Uniform spatial spread of population activity in primate parafoveal V1

Chris R. Palmer,* Yuzhi Chen,* and Eyal Seidemann

Department of Psychology and Center for Perceptual Systems, University of Texas at Austin, Austin, Texas

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What are the shape and size of the region in primate V1 that processes information from a single point in visual space? This region, a fundamental property termed cortical point image (CPI) (McIlwain 1986), represents the minimal population of V1 neurons that can be activated by a visual stimulus and therefore has important implications for population coding in the cortex. Previous indirect attempts to measure the CPI in macaque V1 using sparse microelectrode recordings resulted in conflicting findings. Whereas some early studies suggested that CPI size is constant throughout V1 (e.g., Hubel and Wiesel 1974), others have reported large changes in CPI size in parafoveal V1 (e.g., Van Essen et al. 1984). To resolve this controversy, we used voltage-sensitive dye imaging in V1 of fixating monkeys to directly measure the subthreshold CPI and several related properties across a range of parafoveal eccentricities. We found that despite large changes in other properties of the retinotopic map, the subthreshold CPI is approximately constant and extends over ~6 × 8 mm^2. This large and invariant CPI ensures a uniform representation of each point in visual space, with a complete representation of all visual features in V1, as originally proposed by Hubel and Wiesel (1974). In addition, we found several novel and unexpected asymmetries and anisotropies in the shapes of the CPI and the population receptive field. These results expand our understanding of the representation of visual space in V1 and are likely to be relevant for the representations of stimuli in other sensory cortical areas.

visual cortex; cortical point image; receptive field; cortical magnification factor; voltage-sensitive dye imaging
in the CPI, CMF, and pRF and significant asymmetry in the pRF.

METHODS

Three monkeys (Macaca mulatta) were used in this study. Our general methods for VSDI in behaving monkeys have been described in detail elsewhere (Chen et al. 2006, 2008). All procedures were approved by the University of Texas Institutional Animal Care and Use Committee and conformed to National Institutes of Health standards.

Task and Visual Stimulus

Each trial began when the monkey achieved fixation in a small window (<2° full width) around a 0.1 × 0.1° central fixation point displayed against a uniform gray background. After initial fixation, a circular Gabor patch [a sine wave grating in a circular 2-dimensional (2-D) Gaussian window] was presented for 200 ms. The monkey received a reward at the end of the trial provided its gaze did not leave the fixation window.

The position of the Gabor patch varied pseudorandomly from trial to trial among a total of five to eight positions that spanned a range of eccentricities; all positions were fully represented in the imaged area. Each stimulus position was repeated in at least 10 trials. In different experiments, stimulus position was changed along horizontal or vertical trajectories. The contrast of the Gabor patch was 100%, and it was in sine phase. Stimulus position varied across experiments (mean eccentricity, 2.87°; range across experiments, 1.89–4.74°); the space constant of the Gabor patch (σy7) was 0.167° (i.e., half-width at half-height = 0.2°), the spatial frequency was 2.76 cycles/°, the bandwidth was 1.25, and the orientation was horizontal.

Visual stimuli were presented on a gamma-corrected high-end 21-in. color display (Sony Trinitron GDM-F520) at a fixed mean luminance of 30 cd/m². The display subtended 20.5 × 15.4° at a viewing distance of 108 cm and had a pixel resolution of 1,024 × 768, 30-bit color depth, and a refresh rate of 100 Hz.

Voltage-Sensitive Dye Imaging

The experimental techniques for optical imaging with VSDI in awake, behaving monkeys have been described elsewhere (Arieli et al. 2002; Seidemann et al. 2002; Slovin et al. 2002). Briefly, in the current study we used the voltage-sensitive dyes RH1838 and RH1691 (Shoham et al. 1999) and a high-speed camera (Imager 3001; Optical Imaging, Germantown, NY) to image changes in membrane potentials. The imaged area was 14.4 × 14.4 mm² in the first monkey and 16 × 16 mm² in the second and third monkeys. The camera collected 512 × 512 pixels at 110 Hz.

Behavior Monitoring and Data Acquisition

Behavior monitoring and data acquisition were performed by a personal computer running software for real-time neurophysiological recordings from alert animals (Tempo; Reflective Computing, St. Louis, MO). This computer interfaced with an infrared eye tracker (Dr. Bouis Devices, Karlsruhe, Germany) for high-quality analog eye position monitoring. Eye position signals were sampled with 16-bit resolution at 250 Hz. The data acquisition computer also interfaced with the system used to acquire optical imaging data (Optical Imaging). In addition, this computer controlled a dedicated personal computer with a high-end graphics card that was used for stimulus presentation.

