**Title:** Relationship between spontaneous and evoked spike-time correlations in primate visual cortex

**Authors:** Walter J. Jermakowicz\(^1\),\(^5\), Xin Chen\(^1\),\(^6\), Ilya Khaytin\(^1\),\(^5\), A.B. Bonds\(^4\) and Vivien A. Casagrande\(^1\),\(^2\),\(^3\)

**Affiliation:** Departments of \(^1\)Cell and Developmental Biology, \(^2\)Psychology, \(^3\)Ophthalmology and Visual Sciences, \(^4\)Electrical Engineering and Computer Science and \(^5\)Medical Scientist Training Program, Vanderbilt University, Nashville TN USA.

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\(^+\) Address all correspondence and reprint requests to:
Dr. Vivien A. Casagrande
Department of Cell & Developmental Biology Phone: (615) 343-4538
Vanderbilt Medical School Fax: (615) 936-5673
U3218 Learned Lab
Nashville, TN 37232
vivien.casagrande@vanderbilt.edu

\(^6\)Current address: UC Berkeley Department of Molecular and Cell Biology, 145 LSA, Berkeley, CA 94720

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Abstract

Coincident spikes have been implicated in vision-related processes such as feature binding, gain modulation and long distance communication. The source of these spike-time correlations is unknown. Although several studies have proposed that cortical spikes are correlated based on stimulus structure, others have suggested that spike-time correlations reflect ongoing cortical activity present even in the absence of a coherent visual stimulus. To examine this issue we collected single unit recordings from primary visual cortex (V1) of the anesthetized and paralyzed prosimian bush baby using a 100-electrode array. Spike-time correlations for pairs of cells were compared under three conditions: 1) a moving grating at the cells’ preferred orientation, 2) an equiluminant blank screen and 3) a dark condition with eyes covered. The amplitudes, lags and widths of cross-correlation histograms (CCHs) were strongly correlated between these conditions, although for the blank stimulus and dark condition the CCHs were broader with peaks lower in amplitude. In both preferred stimulus and blank conditions the CCH amplitudes were greater when the cells within the pair had overlapping receptive fields and preferred similar orientations rather than non-overlapping receptive fields and different orientations. These data suggest that spike-time correlations present in evoked activity are generated by mechanisms common to those operating in spontaneous conditions.

Keywords: Synchrony, coincident spikes, multi-electrode, JPSTH, jitter correction
Introduction

Correlated spike times have been implicated in vision related processes, such as feature binding (Engel et al. 1990; Gray et al. 1989), providing stimulus detail (Biederlack et al. 2006; Pillow et al. 2008; Samonds et al. 2004; Zhou et al. 2008), gain modulation (Azouz 2005) and long-distance communication (Fries et al. 2001). Correlated spikes may increase the probability of transmission of salient visual information when they synchronously converge onto their targets. The sources of these correlated spike times remain unclear. Several proposals argue that the spike-time correlations are generated by the spatiotemporal properties of stimuli (Biederlack et al. 2006; Engel et al. 1990; Gray et al. 1989; Zhou et al. 2008). Attentional shifts also have been implicated in correlating spike times in awake animals (Fries et al. 2001), yet several studies also have suggested that spike-time correlations simply reflect network architecture and do not necessarily contain information relevant to stimulus processing (Bair et al. 2001; de la Rocha et al. 2007; Lamme and Spekreijse 1998; Palanca and DeAngelis 2005; Shadlen and Movshon 1999). Understanding the mechanisms underlying spike-time correlations is essential for uncovering their functional relevance.

An important step in reaching this understanding is examining the degree to which these spike-time correlations are inherent in the network, and not generated directly by stimulus properties. If spike-time correlations are very similar in stimulus-evoked and spontaneous states, then it is less likely that they carry stimulus information. Examination of the relationship between stimulus-
evoked and spontaneous forms of neural activity, such as spike rate, variance and spike count correlation (Chiu et al. 2002; Fiser et al. 2004; Haider et al. 2007; Kenet et al. 2003) suggests that, instead of directly representing responses to the attributes of a visual scene, stimulus-evoked responses may reflect the modulation of ongoing cortical activity by the stimulus-dependent input signals. Significant correlations have been detected between stimulus-evoked and spontaneous spike-time correlations in primate visual cortex (Bair et al. 2001; Kohn and Smith 2005; Maldonado et al. 2000, 2008), however, a thorough quantitative analysis of these correlations has not been presented. In addition, it is unclear how spontaneous spike-time correlations are related to the relative orientation preference and receptive field overlap of neurons in a pair, information that may be relevant to understanding the source of these correlations.

