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Response variability in retinal ganglion cells of primates

(noise)

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ABSTRACT **The signal encoded by a sensory neuron is usually characterized as the cell's average response to repeated presentations of a stimulus. However, each stimulus presentation elicits a slightly different response. This response variability may obscure the signal represented by neural activity, but it might also be an important aspect of a neuron's message and in some instances may even serve useful functions. Here we present evidence that response variability (noise) in primate retinal ganglion cells at photopic light levels is (*i*) independent of the amplitude of either the stimulus or the response and is therefore additive, (*ii*) independent of receptive field size and retinal eccentricity, and (*iii*) similar for all primate ganglion cells. Our results show that the primate retina maintains a uniform noise level across the entire visual field and suggest that the noise originates within the ganglion cells themselves.**

The response of a sensory neuron to an external stimulus reflects both the impact of the stimulus and the neuron's internal dynamics. The stimulus itself often includes stochastic components, such as the photon noise that accompanies all visual stimuli (1–3). If response variability were due to a summation of the variability inherent in the stimulus and fluctuations of intracellular and synaptic processes, then large responses would be noisier than small responses. Similarly, large retinal neurons, with large receptive fields and numerous synaptic inputs, would be expected to have proportionately larger response noise than small neurons. On the other hand, if the response integrated from the various sources were averaged and not simply summed, then response noise would be expected to decrease with the number of inputs, and thus with receptive field size (4). Since the input impedance of large neurons is lower than that of small neurons, each synaptic or internal event will have a smaller impact on the membrane potential of larger neurons, and the notion of reduced noise due to averaging is therefore plausible. We investigated these issues by studying the response variability in retinal ganglion cells of monkeys.

METHODS

Ganglion cell activity was recorded extracellularly as synaptic (S) potentials in the lateral geniculate nuclei of anesthetized and paralyzed *Macaca fascicularis* (2.5–4 kg). General anesthesia was induced with ketamine hydrochloride, continued during surgery with thiamylal, and maintained during the recording session with urethane (3–15 mg per kg of body weight per hr). Muscular paralysis was induced by gallamine triethiodide (5–15 $mg \cdot kg^{-1} \cdot hr^{-1}$). Penicillin was injected to prevent infection, and dexamethasone was injected to prevent general edema. Atropine sulfate and phenylephrine hydrochloride were used to dilate the pupils and relax accommodation. A local anesthetic was injected at all incision sites. Cannulae were inserted into both femoral veins for intravenous injections and into one femoral artery to monitor the blood pressure. A tracheotomy allowed artificial respiration after paralysis. A temperature probe inserted just medial to one scapula controlled a dc heating pad wrapped around the animal's torso. Gas-permeable contact lenses protected the corneas from drying, and artificial pupils (3-mm diameter) were placed immediately in front of the contact lenses. Blood pressure, temperature, heart rate, and expired CO_2 were continuously monitored with a Hewlett–Packard patient monitor and maintained within physiological limits. If the animal showed any sign of stress or pain, the anesthetic dose was increased until the animal was completely sedated.

We measured the average responses and response variability of retinal ganglion cells to drifting sinusoidal gratings [mean luminance, 40 candelas (cd)·m^{-2}]. The response measure was the fundamental Fourier component, calculated for each cycle of the drifting grating. We chose to measure variability of the fundamental Fourier component rather than of the more conventional peak or sustained response, to rule out the influence of firing rate on response noise (5, 6). The response average and standard deviation, which was our measure of noise, to 64 cycles of each grating were calculated as illustrated in Fig. 1. Average responses that were greater than the maintained firing rate of the cell were rejected since they rectified during part of the stimulus cycle, so that the amplitude of the fit sinusoid would be an underestimate of the actual response. Cells were identified as parvocellular-projecting (P) or magnocellular-projecting (M) based on the latency of their responses to an electric shock delivered to the optic chiasm and on the depth of their lateral geniculate nuclei targets.