Analysis of the VSDI Signal

VSDI analysis followed five steps. 1) We normalized the response at each location by the average fluorescence at that location across all trials and all frames; this step reduced the effect of uneven illumination and uneven staining. 2) We subtracted from the mean response at each location the average response in blank trials and then removed the mean residual response in the 100-ms interval prior to response onset; this step reduced the effect of sources of noise such as the heart beat artifact and other slow and widespread fluctuations that dominate the variability in the VSDI signals. 3) We averaged the VSDI response during the integration period (36–236 ms after stimulus onset). 4) We removed outlier trials (see below) from each block (<1% of trials). 5) We fitted the averaged VSDI response with a 2-D Gaussian function plus a DC component; the DC component reflected residual widespread fluctuations that were inconsistent across trials and across experiments and were therefore removed. Effective pixel size (after 8 × 8 binning) was ~250 × 250 μm². Outliers (step 4) were trials whose response at the peak position during the integration period was more than 5 SD away from the mean integrated response for that stimulus condition. Outliers, which were very rare, were caused by excessive movements of the animal. All data analysis was performed in Matlab (MathWorks).

In four experiments with a horizontal stimulus configuration, the stimuli closest to the vertical meridian produced a V1 response that partially overlapped the response in V2, reducing our confidence in the measurement of the space constant of the CPI in the direction approximately normal to the V1/V2 border. σmaj. Therefore, we excluded from our σmaj database 8 data points where the stimulus was 0.75° or less away from the vertical meridian. In those cases, we were still able to confidently measure the space constant of the CPI in the direction approximately parallel to the V1/V2 border, σmaj.

Details regarding the methods used for estimating the three key retinotopic properties (CPI, CMF, and pRF) are described in RESULTS and summarized in Table 1.

Analysis of Change in Retinotopic Properties as a Function of Eccentricity

Previous studies have shown that changes in CMF and pRF with eccentricity over a large range of eccentricities in primates V1 are well fitted by power functions (e.g., Adams and Horton 2003; Schwartz 1977; Van Essen et al. 1984). In the current study, we only examined a narrow range of eccentricities in parietofoveal V1. We therefore elected to use a simple linear regression to fit our results. Our goals in fitting the data were 1) to determine whether the three retinotopic properties (CPI, CMF, and pRF) vary significantly with eccentricity in parietofoveal V1 and 2) to estimate the anisotropy in these retinotopic properties.

To estimate the anisotropy (e.g., anisotropy in CMF in vertical vs. horizontal directions; see Fig. 2A), we fitted the two data sets simultaneously with a common slope term, allowing only the offset term to vary between the two sets. The magnitude of the anisotropy was then taken as the ratio of the fitted values at the middle of the eccentricity range.

We used a simple permutation procedure to determine if the slope of the regression was significantly different from zero. For each data set (e.g., PRF size as a function of eccentricity), we randomly shuffled the size values among all of the eccentricity values and fitted the shuffled data with linear regression to obtain a null distribution of slopes (n = 1,000). The slope of the original data set was considered significantly different from zero if it fell outside of the 95% confidence interval of the null distribution of slopes.

RESULTS

The goal of the current study was to characterize quantitatively three interrelated properties that influence the spatial distribution of V1 population responses to visual stimuli: the cortical point image (CPI), the population receptive field (pRF), and the cortical magnification factor (CMF). To achieve
this goal, we used VSDI in fixating monkeys to directly measure the spatial profiles of V1 population responses to small Gabor patches while stimulus position was varied systematically in the visual field. In each experiment, stimulus position was varied along the horizontal (e.g., Fig. 1A) or the vertical (e.g., Fig. 3A) direction. Gabor stimuli are advantageous for studying V1 responses because they are localized in both space and Fourier domains. In addition, they strongly

Table 1. Description of retinotopic variables and space constants

<table>
<thead>
<tr>
<th>Abbreviation (Units)</th>
<th>Brief Description</th>
<th>Relationship to Other Retinotopic Variables</th>
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<tbody>
<tr>
<td>Retinotopic variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical point image</td>
<td>CPI (mm)</td>
<td>Cortical region that is activated by a point in visual space</td>
</tr>
<tr>
<td>Cortical magnification factor</td>
<td>CMF (mm/°)</td>
<td>Distance in cortex that corresponds to a given distance in visual space</td>
</tr>
<tr>
<td>Population receptive field</td>
<td>pRF (°)</td>
<td>Aggregate receptive field of a local population of neurons</td>
</tr>
<tr>
<td>Space constants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Space constant of cortical response</td>
<td>σp (mm)</td>
<td>Size of response profile in V1 to a visual stimulus</td>
</tr>
<tr>
<td>Space constant of stimulus</td>
<td>σST (°)</td>
<td>Size of Gabor patch</td>
</tr>
<tr>
<td>Space constant of population receptive field</td>
<td>σpRF (°)</td>
<td>Size of the pRF after removing the effect of stimulus size</td>
</tr>
<tr>
<td>Space constant of position tuning function</td>
<td>σPT (°)</td>
<td>Size of the function plotting neural response amplitude as a function of stimulus distance from location corresponding to the peak</td>
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Fig. 1. Spatial response profiles measured from V1 in the right hemisphere of monkey 1 in one voltage-sensitive dye imaging (VSDI) experiment. A: stimulus coordinates in degrees of visual angle, with fixation point at the origin. Blue rectangle corresponds to blue arc in B showing the approximate locations of the representation of the various stimulus positions in V1. The white arrow and red line correspond to the arrow and line in B. B: top: image of cortical vasculature with scale and landmark information. Red rectangle indicates the 10 × 10-mm² region of interest for the response maps below. Bottom: spatial distribution of response amplitudes for different stimulus positions. The center coordinates of each stimulus are given above each panel. To compute response amplitude, the response at each site is time-averaged during a short interval after target onset (36–236 ms) and then averaged across repetitions (n = 10). Ellipsoids show 1 standard deviation (SD) of the 2-dimensional (2-D) Gaussian function used to fit the VSDI response maps. Colored squares (1.25 × 1.25 mm²) denote the center of the 2-D Gaussian function. The pink square added to the panel labeled “−3.25, −1.95” and the blue square added to the panel labeled “−1.75, −1.95” illustrate the change in cortical magnification factor (CMF) across eccentricity. In both cases, the 2 stimuli are 1 deg apart in visual space, but the responses are further apart for the pair of stimuli closer to the fovea, indicating that the CMF decreases with eccentricity. All squares are superimposed in the panel at bottom right. C: CMF as a function of eccentricity. Black curve is a linear function fitted to data. D: size of the cortical point image (CPI) as a function of eccentricity approximately parallel (squares; solid line) and perpendicular (diamonds; dashed line) to the V1/V2 border. E: orientation (relative to a line parallel to V1/V2 border) of the major axis of the CPI as a function of eccentricity. Dashed line denotes the mean orientation difference from a line parallel to V1/V2 border. Ant, anterior; Lat, lateral; ∆F/F, response amplitude.
activate V1 neurons, which are highly sensitive to contour orientation (Hubel and Wiesel 1959).

