Macaque retinal ganglion cell responses to visual patterns: harmonic composition, noise, and psychophysical detectability

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Cooper B, Lee BB, Cao D. Macaque retinal ganglion cell responses to visual patterns: harmonic composition, noise, and psychophysical detectability. J Neurophysiol 115: 2976–2988, 2016. First published March 2, 2016; doi:10.1152/jn.00411.2015.—The goal of these experiments was to test how well cell responses to visual patterns can be predicted from the sinewave tuning curve. Magnocellular (MC) and parvocellular (PC) ganglion cell responses to different spatial waveforms (sinewave, squarewave, and ramp waveforms) were measured across a range of spatial frequencies. Sinewave spatial tuning curves were fit with standard Gaussian models. From these fits, waveforms and spatial tuning of a cell’s responses to the other waveforms were predicted for different harmonics by scaling in amplitude for the power in the waveform’s Fourier expansion series over spatial frequency. Since higher spatial harmonics move at a higher temporal frequency, an additional scaling for each harmonic by the MC (bandpass) or PC (lowpass) temporal response was included, together with response phase. Finally, the model included a rectifying nonlinearity. This provided a largely satisfactory estimation of MC and PC cell responses to complex waveforms. As a consequence of their transient responses, MC responses to complex waveforms were found to have significantly more energy in higher spatial harmonic components than PC responses. Response variance (noise) was also quantified as a function of harmonic component. Noise increased to some degree for the higher harmonics. The data are relevant for psychophysical detection or discrimination of visual patterns, and we discuss the results in this context.

magnocellular; parvocellular; ganglion cell; grating

SINEWAVE GRATINGS ARE A STANDARD tool in investigation of spatial vision. Visual patterns such as squarewave gratings have a complex spatial frequency spectrum, as do natural scenes. As an early example of the use of such patterns, Campbell and Robson (1968) tried to predict psychophysical detection and discrimination of squarewave from sinewave gratings based on the sinewave grating spatial tuning curve. They found discrepancies at low spatial frequencies, and this was adduced as evidence for multiple spatial channels in vision. Many later studies grew from this approach (Graham and Nachmias 1971; Nachmias and Weber 1975). Putative multiple spatial channels are now thought to be manifest at cortical rather than subcortical levels. However, they must rest on retinal inputs from ganglion cells. One assumption in these analyses is that responses to visual patterns can be predicted from responses to sinewave gratings. For example, responses to squarewave patterns of cells in the limulus retina can be predicted on the basis of their sinewave tuning (Brodie et al. 1978).

For temporal modulation of large fields, responses of macaque ganglion cells to squarewave and ramp waveforms can be reasonably predicted from sinewave responses (Kremers et al. 1992). We test here if this is the case with spatial patterns. A key issue here is spatiotemporal separability. If this holds, the spatial frequency tuning curve (amplitude and phase) is independent of temporal frequency. This is important because with a drifting squarewave, for example, the higher spatial harmonics are drifting at higher temporal frequencies. In a study of cat X cells (Dawis et al. 1984), deviations from spatiotemporal separability were found, and these authors cite other work noting spatiotemporal inseparability. Such effects would affect simple summation of response to the different harmonics. From a functional perspective, another issue is response variance (noise) in different frequency components of a response. With sinusoidal modulation, ganglion cell response amplitude changes with contrast and spatial frequency, but noise remains similar (Croner et al. 1993; Sun et al. 2004; Yeh et al. 1995). However, noise increases with temporal frequency (Lee et al. 2007; Sun et al. 2004). If noise varies as a function of harmonic component in responses to complex gratings, this would contradict a further assumption of Campbell and Robson (1968).

We have recently considered physiological and psychophysical performance with both luminance and chromatic gratings with multiple spatial frequency components (Cooper et al. 2012; Lee et al. 2011). We now consider how far responses of macaque retinal ganglion cells to visual patterns (in this case squarewave and ramp gratings) can be predicted from their responses to sinewave gratings. In addition, we examine the variation in noise in different harmonics of the response. In the discussion we also consider some other assumptions inherent in earlier psychophysical analysis.

We collected spatial tuning curves from ganglion cells in vivo for sinewave, squarewave, and ramp (rapid on- and off-going) drifting gratings. Luminance gratings were used for magnocellular (MC) pathway cells and red-green chromatic gratings for parvocellular (PC) pathway cells; some PC cells were also tested with luminance stimuli. MC cells’ responsivity increases rapidly with temporal frequency, and PC cells’ responses are more sustained (Derrington and Lennie 1984; Lee et al. 1989, 1990, 2007). Because of the link between spatial and temporal frequency, this amplifies MC cell’s responsivity to higher harmonic components in the waveform. We constructed a model incorporating spatial and temporal cell
properties that largely captured cell responses to the different waveforms. In a second analysis, we measured response variability through the harmonic spectrum of cells’ responses and found some increase as a function of harmonic component.

From these analyses, it became apparent that there are minor deviations from linearity in MC cell responses, and noise increases in cells’ responses through the frequency spectrum. As we used drifting gratings, it became clear that visual pattern movement across the retina is an additional complication for spatial processing from a psychophysical perspective. Campbell and Robson (1968) used free viewing, so that eye movements provided a moving stimulus. This raises the issue of eye movement in perception of spatial patterns. We discuss these factors in terms of psychophysical detectability.

