coin. Thus, it is suggested to determine the optimal stimulus for magnocellular-projecting retinal ganglion cells as brightness change according to concentric center–surround receptive field structure.

Main Text

Neurophysiological studies of the retina gradually brings us closer to understanding of visual perception. It was found that the one cell of retina responds to stimulation by light in its small area of responsibility - receptive field[1]. According to receptive field structure, retinal ganglion cell (RGC) has corresponding form of the optimal stimulus that elicits a spike train[2]. Moreover, presenting the optimal stimulus is not the only way to make a retinal cell respond with spikes. Rebound excitation, also termed post-inhibitory rebound, is a spike train that arised after canceling hyperpolarization below the resting membrane potential[3,4]. The natural way to cause rebound excitation is to present opposite visual stimulus for some period of time and then remove it.

After long and intensive stimulation retina percept long-lasting negative afterimage, and rebound excitation takes place in that physiological aftereffect[3]. RGCs, for which presented stimulus was opposite, keep firing and give us information where in sight of view stimulus was. But what for natural stimulus with short period of time? Spikes of retinal rebound excitation are no different from spikes caused by optimal stimulus, that what if RGC rebound excitation is fast and sensitive enough to percept of removal of the visual opposite stimulus at same level as perception of optimal stimulus, it could be the key of motion perception.

It was already suggested to add rebound excitation in motion perception model[5], but the model of rebound excitation had a disadvantage. Spike train appeared only after opposite stimulus 300 ms duration. Currently there is no information about required period of time to cause rebound excitation for different types of RGCs.

I assumed that in order to be useful, rebound excitation should leave a trace on spike triggered average[6] (STA). There must be a peak for the opposite stimulus that corresponds to the cell's response to the removing opposite stimulus. RGCs with biphasic STA can fulfill this condition. However, currently biphasic STA is interpreted in following way for RGC with transient response. The first peak determines

the value of the optimal stimulus, while the second opposite peak determines how short the response to the long-term optimal stimulus will be. This interpretation is conditioned upon the fact that the linear filter in the linear-nonlinear model actually repeats the STA shape[7]. Whether there is a place for rebound excitation behind the second peak, I will consider in this paper.

Behavior of the rebound excitation

Different implementations of the reverse correlation algorithm reveal biphasic temporal properties for magnocellular visual pathway starting from retina to primary visual cortex[8,9,10]. Also, other studies with inactivating magnocellular-projecting RGCs show weak influence on spatial vision, but instead seriously affects motion detection[11,12,13,14]. Thus, in this study I focused on magnocellular-projecting RGCs to find evidence that rebound excitation participates in visual perception not only as part of afterimage, but at the same level as optimal stimulus reaction.

First of all, I checked how fast is the reaction on removing opposite stimulus. For cats, response latency on removing opposite stimulus faster than response latency on optimal stimulus for case of 300 ms stimulus duration[4]. OFF cells: 31.39 ± 2.32 ms for the removal of opposite stimulus vs 52.55 ± 3.08 ms for the optimal stimulus. ON cells: 37.39 ± 2.27 ms for the removal of opposite stimulus vs 48.37 ± 2.34 ms for the optimal stimulus. For measurement, lateral geniculate nucleus X and Y type neurons were used. Response latency for removing opposite stimulus only for Y type neurons: 18 Y-ON 39.67 ± 4.87 ms, 20 Y-OFF 29.80 ± 3.72 ms. Those measurements are a perfect example of reaction speed in retina too, because lateral geniculate nucleus ON and OFF neurons inherit the spatio-temporal receptive field organization of ON and OFF RGCs[15].

Second, I checked how short could be opposite stimulus to cause rebound excitation. The best result was obtained during the study[16] with macaque monkeys ON and OFF parasol cells reaction for 25 ms flashes with contrasts were ±12, ±24, ±48, and ±96% for gray screen. Response for removing opposite stimulus flash took place. With regard to participation in visual perception, the duration of the flash of 25 ms is close to the limits of perception. A person can easily see a picture in 20 ms if it is followed by a blank screen[17]. For sequences of pictures, 13 ms is sufficient only if it is specified in advance which picture he may or may not see in the sequence[18] with some conditions[19].

