Temporal and Spatial Dependence of Adaptation on Ganglion Cells

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ABSTRACT

One of the visual system's many tasks is to be able to distinguish objects from the background. The ability to do this is limited and affected by the relationship between the object (or stimulus) of interest and the background. Adaptation in retinal neurons is the process of changing the cell's response to a stimulus according to that stimulus's background. When the stimulus is hard to discern from the background, the retina adapts by improving its sensitivity to low contrast. The large response range maintained by adaptation comes at a cost, however. Adaptation complicates neural coding by making the brain interpret identical stimuli as different based on differences in background. In order to further our understanding of adaptation, this study modified the background to be in terms of time and space rather than light intensity as is the norm. By changing the interval between two circular stimuli (inter-stimuli interval; ISI) of the same diameter, and by changing the diameter over a common ISI, we measured a ganglion cell's output for one stimulus relative to another stimulus. The results show saturation (loss of output to the 2nd stimulus) of stimuli at lower ISIs. Also, the degree of saturation for a given ISI depends on the diameter of the stimulus. These combinations of results illustrate the temporal and spatial dependence of adaptation on ganglion cells. A larger-diameter stimulus involves multiple neurons surrounding the ganglion cell being recorded so various pathways most likely influence that cell's ultimate output. Rapid stimuli (low ISI) can be defined as having large mean luminosity that directly affects ganglion cell output.

INTRODUCTION

Adaptation is a common property of biological systems, and obvious in visual processing where stimuli of different intensity and contrast initiate retinal processes that increase or decrease the gain and dynamics of retinal neurons to maintain optimum visual sensitivity. The incremental change in a threshold response is always proportional to the ambient intensity level. More specifically, the sensitivity of retinal neurons is known to decrease according to Weber's Law – that is, inversely with flash intensity (Pugh, et al. 1999). In other words, as the mean luminance of the input increases, the gain decreases so that the incremental response remains constant. (The percent of gain is defined as the ratio of output to input). This coincides with the two purposes of adaptation in the retina: to improve signal-to-noise ratio when input signals are weak, and to prevent response saturation and the loss of information when input signals are strong (Demb, 2008).

Adaptation ultimately adjusts the spike output of ganglion cells to optimize the response to changes in two primary properties of light: the mean intensity and the variance of intensity over time, otherwise known as contrast (Fairhall, et al., 2001; Demb, 2008). The retina's adaptation to luminance involves both large- and small-scale fluctuations in light levels (Freeman, et al., 2010), illustrating the retina's incredible flexibility in terms of sensation. Although the ganglion cells are ultimately responsible for transmitting electrical signals to the brain, these large-scale changes in sensitivity begin with the photoreceptors and the changes are more finely tuned at

every stage of the visual processing pathway in the retina until the ganglion cells receive a very refined and specific input.

Adaptation in Photoreceptors

Photoreceptors must generate reliable signals at night when long intervals of darkness are interrupted by few photons, and must also continue to signal at the very high light intensities encountered on a bright day (Govardovskii, et al. 2000). Two hallmarks of photoreceptor light adaptation are the reduction in sensitivity and the acceleration in response kinetics that occur in the presence of background illumination (Pugh, et al. 1999).

There are two broad classes of photoreceptors: rods and cones. To begin with, it is worth noting two properties of cone photoreceptors relative to rods: 1) they require about 100 times greater light intensity for stimulation; and 2) their photocurrents do not saturate, so their operating curves shift along the light intensity axis without modification or adaptation (Werblin, 1972), thereby maintaining the same level of sensitivity (fig. 1). The discrepancy between rods and cones can be attributed to the rod photoreceptors' ability to exhibit a form of adaptation by changes in the transduction cascade that modulate the absorption of photons by neighboring photoreceptors.