Consider the spread of activity in a patch of cortex in the dorsal portion of macaque V1 (such as the one shown in Fig. 1B) in response to a small Gabor stimulus. The spread of V1 population response depends on two factors: first, the direct projection of the stimulus to V1’s retinotopic map, and second, the size and scatter of V1 neurons’ receptive fields (RF) in this region.

At any given location in V1, there is significant heterogeneity in RF size (Jones et al. 2001; Levitt and Lund 2002; Snodderly and Gur 1995; Van Essen et al. 1984). In addition, there is significant scatter in RF centers (Dow et al. 1981; Hubel and Wiesel 1974; Van Essen et al. 1984). Thus the pRF, which is the combined RF of a local population of V1 neurons, is likely to be larger than the average RF of the single neurons at that location. The pRF has an important effect on the response spatial profile, particularly for small stimuli, because neurons that fall outside of the direct mapping of the stimulus to the cortex will continue to respond to the stimulus as long as it overlaps their RF. Therefore, the larger the pRF, the larger the response spread will be.

For small local stimuli, the spatial spread of the response can be approximated by convolving the direct retinotopic projection of the stimulus to V1 with the CPI. The CPI is approximately equivalent to the pRF expressed in units of millimeters of cortex. Under the assumptions that the pRF can be approximated by a 2-D Gaussian and that the pRF and CMF are approximately constant within the activated region, the response profile in V1 to a small stimulus with a 2-D Gaussian contrast envelope (such as a Gabor patch) will also be a 2-D Gaussian with a space constant $\sigma_R$ (in mm) given by

$$\sigma_R \approx \sqrt{(\alpha_{ST} \cdot \text{CMF})^2 + \sigma_{CPI}^2} \quad (1)$$

where $\sigma_{ST}$ (in °) is the space constant of the stimulus, CMF (in mm/°) is the local cortical magnification factor, and $\sigma_{CPI}$ (in mm) is the space constant of the CPI. The space constant of the CPI can be approximated by $\sigma_{CPI} \approx \sigma_{pRF} \cdot \text{CMF}$, where $\sigma_{pRF}$ (in °) is the space constant of the pRF (see Table 1 for a list of all retinotopic variables and space constants). The first item under the square root captures the contribution of the stimulus to response spread (the direct projection of the stimulus to the retinotopic map). The second item under the square root captures the contribution of the CPI to response spread, which dominates $\sigma_R$ when the stimulus is smaller than the pRF (see Seidemann et al. 2009 for additional discussion). Importantly, Eq. 1 implies that the response in the cortex has a minimal spread that is determined by the product of the size of the pRF and the CMF.

This results section is divided into two parts. In the first part, we characterize the CPI by directly measuring the 2-D spatial profile of V1 responses to Gabor patches at different positions. Specifically, we ask whether CPI size depends on eccentricity or remains constant in parafoveal V1. In the second part, we characterize the pRF by measuring VSDI response at a single V1 location as a function of the position of the Gabor patch in visual space. In both parts, we also examine in more detail the shapes of the CPI and the pRF, looking specifically for possible anisotropies and asymmetries.

We imaged V1 in 11 experiments from 3 hemispheres of 3 monkeys, with monkey 1 contributing 5 experiments and 36 stimulus positions (sites), monkey 2 contributing 2 experiments and 13 sites, and monkey 3 contributing 4 experiments and 19 sites (total of 68 sites). Because we found no systematic differences between the results from the three monkeys, data from all monkeys were combined. Most main findings were also replicated separately in each monkey (exceptions are noted).