To determine the size of the receptive field centers of these cells, we calculated the average responses to gratings of increasing spatial frequency and fit these average responses with a "Difference-of-Gaussians" model (7, 8) convolved with a modulation transfer function (MTF) for the optics of the human eye at various retinal eccentricities (9). We used the human MTF because our studies of the monkey eye have shown that the monkey MTF is very similar to the human MTF (L.J.C. and E.K., unpublished data) and because the available human MTFs extend to higher spatial frequencies than do our own data for monkeys. From the fit we determined the size of each receptive field center region at the point where response fell to $1/e$ of its maximum level.

RESULTS

Fig. 2 shows response amplitude and noise plotted as a function of stimulus contrast for four typical ganglion cells located at 15°–22° retinal eccentricity. For each cell, the

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Abbreviations: P, parvocellular-projecting; M, magnocellular-projecting.

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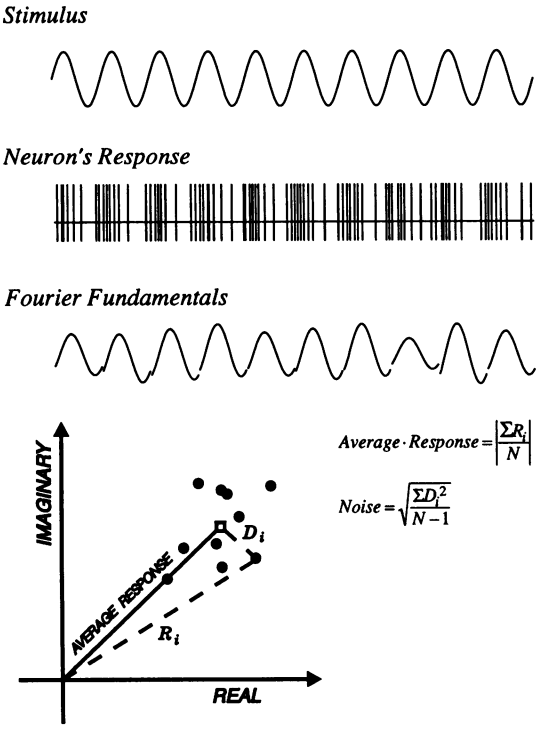

FIG. 1. Calculation of a ganglion cell's average response and response noise to 10 cycles of a drifting black-and-white sine-wave grating presented on a cathode ray tube: the light intensity at any point on the screen varied with time as illustrated at the top, at 4 cycles·sec^{-1}; the contrast was the ratio of the greatest difference from the mean luminance to the mean luminance. The S potentials during the same time period as the stimulus are represented just below as spikes labeled "Neuron's Response." "Fourier Fundamentals" are the sinusoids fit (with a Fast Fourier Transform) to the rate at which S potentials occurred during each cycle of the stimulus. In order to evaluate variability in both the amplitude and the timing of the responses, each fit sinusoid is plotted as a point (vector tip) in the complex plane, as shown on the lower left. The distance of each vector tip from the origin represents the amplitude of the sinusoidal response, and the angle between the vector and the positive x axis represents the phase lag between the stimulus and the response. The amplitude of the average response vector (open square) is the average response of the cell. We define noise as the sample standard deviation of all the geometric distances between the average response vector and the individual vector tips: it represents the dispersion of all the response vectors around the average response vector.

response increased with increasing contrast, but the noise remained constant. This behavior is seen in every cell (10). This result is consistent with the idea that the noise is additive—that is, a baseline noise that is unaffected by either stimulus or response magnitude is added to the response. This additivity is in clear distinction to what was found in neurons in the visual cortex, where response noise was shown to increase with stimulus contrast (11).