We examined the relationship of stimulus-evoked and spontaneous spike-time correlations by recording single unit data from bush baby V1 using a 100 electrode array. V1 is ideal for such studies because in few other cortical areas have connections been as well defined (Angelucci et al. 2003; Malach et al. 1993; see Casagrande and Kaas 1994 for review). The bush baby is also well-suited for these studies since its visual system has been intensively studied, the early cortical visual areas are exposed on the brain surface and the brain is lissencephalic, maximizing the number of neurons that can be recorded simultaneously (Bonds et al. 1987; Collins et al. 2005; Debruyn et al. 1993; Jermakowicz et al. 2006, 2007; Xu et al. 2005). This arrangement allowed for
the computation of thousands of cross-correlation histograms (CCHs) for many pairs of V1 neurons. Evoked and spontaneous spike-time correlations were compared by recording spike activity in response to drifting sine wave gratings of a preferred orientation and in response to an equiluminant blank stimulus or to no stimulus, respectively. We compared CCH peak amplitudes, lags and widths in response to these different conditions. In addition, the influence of receptive field overlap and similarity in orientation tuning preference on the CCH peaks was examined for the two conditions. Our data show that there is a strong relationship between spike-time correlations evoked by a preferred stimulus and those evoked by a blank stimulus or dark condition.

Materials and Methods

Physiological preparation and recording

These experiments were performed on three prosimian bush babies (Otolemur garnetti). All experiments were performed under the guidelines of the American Physiological Society and Vanderbilt University Institutional Animal Care and Use Committee under an approved protocol. Each animal received 1.0 mg of dexamethasone roughly one hour prior to surgery to control for potential inflammation. After induction of anesthesia with ketamine (10 mg · kg⁻¹), implantation of two venous catheters and insertion of an exotracheal tube, the animals were placed into a stereotaxic apparatus. Through one of the catheters, 10 mg · kg⁻¹ · h⁻¹ of Propofol was infused continuously to maintain general anesthesia. Through the other catheter, a neuromuscular blockade was initiated
with 3.0 mg Pancuronium bromide (in 5% dextrose lactated Ringers) and then maintained by infusion of the drug at 0.1 – 0.3 mg · kg\(^{-1}\) · h\(^{-1}\). Throughout the experiment the animals were artificially ventilated with NO\(_2\) (75%), O\(_2\) (23.5%) and CO\(_2\) (1.5%) at a rate sufficient to maintain the peak end tidal CO\(_2\) level at around 4%. At the onset of the procedure pupils were dilated with 1% atropine eye drops. Then, to ensure protection of the cornea and render the retina conjugate with the viewing screen 57 cm distant, contact lenses of appropriate power and with artificial 3 mm pupils were applied to the eyes. The optic discs and *areae centralii* (ACs) were plotted via a tangent screen onto a plotting table by back reflection of the retinal image from the tapetum using a fiber optic light source.

An 8 X 8 mm craniotomy was performed and the dura resected over the region corresponding to V1. A digital picture was taken of the cortical surface and a 10 X 10 Cyberkinetics multielectrode array was pneumatically inserted. The array was injected to a depth of about 600 µm (cortical layers 2 and 3) and then the surface and array were covered with 1% agar to prevent dehydration. To remove noise at each channel, spike sorting was performed using a method widely used with this array (Shoham et al. 2003). This spike sorting method models the distribution of waveforms recorded on each channel as a multivariate t-distribution and uses an expectation-maximization algorithm to distinguish spikes from noise on each electrode.