METHODS

Physiological recordings. Single-unit recordings were made in vivo from macaque monkeys. All procedures conformed to the National Institutes of Health Guide for the Care and Use of Laboratory Animals, were approved by the State University of New York College of Optometry Animal Care and Use Committee, and conformed to the Society for Neuroscience Policy on the Use of Animals in Neuroscience Research. Macaques (5 Macaca fascicularis, male 2.8–4.0 kg) were initially sedated with an intramuscular injection of ketamine (10 mg/kg). Local analgesic was then applied to surgical points of intervention. Anesthesia was induced with sodium thiopental (10 mg/kg) and maintained with inhaled isoflurane (0.2–3%) in a 70:30 N₂O-O₂ mixture. Muscle relaxation was maintained by an infusion of gallamine triethiodide (5 mg·kg⁻¹·h⁻¹) iv with accompanying dextrose Ringer solution (5 mL·kg⁻¹·h⁻¹ iv). To ensure the proper depth of anesthesia, the electroencephalogram and electrocardiogram were continuously monitored. Body temperature was kept close to 37.5°C, and the end-tidal CO₂ was kept close to 4% by adjusting the rate and depth of respiration.

Neuronal activity was recorded directly from retinal ganglion cells by a tungsten-in-glass electrode inserted via a cannula entering the eye behind the limbus. The details of the preparation can be found elsewhere (Crook et al. 1988). To bring stimuli into focus on the retina, a gas-permeable contact lens of the appropriate power was used. The fovea was located and back-projected onto a screen, from which we could determine receptive field location. Ganglion cells were recorded with receptive fields between 4 and 12° eccentricities. Cell identification was achieved through standard tests (Lee et al. 1989). Initially, this included basic response properties such as spectral opponency and temporal response properties. For instance, PC retinal ganglion cells can be identified by strong tonic, chromatic responses, while MC retinal ganglion cells exhibit phasic responses, strong response to achromatic modulation, and weak response to equiluminant chromatic stimuli. For each cell, the locus of the receptive field center was determined by seeking the response minimum with temporally modulated horizontal and vertical bipartite fields. Times of spike occurrence were recorded to an accuracy of 0.1 ms, and averaged histograms of spike trains were simultaneously accumulated with 64 bins per cycle of modulation. The histograms were Fourier analyzed to give amplitudes and phases of the response spectra.

Visual stimuli. Responses to spatial waveforms were measured using drifting gratings of different spatial frequencies generated on a SONY Trinitron CRT display driven by a Cambridge Research Systems Visage (frame rate 120 Hz at a resolution of 800 × 600, 2.28 m away from the monkey, usually at 30 and 60% contrast). The Visage was controlled by CRS Stimulus Description Language programs governed by C wrapper programs running on a Macintosh Quadra 950 computer. Stimuli were horizontal gratings presented in a 5 × 5 deg window. Sinewave, squarewave, and rapid-on and rapid-off ramp gratings were used. A 2 Hz drifting rate was usually used, but 1 and 4 Hz were also tested. The mean luminances of the red and green phosphors were set equal to give a mean luminance (L₀) of 31.34 cd/m² and chromaticity of (0.436, 0.476) in CIE 2° x-, y-coordinates. Red and green phosphors were modulated in phase or out of phase to produce luminance or chromatic gratings.

Sinewave, squarewave, and the two ramp grating luminance (L) profiles over space (x) at a contrast C, are described by

\[ L(x) = L_0 \left[ 1 + \frac{2}{\pi} \sum_{n=1}^{\infty} \sin(2\pi n x) \right] \]

where \( k \) is spatial frequency and \( n \) is the harmonic sequence. These patterns drift with a velocity, \( v \), in visual angle/s, so that

\[ v = \frac{1}{k} \quad \text{or} \quad f = \frac{v}{k} \]

where \( f \) is the temporal frequency. As spatial frequency increases through the Fourier expansion for the squarewave and ramp gratings, temporal frequency, \( f \), must increase in proportion in order that velocity, \( v \), remain constant for each harmonic.

Cell sample. From a sample of 41 neurons, eight MC (4 on- and 4 off-center) and eight PC retinal ganglion cells (4 +M/L–L/M and 4 –M/L+L/M) were used for detailed analysis; partial datasets from the other cells were similar. Spatial tuning curves were collected for drifting sinewave, squarewave, on- and off-ramp waveforms at two suprathreshold contrast values (30 and 60%) for MC (luminance modulation, red and green guns modulated in phase), and 50 and 100% for PC cells (chromatic modulation, red and green guns modulated in counterphase).

Responses to full-field temporal waveforms were also measured, using stimuli generated on a three-channel Maxwellian view system as described in detail elsewhere (Lee et al. 1990). Two light-emitting diode (LEDs) sources with dominant wavelengths of 638 and 554 nm were used. The LEDs were driven by pulse-train frequency modulation to achieve a highly linear relationship between driving voltage and LED light output. They were usually modulated at a time-averaged retinal illuminance close to 200 Td at a range of modulation contrasts.

RESULTS

Harmonic spatial tuning of cells to sinusoid and complex waveforms. In this section we qualitatively describe the responses of macaque retinal ganglion cells to sinewave, squarewave, and ramp gratings. Figure 1, A and B, shows waveforms and histograms from an MC (off-center) and a PC ganglion cell (+L–M) for all four waveforms at two of the 14 spatial frequencies tested (0.1 and 1.6 cd·°⁻¹, 60% contrast for the MC cell and 100% contrast for the PC cell). The solid lines derive from a model described later. Upon inspection, at low spatial frequencies (0.1 cpd), MC cells gave more transient edge responses than PC cells (Dreher et al. 1976; Lee et al. 1990). PC cells’ responses were more sustained and do not display the sharp high-amplitude transient at the edge that are seen in MC cell responses. For instance, the PC response to a squarewave or ramps approximates more closely the stimulus waveform, whereas the MC cell responded transiently to the edge crossing the receptive field center. MC on-center cells gave peak responses to on transitions in squareswaves and ramps, while off-center MC cells responded sharply to the off transitions. Such an effect is weakly present in PC retinal ganglion cells to
chromatic ramp waveforms. For MC cells, at 1.6 cpd responses appear less transient due to a combination of spatial and temporal factors.