The mechanism for adaptation in rod photoreceptors has been outlined previously (Hodgkin and Nunn, 1988)

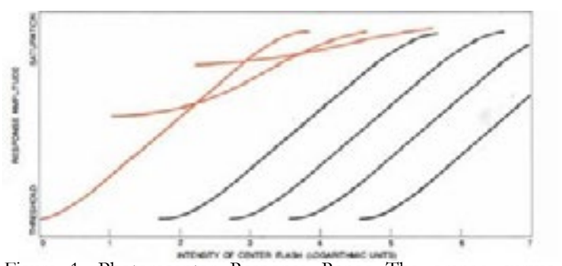

Figure 1. Photoreceptor Response Range The orange curves correspond to rod photoreceptors whose response range is modified (adapted) in terms of changing light intensities to avoid saturation. The black curves correspond to cone photoreceptor's operating curves and depict the cone's ability to avoid saturation at higher light intensities without adaptation (Figure from Werblin, 1972).

The dark-adapted photoreceptor maintains a steady concentration of cGMP, keeping a fraction of cGMP-gated cationic channels open and the membrane depolarized. Light initiates an enzymatic cascade (fig. 2) involving rhodopsin, the G-protein transducin, and ultimately activating the effector phosphodiesterase (PDE). PDE hydrolyzes cGMP, decreasing the influx of Ca2+ and Na+ and thereby hyperpolarizing the photoreceptor and reducing the response level. The light-adapted photoreceptor is, therefore, less sensitive to light, preventing them from becoming blind at high light intensities; and they produce quicker photoresponses, improving the temporal resolution in the visual system (Blumer, 2004). Offset of light inactivates the cascade, allowing cGMP levels to be restored by guanylyl cyclase. In this fashion the photoreceptors are able to regulate their response to a stimulus (i.e. greater intensity corresponds to more photons which target more rhodopsins which initiate more enzymatic cascades).

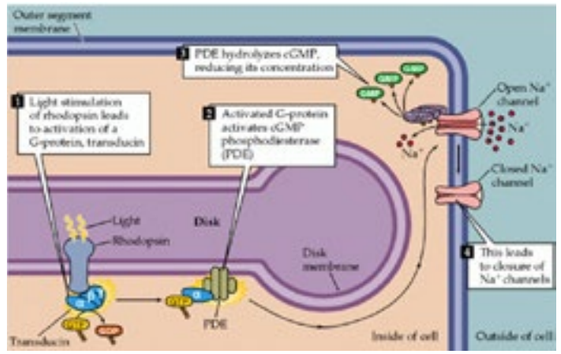

Figure 2. Second Messenger Cascade of Phototransduction In the rod class of photoreceptors, the pigment-containing protein, rhodopsin, absorbs light (1) and activates transducin by causing it to release GDP and bind GTP. GTP-bound transducin binds to and activates a phosphodiesterase (PDE) (2), which converts cGMP to GMP (3). The concentration of cGMP decreases below what is required to open cGMP-gated ion channels, reducing the flow of cations across the cellular membrane (4), thereby hyperpolarizing the cell. (Blumer, 2004) (Figure from Purves, et al, 2001).

The Role of Lateral Interneurons

Located just proximal to the photoreceptors in the retinal hypercircuit (i.e. the layout and connectivity of the different layers in the retina) are the horizontal cells in the outer plexiform layer. Like the photoreceptors, they, too, exhibit polarization in the negative-going direction, or hyperpolarization, not in response to light, but in response to glutamate release from photoreceptors (Werblin, 1972). They are laterally interconnecting neurons whose strong electrical coupling to one another enables them to function as a single unit. Consequently, they cause a blurring of the immediate image, which modulates the gain from photoreceptors that carry the high-resolution image, leaving small differences in intensity (contrast). Horizontal cells receive input from cone photoreceptors, and these cone signals are relayed to ganglion cells by two classes of excitatory neurons known as ON and OFF type bipolar cells. Since adaptation in photoreceptors only exists in rods and not cones, gain control is absent in horizontal cells (Beaudoin et al. 2007); thus, gain control in ganglion cell synaptic inputs is consequently explained by mechanisms at the level of bipolar cells (Demb, 2008). Horizontal cells do, however, influence bipolar cells via feedback to the photoreceptors (Werblin, 1972) so they are not entirely inconsequential in adaptation mechanism. For example, an ON bipolar cell will depolarize when it is in direct synaptic connection (the center) with illuminated ON cone photoreceptors, or hyperpolarize when illuminated photoreceptors that lack direct connection to it (the surround) communicate with it via horizontal cells. The antagonistic effect horizontal cells have is responsible for shifting the bipolar-cell operating curve to a higher range of intensities. Thus, the stimulus is finely tuned as a specific function of the local intensity level (Werblin, 1972).

