HOW EFFICIENTLY A GANGLION CELL CODES THE VISUAL SIGNAL

R. G. Smith, N. K. Dhingra, Y. H. Kao, and P. Sterling
Department of Neuroscience, University of Pennsylvania, Philadelphia, PA 19104-6058 USA

Abstract-**The retina's visual message is transmitted to the brain by ganglion cells that integrate noisy synaptic inputs to create a spike train. We asked how efficiently the retinal ganglion cell spike generator creates the spike train message. Intracellular and extracellular recordings were made from *in vitro* guinea pig retina, in response to a spot of light flashed over the receptive field center. Responses were analyzed with an "ideal observer," a program that discriminated between two contrasts based on an optimal decision rule. Spike trains from ganglion cells had thresholds as low as 1% contrast, but thresholds for the corresponding graded potentials were lower by a factor of 2. Using a computational model of the ganglion cell, we asked what factors in the spike generator mechanism are responsible for the spike train's loss in performance. The model included dendritic/axonal morphology, noisy synaptic inputs and membrane channels. Adaptation of spike rate was provided by K(Ca) channels which were activated by Ca^{2+} flux during spikes. When K(Ca) channels were included, they controlled the duration of the inter-spike interval and thus set the level of noise in the spike train. These results imply that the spike generator adds noise to the spike train signal**.

Keywords **- Computational model, retina, spike generator, membrane channel, noise, ideal observer.**

I. INTRODUCTION

Humans can detect a small stimulus at contrasts as low as 0.2% [1]. This visual message is transmitted to the brain by retinal ganglion cells, which integrate their synaptic inputs to create a spike train. Precisely how the ganglion cell creates the spike train, and what code it utilizes are not known. The signal received by the ganglion cell from presynaptic circuits contains noise from several sources, which limit its sensitivity to contrast and reliability of timing. Different spike generator codes would give different proportions of signal and noise, which implies that the ganglion cell's performance depends on the particular code one assumes. Since a ganglion cell can simultaneously code for multiple features of a stimulus, it is difficult to know which code is most essential.

Ganglion cells sum signals from several dozen to several hundred synapses [2,3]. The noise from Poisson fluctuation of synaptic quanta would be expected to improve with larger numbers of synapses because the S/N ratio of Poisson distributed events improves as the square root of the mean. However, the S/N ratio of ganglion cells has been measured and is relatively constant across variations in size [4]. This implies that all ganglion cells have a noise source in common.

One potential source of noise shared by all ganglion cells is the spike generator itself. Na^+ channels are opened by a depolarization in a neuron's membrane and this leads to regenerative "spike" which is terminated by delayed opening of K^+ channels. The spike rate is controlled by other channel types that open during the inter-spike interval. All of these membrane channels are known to be gated stochastically, which suggests they might add noise to the signal coded by the neuron.

To understand how the spike generator codes its signal, we asked how efficiently it creates the spike train message and which neural codes give the best performance. We obtained performance with an experimental paradigm similar to psychophysical methods that measure absolute behavioral sensitivity to a stimulus parameter, e.g. contrast. This allowed testing the performance of different codes and comparing performance of graded potential with the spike train. We then compared the empirical measurements of the ganglion cell's performance with those from a computational model of the ganglion cell spike generator.

II. METHODOLOGY

A. Physiology

Recordings were made from an in vitro guinea pig retina at 35^{O}C, both intracellular and extracellular in response to a spot of light flashed over the receptive field center [5]. Light from a computer monitor was projected through the camera port of a microscope to the retina at an intensity equivalent to low photopic (daylight) [5]. Spot size and temporal frequency were varied parametrically in initial tests for each neuron recorded to identify the optimal values.