Response histograms were Fourier analyzed to extract response amplitudes to different harmonic components. Figure 2, A and B, shows the amplitude of selected components for the MC and PC cells for sinewave, squarewave, rapid-on, and rapid-off ramp gratings as a function of spatial frequency. The solid curves represent the fit of the model described in the next section. For sinewaves, the responses in harmonics beyond the fundamental are small and are associated with response shaping, including response rectification. For the MC cell, the 1st harmonic shows the bandpass shape associated with antagonistic center/surround structure. For the PC cell, the 1st harmonic shows a low-pass shape, due to additive center and surround responses to the chromatic gratings.

For waveforms other than sinewave, there is, as expected, significant energy in higher response harmonics, especially for the MC cell. Squarewave grating stimuli have energy in the odd harmonics with amplitudes: $2/\pi, 2/3\pi, 2/5\pi...$ for the 1st, 3rd, and 5th harmonics, respectively (Eq. 2). For the MC cell, comparing the response amplitude for the higher harmonics with the fundamental, there is more energy present than expected from the ratios in the Fourier expansion of the stimulus waveform. This is due to MC cells’ transient responses, as discussed in the next section. This disparity is less marked for the PC cell, since their responses are more sustained. For both cell types, there was also significant energy in the even harmonics of the squarewave response, because of response rectification. Ramp waveforms have energy in both even and odd harmonics with amplitudes: $2/\pi, 2/2\pi, 2/3\pi...$ for the 1st, 2nd, and 3rd harmonics. Again, especially for the MC cell, there was more response energy in the higher harmonics than expected from these ratios. We now consider how the responses shown can be described based on a simple receptive field model.

Modeling retinal ganglion cell responses to squarewave and ramp waveforms. We have previously shown that responses to squarewave and ramp temporal waveforms can be predicted from the sinewave temporal modulation transfer function (tMTF) (Kremers et al. 1993). Spatial patterns bring an additional complication. That is, when visual patterns such as squarewaves are drifted across the retina, the higher spatial frequency components in the stimulus move at proportionally higher temporal frequencies (Eq. 4).

If neuronal spatial tuning were independent of the temporal frequency of a drifting sinewave, spatiotemporal separability would hold, and modeling would be straightforward. However, this is generally not the case. Dawis et al. (1984) provided detailed analysis of such deviations for cat X cells and found two factors, center/surround latency differences (this causes a decrease of center/surround opponency as spatial frequency increases) and a positional mismatch between center and surround. These factors change both response amplitudes and phases, causing deviation from spatiotemporal separability. We now consider how well we can predict responses to other waveforms despite these factors.
The response of a ganglion cell, $R_g$, to a visual pattern can be described by the difference of center and surround Gaussians for MC cells for luminance patterns, and the sum of Gaussians for PC cells for chromatic patterns (Eq. 5).

$$R_g(k) = R_C(k) \pm R_S(k) = l_c r_c^2 \pi \exp(-\pi k r_c^2) \pm l_s r_s^2 \pi \exp(-\pi (k + \delta k)^2) \quad (5)$$

where $l_c$ and $l_s$ are amplitude scalars and $r_c$ and $r_s$ are center and surround radii. A spatial displacement of center and surround, one of the factors causing spatiotemporal inseparability (Dawis et al. 1984), is represented by $\delta k$. However, we had no means of estimating this factor, which appears small compared with center size and thus has been ignored. The sign of the summation is negative (i.e., the difference of Gaussians, DoG) for MC-cell luminance processing and positive (i.e., the sum of Gaussians, SoG) for PC-cell chromatic processing.

A schematic is shown in Fig. 3A. The sinewave spatial tuning curves were fitted with the DoG and SoG functions (Eq. 5, Fig. 3B). The data and fits for the cells of Figs. 1 and 2 are shown. The fits were satisfactory. Fit parameters, e.g., center and surround Gaussian radii, were consistent with values in the literature (Lee 2011). The SoG function shows an inflection near 1 cpd reflecting the contributions from center and surround mechanisms.

To predict responses to squarewave or ramp patterns, we also required a description of center and surround temporal responses; as mentioned above, a second source of spatiotemporal inseparability is a difference in temporal tuning of center and surround. This causes spatial frequency tuning curves of ganglion and LGN cells to become less bandpass with increasing temporal frequency (Dawis et al. 1984; Lee et al. 1981), as the delay in the surround response Lessens spatial opponency at high temporal frequencies on vector summation of center and surround signals. Detailed description of this effect can be found elsewhere (Dawis et al. 1984; Frishman et al. 1987). We found such temporal effects in MC cells (Nadig et al. 1995) and later modeled MC cells temporal tuning based on a similar temporal tuning of center and surround but with a surround lag of $\sim 5$ ms (Smith et al. 2008).

We incorporate these temporal tuning characteristics into the model. We base our analysis (Fig. 3C) on the tMTF of MC (squares) and PC (triangles) cells as a function of temporal frequency. The MC curves were obtained by selectively stimulating the center with a small modulated spot (0.5°) set in an isoluminant surround (Nadig et al. 1995); details of stimulation conditions are given in the figure legend. The PC curves were obtained using silent substitution to isolate center and surround (Yeh et al. 1995). Data have been fitted with a third-order polynomial for amplitude $[A(f)]$ or a linear function $[P(f)]$ for phase. The same tMTF curves were used for the surround with a delay of 5 ms.