Third, I checked how low contrast could be to cause rebound excitation. During testing of visually guided behavior, mice starts to achieve 100% correct choices for 20 ms flashes with flash intensities 0.01 R*/rod/flash[20]. The test was carried out after 2 hours of dark adaptation of mice. Subsequent study of the response of the removed retina to the same series of flashes increasing in brightness in complete darkness shows the appearance of a section of silence (inhibition) during presentation of an opposite stimulus much earlier than intensities of 0.01 R */rod/flash are reached. Complete darkness is the optimal stimulus after a flash for OFF RGCs, the resulting spike train hides a possible rebound excitation. But since rebound excitation arised after canceling hyperpolarization below the resting membrane

potential it is no evidence of its absence, because sensitivity for opposite stimulus remains. These results are obtained for OFF-Transient alpha RGCs most sensitive RGCs type of the mouse[21].

Visualisation

It is obvious that white noise stimulation reveals response properties of magnocellular-projecting RGCs for both types of responses. However, this is not enough to fully appreciate the behavior of RGCs before spike. The STA does not provide an idea of where the separation between the two types of RGCs reactions is and what they would look like in isolation. In fact, biphasic STA shows an average between the two types of response, distorting the overall picture.

For visualization, I chose freely available white noise subregions stimulation data[22] of parasol (magnocellular-projecting) RGCs of the macaque monkey retina. Visual stimuli consist of two parts ‘center region’ and ‘surround region’ according to center/surround receptive field organization for each cell. Stimuli for each part are fulfilled region with Gaussian-distributed random luminance values on gray background with change each 33 ms. Responses available alone for ‘center region’ stimulation, alone for ‘surround region’ stimulation and for combination of both.

First of all, I checked whether there are sequences of stimuli leading to spikes separately for "center" and "surround" which can easily be interpreted as a response to a removing opposite stimulus. Figure 1 shows examples for the ‘center region’ and ‘surround region’ STA of ON and OFF cells, as well as selected cases of stimuli causing spikes and which can be interpreted as a response to a removing opposite stimulus.

Then I try to show all stimuli which leads to spike frame by frame with saving connection of sequence. (Figure 2) With a step of 10 ms on each scatter plot, I show the correlation of stimulus values at the moment and one step before. If the value has not changed in 10 ms, then it lies on the diagonal. If the point of the stimulus lies below the diagonal, then the stimulus has become brighter than 10 ms earlier, If the point is above the diagonal, then the stimulus has become darker than 10 ms earlier. The red square shows the change in STA values. I named this graph the spike-triggered behavior map (STBM).

The peculiarity of white noise stimulation is such that the stimulus most often takes the form of a combination of optimal and opposite stimuli in different ratios. On STBM, this allows one to observe a smooth transition from the optimal stimulus 30 ms before the spike and a gradual filling of the space above the diagonal up to 80 ms before the spike. The continuity of the transition allows us to assume the commonality of these incentives. The response to optimal stimulus and reaction on removing opposite stimulus is only two extremes of the same difference in brightness in the direction in accordance with the cell type. For convenience, I have chosen to refer to this combined stimulus as optimal dynamic stimulus (DS). Then its main feature is insensitivity to the nominal values of brightness at the points of the beginning and end of the difference, only the magnitude of the brightness difference will have a central value. A similar behavior has already been observed in cat RGCs in the Enroth-Cugell experiment[23], and it was even suggested that when the full-field light intensity changes in some moments, Y type RGCs rather reacts to a brightness difference than to its nominal value.

Previously, I assumed that STA shows an average between the two types of reactions. However, if the optimal DS is the only way to make the parasol cell issue a spike train, then the STA should not carry distorted information about the cell's behavior. What is possible and happens if you use STA as a linear filter in linear-nonlinear model[7], then under one condition it will be immune to the general illumination level and will only respond to changes in brightness. The condition is simple - it should work as filter with derivative kernel. In other words, on a biphasic STA plot, the area above the axis must be equal to the area below the axis. Then, at any stable brightness value, the linear filter will output zero and react only on changes (Figure 3, d).

I have plotted the correlation of the areas of these STA plots for all cells of dataset (Figure 3,c). Thus, the STA shape does not contradict the assumption about the dynamic nature of the optimal stimulus parasol cells at least for chosen dataset. However, other stimulation methods to obtain STA as a full-field flicker that do not separate the central region and the surround region will most likely not produce the same result due to overlap.

If there is an optimal DS, then naturally there must be an opposite DS. I assume that due to the white noise with a Gaussian distribution, one can see its influence on the response to the optimal DS. In the work[4] already mentioned when the opposite stimulus (non-DS) is held for 300 ms, the response to its withdrawal is faster than the response to the presentation of the optimal stimulus. At the same time, on STA, the second peak is at a distance twice as far as the first. Examples of opposing stimuli in Figure 1 also show that the response to the removal of the opposing stimulus is almost twice as long as the optimal one. The peculiarity of Gaussian white noise stimulation is such that it leaves an extremely low probability of receiving a pronounced long-term opposing stimulus (the probability of sequential appearance of extreme values of the range is very small).