At the end of each experiment the animal was euthanized with an overdose of Sodium pentobarbital and perfused transcardially, first with a saline
rinse and followed by a fixative consisting of 2% paraformaldehyde in 0.1 M phosphate buffer. The brain then was removed and the visual cortex was resected and flattened. After soaking overnight in a 30% sucrose solution, the visual cortical tissue was frozen and 52 µm sections were cut tangentially. Cytochrome oxidase (CO) staining was then performed using methods described previously (Boyd and Matsubara 1996; Xu et al. 2005). For each case, proper placement of the array in V1 was confirmed by observing that the array lay within the CO blob region of the tissue (Fig. S1), which corresponds to area V1 in the bush baby (Xu et al. 2005). All electrode positions were subsequently reconstructed through serial sections (Fig. S2) in order to determine their exact location in V1. Although depth is more difficult to calculate relative to cortical layers in tangential reconstructions several pieces of information helped us. First, 3 holes were made at the edge of the sections to align all sections after cutting. The first section was cut thicker (~150 microns) in order to align blood vessel patterns with digital photographs taken before the insertion of the array. Second, cortical layers show distinct differences in CO staining in any plane of cut with layer 3B showing the patchy CO pattern known as the CO blobs, layer 3C (4B of Brodmann) staining more lightly and layer 4 (4C of Brodmann) showing a more uniform dark CO staining pattern. For CO, layer 5 stains lightly and layer 6 stains more darkly and shows hints of patches that align with the CO blobs in layer 3B. These laminar differences helped us determine depth. Third, we knew, based on prior measurements, the total depth of cortex and the approximate width of each layer and so could calculate the likely layer of the terminal point of
each electrode in the array. Reconstructions showed that no electrode penetrated below layer 4 of cortex and the vast majority were located in layer 3.

**Stimulus conditions**

A 21 inch Sony (Tokyo, Japan) Trinitron monitor with a refresh rate set to 120 Hz was used to present the stimuli. Good orientation tuning (see below) was used as a criterion to select cells for receptive field mapping and was measured with 15 two-second trials of drifting sine wave gratings varying in orientation from 10 - 180° presented at 60% contrast at the preferred spatial (0.5 cyc/deg) and temporal (2.0 Hz) frequencies previously reported for bush baby V1 cells (DeBruyn et al. 1993). These stimuli were interleaved with an equiluminant (73 cd/mm²) blank stimulus. To examine preferred spatial and temporal frequencies of individual neurons, we also tested 20 spatial frequencies from 0.1 to 2.0 cyc/deg and 20 temporal frequencies from 0.5 to 10.0 Hz. The locations of the receptive fields of individual neurons were plotted with a manually controlled bar of light projected simultaneously on a tangent screen and on a plotting table (Fig. S1; see DeBruyn et al. 1993).

After receptive field plotting, stimuli were presented in the following blocks. First, two blocks each with 30 two-second trials consisting of 18 orientations and one blank (interleaved) were presented. Following these two ~ 30 minute blocks the dark condition was presented. For this condition the animal’s eyes were covered with opaque paper, the room lights and monitor turned off and activity was recorded continuously for 10 minutes. This set of two stimulus blocks and a
dark condition then were repeated again in the same order. Finally, at the end of the experiment a fifth stimulus block (identical to block 1) was presented again. Unless otherwise stated, in the Results “blank” stimulus refers to the isoluminant gray screen stimulus.

**Selection of neuron pairs**

Three criteria were used for the initial selection of cells. First, the cell had to produce a vigorous response to hand plotting. Second, the response at the preferred orientation needed to be at least twice that at the non-preferred orientation. Finally, the preferred orientation and spike waveform (Fig. S3) of that cell needed to remain stationary for the duration of the entire recording session (~3.5 hours). These restrictions yielded 135 V1 neurons. From this population we selected only those cells with a minimum spike rate of 2 sp/s in response to the blank stimulus. This fourth criterion yielded a final total of 81 neurons. The average spike rates of these neurons in response to the preferred orientation and blank stimulus did not change throughout each experiment (Fig. S4). Spike-time correlations were examined for all possible combinations of these 81 remaining neurons, yielding 1236 neuron pairs.