The amplitude curve (Fig. 3C, left) for MC cells is much more bandpass in shape than that for PC cells. This reflects the more transient MC cell responses. In the phase curve (Fig. 3C, right), there is an increasing phase lag with temporal frequency; at low frequency, the MC cell curve shows a phase advance as expected from their transient response.

We predicted the responses to all waveforms from the equations above. For example, for the squarewave at a drift frequency of $f$ Hz, we used the following expansion. A delay term ($\delta$) has been inserted in the surround contribution to represent the center-surround delay.
For each cell, the spatial tuning functions were obtained from the sinewave responses. The temporal tuning functions were obtained from Fig. 3C. In addition, two further parameters are used. M represents the maintained firing of the cell; this determines the baseline about which modulated responses occur, and was measured for each cell. S is a scaling factor; it is required since part of the response in the prediction is lost by response rectification, and this is not taken into account in the DoG or SoG fits. Similar expansions were used for ramp waveforms.

Figure 3D shows example squarewave predictions for 0.1 cpd, for an MC and PC cell. The baseline is elevated above zero since maintained firing is present. The last stage in the model is rectification due to the impossibility of negative firing rates. The response waveform lost is drawn in gray. It should be stressed that for a given cell in the simulation there is only one free parameter, S. All other parameters, e.g., center and surround radii, their relative strengths and their tMTFs, were derived from the sinewave data.

Model curves are provided for the histograms in Fig. 1 and can be seen to reasonably capture the timing, shape, and major features of the responses, especially for the PC cell. For the MC cell, the sharpness of the response peaks was not fully captured, and there are other differences in detail. In Fig. 2, the harmonic spectra are shown for the rectified model analysis and can be compared with the measured values. Again (especially for the PC cell) most aspects of the data are captured. This suggests that it is appropriate to approximate MC and PC responses by a linear prediction, with certain exceptions noted below.

A similar approach was used by Brodie et al. (1978) to predict responses in the Limulus retina to drifting squarewaves, based on the ommatidia’s spatial and temporal tuning to sinusoidal stimulation. In their case, spatial and temporal tuning was estimated using a sum-of-sinusoids stimulation technique, from which the spatiotemporal transfer function can be recovered. They discussed in detail the linear systems principles underlying their approach and achieved satisfactory predictions. Equation 6 above is equivalent to their convolution of the stimulus with each cell’s spatiotemporal tuning.

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We pursued the analysis into the frequency domain. We took the Fourier transform of the rectified model waveform and
compared the resultant spatial tuning surface to that of cell responses. An example is shown in Fig. 4 for the MC and PC cells of Figs 1 and 2. It should be stressed that the same scaling parameter was used for all fits for a given cell. Harmonic amplitude is plotted against spatial frequency up to the 15th harmonic. Generally, cell and model surfaces correspond well. There is little energy beyond the second harmonic for the sinewave. The surfaces for the squarewave show a corrugated shape because of the concentration of energy in the odd harmonics. However, the spillover of energy (primarily due to response rectification) into the even harmonics was reasonably described. The different surfaces for different polarity ramps are also captured. At low spatial frequency most of the energy in MC cell responses to complex waveforms is at higher harmonics, beyond the 1st harmonic.

However, certain discrepancies are apparent. Energy in the PC cell harmonic surface is well accounted for by the model output under all conditions. But MC cell responses to complex waveforms showed two consistent discrepancies for all cells analyzed. The predictions of 1st harmonic energy at low spatial frequency for complex waveforms are higher than those actually measured (marked for emphasis in Fig. 4A). At higher harmonics, actual responses are more vigorous and extend to higher frequency. This is reflected in the response histograms, where the response peaks are sharper than the model prediction. Operation of contrast gain controls might cause this.

Fig. 4. A: on-center MC cell response harmonic surfaces and modeled MC harmonic surfaces as a function of spatial frequency to sinewave and complex waveforms. For sinewaves, both cell and model sinewave surfaces (1st column) have the majority of energy in the fundamental and some energy in the second harmonic due to response rectification. For the other waveforms, MC cell responses have much energy in higher harmonic components; the model is able to capture some, but not all, of this behavior. Also, the model prediction of the fundamental harmonic at low spatial frequencies is much higher in the model prediction than in the cell’s response (starred for squarewave and ramp responses). B: PC cell response harmonic surfaces and modeled +L−M PC harmonic surfaces for sinewave and complex waveforms. There is comparatively less energy in the higher harmonics of the PC cell responses and this is reflected in the model output. For PC cells, the model captures the amplitude of the cell’s response as a function of harmonic component and spatial frequency.
phenomenon (Benardete and Kaplan 1999; Lee et al. 1994; Shapley and Victor 1978, 1981), but we did not incorporate this into the analysis.

Satisfactory fits were also found for the other cells in the sample. Table 1 summarizes cell parameters. Center and surround Gaussian radii are consistent with those in the literature for 5–10° eccentricity. Over the sample of MC and PC cells, for MC cells 85% (SD 6.2%; $n = 8$, harmonics 1–10) of the variance in harmonic composition was accounted for by the analysis, and for PC cells 92% (SD 3.0%; $n = 8$). The difference between the two cell types was primarily due to poor prediction of the first harmonics for the complex waveforms at low spatial frequencies.

We also obtained similar datasets at a lower stimulus contrast (30% MC cells, 50% PC cells). For PC cells, their behavior showed little deviation from the linear prediction even at higher contrast, and the 50% contrast analysis also yielded satisfactory results. An example of an analysis for an off-center MC cell is shown in Fig. 5. Response histograms to sinewaves and squarewaves (Fig. 5A) and ramps (not shown) could be well predicted. Contrast gain control is expected be less manifest at 30% contrast, and response peaks were better captured. However, in the spatial frequency tuning curves, actual response to squarewaves and ramps were, at lower spatial frequencies, smaller than the prediction, as shown in the squarewave example in Fig. 5B.