Characterizing the CPI in V1

Our first goal was to characterize the CPI using VSDI and determine its dependency on eccentricity. VSDI allowed us to estimate the CPI directly by measuring the spatial distribution of V1 responses to small Gabor patches. This direct approach contrasts with the previous electrophysiological studies that had to compute the CPI indirectly by computing the product of the average RF size with the estimated CMF (Dow et al. 1981; Hubel and Wiesel 1974; Van Essen et al. 1984). As discussed above (Eq. 1), the spread of V1 responses can also be affected by the direct projection of the stimulus to the cortex, which depends on the CMF. Therefore, our first step was to measure the CMF. We then proceeded to examine the CPI.

CMF depends on eccentricity and direction. VSDI allowed us to directly measure the response to stimuli that fall within a limited region of the visual field. The imaged regions of cortex represented a wedge-shaped region in the contralateral visual field, extending from eccentricities of 1.89° to 4.74° (degrees of visual angle) and representing directions about the visual axis of up to 60° (degrees of polar angle) from the lower vertical meridian (270°). Predictably, as we varied the position of the stimulus within this region, the population response moved systematically across the surface of the cortex.

Figure 1 shows VSDI population responses to varying stimulus positions from a typical experiment. The positions of the stimuli in this experiment were varied along the horizontal direction (Fig. 1A). The VSDI response maps for each stimulus position are shown in Fig. 1B. Each VSDI response map was fitted with a 2-D Gaussian function (see METHODS); the dashed ellipsoid in each panel shows the contour of the 2-D Gaussian fit (at 1 σ). As the stimulus moved from the leftmost position toward the vertical meridian, the center of the response moved noticeably from the medial posterior corner of the imaged area to the anterior lateral corner.

To compute the local CMF, we considered the cortical representation of three neighboring visual stimuli. We measured the distance between the cortical representations of the middle stimulus and its two neighboring stimuli. We then plotted the two cortical distances as a function of the distances between the stimuli in visual space. The CMF at the middle position was taken to be the slope of the linear regression for this triplet. Six estimates of CMF are plotted in Fig. 1C. The CMF estimates were fitted with linear regression (see METHODS). Although the individual values of the CMF were noisy, there was a clear trend for the CMF to decrease with increasing eccentricity.

Figure 2A summarizes our CMF measurements across the 11 VSDI experiments. Across both horizontal and vertical configuration experiments, the CMF decreased dramatically from the most foveal location to the most peripheral location ($P < 0.01$,
permutation test combined across horizontal and vertical configurations; see METHODS). However, at each eccentricity, the CMF values along the vertical direction (gray symbols) were larger than the CMF values along the horizontal direction (black symbols), revealing an anisotropy in the CMF along larger than the CMF values along the horizontal direction (gray symbols) were from midpoint between 2.0° and 4.5° eccentricity. CMF values are from midpoint between 2.0° and 4.5° (taken from linear fits in Fig. 2A). For CMF and pRF, the ratio of vertical to horizontal configurations (V/H) is taken from the fitted values at midpoint between 2.0° and 4.5° (Fig. 2B and Fig. 4).

Table 2. Anisotropy in CPI, CMF, and pRF

<table>
<thead>
<tr>
<th>Configuration</th>
<th>CPI</th>
<th>CMF</th>
<th>pRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal</td>
<td>Minor–1.41 mm (0.19 mm)</td>
<td>1.72 mm/°</td>
<td>0.62° (0.11°)</td>
</tr>
<tr>
<td>Vertical</td>
<td>Major–1.95 mm (0.27 mm)</td>
<td>3.72 mm/°</td>
<td>0.44° (0.11°)</td>
</tr>
<tr>
<td>Ratio V/H</td>
<td>1.38</td>
<td>2.16</td>
<td>0.71</td>
</tr>
</tbody>
</table>

As mentioned above, the spatial spread of the cortical response depends on the local CMF. Having measured the CMF, we next turned to measure the CPI.

**CPI is constant across eccentricity and is anisotropic and asymmetric.** To derive the CPI, VSDI responses for each stimulus position were first fitted with a 2-D Gaussian function. To capture potential anisotropies in the spatial response profiles, we included three free parameters: one each for the space constants along the major (\(\sigma_{\text{maj}}\)) and minor (\(\sigma_{\text{min}}\)) axes and one for the orientation of the 2-D Gaussian function (see METHODS).

The spatial response profiles were noticeably anisotropic. In the experiment illustrated in Fig. 1, the mean \(\sigma_{\text{maj}}\) was 2.01 mm and the mean \(\sigma_{\text{min}}\) was 1.55 mm. By removing the contribution of the direct projection of the stimulus from the response profile (Eq. 1), we derived estimates for the CPI along the major and minor directions (Fig. 1D). Because the direct projection of the stimulus to V1 [the product of \(\sigma_{\text{ST}}\) (0.167°) with the local CMF (~3 mm²)] was much smaller than \(\sigma_{\text{ST}}\), the CPIs were almost identical to the response profile values (Eq. 1). In this example experiment, CPImaj (mean = 1.99 mm) was 1.30 times larger, on average, than CPImin (mean = 1.53 mm).