B. Ideal observer analysis

Responses to both spike train and graded potential were gathered from several contrasts for 200-400 trials, and these were analyzed in a two-alternative forced-choice paradigm similar to that used in behavioral tests on human subjects. Spikes were separated from the underlying graded potentials by a standard thresholding and interpolation algorithm. The data were analyzed with an "ideal observer", a computer program that discriminated between a pair of contrasts based on an optimal decision rule [6]. Response data were binned according to the particular code to be tested, and bin size was varied parametrically to find the optimum. Autocorrelograms of the graded potential typically gave an equivalent width of 10 msec which was much shorter than the bin width (40-100 ms.). Four neural codes were implemented: total spike count (1 bin), spike time (1 bin for each spike time), spike pattern (typically 5-10 bins), and graded potential pattern. To discriminate a pair of stimuli, a probability distribution function was constructed for each combination of bin and stimulus from half of the trials. Performance was tested with the other half of the trials on a trial-by-trial basis by comparing for each stimulus the bins' joint probabilities (Fig 1). Threshold was defined as the contrast that produced 75% correct responses [6].

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle How Efficiently A Ganglion Cell Codes The Visual Signal	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Department of Neuroscience University of Pennsylvania Philadephia, PA 19104-6058	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) sponsoring agency and address	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom., The original document contains color images.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
3

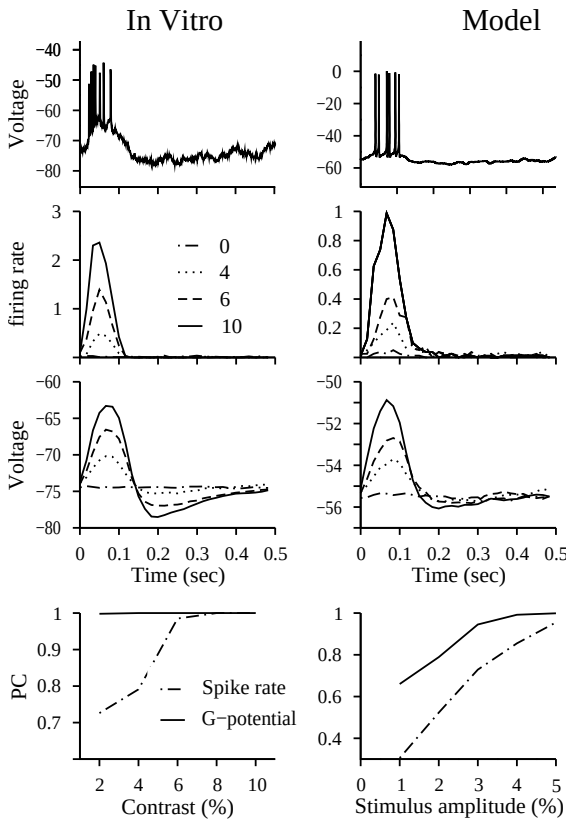

Fig 1. Comparison of performance for real cell and model. Left, *in vitro* ganglion cell, stimulus was photopic spot increment of light in receptive field center. Right, model, stimulus was voltage clamp in presynaptic terminal adjusted to give response amplitude similar to real spot. Top, typical responses to spot that flashed on at 0 and off at 100 msec (left, 8% contrast, right stimulus to give similar response). Second row, average graded potential with spikes removed in response to flashes of different contrasts.. Third row, average graded potential with spikes removed. Bottom, performance (proportion correct) of ideal observer. Performance for spike rate pattern crosses threshold (75% correct) at higher contrast than graded potential.

C. Simulations

A computational model was developed in the simulation language Neuron-C [7] based on prior models in salamander and cat [8,9]. With this simulator we could perform a complete physiology experiment on a neural circuit, including optical stimulus, realistic morphology and biophysics, and voltage clamp recording [7,10]. The model included the ganglion cell's dendritic and axonal morphology, 500 synaptic inputs, 7 membrane channel types (Na, Kdr, KA, L-type Ca, SK1, SK2, BK) and noise from synaptic inputs and membrane channels. Channel kinetics were implemented in the simulator with Markov diagrams taken from the literature for each channel type, adjusted for temperature with appropriate Q10 values (for recordings and simulations, T=35^{o}C). Synaptic inputs were driven to release at a low (~5/sec) quantal background rate and a higher rate during the stimulus. Synaptic noise was implemented by setting quantal release with a gamma interval distribution function modulated by an exponential function of voltage. Channel noise was implemented by setting the Markov transition rates to binomial functions of the channel populations in each state. We calibrated the model by adjusting channel kinetics and densities to give similar spike shapes and firing rates to empirical recordings.