The goal in this analysis was to test if a straightforward linear analysis could account for responses to complex waveforms. This would appear to be the case to a first approximation for the contrast range we tested, although the simple model neglected such effects as nonlinear contrast response in MC cells or contrast gain control. We did incorporate, however, center surround latency differences but manipulating the surround delay relative to the center ($\delta$, Eq. 6) did not improve fits.

Harmonic composition of cell responses. From the preceding section we showed that, with complex moving patterns, the higher temporal frequency of higher spatial harmonic components are a critical determinant of response waveform in MC cells. Put another way, the higher spatial frequency components of a pattern are selectively amplified in the responses of MC cells due to their transient responses and band-pass TMTF. To illustrate this further, we plot in Fig. 6A the amplitude spectra for representative MC and PC cells for the four different waveforms at two spatial frequencies, 0.1 and 1.6 cpd.

For the MC cell (Fig. 6A), for sinewave gratings at 0.1 cpd there was energy in the 1st harmonic and little energy beyond the 2nd harmonic. This pattern changes dramatically for squarewave and ramp gratings of the preferred polarity (i.e., rapid-on ramps for on-center cells and rapid-off ramps for off-center cells). Higher harmonic components dominate the spectrum; individually each harmonic component may have less energy than the first harmonic, but the summed energy in the higher harmonics is much larger than the first harmonic. For the nonpreferred ramp grating, the amplitude spectrum is

<table>
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<th>Table 1. Parameters for cell sample</th>
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<tr>
<td><strong>MC Cells ($n = 8$)</strong></td>
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<td><strong>PC Cells ($n = 8$)</strong></td>
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<tr>
<td>$r_c$  0.069 ± 0.021</td>
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<tr>
<td>$l_c$  2.622 ± 1.010</td>
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<tr>
<td>$r_s$  0.287 ± 0.11</td>
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<tr>
<td>$l_s$  170 ± 100</td>
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<tr>
<td>$M$    6.3 ± 3.9</td>
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<tr>
<td>$S$    1.78 ± 0.17</td>
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<tr>
<td>Res. error 14.8 ± 6.2</td>
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<tr>
<td><strong>MC Cells ($n = 8$)</strong></td>
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<tr>
<td><strong>PC Cells ($n = 8$)</strong></td>
</tr>
<tr>
<td>$r_c$  0.050 ± 0.018</td>
</tr>
<tr>
<td>$l_c$  4.760 ± 2.520</td>
</tr>
<tr>
<td>$r_s$  0.35 ± 0.28</td>
</tr>
<tr>
<td>$l_s$  384 ± 499</td>
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<tr>
<td>$M$    15 ± 8</td>
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<tr>
<td>$S$    1.46 ± 0.2</td>
</tr>
<tr>
<td>Res. error 8.2 ± 3.0</td>
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Means and SD for parameters. Center and surround parameters were derived from fits to spatial frequency tuning curves. M (maintained firing) was directly measured. $S$ is the free scaling parameter.

Fig. 5. A: responses of off-center MC cell to sinewaves and squarewaves, together with predictions from the model as in Fig. 1. The shape of the response is well captured. B: amplitudes of selected harmonic as a function of spatial frequency as in Fig. 2. Shapes of the tuning curves are generally well captured, except for the squarewave at the lowest spatial frequencies.
overall much lower in amplitude but again biased toward higher harmonics. For PC cells (Fig. 6B), for the sinewave, most energy is again in the first harmonic with little energy beyond the second harmonic. For the other waveforms there is an increase in energy in the higher harmonics but much less change in the harmonic spectrum than with the MC cell. As discussed in the previous section, this is accounted for by the difference in temporal response of the two pathways. At 1.6 cpd, there is little difference between the spectra for different waveforms for either cell type, although responses are still vigorous at this spatial frequency. This indicates that the change in harmonic spectrum with the different waveforms is primarily due to temporal frequency effects rather than the effects of response rectification.

To further quantify this result, we calculated the ratio of the 1st harmonic to the sum of energies in higher harmonics. To discount the effect of noise, for each cell we subtracted the mean energy averaged over all harmonics in the absence of response for this calculation. It should be noted that the energy spectrum of the maintained activity of cat (Troy and Robson 1992) and monkey (Troy and Lee 1994) is flat up to temporal frequencies corresponding to the maintained activity rate (~10–20 Hz).

Harmonic ratios (averaged over 8 MC and 8 PC cells) are shown in Fig. 6, C and D. The responses of PC cells to sinewaves show less higher harmonic components than those of MC cells ($P < 0.001$, t-test), and the ratio of 1st to other harmonics is higher. This is partially due to the higher maintained activity of PC cells. For complex waveforms, for MC cells the ratio of higher harmonic to the first harmonic energy drops to ~5%, a factor of 5.72. For PC cells this factor is lower, 1.35. Analysis of variance showed these differences to be significant at the 0.001 level.