In this study, when we discuss the activity of pairs of neurons, “preferred” stimulus is defined as the drifting grating stimulus with an orientation midway between the preferred orientations of each individual neuron in the two neuron pair. This orientation was presented at a spatial frequency of 0.5 cyc/deg and temporal frequency of 2.0 Hz. Although, spatial and temporal frequencies were
not tailored to each pair, the frequencies used were similar to the average preferred spatial (0.54 ± 0.06 cyc/deg; mean ± SEM; 81 neurons) and temporal frequencies (2.22 ± 0.19 Hz; mean ± SEM; 81 neurons) measured for the population. The average difference between the midpoint of the pairs’ spatial frequencies and the 0.5 cyc/deg used for the stimulus was 0.16 ± 0.01 cyc/deg (mean ± SEM; 209 pairs). The average difference between the midpoint of the pairs’ temporal frequencies and the 2.0 Hz temporal frequency of the stimulus used was 0.82 ± 0.06 Hz (mean ± SEM; 209 pairs). Additionally, although the stimulus was not at the preferred orientation for either neuron in the pair (unless the neurons had similar orientation tuning) it was important to use the midway orientation because driving both neurons in the pair to a similar extent reduces artifactual shifts in the CCH time lags that may be caused by changes in response onset for each neuron (Maldonado et al. 2000; Nowak et al. 1999). For this study, the average difference in orientation between the preferred orientations of the neurons in each pair and the orientation of the stimulus used to drive the neurons was 24.6 ± 1.1° (mean ± SEM; 209 pairs).

Quantifying spike-time correlations

Two different correction methods were used to compute CCHs adjusted to take into account correlations caused by changes in spike rate. The method used for the bulk of the analyses in this paper was the jitter correction method (Harrison et al. 2007; Smith and Kohn 2008). This technique is proposed as a more effective method for removing spike-time correlations caused by the
covariation of spike rates because trial to trial variations in spike count are taken into account. Correlations caused by spike interactions on scales greater than the size of the jitter window used (50 msec in this case) are effectively removed. First, raw coincidences are computed by plotting all the coincidences between all spikes within a trial for both neurons with millisecond resolution on a 2000 X 2000 plot (corresponding to the 2000 msec stimulus duration), and the coincidences are then summed across trials. The raw CCH is then obtained by integrating across the diagonal of the plot. For the jitter correction method each trial is divided into 50 msec bins and each spike within each bin is randomly replaced with another spike occurring in that jitter window, but from another trial. This preserves the spike count for each trial and also the neurons’ peristimulus time histograms (PSTHs). The CCHs are then re-computed as described for the raw CCH. To obtain the corrected CCH, the averaged jittered CCHs from one hundred resamples of the data were subtracted from the raw CCH. The data are presented as coincidences per spike (s\(^{-1}\)). Fifty milliseconds was used as the jitter window because most spike-time correlations measured are correlated at scales shorter than this interval (Bair et al. 2001; Samonds and Bonds 2005; Kohn and Smith 2005). In the Results, the widths of jitter-corrected CCH peaks are compared. By definition, the jitter correction method restricts the overall width of CCH peaks. Because this method was used for all examined CCHs, however, this allowed for a fair comparison of the durations of more tightly correlated spiking events. As an additional control, however, CCHs were also computed with 100 msec jitter windows.
The CCH peaks, as well as the orientation tuning curves (described above), were fit with Gaussian curves of the following form:

\[ f(x) = a + b \exp\left(-\frac{(x - \mu)^2}{\nu}\right) \]

Where \( a \) is the offset, \( b \) is the amplitude, \( \mu \) is the mean and \( \nu \) is the variance. The equation was fit by finding the values of the parameters that minimize the least squared error between the equation and the correlation data. These best-fit Gaussian curves were used to examine the amplitude, lag (commonly referred to as latency) and width at half-height of the CCHs. The average \( R^2 \) value of the fits for the preferred and blank stimulus CCHs was 0.68 ± 0.01 (mean ± SEM; 418 CCHs).