In a similar fashion, amacrine cells have an antagonistic-surround effect on change-detecting ganglion cells. Amacrine cells are activated by change in luminance (i.e. contrast detected by bipolar cells), and reduce ganglion cell activity (when exposed to high intensity or high contrast) by reducing the strength of the bipolar-to-ganglion signal and shifting the operating curve to cover a different, higher range of intensities. As a result, change that occurs over multiple retinal hypercircuits acts to reduce the response to change occurring locally. This allows the detection of movement of small objects without overwhelming the visual field with vast changes in contrast (Brown & Masland, 2001).

The effects of these lateral interneurons can be summarized as follows: horizontal cells responding to sustained levels of illumination affect the magnitude of the sustained bipolar cell signal; and amacrine cells, responding to contrast, affect the responsiveness of the change-detecting ganglion cells (Werblin, 1972). Essentially, the operating curves at each level of processing in the retina gets more and more finely tuned, leading finally to a high contrast output at the ganglion cells. Thus, the rod and cone photoreceptors are capable of detecting a wide range of light intensities, but the ganglion cells receive a more narrow and specific range.

Adaptation at the Bipolar Cell, Ganglion Cell Synapse

The actions of photoreceptors, horizontal cells, and amacrine cells outlined above contribute to bipolar cell's control of gain and the input level observed by ganglion cells. This so-called gain change is one aspect of adaptation in ganglion cells to prevent response saturation; the other is membrane after-hyperpolarization (Demb, 2008; Fig. 3). These two mechanisms need not occur independently, and indeed in the retina gain control and hyperpolarization co-occur (Baccus & Meister, 2002; Zaghloul, et al,. 2007; Lesica, et al., 2007).

Gain control in ganglion cells begins at its dendrites where bipolar cells' and amacrine cells' axon terminals synapse. Previous studies have shown that contrast gain control at the level of the bipolar terminals persists even when inhibitory neurotransmitter receptors are blocked on ganglion cells, thereby ruling out amacrine cell signaling as a requirement for gain control. Rather, gain control depends on adequate stimulation of bipolar cells, which provide one of the mechanisms for gain control over the ganglion cell receptive field center (Beaudoin et al. 2007). Furthermore, another form of gain control is intrinsic to ganglion cells. The mechanism can be explained by sodium channel inactivation. When ganglion cells respond to high contrast, their frequent spike bursts reduces the available Na+ current through slow inactivation, resulting in a persistent depression of spiking output and reduced excitability (Kim and Rieke, 2003; Demb, 2008). The other mechanism of adaptation in GC is membrane after-hyperpolarzation. Prolonged membrane after-hyperpolarization (AHP) follows strong stimulation of ganglion cells, and pharmacological studies have shown that AHP does not depend on synaptic inhibition, Ca2+-activated K+ channels or mGluRs; rather, AHP is driven by prolonged suppression of glutamate release at bipolar cells synapse although the mechanism of vesicle depletion is not well understood (Brown & Masland, 2001; Manookin & Demb, 2006; Demb, 2008) (fig. 3).