Next we examine the dependence of response noise on receptive field size and on retinal eccentricity. Fig. 3 *Upper* shows the response noise for 75 P and 9 M retinal ganglion cells recorded from 15 animals, plotted as a function of the area of the receptive field center on logarithmic axes. The regression line (slope = 0.003, P = 0.939) shows that response noise is independent of receptive field size. Fig. 3 *Lower* shows response noise for the same cells plotted as a function of retinal eccentricity on linear axes; response noise is virtually constant at all retinal eccentricities (slope = -0.035, $P = 0.075$). In other studies we have found that P and M cells' characteristic responses to contrast are also independent of retinal eccentricity (13). These two results show

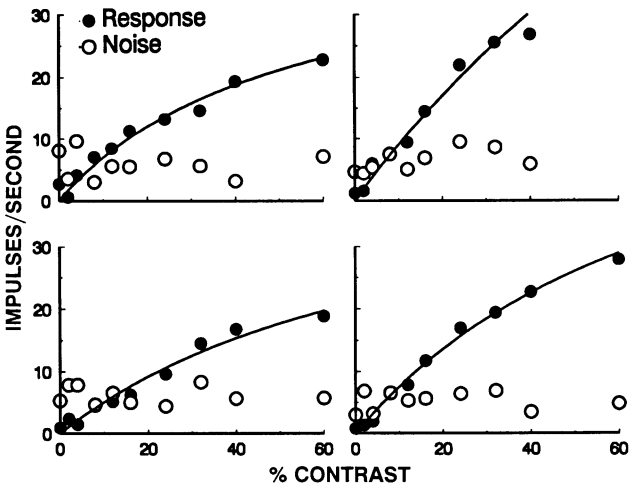

FIG. 2. Average responses (●) and response noise (○) of four P ganglion cells plotted as a function of contrast. The smooth curves through the response data are Michaelis–Menten functions, $R = aC/(b + C)$, where R is response, C is contrast, a is the maximal response, and b is the contrast which elicited half the maximal response. The slopes of regression lines through the noise data are not significantly different from 0. These four cells were recorded from one monkey and were located between 15 and 22 degrees from the fovea. Each cell was stimulated with drifting gratings of a spatial frequency fine enough to be resolved by the cell's receptive field center region but not by its surround.

that the signal/noise ratios of P and M cells are distinct from each other and are constant across the retina (see also refs. 14 and 15).

Previous studies have shown that response variability is related to maintained firing rate (5, 6), and Fig. 4 shows that this was also true of the cells we studied (slope = 0.223, $P < 0.001$). However, for the range of mean firing rates we observed, this relation predicts only 2-fold variation in response noise, and we found 5-fold variation among the 84 cells presented here. This is quite small when compared with the 10,000-fold variation in center area in our sample. Whatever the causes of response noise, the similarity of noise from ganglion cells at different eccentricities and with receptive field centers of widely different sizes suggests that all primate ganglion cells have similar response variability.

DISCUSSION

Several reasons might account for the independence of response noise and receptive field center area. (*i*) The total number of synaptic inputs that contribute to a ganglion cell's response may not increase with the area of the cell's receptive field center. If this were so, response noise that is due to summation of the variability of synaptic processes will not vary with center area. Cells with large receptive fields may have synapses that are more sparsely distributed across their dendritic trees, which will contribute to a lowering of their point sensitivity (13, 16). (*ii*) The fluctuations of the inputs that contribute to the noise may be correlated, so that averaging will not reduce noise. This would be the case if the seemingly random fluctuations of the inputs were driven by a common source or if retinal cells were coupled to each other (17–23). (*iii*) Some large source of noise, perhaps located in the ganglion cell itself, may swamp the effects of the smaller contributions from uncorrelated inputs. Other studies also suggest that ganglion cells generate their own variability (24, 25), independent of synaptic inputs.

The detection of sensory stimuli requires a discrimination between signal and noise. Our results indicate that the noise in retinal ganglion cells is additive and may originate primar-