As expected from the anisotropy observed in the CMF (Fig. 2A), where the CMF in the direction parallel to the V1/V2 border was much larger than in the direction normal to the V1/V2 border, the orientation of the major axis of the CPI was nearly parallel to the V1/V2 border (Fig. 1E; mean orientation relative to border = –8.50°; SD = 9.90°, n = 8).

Figure 2, B–D, summarizes our CPI measurements from all VSDI experiments. Across experiments the major axis tended to be oriented parallel to the V1/V2 border (Fig. 2B; mean orientation relative to border = –1.98°, SD = 19.45°, for all stimuli with a ratio CPImaj/CPImin > 1.1, n = 66). The mean space constants of the CPIs were 1.95 mm along the major axis (SD = 0.27 mm, n = 68; Fig. 2C) and 1.41 mm along the minor axis (SD = 0.19 mm, n = 60; Fig. 2D). Importantly, despite large changes in CMF over the same range of eccentricities (Fig. 2A), the size of the CPI did not change significantly as a function of eccentricity (CPImaj: \(P = 0.12\); CPImin: \(P = 0.61\); permutation test combined across horizontal and vertical configurations), providing direct evidence that the CPI is approximately constant in parafocal V1.

The CPI is approximately the product of the pRF and the CMF. Therefore, if the pRFs were isotropic, the anisotropy of the CPI should match the anisotropy of the CMF. However, the average CPI anisotropy (CPImaj = ~1.4 × CPImin) was much smaller than the average CMF anisotropy (CMFV = ~1.9 × CMFH) (Table 2). Part of this difference could be attributed to the fact that the vertical and horizontal directions only approximately correspond to the major and minor directions of the CPI (note progression of squares in Figs. 1B and 3B).
addition, it is possible anisotropy in the pRF contributes to these differences. Specifically, because we used horizontal Gabor patches, it is possible that the observed pRFs tend to be larger in the horizontal direction than in the vertical direction, thus reducing the CPI anisotropy relative to the value expected based on CMF anisotropy. This prediction is verified in the next section (see Fig. 4).

In addition, because the CMF decreases with eccentricity, it is possible that the CPI would show a significant asymmetry along the isopolar direction (toward and away from the fovea).

To test for such asymmetry, we collapsed the VSDI response maps (e.g., Fig. 1B) along the major axis of the CPI (which is close to isopolar) and fitted the 1-D spatial profile on each side of the peak with a separate half-Gaussian function. We found significant asymmetry along CPImaj in the combined data set (mean σ toward fovea = 2.13 mm, SD = 0.48 mm; mean σ toward periphery = 1.80 mm, SD = 0.47 mm; paired t-test, P < 0.01; n = 68). However, the asymmetry was dominated by the data from monkey 1 (mean σ toward fovea = 2.33 mm, SD = 0.33 mm; mean σ toward periphery = 1.66 mm, SD = 0.35 mm; paired t-test, P < 0.01; n = 28): CPImaj was not significantly asymmetric in monkeys 2 (mean σ toward fovea = 2.05 mm, SD = 0.54 mm; mean σ toward periphery = 2.03 mm, SD = 0.42 mm; paired t-test, P = 0.90; n = 13) and 3 (mean σ toward fovea = 1.90 mm, SD = 0.58 mm; mean σ toward periphery = 1.82 mm, SD = 0.54 mm; paired t-test, P = 0.68; n = 19). In the next section, we test for asymmetry in the pRF.

In summary, using direct VSDI measurements of the spatial response profiles, we found that the CPI is approximately constant across eccentricity in parafoveal V1, despite large changes in the CMF. In addition, we found significant anisotropy in the CPI, but less than predicted by CMF anisotropy. Finally, we found that the CPI is significantly asymmetric (larger toward the fovea than toward the periphery) in one of the three monkeys. These results are illustrated schematically in Fig. 6A. In the next section, we shift to measurements of the pRF.

Characterizing the pRF in V1

Our goal here was to determine how the size and shape of the pRF depend on eccentricity. The pRF was estimated by measuring the response amplitude of a local population of neurons as stimulus position was varied. We refer to the amplitudes of the neural response as a function of stimulus distance from the pRF center as position tuning (PT) functions.

PT function is equal to convolving the stimulus with the pRF. Mathematically, the PT size, a larger stimulus would lead to a PT function with a larger size of the pRF but also on stimulus size; for the same pRF size, a larger stimulus would lead to a PT function with a larger space constant than a smaller stimulus. Mathematically, the PT function is equal to convolving the stimulus with the pRF. Therefore, to obtain the space constant of the pRF, σpRF, we removed the effect of stimulus size using the following equation:

$$\sigma_{\text{pRF}} = \sqrt{\sigma_{\text{PT}}^2 - \sigma_{\text{ST}}^2}$$

where σPT is the space constant of the PT function and σST is the space constant of the Gabor stimulus (0.167°). This method was repeated for each stimulus position to obtain an estimate of the pRF size at each stimulus position.