III. Results

A. Ganglion cell recordings

Spike trains from ganglion cells had thresholds for flashed spots as low as 1% contrast. However, thresholds for the corresponding graded potentials were lower by about a factor of 2 (Fig 1). For near-threshold stimuli, noise was relatively constant, but the S/N ratio for the graded potentials was greater than for spikes. This implies that the spike generator contains an additional noise source not present in the graded potential.

Of the 3 spike codes, spike count performed the lowest, spike time performed typically 30% better, and spike pattern had the best performance (50% better than spike count) (Fig 2). For the spike count code, noise in the tail end of the response period, when summed in one bin with the main response tended to reduce performance. The reason for the higher performance of the pattern code was that the ideal observer could weight each bin differently because the response waveshape gave each bin different S/N ratios. When the bin size was shorter than the 100 msec stimulus duration, noise appearing later in the response was summed in separate bins and automatically given lower weight by the joint probability, thus preserving performance. Bin sizes shorter than 25 msec were less accurate for several reasons so most data sets were analyzed with a 40 ms. bin size.

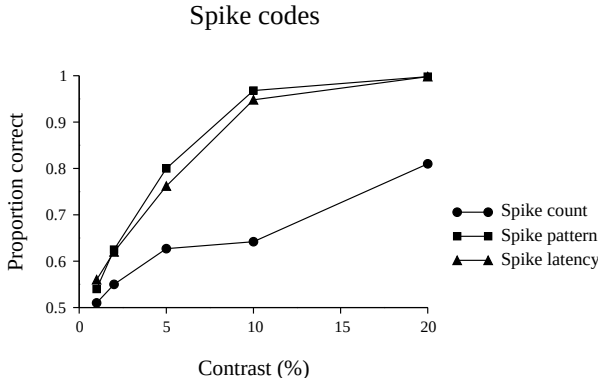

Fig 2. Comparison of performance for differnt types of spike codes for a typical ganglion cell. Spike count is total number of spikes in response interval, spike pattern is numbers of spikes binned into 40 msec bins, spike latency is time to first spike. Spike count performs worst, spike pattern is slightly better than latency code.

B. Computational model

We calibrated the model to give spiking properties similar to live recordings, and then asked what channel types were responsible for the additional variability in the spike train. When K(Ca) channels were omitted, there was no

accomodation of spike rate and noise originated mostly in Na and Kdr channels. Spike rate accommodation was provided by K(Ca) channels which were activated by Ca^{2+} flux during spikes. When the density of K(Ca) channels was set to the level necessary to provide ~50% spike rate accommodation, they controlled the duration of the inter-spike interval and thus set the level of noise in the spike train (Fig 3).