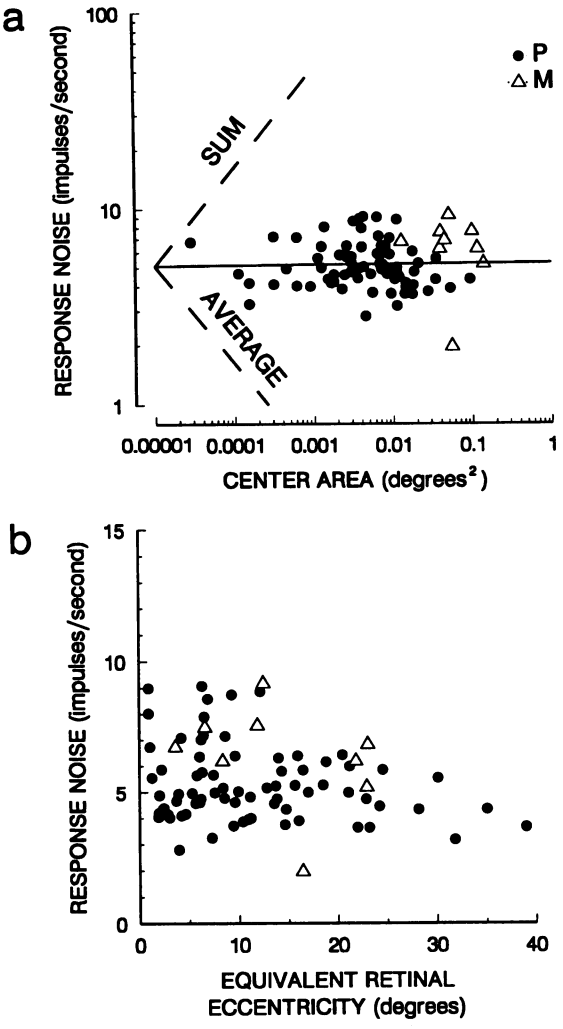

FIG. 3. (*Upper*) Response noise as a function of receptive field center area for 75 P and 9 M ganglion cells located between 0 and 40 degrees from the fovea. The lines labeled AVERAGE and SUM with slopes of $-1/2$ and $+1/2$, respectively, represent the relations expected if the number of inputs were linearly related to center area and if ganglion cells averaged or summed their inputs. The slope of the regression line through the data is not significantly different from 0 (slope = 0.003, $P = 0.939$). Response noise was calculated for each cell as the average of the response noise to center-isolating gratings of contrasts that evoked a reliable average response. (*Lower*) Response noise plotted as a function of temporal equivalent retinal eccentricity for the same cells shown in *Upper*. The slope of a regression line through the data is not significantly different from 0 (slope = -0.035, $P = 0.075$). The temporal equivalent eccentricity of any cell that lay in the nasal retina was calculated by multiplying nasal eccentricity by 0.61 to give the temporal eccentricity at which cell density is the same as that in the nasal retina (12) and then using the Pythagorean theorem to calculate temporal equivalent eccentricity.

ily within the ganglion cell itself. Furthermore, it appears that the retina maintains a constant noise level for all ganglion cells regardless of size and retinal eccentricity. The precise function of noise in the processing of information by the visual system remains to be established.

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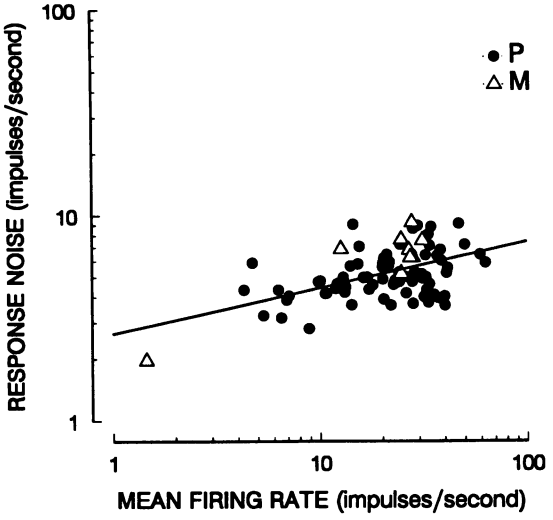

FIG. 4. Response noise plotted as a function of mean firing rate for the same cells shown in Fig. 3. The regression line through the data (slope = 0.223, $P < 0.001$) shows that there is a significant relationship between noise and mean firing rate, as found by others (5, 6). Mean firing rate was calculated for each cell as the average firing rate during presentation of 64 cycles of several sinusoidal stimuli and was the same as the maintained firing rate with no visual stimulation.

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