To test whether the pRFs are asymmetrical with respect to the isopolar direction (toward and away from the fovea), we fitted each PT function in Fig. 3C with two half 1-D Gaussian functions, one toward the fovea and one toward the periphery (requiring each half to have at least 2 data points). We then combined the results from all PT functions and fitted each set of pRF sizes as a function of eccentricity [toward the fovea (circles) and toward the periphery (triangles)] with two linear regressions (Fig. 3D) using a common slope (see METHODS). pRF size increased with eccentricity. In this typical example, pRFs measured toward the periphery tended to be larger than the ones measured toward the fovea, suggesting that the pRF is indeed asymmetric.

A summary of pRF size as a function of eccentricity for all of the VSDI experiments is shown in Fig. 4. Given the differences between the CMF and CPI anisotropies, we expected some anisotropy in the pRF. Therefore, we computed pRFs separately for horizontal (black) and vertical (gray) stimulus configurations.

As predicted based on our CPI and CMF measurements, the pRF also showed significant anisotropy. pRF sizes measured with horizontally configured stimuli (mean = 0.62°, SD = 0.11°, n = 38) were significantly larger (unpaired t-test, P < 0.01) than those measured with vertically configured stimuli (mean = 0.46°, SD = 0.14°, n = 30). This result confirms our prediction that the pRF would be larger in the horizontal direction, leading to reduced CPI anisotropy relative to the CMF anisotropy (Table 2). This pRF anisotropy is likely to be related to the horizontal orientation of the Gabor patch used in our measurements (see DISCUSSION).

Each set of pRF sizes as a function of eccentricity was fitted with linear regression (Fig. 4) using a common slope (see METHODS). There was a significant increase in the pRF size with eccentricity for the combined horizontal and vertical stimulus configuration measurements (permutation test, P < 0.01).

We next tested for possible fovea-periphery asymmetry in the pRF. As with the CPI, we only tested for asymmetry for vertically configured stimuli because the vertical direction in our imaging chambers was closer to the isopolar direction. For the cases where we could estimate pRF with the vertically configured stimuli both toward the fovea and toward the periphery, pRF sizes measured toward the fovea (VF) tended to be smaller than pRF sizes measured toward the periphery (VP),
but this effect was not significant (mean $V_F = 0.40^\circ$, SD = 0.10; mean $V_P = 0.46^\circ$, SD = 0.21; paired $t$-test, $P = 0.24$; $n = 13$). This effect was significant when we considered a larger VSDI integration area of $1.25 \times 1.25$ mm$^2$ (mean $V_F = 0.41^\circ$, SD = 0.06; mean $V_P = 0.51^\circ$, SD = 0.18; paired $t$-test, $P = 0.03$; $n = 13$), most likely because the measurements were less noisy with a larger integration area.

Since we obtained estimates of pRF at each eccentricity in the horizontal and vertical directions, we could compare the values of the CPI obtained directly, as described in the previous section, with the expected values of the CPI obtained by computing the product of the measured pRFs with the measured CMFs. The predicted CPI values (right column in Table 2) and the directly measured CPI values (left column in Table 2) are very similar, providing support for our assumptions and demonstrating the reliability of our measurements.

To summarize, we found that 1) pRF size increases with eccentricity; 2) for horizontal stimuli, pRF size is larger in the horizontal direction than in the vertical direction; and 3) pRF tends to be larger when measured toward the periphery than toward the fovea. These results are illustrated schematically in Fig. 6B.

Possible Effect of Eye Movements

Small fixational eye movements could lead to significant biases in our estimates of the CPI and pRF. To test for such an effect, we computed two eye movement metrics: 1) to capture eye movements within trial, we computed the SD of the eye position during stimulus presentation and averaged this value across all trials associated with each stimulus position; 2) to capture the scatter in the average eye position across trials, we measured the distance of the mean eye position during the stimulus presentation interval from the fixation point in each trial and then computed the SD of this offset across all trials associated with each stimulus position. The average values of the “within-trial” metric (0.08 ± 0.02°, $n = 68$ sites) and the “across-trials” metric (0.19 ± 0.08°, $n = 68$ sites) were very small and uncorrelated with target eccentricity (within trial: $r = 0.10$, $P = 0.38$; across trials: $r = 0.04$, $P = 0.71$; Fig. 5). Furthermore, some of this variability was likely to be due to noise in our eye position measurements rather than due to poor fixation. Nevertheless, to determine if the small amount of variability in eye position had an impact on our results, we compared CPI size in sites in which the within-trial or across-trials metrics were above and below their median value across

![Figure 3. Measurements of population receptive field (pRF) in one VSDI experiment from V1 in the right hemisphere of monkey 3. A: stimulus coordinates in degrees of visual angle (same conventions as Fig. 1A). B: spatial distribution of response amplitudes for different stimulus positions (same conventions as Fig. 1B). C: response amplitude ($\Delta F/F$, %) as a function of vertical stimulus position. For each panel, the responses to all stimuli are measured at the center location (colored squares in panel B) for each stimulus position. Data points are fitted with 2 half 1-D Gaussian functions, one for points moving toward the fovea (relative to the location listed at the top of each panel) and one for points moving toward the periphery. D: pRF size as a function of eccentricity, measured toward the fovea (circles; solid curve) and toward the periphery (triangles; dashed curve). Stim, stimulus.](image-url)
The CPI values were not significantly different in these two groups for the within-trial metric (t-test, \( P / H 0.24 \) and \( P / H 0.22 \) for \( / H \) maj and \( / H \) min, respectively; Fig. 5, A–C) and for the across-trials metric (t-test, \( P / H 0.51 \) and \( P / H 0.26 \) for \( / H \) maj and \( / H \) min, respectively; Fig. 5, D–F), demonstrating that our monkeys maintained tight fixation and that fixational eye movements had negligible impact on our result.