It could be argued that this finding partly results from the high contrasts used; data in Fig. 6 were obtained with 60% contrast for MC cells and 100% contrast for PC cells (where contrast is in terms of red/green gun modulation). Similar results were found with 30% contrast for MC cells and 50% for PC cells. To further investigate contrast effects we considered previously acquired data obtained over a large range of contrasts with full-field temporal stimuli (Kremers et al. 1993). Stimuli were uniform fields 4° in diameter modulated in luminance or chromaticity, at contrasts ranging from 0.75 to 100%. In a first analysis, the 1st harmonic ratio was calculated as a function of contrast for squarewave, ramp, and sinewave waveforms (not shown; data averaged data over 5 MC cells and 5 PC cells). For MC cells, the low ratios for complex waveforms (as in Fig. 6B) persisted down to low contrast. This is to be expected since the temporal properties of MC and PC cells are not very contrast dependent, i.e., MC cells are transient whatever the contrast.

In a second analysis we assessed how much distortion of the harmonic spectra (relative to the linear prediction) might be associated with rectification. At low contrast when responses are small there will be less response rectification, so that response spectra might correspond more closely to that expected from the Fourier series of the waveform. This was the case for PC cells (not shown; data were averaged over 5 MC
cells and 5 PC cells), but for MC cells distortion of the harmonic spectra began at low contrast (<5%). Results indicated that even at low contrast the peak firing rates associated with step changes (in sinewave and ramp gratings) are ~20–30 imp/s, well exceeding the usual level of maintained activity (see values in Table 1). The consequences of this result for discrimination experiments [e.g., between square and sinewaves (Campbell and Robson 1968)] remain uncertain.

This finding suggests that cells of the MC pathway preferentially code the higher spatial harmonic energy of sharp luminance transitions of complex spatial patterns, such as the edges in drifting square and ramp waveforms. Responses of PC cells, on the other hand, primarily carry information of the patterns’ fundamental spatial frequency.

**Harmonic composition and noise in cell responses.** We now consider a further assumption of Campbell and Robson (1968) that noise is constant through the harmonic spectrum of a cell’s response. The detection of information in complex patterns coded in higher harmonic components will be a function of noise in harmonic components. Retinal ganglion cell response variance, as a measure of noise, has been found to remain constant as a function of contrast (Croner et al. 1993) and spatial frequency but increase roughly linearly as the square root of temporal frequency (Lee et al. 2007; Sun et al. 2004). If this were so in the harmonic spectrum of the response to a pattern, this noise would be expected to affect psychophysical detectability. Here we quantify response variance through the harmonic components of the response.

Each waveform condition for a given spatial frequency was presented for 20 cycles and resulting spike trains, while similar, varied in spike timing and numbers of spikes. To measure this variance, the Fourier transform was calculated for each cycle, and the resulting real and imaginary components were plotted in the complex plane. Figure 7 shows the 1st, 3rd, and 5th harmonic components for an MC (Fig. 7A) and a PC cell (Fig. 7B) for different waveforms at a low spatial frequency. The harmonic components cluster into groups where each point corresponds to one sweep. Response variance is the radial standard deviation of the points about the mean (Eq. 7) (Croner et al. 1993),

\[
\text{Noise} = \sqrt{\frac{\sum_{1}^{n} d_i^2}{n-1}}
\]

where, \(d_i\) is the radial distance of a point from the mean and \(n\) is the number of points. This is illustrated for the sinewave 1st harmonic response of the MC cell in Fig. 7A.

Variance measured in this way captures the degree of clustering for each harmonic. As in earlier work (Croner et al. 1993; Sun et al. 2004), the distributions of individual sweep points were approximately circular, for different waveforms and at different harmonics. There was little indication that, for example, variability along a radial axis was greater than variability along a tangential axis; such a difference would indicate more variation in response amplitude than in response phase. However, for MC cells with vigorous response peaks, the distribution of points occasionally arranges in step patterns on a radial axis, seen mostly for MC cell “preferred” ramp responses (Fig. 7A “Off Ramp” response). This is due to a transient response with few impulses to the edge present in the stimulus (Victor and Purpura 1996). Regression analysis showed that only under this condition did the sweep distribution deviate from circularity (\(P < 0.001\)); all other conditions in Fig. 7 showed no such effect (\(P > 0.05\)). Similar results were found for other PC and MC cells.

The data in Fig. 7 show only a small increase in noise (the size of the cloud of points) in the higher harmonics compared with noise for the fundamental. This contrasts with the effect of increasing temporal frequency per se; noise increases markedly with temporal frequency in Fig. 4 in Sun et al. (Sun et al. 2004).

The increase in noise through the higher harmonics is plotted in Fig. 8 for the mean of eight MC and eight PC cell’s response for the different waveforms. Data showed no spatial frequency dependence and have been averaged across spatial frequency.

For the MC cells across all conditions, there was a roughly linear increase in variance with harmonic number. There was no significant difference between waveforms, and data have been fit with a single straight line. For PC cells, there was a similar gradual increase but the curve flattens out beyond about the 5th harmonic. Again there was no difference between waveforms.

The increase in noise with temporal frequency was shown to be mostly due to the fewer impulses within the shorter cycle period at higher frequencies (Sun et al. 2004; Victor and Purpura 1996). With our waveforms, higher harmonics (which represent higher temporal frequencies) showed much less increase in noise. Perhaps, since higher harmonics derive from the whole cycle, this impulse number effect does not occur. However, some increase in variance did occur in our data, which may affect psychophysical detectability to some degree. This issue is addressed in the next section.

**DISCUSSION**

**Cell responses to complex waveforms and their analysis.** We have described an analysis of in vivo macaque retinal ganglion cell responses to visual spatial patterns, such as sinewaves and ramp gratings. To predict responses to these waveforms, we scaled cell spatial tuning curves for sinewaves with the coefficients of the Fourier expansion for the complex waveforms. Such scaling has been used in human psychophysics (Blakemore and Campbell 1969; Campbell and Robson 1968; Graham and Nachmias 1971; Tolhurst 1972; for review see DeValois and DeValois 1988 or Shapley and Lennie 1985), but it has seldom been implemented in physiological analysis except for a study of the spatiotemporal response of the limulus retina (Brodie et al. 1978).