It can be assumed that when the opposite stimulus (non-DS) is short, then the reaction to its removal is slow, and when it is prolonged, the reaction is fast. Taking into account the definitions of optimal and opposed DSs, the usual opposite (non-DS) stimulus consists of a sequence of opposed DS and optimal DS, and the smaller the distance between them, the slower the parasol cell response to the optimal DS. This property has already been investigated earlier[24]. For clarity, I built the OFF cell behavior for known data (Figure 4). Whether the same delay is repeated if the stimuli are below the average brightness level for the OFF cell can only be found in practice by creating a new experiment, since the probability of encountering such a sequence of stimuli in white noise is extremely low. Thus, Gaussian distribution is not a sufficiently suitable stimulus and must be replaced by an independent and identically distribution for brightness values, since the time sequence of brightness values is important for magnocellular-projecting RGCs.

A new motion perception foundation

This study provides an arguments to change the foundation of magnocellular visual pathway as follows. The signal going to the brain along the magnocellular visual pathway carries information of a dynamic

nature about the magnitude of the brightness difference without the influence of the nominal values. For OFF parasol cell, the optimal DS consists of decrements in light intensity for the "center" and increments in light intensity for the "surround", while the final nominal light intensity in the "center" may be greater than in the "surround", less than in "surround", or equal. In other words, magnocellular visual pathway signal looks like the first derivative of light intensity and this is quite enough to cover all the needs for perception of movement in the brain. An ideal temporal linear filter for obtaining a dynamic signal would use a derivative kernel with upper and lower peaks of equal strength. The transition from the upper to the lower peak will correspond to the speed of the cell's response to the stimulus.

DS is also a reason to rethink rebound excitation for magnocellular-projecting RGCs. If for various neurons in the nervous system rebound excitation is spikes after removing of a sustained hyperpolarizing stimulus[4,25], then for magnocellular-projecting RGCs the question arises with a long-term opposed DS. In addition, it should be borne in mind that all previous experiments with rebound excitation for magnocellular-projecting RGCs were amplified by spikes from the response to the optimal DS.

This study also raises the question of the effect of opposite DS on spike release timing when opposite DS is close to optimal DS. This question has already been awarded a separate study[24]. To clarify the effect on the timing of spikes, it is necessary to modify the white noise stimulation by abandoning the Gaussian distribution. This is necessary in order to capture complete information about the spikes' timings and build a more accurate RGC model. The luminance boundary values should be represented in the stimulus sequence in the same way as the average values from the stimulation range. Some of the non-binary pseudorandom M-sequences[26] are better suited for this.

Materials And Methods

Stimuli and corresponding responses of On and Off parasol RGCs to center-surround white noise stimulation from Macaque monkeys (M. nemestrina, M. mulatta, or M. fascicularis) retina were taken from the public domain. Data are sampled at 10 Khz. For details, please see the following paper by Turner et al., 2018[22]. Data analysis was performed using custom written scripts in MATLAB (Mathworks). The code used to analyze the data and generate the figures can be found at ***https://github.com/PinchukKPI/optimal_stimulus***. Responses of ON and OFF parasol RGCs electrical conductance filtered with hi-pass filter and detected spikes with threshold.

Declarations

Author Contributions and Notes

A.P performed research, wrote software, analyzed data and wrote the paper.