**DISCUSSION**

The primary goal of this study was to characterize the size and shape of the CPI in macaque V1 and to determine if and how it varies with eccentricity. We found that, across a range of parafoveal eccentricities, CPI size remains constant, whereas the pRF size increases with eccentricity and the CMF value decreases with eccentricity. We also found significant anisotropies in all three properties, as well as significant asymmetry in the CPI in one of the three monkeys. These results are summarized schematically in Fig. 6. Below, we discuss our main findings and their significance.

**Cortical Point Image**

The CPI is a fundamental property of the representation of visual space in V1. It describes the size and shape of the cortical region in V1 that is activated by a given point in visual space. We found that despite large changes in the sizes of the pRF and CMF with eccentricity, the CPI size is nearly constant across eccentricity in parafoveal V1 (Fig. 2, C and D), suggesting that each point in visual space activates an equivalent amount of cortical machinery, as originally proposed by Hubel and Wiesel (1974). Similar results have been obtained recently using functional MRI in human subjects (Harvey and Dumoulin 2011). These findings are inconsistent with previous studies (Dow et al. 1981; Van Essen et al. 1984) that used microelectrode recordings to estimate the CPI and reported large variations in CPI in parafoveal V1. The discrepancy is likely to be due to the inaccuracies inherent in using sparse microelectrode recordings for measuring retinotopic properties across the cortex and the indirect approximation of the CPI as the product of the pRF and CMF (see Table 2). Additional factors that could have contributed to this discrepancy are the large heterogeneity in RF properties of neighboring single neurons (DeAngelis et al. 1999) and the large individual variability in cortical properties such as local CMF and overall size of V1 (Dow et al. 1981; Van Essen et al. 1984).

Our cranial windows covered a small portion of macaque V1 that represented a limited range of eccentricities. Nevertheless, within this range, we observed an approximately twofold change in CMF and pRF, indicating that the nearly constant CPI is due to neither the limited eccentricity range examined...
with a SD of membrane potentials, pooled within a Gaussian shaped region signal at a given location is equivalent to the weighted sum of study (Seidemann et al. 2010) also showed that the VSDI relationship implies that the CPI and pRF for spiking activity in neurons (reviewed in Priebe and Ferster 2008). This nonlinear relationship between membrane potential and spike rate in single V1 neurons revealed that for high-contrast stimuli, this uniformity might extend to extrastriate cortical areas (Hartve and Dumoulin 2011; Motter 2009).

The large CPI obtained in the present study reflects the dominant contribution of subthreshold responses to VSDI signals. A recent study that examined the quantitative relationship between the VSDI signal and spiking activity in populations of V1 neurons revealed that for high-contrast stimuli, this relationship is described by a power function with an exponent of \(-4\) (Seidemann et al. 2010), similar to the relationship between membrane potential and spike rate in single V1 neurons (reviewed in Priebe and Ferster 2008). This nonlinear relationship implies that the CPI and pRF for spiking activity in V1 are about one-half the values obtained with VSDI. Our study (Seidemann et al. 2010) also showed that the VSDI signal at a given location is equivalent to the weighted sum of membrane potentials, pooled within a Gaussian shaped region with a SD of \(\sim 230\) \(\mu m\). This result implies that the effects of optical blurring, light scattering, and blurring due to the lateral spread of axons and dendrites in the cortex are negligible relative to the size of the CPI. A further analysis of our results suggests that the relationship between VSDI and spiking activity is independent of eccentricity in parafoveal V1 (i.e., the exponent of the VSDI-to-spikes transfer function was indistinguishable between the more foveal and the more peripheral halves of the data set, \(P > 0.9\), bootstrap test). This analysis, therefore, shows that the results reported here using VSDI, and specifically, the invariance of the CPI with eccentricity, are likely to also hold for spiking activity.

Our results show that the VSDI-measured CPI is very large, spanning a region of \(-6 \times 8\) \(mm^2\) of cortex in V1 (this value represents the \(\pm 2\sigma_{\text{CPI}}\) region based on our estimates of \(\sigma_{\text{maj}}\) and \(\sigma_{\text{min}}\); Fig. 2, C and D), a region containing millions of neurons. Based on the relationship between VSDI signals and spiking activity discussed above, we estimate that the CPI of spiking activity spreads over \(-3 \times 4\) \(mm^2\) of cortex. The size of the suprathreshold CPI is therefore sufficiently large to contain the representation of all possible orientations and several ocular dominance columns, as originally proposed by Hubel and Wiesel (1974, 1977) when they introduced the concept of a hypercolumn.