These aforementioned properties of adaptation

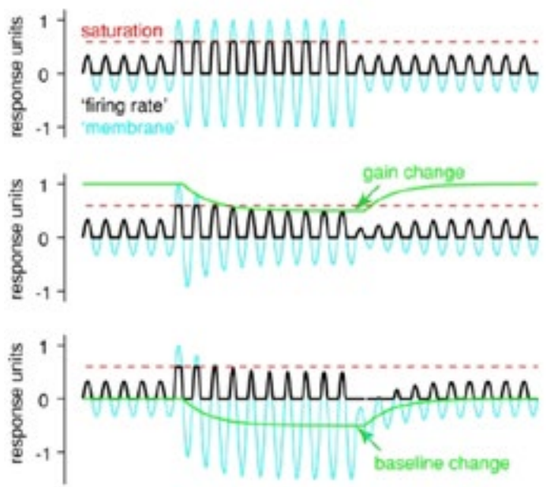

Figure 3. Two General Mechanisms for Contrast Adaptation and Illustration of Rectification and Saturation in Ganglion Cells. In the top panel the firing rate (black) does not go below zero (i.e. it is rectified) nor does it go above a certain value (i.e. said to be saturated). The middle panel depicts one mechanism of adaptation, which is a reduction in gain to avoid saturation. This phase of adaptation where the ganglion cell's sensitivity decreases in response to a strong stimulation is considered the fast change (occurs <.1s) and is accompanied by depolarization of baseline membrane potential. The bottom panel depicts the second mechanism: response adapts by gradual hyperpolarization in response to high contrast or high light intensity. This mechanism is considered the slow change (occurs in ~10s). Both mechanisms effectively reduce the firing rate of the ganglion cell (Baccus & Meister, 2002).

are in the context of a static background, one with a defined luminance level. Dynamic backgrounds also affect response properties and in this study we show the simplest form: response to stimuli with changing temporal and spatial frequencies. This study measures ganglion cell output following two-stimuli-input that is varied in terms of the time between the two stimuli as well as the diameter of the set of stimuli. The background that accompanies stimuli is usually represented by luminescence, but in our study we have manipulated the background so that it is represented by time or space. Since the background is still maintained, we are able to analyze the retina's inherent tendency to discriminate otherwise equivalent stimuli based on differences in their backgrounds. Although our study is conducted in vitro, it is an accurate reflection of adaptation in vivo because the retina remains intact and still responds to light (Demb, 2008). Thus, the firing rate of the ganglion cell can be observed as it would be in vivo – that is, exhibiting saturation (the rate cannot increase despite increase in stimulus intensity of contrast) and rectification (negative values are set to zero) (fig. 3).

METHODS

The retina-sclera preparations used in this study have been previously described (Farajian, 2011). The adult, wild-type New Zealand White rabbits used in this study were first anesthetized with a 1.5ml of ketamine and .2ml of xyline injection into spinal tissue followed by a 1.5ml intracardial injection of euthanasia solution comprised of pentobarbital sodium and phenytoin sodium. The eyes were enucleated under dim red illumination and subsequently hemisected anterior to the ora serrata. The resultant retina-eyecup was flattened by making radial incision at the periphery, and then sliced into six pieces (3 visual streaks, 2 dorsal pieces, and 1 ventral piece).
All procedures were done in accordance with the rules and regulations established by the Institutional Animal Care and Use Committee (IACUC) at UC Berkeley.

When running the experiment, the retinal piece was placed on a MicroElectrode Array (MEA; sixty 30µm-diameter electrodes spaced 200µm apart in a square layout) and superfused at a rate of roughly 15ml/min with AMES solution that was prepared by mixing AMES Medium (w/ L-Glutamine) with kanamycin sulfate, sodium bicarbonate, and gaseous carbon dioxide. The superfusate was kept at a constant temperature of 34°C, and a pH of 7.4 was maintained by bubbling with a gaseous mixture of 95% O2-5% CO2. The MicroElectrode Array (MEA) is a glass plate with electrodes that capture electric signals generated by neurons.

With the retina on the MEA, the first task is to map the cell's operating curve and corresponding receptive field size. This was accomplished by flashing a set of stimuli spaced 5s apart in increments of 50µm from 250µm to 650µm and measuring the graded amplitude of the response. We then chose to focus on three particular diameters: 300µm, 450µm, and 600µm. We also chose to use three different inter-stimuli intervals (ISIs): .5s, 1s, and 5s. The ganglion cells were tested for adaptation by flashing two consecutive spots of a fixed diameter while changing the ISI from 5s to 1s and then .5s. We then changed the diameter of the spot and ran through the series of ISIs. We did this a third time so that all three diameters were used and all three ISIs were used for each diameter, thus, we had a total of 9 combinations. In this manner we were able to change the ambient conditions in terms of both ISI and spot diameter.