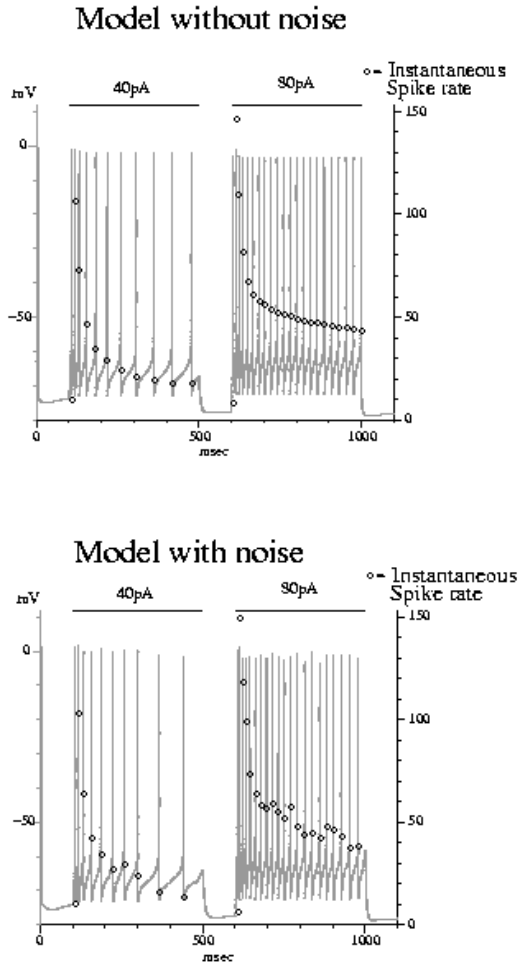

Fig 3. Simulation of spike generator with 40 pA (left) and 80 pA (right) of current injected into soma. Top, model without noise KCa channels provide spike accomodation with sharply falling spike rate after first few spikes. Bottom, spike generator model with all noise sources included. Variability in spike rate originates mostly in K^+ channels open during inter-spike interval.

IV. Discussion

Our result that contrast threshold for the graded potential is about 50% of the threshold for the best-performing spike code implies that the ganglion cell at threshold transmits in its spike train only 50% of the information it receives from the presynaptic circuit [6]. Our simulation result that the spike generator adds variability to the signal it codes into a spike train suggests that the ganglion cell's contrast threshold is determined to a great extent by its intrinsic variability. This is surprising in comparison to engineered devices such as radio receivers where noise in the first stage sets the S/N ratio for all successive stages. Since a different spike generator mechanism could conceivably produce less variability, it is interesting to speculate that the ganglion cell adds noise to gain some information processing advantage in a compromise with the fineness of detail it can transmit.

V. Conclusion

The ganglion cell is responsible for transmitting subtle changes in contrast in the visual signal transmitted to the brain. We show with ideal observer analysis that about half of the information about contrast from a flashed spot is lost in the ganglion cell by the spike generator, and that the level of performance of the spike train depends on the particular code tested. We further show with a compartmental model of the spike generator that noise from stochastic gating of membrane channels active during the inter-spike interval add considerably to the variability observed in the spike train.

Acknowledgment

We thank M.A. Freed, W.S. Geisler, J. Nachmias, F. Rieke, M.C.W. van Rossum, and J. Victor for helpful discussions. Supported by MH48168, EY00828.

References

[1] H.B. Barlow and J.D. Mollon (eds.) *The Senses.* Cambridge: Cambridge Univ. Press, 1982.
[2] C.K. Kier, G. Buchsbaum, and P. Sterling, "How retinal microcircuits scale for ganglion cells of different size," *J. Neurosci*. vol 15, pp.7673-7683, 1995.
[3] D.J. Calkins, S.J. Schein, Y.Tsukamoto, and P. Sterling. "M and L cones in macaque fovea connect to midget ganglion cells by different numbers of excitatory synapses," *Nature*. vol 371, pp. 70-72, 1994.
[4] L.J. Croner and E. Kaplan, "Receptive fields of P and M ganglion cells across the primate retina," *V*ision Res., vol 35, pp. 7-24, 1993.
[5] J.B. Demb, L. Haarsma, M.A. Freed, and P. Sterling, "Functional circuitry of the retinal ganglion cell's nonlinear receptive field," *J.Neurosci.*, vol 19, pp. 9756-9767, 1999.
[6] W.S. Geisler, D.G. Albrecht, R.J. Salvi, and S.S. Saunders, "Discrimination performance of single neurons: rate and temporal-pattern information," *J. Neurophysiol.*, vol 66, pp. 334-362, 1991.
[7] R.G. Smith, "Neuron-C: a computational language for investigating functional architecture of neural circuits," *J. Neurosci. Meth.*, vol 43, pp. 83-108, 1992.
[8] J.F. Fohlmeister and R.F. Miller, "Mechanisms by which cell geometry controls repetitive impulse firing in retinal ganglion cells," *J. Neurophysiol.*, vol 78, pp. 1948-1964, 1997.
[9] G. Benison, J. Keizer, L.M. Chalupa, and D.W. Robinson, "Modeling temporal behavior of postnatal cat retinal ganglion cells," *J. theor. Biol.*, in press, 2001.
[10] http://retina.anatomy.upenn.edu/~rob/neuronc.html