In physiological analysis it is necessary to incorporate cells’ temporal tuning properties. As explained in Methods and Fig. 3, higher harmonic components of visual patterns drift at a higher temporal frequency. MC cells show a highly bandpass temporal tuning (Fig. 3) so response amplitude increases rapidly with temporal frequency up to 20–30 Hz (Lee et al. 1990). This amplifies the contribution of high harmonic components to their responses to visual patterns. PC neurons are more low-pass in their temporal response, and this amplification does not occur. We therefore scaled different frequency components by the corresponding MTMFs of MC and PC cell classes. Cells’ responses to complex waveforms were then largely predictable from the response to sinusoidal modulation,
Fig. 7. Response variance analysis in the complex plane. Real and imaginary components for each sweep of the stimulus (20) are plotting in the complex plane. Response variance is defined as the SD of the distances ($d_i$) of the response vectors from the mean response vector (demonstrated in A, sinewave). The first 3 odd harmonics for sinewave and complex waveforms are given for an off-center MC cell in A and a +L–M PC cell in B.
after incorporation of thresholding nonlinearity. This is apparent in the fit curves in Figs. 1 and 2 and the 3D power spectrum plots in Fig. 4. This suggests that linearity and spatiotemporal separability holds to a first approximation. We specifically explored one cause of a breakdown of separability, the center-surround latency difference, but this had only a minor effect on model predictions.

The goal of this analysis was to test how far a simple model could account for responses, rather than to provide a precise model of the underlying mechanisms present. The model (Fig. 3) omits established features of ganglion cell physiology, e.g., the presence of contrast gain control, which is present in MC cells but not in PC cells (Benardete et al. 1992; Kaplan and Shapley 1986). Contrast gain control is a contrast-dependent feedback compression, which leads to some degree of response saturation, a characteristic contrast-dependent change in temporal tuning, and a briefer response to flash stimuli at high contrast (Lee et al. 1994; Shapley and Victor 1978). The sharper MC cell response to the squarewave or ramp edge compared with the model is likely to derive from this source. In the similar analysis of the limulus retinal response (Brodie et al. 1978), this effect does not seem to be present.

The other consistent deviation between cell responses and model was for MC cells at low spatial frequencies. Measured low-harmonic response amplitudes were lower than the prediction. Conversely, response amplitudes persisted to higher harmonics than predicted; this is due to the briefer duration of the edge response compared with its prediction. It is possible that both these effects were associated with contrast gain controls, but other mechanisms may also be involved.

These results demonstrate that, with moving visual patterns, spatial structure interacts with temporal frequency so that information about fine spatial detail is carried by MC cells. The sustained responses of PC cells result in most of their response energy being devoted to harmonics of low spatial frequencies.

We also considered response noise (or variability) as a function of harmonic composition. In the retina, cell response amplitude increases with contrast, while noise remains constant (Croner et al. 1993). In the lateral geniculate nucleus there is some increase (Victor et al. 2007), and a further increase in cortex (Tolhurst et al. 1983). There is no increase in noise with spatial frequency, but there is a marked increase with temporal frequency (Lee et al. 2007; Sun et al. 2004). Given that the higher spatial harmonics of a complex waveform have a higher temporal frequency, we wished to test if the variance of these responses increased. Noise was not invariant and increased in higher harmonic response components although not as much as for temporal frequency. In the earlier studies, it was found that the increase in noise with temporal frequency had to do with impulse statistics. There are fewer impulses per cycle at higher frequency (due to decreased cycle duration) and if impulse generation can be approximated by a modulated Poisson process (Reich et al. 1997), then variance will increase. However, higher harmonics with visual patterns derive from a whole cycle of the fundamental, so the number of impulses from which harmonic estimates derive did not change so much. However, a small but consistent increase in noise was found.

**Implications for perceptual mechanisms.** With visual patterns, we show here that most energy of MC cell responses is shifted toward higher spatial harmonics, because of MC cells’ bandpass temporal response. Data were obtained from squarewave and ramp waveforms, but the same result is expected for natural scenes with more elaborate spatial spectra. It is also likely to hold with eye movement as well as stimulus movement. There has been a recent resurgence of interest in the role of eye movements in perceptual processing (Martinez-Condes et al. 2013; Rucci and Victor 2015). For example, eye movements and the fast temporal response they evoke have been shown to be critical in detection of detailed structure during high visual acuity tasks (Ko et al. 2010; Martinez-Conde et al. 2000; Rucci and Victor 2015).

Our data add a physiological context to this prediction. In complex patterns, high spatial frequency harmonic information is amplified in the MC pathway due to the bandpass temporal response of MC cells. On the other hand, energy in the sustained responses of PC cells is biased more toward the fundamental components of the complex pattern; in a theoretical analysis, Rucci and colleagues (Rucci et al. 2007) suggested that eye movements play less of a role in a low-frequency range and may serve to functionally shift neural...
representation toward high spatial frequencies (i.e., edges and contour features).

Furthermore, there is evidence that PC pathway signals undergo temporal low-pass filtering at a central site. Psycho-physical thresholds for chromatic flicker decrease rapidly beyond 4 Hz, whereas PC cells respond to much higher frequencies (Lee et al. 1990; Lee et al. 2007; Yeh et al. 1995). Such PC pathway lowpass temporal filtering would further concentrate information in the PC pathway toward lower spatial and temporal frequencies. Such a conclusion about the division of spatial information between these pathways contradicts the common assumption that higher spatial frequency signals are carried in the PC pathway and lower spatial frequencies in the MC pathway.