After acquiring the spike response data via the MC_Rack software that accompanies the MEA, we used Plexon Offline Sorter and its k-means spike sorting tool in order to sort action potentials of one neuron from that of all other neurons recorded by our particular channel as well as from background noise. This function has been described previously (Lewicki, 1998). Following spike sorting and with the help of MatLab, we simply coordinated the cell's spike output with the onset of the stimuli to produce a series of plots to analyze the effects of adaptation given the stimulus' parameters (figs. 4 - 9)

Finally, we outlined two technical notes that would facilitate interpretation of the following results:

1. The amount adapted is defined as (1 – % of Gain). The percent of gain is defined as the ratio of output to input, or in the context of this study, how much the second-response to a stimulus changes in the event that first-response to a stimulus has already occurred (r2/r1)
2. In the plots that follow where diameter is labeled on the x-axis, the x-values represent the diameter in pixels; to get the diameter in micrometers simply multiply the value by 5. In the text that follows the diameter has been stated in µm.

RESULTS

The goal of our study was to measure the effects that changing spatial and temporal properties of a stimulus' background would have on contrast sensitivity of retinal ganglion cells. To do this, we acutely dissected retinas from rabbits, and measured their output evoked by light stimulation using a MicroElectrode Array. When the first and second stimuli were separated by 1 second (ISI=1s), there was a linear decrease in spike output across the three diameters (fig. 4-left). Since this linear decrease in second-stimulus-response mirrors the linear decrease in gain change (fig. 4-right), we know that the trend is independent of ISI. In other words, the ganglion cell would react to the second-stimulus just as it would to a single-stimulus that is not followed by another stimulus. Thus, this data represents the spatial dependence of adaptation in ganglion cells. Likewise, ISI=.5s is also indicative of the effects that stimulus size has on ganglion cell response (fig. 5). However, the lack of spiking output at D=450µm (D=90 on the x-axis of fig. 5) results in a plot that has little predictability in its trend (fig. 5).

In order to observe the temporal dependence of adaptation on ganglion cells we looked at the data produced by two sequential stimuli whose diameter was fixed and ISIs varied. Both D=300µm and D=600µm plots

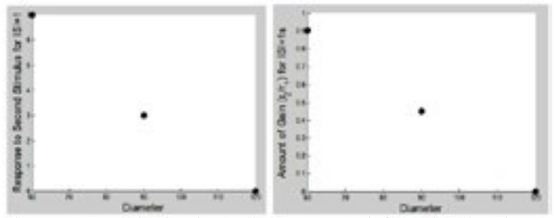

Figure 4. Second-Stimulus Spike Response (left) and Gain Change (right) For ISI=1s. Both plots show a negative correlation between diameter size and the amount of response by the ganglion cell at the onset of the 2nd flash. Since the response level decreases at the onset of the 1st flash, there is a corresponding reduction in gain (right). This linearity shows that diameter affects the ganglion cell's response prior to any adaptive effects.

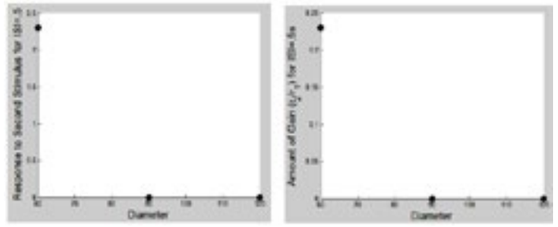

Figure 5. Second-Stimulus Spike Response (left) and Gain Change (right) For ISI=.5s. Like the plots for ISI=1s, these plots show a negative correlation between response and diameter size, suggesting the inhibitory effects large diameter size has on ganglion cells.

depict a positive correlation between second-stimulus response and ISI (fig. 6 and fig. 7, respectively) although the trend is not linear in either plot and the predictability is reduced in D=600µm since ISI=1s registered 0 spikes. Regardless, we can interpret the data as follows: larger diameters influence adaptation more at low ISIs than at high ISIs. Also, stimuli with larger diameter (i.e. 600µm vs. 300µm) produced less spikes in first-response (fig. 8) indicating that there is an overall reduction in responsiveness at large diameters prior to any adaptive effects. The intensity of first-response also decreases linearly with increasing diameter (fig. 9) at a set ISI to further support the notion that larger stimuli elicit greater inhibitory effects that work to reduce spike output of ganglion cells.