Competing interests

No competing interests declared

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Figures

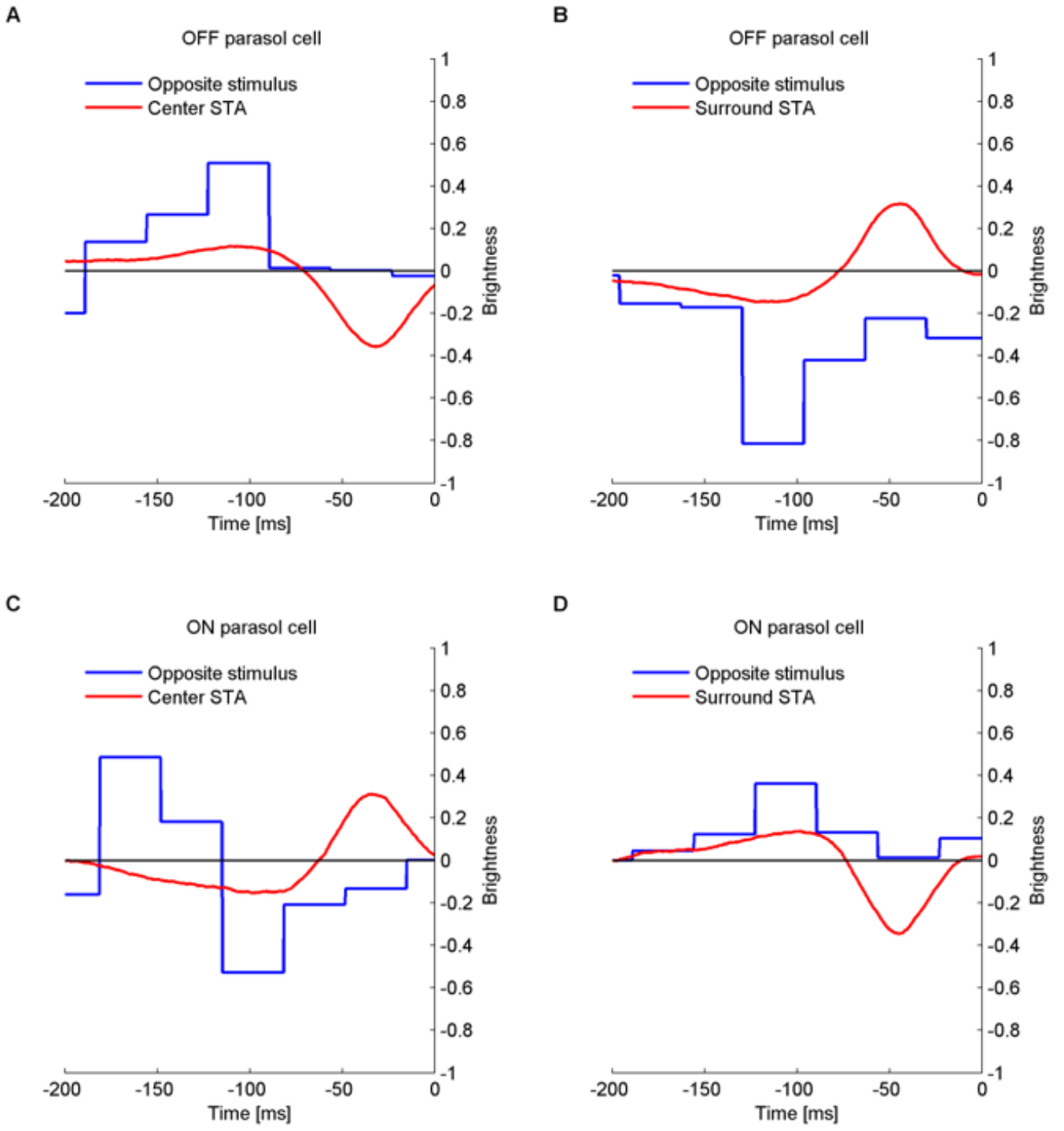

Figure 1

STA of cells and opposite stimulus caused spikes. (A, B) STA for "center region" and "surround region" of OFF parasol RGC and example of 200 ms white noise stimuli which look like opposite stimuli for those regions and produce spike. The reaction of the cell in this case can be interpreted as a reaction to removing opposite stimulus. (C, D) STA for "center region" and "surround region" of ON parasol RGC and

example of 200 ms white noise stimuli which look like opposite stimuli for those regions and produce spike.

Figure 2

Spike-triggered behavior map. (A, K) Scatter plots with step 10 ms of the spike triggered stimuli of central region Off parasol cell. The red square corresponds to the change in STA values with a time step of 10 ms. The points on the diagonal are stimuli that did not change their value in 10 ms. The data contains a sequence of stimuli with a period of 33 ms. (L) Spike-triggered average for Off parasol cell center region.

Figure 3

Spike-triggered average as filter with derivate kernel. (A, B) On and Off parasol cells STA for center and surround regions. (C) Scatter plot of the areas above axis versus the areas under axis for all STA from (A, B). The more the values of the areas coincide, the more their behavior is equal to filter with derivative kernel. (D) Using On center STA as filter. Response to stimulus with the best behavior as derivate kernel.

Figure 4

Influence of combination of optimal and opposite dynamic stimulus on spike timing. The proximity and magnitude of the preceding opposite DS affects the rate at which spike appears after presentation of the optimal DS. On the left are stimuli with normal response rates for optimal DS. On the right is the maximum response delay for optimal DS.