We now consider the relation between psychophysical detection and discrimination of different waveforms and the physiological substrates. Almost all psychophysical studies with different waveforms have used achromatic patterns. The following discussion thus concentrates on these achromatic psychophysical data and MC cells; equivalent psychophysical data with chromatic gratings would be of interest, but are difficult to find.

We consider the seminal paper of Campbell and Robson (1968). They measured detection and discrimination thresholds for sinewave gratings and other visual patterns. Their sinewave detection curve showed the characteristic bandpass shape. Observers used free viewing, and so their eyes scanned across the different waveforms. If images are stabilized on the retina and gratings drifted at fixed temporal frequencies, the resulting psychophysical sinewave tuning curve loses much of its low spatial frequency attenuation (Kelly 1979). His results implied that the strong low spatial frequency attenuation found psychophysically has a largely temporal origin; the implication is that this is due to the low amplitude of eye movements relative to the wavelength of coarse gratings. With briefly presented gratings, the human contrast sensitivity curve becomes much more low-pass (Leonova et al. 2003). Kelly (1979) concluded that eye movements play a critical role in the standard spatial tuning curves; they are the “sine qua non of spatial vision” [sic]. Physiologically, we have found that MC cells show a similar spatiotemporal sensitivity surface to Kelly’s psychophysical data (not shown). Recent physiological data have shown that eye movements play a critical role in detection of slowly modulated targets set in equiluminant surrounds (Ennis et al. 2014), as eye movements displace the target edge over the retina. We stress this point to underline the importance of eye movements in visual pattern detection, including grating tuning curves.

Campbell and Robson (1968) found that at low spatial frequencies detection thresholds for square waves were higher (by a factor of ~2) than a prediction based on a broad-band peak detector model based on the sinewave detection curve. They proposed the presence of multiple spatial channels in the visual system to account for this. Shapley and Tolhurst (1973) found a similar result with other spatial waveforms and discussed other possible explanations. Other early results implying the existence of multiple spatial channels are, for example, those of Graham and Nachmias (1971) and Nachmias and Weber (1975). Such multiple spatial channels are now thought to be manifest at cortical rather than subcortical levels, although they must rely on retinal inputs from ganglion cells. We would stress that the current study is neutral with regard to the multiple channel hypothesis; we are simply concerned with testing underlying physiological assumptions.

The current study was intended to test some physiological assumptions of this approach. We first tested if cell responses to other waveforms could be predicted from cell responses to sinewaves. Cells largely passed this test; >85% (MC cells) or 90% (PC cells) of response variance could be accounted for by a linear model, as long as cell tMTFs were taken into account. This conforms with earlier results using flickering stimuli (Kremers et al. 1993).

Campbell and Robson (1968) remark that higher harmonic amplitudes of a squarewave fall off rapidly with spatial frequency and become negligible. However, the tMTF of MC cells amplifies the higher harmonic components so that they play a much larger role in cell responses than expected (Fig. 6). This may not be relevant to their analysis. If, as discussed above, the human sinewave detection curve is heavily influenced by eye movements, then tMTF effects are inherent in the sinewave detection curve, and thus (by accident) incorporated in their analysis. However, if the eye movement pattern depended on the structure of the grating, this assumption would be invalid.

If noise increased through the harmonic spectrum of a cell’s response to complex patterns, this might partially account for the kind of discrepancy shown by Campbell and Robson (1968); they explicitly assumed that noise was similar for different harmonics. We show here some increase in response variance, or noise, through the harmonic spectrum, but that this is minor. Nevertheless, much energy in MC cell responses is concentrated in higher harmonics (to the 10th harmonic and beyond), and this would imply a significant increase in noise. We estimated the decrease in signal-to-noise ratio that might be expected for squarewave gratings based on the data curves in Fig. 8. For MC cells and achromatic gratings, the increase in noise through the harmonic spectrum would be anticipated to increase thresholds by a factor of 1.4. This is substantial but less than the factor of 2 found by Campbell and Robson (1968), and results of other authors. However, a proper analysis of this issue would require elaboration of a full model for detection, including, for example, a peak (or peak to trough; see below) detector with a fixed temporal window. We have constructed such models for temporal modulation (Lee et al. 2007), but such an analysis is beyond the scope of the current paper.

A further assumption in most psychophysical analyses is linearity near threshold. In the high-contrast results shown here, linearity held to a first approximation, but with some deviations. One distortion is thresholding nonlinearity due to the impossibility of negative firing rates. We estimated MC cell contrast gain for the sharp response peak evoked of squarewave stimuli. For MC cells and achromatic modulation, mean contrast gain was 15.8 imp/s% contrast (n = 5). Maintained firing of MC cells is ~5 imp/s, as in Table 1 (Troy and Lee 1994), and so rectification effects on response waveforms are likely to be present event at 1% contrast. This contrast level is in the threshold range for many of the above psychophysical studies. Response rectification will abolish negative-going responses. This would not affect a simple peak detector but would affect a peak-to-trough detector (Lee et al. 2007). The importance of all these considerations remains uncertain; in any event, the relation of physiological responses to psycho-
physical detection of complex waveforms is more complex than expected.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

B.C., B.B.L., and D.C. conception and design of research; B.C., B.B.L., and D.C. performed experiments; B.C. and B.B.L. analyzed data; B.C., B.B.L., and D.C. interpreted results of experiments; B.C. and B.B.L. prepared figures; B.C., B.B.L., and D.C. drafted manuscript; B.C., B.B.L., and D.C. edited and revised manuscript; B.C., B.B.L., and D.C. approved final version of manuscript.

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