One set of three trials (D=90, ISI=5s) was originally viewed as an outlier because our calculations showed a 237% increase in spiking output for the cell's 2nd respond. This finding was particularly improbable since ganglion cells recover in as little as 5s (Manookin and Demb, 2006) following a switch from high to low contrast or high to low luminosity, i.e. from first stimulus flash to offset of that flash so that by the time the second stimulus is presented, the ganglion cell has recovered and elicits a response nearly equivalent to the first response. Although ganglion cells can require up to ~10s to recover from prolonged suppression of firing after strong stimulation (Victor, 1987; Smirnakis et al. 1997; Brown & Masland, 2001; Kim & Rieke, 2001; Baccus & Meister, 2002; Zaghloul

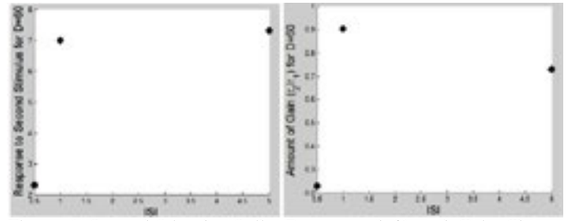

Figure 6. Second-Stimulus Spike Response (left) and Gain Change (right) For D=300µm. The greater than expected value of amount of gain for ISI=1s is due to a relatively low first stimulus response (r1). ISI=.5s and ISI=5s both had r1 = 10. However, the overall effect the diameter has on adaptation can still be deduced

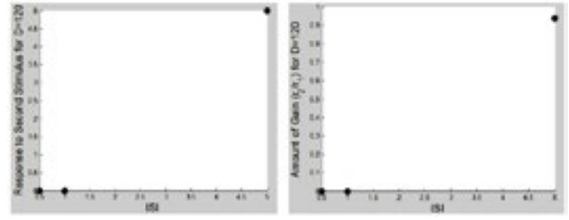

Figure 7. Second-Stimulus Spike Response (left) and Gain Change (right) For D=600µm. The similarity between the two plots compensates for the discrepancy found in figure 7 above and more clearly illustrates the increase in adaptation with a decrease in ISI.

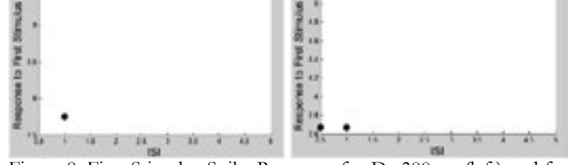

Figure 8. First-Stimulus Spike Response for D=300µm (left) and for D=600µm (right) Disregarding the lack of linearity in the left plot and considering only the absolute values at each ISI, there is an overall reduction in spike response at the larger diameter (right) at the onset of the first stimulus, prior to any adaptive effects.

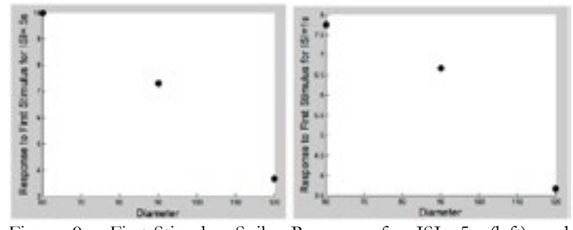

Figure 9. First-Stimulus Spike Response for ISI=.5s (left) and for ISI=1s (right) As these plots show, as you increase the size of diameter, the response is decreased, which indicates the effects of inhibitory mechanisms.

et al. 2005;Manookin & Demb, 2006; Demb, 2008) all other ISI=5s trials responded according to our expectations. Upon closer inspection of this particular set of trials, we discovered the effects of spontaneous spiking on the neurons ability to respond to light (Fig. 10). In all three trials there was very little to no spontaneous spiking preceding

the second stimulus. Consequently, each trial exhibited light response to the onset of the second stimulus. On the other hand, two out of three trials showed robust spontaneous spiking immediately preceding the onset of the first stimulus, and, thus, showed negligibly little to no light response to the first stimulus. In one trial robust spontaneous activity took place about .5s, rather than .1s or less, before onset of the stimulus. In this trial the ganglion cell exhibited light response.

DISCUSSION

This study determined that retinal ganglion cells reduce their sensitivity when presented with stimuli with increasing diameters or in increasingly rapid succession. This modifying of activity is defined as adaptation, and helps to prevent saturation of the ganglion cells. The study is, however, limited by the equipment used: the MEA measures ganglion cell output and offers no means of tracing the activity and mechanisms that contributed to that output. Thus, it was impossible for us to accurately determine the mechanisms that produced the previous described results. However, we are not prevented from making plausible conjectures based on our observations. Overall, in terms of our definition of adaptation (1 – percentage of gain) there was an increase in adaptation following an increase in stimulus diameter. Also, there was an increase in adaptation following a decrease in ISI although this effect was depicted less vividly by our results.