Our estimates of the CPI size are somewhat lower than those obtained in previous studies using VSDI in macaque V1 (Grinvald et al. 1994; Slovin et al. 2002). These previous studies used stimuli that were larger than the stimuli employed here, and they did not measure directly the retinotopic representation in the imaged areas. It is therefore possible that their spread measurements were inflated by the direct retinotopic projection of the stimulus to V1.

The CPI could be dominated by cells with larger RFs, which tend to be selective to lower spatial frequencies (Victor et al. 1994). It is therefore possible that the estimated size of the CPI depends on the spatial frequency (SF) of the stimulus. However, preliminary results from our laboratory suggest that whereas response spread increases systematically with stimulus size as predicted by Eq. 1 (Fig. 7B), SF has negligible impact on response spread and, therefore, on the size of the CPI in parafoveal V1 (Fig. 7A).

Our results suggest that the CPI is asymmetric in V1. The CPI is larger toward the fovea than toward the periphery. This
trend was observed in all three monkeys, but it only reached significance in one monkey. More studies are needed to determine whether this finding is robust. The asymmetry in the CPI could be a by-product of the change in CMF with eccentricity and the asymmetry in the pRF (discussed below).

Population Receptive Field

The pRF is the aggregate RF of a local population of neurons. Consistent with previous studies, we observed a significant increase in pRF size with increasing eccentricity (Dow et al. 1981, 1985; Dumoulin and Wandell 2008; Gattass et al. 1987; Hubel and Wiesel 1974) (Fig. 4). This increase in pRF size with eccentricity counteracts the decrease in CMF with eccentricity, leading to a CPI that is nearly eccentricity invariant.

Our results provide the first evidence that the pRF is asymmetric in parafoveal V1. At a given eccentricity, the pRF was larger on average when tested toward the periphery than when tested toward the fovea. A similar result was observed recently in area V4 (Motter 2009). These results suggest that within the local population of neurons that contribute to the pRF, there is a systematic relationship between RF size and RF center; neurons with larger RFs tend to have RF centers that are more peripheral than neurons with smaller RFs. In addition, it is possible that some foveal/peripheral asymmetry could also be observed in the subthreshold and/or suprathreshold RFs of single V1 neurons. These possibilities should be addressed in future studies.

We find significant anisotropy in the measured pRFs; the pRFs are larger in the horizontal direction than in the vertical direction. This specific anisotropy is likely to be related to the horizontal orientation of the Gabor patches used in our study. Consistent with this possibility, preliminary results from our laboratory suggest that pRF anisotropy depends on stimulus orientation, with the pRF larger in the direction of the stimulus (Chen and Seidemann 2011). These results are likely to be related to the observation that the RFs of individual V1 neurons tend to be elongated along their preferred orientation (Hubel and Wiesel 1962; Jones and Palmer 1987).

Cortical Magnification Factor

Despite the limited range of eccentricities tested in this study, our results reveal significant decreases in CMF with eccentricity in parafoveal V1, consistent with previous studies (Adams and Horton 2003; Daniel and Whitteridge 1961; Dow et al. 1981, 1985; Engel et al. 1997; Hubel and Wiesel 1974; Schwartz 1977; Talbot and Marshall 1944; Tootell et al. 1982, 1988; Van Essen et al. 1984; Yang et al. 2007). In general, the shape of the retinotopic map in V1 appears to be consistent with a log-polar mapping (Adams and Horton 2003; Schwartz 1977; Tootell et al. 1988). As in previous studies, our results demonstrate that the CMF is significantly anisotropic near the V1/V2 border, with CMF being larger in the direction parallel to the V1/V2 border than normal to the V1/V2 border (Adams and Horton 2003; Dow et al. 1985; Tootell et al. 1988; Van Essen et al. 1984). These physiological results are also consistent with anatomic evidence for anisotropy in the extent of horizontal connections in V1 (Malach et al. 1993; Yoshioka et al. 1996).

Conclusion

By combining VSDI in fixating monkeys with quantitative analysis of the spatial distribution of V1 responses to small Gabor patches, we have expanded our understanding of the representation of visual stimuli by populations of neurons in V1. We found that the size of the cortical point image is constant across eccentricity in parafoveal V1, suggesting that each point in visual space is processed by an equivalent amount of cortical tissue in V1. We also observed significant anisotropy in the shape of the CPI and significant asymmetries and anisotropies in the shape of the pRF, as well as preliminary evidence that the CPI is also asymmetric. The uniform representation of each point in visual space by a large and fixed-size population of neurons in V1 is likely to be a general principle of sensory cortical processing and to extend to other sensory modalities.

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Present address of C. R. Palmer: Division of Biological Sciences, University of California, San Diego, CA.

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AUTHOR CONTRIBUTIONS

Author contributions: C.R.P., Y.C., and E.S. conception and design of version of manuscript; E.S. edited and revised manuscript; C.R.P., Y.C., and E.S. approved final version of manuscript.

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