Increasing the diameter of the stimulus caused the ganglion cells to decrease their level of output, thereby decreasing the amount of gain and increasing the amount of adaptation. Thus, based on figures 5 and 6, there is clearly an inverse relationship between diameter size and the amount of gain. Consequently, there is a direct relationship between diameter size and amount of adaptation. This can be reasoned in various ways beginning with "surround" activation. Large diameters exceeded the diameter of the ganglion cell's excitatory center-receptive field, which is usually no greater than 500µm (Peichl & Wassle, 1979), and thereby activating the inhibitory surround which lies around the excitatory field. This surround is comprised of retinal hypercircuits similar to the one our ganglion cell belongs to; thus, the surround exhibits layer-by-layer adaption as outlined in the introduction. The resulting adaptive effects in the surrounding hypercircuit are directly communicated to our ganglion cell being measured via inhibitory amacrine cells (Werblin, 1973).

Although amacrine cell signaling is not a requirement for gain control, they do, however, mediate response between bipolar cells and ganglion cells. For example, they indirectly affect GC gain by inhibiting glutamate release at bipolar cell terminals. This reduction in glutamate corresponds to a reduced input to GCs. Also, the AII amacrine cell is specifically responsible for relaying the gain control that arises in ON bipolar cells to ganglion cells (Beaudoin et al. 2007). These functions of some amacrine

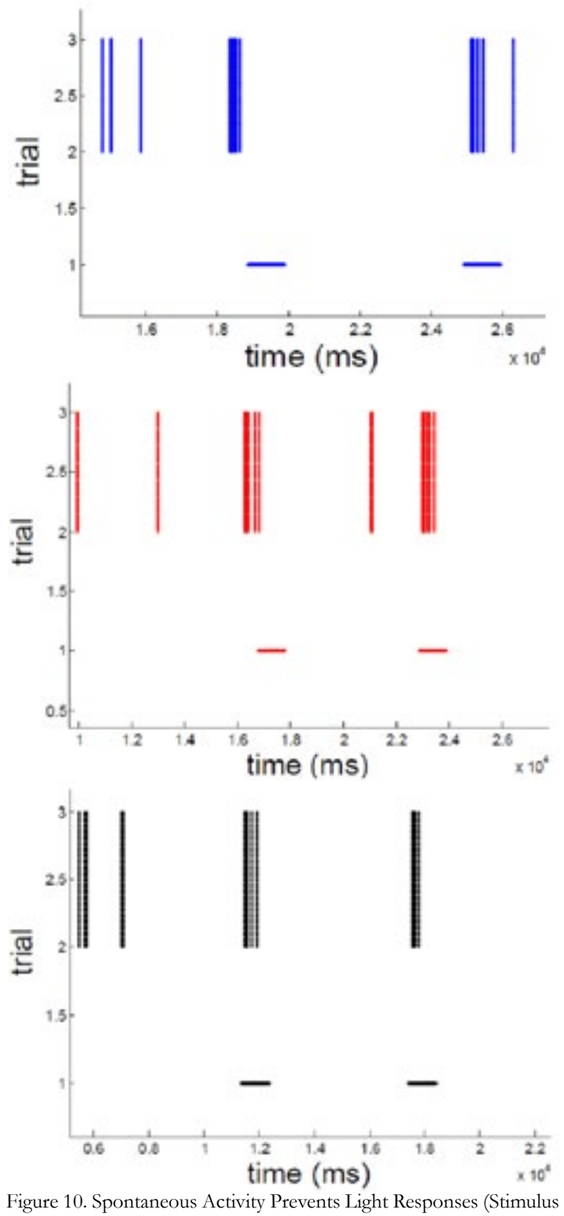

Figure 10. Spontaneous Activity Prevents Light Responses (Stimulus represented by horizontal dash; Spike Output represented by vertical lines; Trial Conditions: D=90, ISI=5s) Two trials show very little to no light response to onset of first stimulus (RED: # of spikes = 1; BLUE: # of spikes = 0), which is preceded by robust spontaneous activity in both trials. One trial (BLACK) lacked spontaneous spiking within ~.5s of first stimulus onset, and exhibited robust light response to this stimulus.

cells explain the mechanism for peripheral adaptation (Demb, 2008; Zaghloul, 2007). Future experiments need to test whether excitatory (e.g. cholinergic, dopaminergic) amacrine cells play any role in contrast adaptation (Demb, 2008). Also worth testing is how narrow-field amacrine cells – which are known to function in feedback inhibition onto bipolar terminals and feed-forward inhibition onto ganglion cells – contribute to adaptation (Demb, 2008).

Furthermore, the amount of adaptation experienced by the ganglion cell depends on the interstimulus interval; that is, we observed the temporal effects of adaptation. For example, in the plot for D=300µm where the ISI varied, we saw greater adaptive effect (less spike output) at ISI=5s than we did at ISI=1s. This disagrees with our hypothesis that the greater the ISI, the more independent the second-response is from the first-response. In other words, according to our hypothesis, we expect the degree of spike output of both responses to be more equivalent (i.e. exhibit less gain change) at ISI=5s than at ISI=1s. Although the results for D=300µm slightly deviate from this expectancy, D=600µm validates our hypothesis.

There is an increased sensitivity to high temporal frequency (low ISI) resulting in low second-response spike output and corresponding gain (Zaghloul, et al., 2005; Beaudoin, et al., 2007). This may be because the integration time for an ON ganglion cell increases under these conditions (Demb, 2008). Rapid presentation of the two stimuli (low ISI) might also be interpreted by the ganglion cell as a single, high intensity flash so the cell is only capable of eliciting one response. Considering the actual nature of the environment as two distinct stimuli, this behavior seems problematic for accurate neuronal coding. Interestingly, however, this very rapid component of adaptation may actually resolve potential ambiguities by optimizing the information that action potentials carry about rapid stimulus variations (Fairhall, et al., 2001). In other words, simpler spiking paradigms may improve neuronal coding despite sacrificing precision. Taking this into account, it seems reasonable to further investigate the circumstances under which ganglion cells maintain complex spike patterns (i.e. perceive the two stimuli as distinct) at this low of an ISI. The stimulus itself may need modification so it more closely resembles natural conditions. Although such stimuli have been developed, quantifying the stimuli's specific effects has proven to be a challenge since the relationship between the stimuli's complex properties and the spike pattern is not linear or directly correlatable, which is the case with simple stimuli like spots, flashes, and rings. Hopefully future studies uncover adaptive properties of the retina under natural conditions.

Finally, the effect that spontaneous activity had on the prevention of light response implies that adaptive effects take place even without specific stimuli with specific properties. As our results show, spontaneous activity can and does affect the cell's ability to respond to stimuli for roughly .5s after the end of spontaneous activity (fig. 10). Thus, external stimulation is not required to elicit adaptation; rather, the cell's intrinsic nature to experience fatigue modulates the cell's response potential. Although spontaneous activity allows the visual system to bootstrap an efficient neuronal code for its natural environment prior to external visual experience (Albert, et al., 2008), the .5s recovery period hinders accurate perception of the environment. Thus, spontaneous activity, which is inherent to neurons, enables "predictive" perception to compensate for the cell's inability to respond to stimuli following fatigue and its inability to respond continuously.

CONCLUSIONS

The mammalian retina constantly strives to maintain a precise range of sensitivity in accordance with ambient stimuli. The retina simplifies stimuli into two basic properties: luminosity and contrast. Given these two properties, the retina will correspondingly amplify or reduce ganglion cell spiking output so information is neither lost (when input is strong) nor convoluted (when input is weak). This process, known as adaptation, begins in photoreceptors and is refined at every stage and every synapse of the visual pathway in retinas until ganglion cells' outputs are ultimately modulated. As the study shows, the modulation of ganglion cells is not limited to stimuli that differ in luminosity alone. Two identical stimuli that differ in their temporal and spatial properties also affect the degree of adaptation exhibited by ganglion cells. These varying features of stimuli that affect the retina and all of its interactive components illustrate the retina's remarkable precision that allows it to perceive the myriad features of our external environment.

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