Peaks were considered significant if they exceeded the CCH mean by two standard deviations, where CCH mean was measured over the range -100 to 100 msec. Using this criterion 22% of preferred stimulus and 18% of blank stimulus peaks were significant. These significance percentages are consistent with other studies (de Oliveira et al. 1997; Nowak et al. 1999; Maldonado et al. 2000; Samonds et al. 2004). Based on anatomical connectivity not all neurons in V1 are expected to share common connections, however, as a control to examine the influence of using these significance criteria to limit pairs used in the analysis we also examined the relationships of preferred and blank stimulus spike-time correlations using all 1236 pairs (Fig. S5). When all neuron pairs, regardless of whether they met our significance criteria, were analyzed in relationship to orientation preference, no significant relationship was found.
between CCH peak amplitude and relative orientation preference \((P > 0.05,\) one-way ANOVA).

The second method used to correct the CCHs for spike-time correlations caused by the covariation of spike rates was a modification of the joint-peristimulus time histogram (JPSTH) method (Aertsen et al. 1989; Zhou et al. 2008). This method removes correlations locked to the stimulus, however, unlike the jitter-corrected CCHs, influences of events correlated over longer time scales are not removed. Raw coincidences are plotted in the same manner as with the jitter correction method, however, the cross-product of each cell’s peristimulus time histogram is subtracted from the raw JPSTH and normalized by the SD of the PSTHs to remove correlations caused by chance. The magnitude of spike-time correlation is also represented as the number of coincidences per spike \((s^{-1})\). Gaussian curves also were fit to these data. Spike-time correlations measured with this shift predictor were included for comparison with previous studies and as a control for comparing preferred and blank stimulus CCH amplitudes. The analysis of these CCHs is predominantly presented in the supplement. CCHs computed with this method had significantly greater stimulus-evoked peak amplitudes than peaks computed with the jitter method \((17.2 \times 10^{-3} \pm 0.5 \times 10^{-3} s^{-1} vs. 9.6 \times 10^{-3} \pm 0.3 \times 10^{-3} s^{-1}; mean \pm SEM; P < 10^{-23},\) Wilcoxon signed-rank test; 209 pairs). Correlations of preferred stimulus and blank CCH properties for correlograms computed with the JPSTH method are shown in Figure S4.
To compute mean spike rates for neuron pairs, we measured the geometric mean spike rate (GMSR) (Bair et al. 2001). This was measured as the square root of the product of each neuron’s spike rate. Second order linear partial correlation analyses were computed in order to compare correlation coefficients between CCH peak amplitudes of different pairs with GMSR controlled. All variables were z-normalized. Multiple regression analysis was used to compute the residuals of the CCH peak amplitudes controlling for the GMSRs. The partial correlation then represented the correlation of the residuals.

**Results**

*Detection of significant CCH peaks for preferred and blank stimuli*

We examined spike-time correlations computed with jitter correction for all combinations of V1 neurons. Similar to previous studies examining spike-time correlations for neurons within a cortical area (Bair et al. 2001; Bruno and Sakmann 2006; Kohn and Smith 2005; Maldonado et al. 2000; Nowak et al. 1995; Samonds et al. 2005), CCH shapes varied greatly among neuron pairs, but the peaks were generally centered around zero millisecond lag. Figure 1 shows the evoked and spontaneous CCH peaks from the preferred and blank (isoluminant gray screen) stimuli, respectively, computed for a representative neuron pair. Qualitative examination shows that the CCHs of this pair had peaks at similar lags, but the blank CCHs had lower amplitudes and broader widths at half-height than the preferred stimulus CCHs. Below we describe efforts to quantify these observations for the population.
Using our four criteria for selecting cell pairs for analysis (see Materials and Methods), we examined 1236 pairs from 81 neurons. CCH peaks were considered significant if a Gaussian curve fit to the peak was greater than two standard deviations above the mean of the CCH integrated over lag ranges of -100 to 100 msec (Maldonado et al. 2000; Nowak et al. 1999). Of the V1 pairs, 22% (273/1236) had a significant CCH peak in response to the preferred stimulus with an average difference in peak amplitude and CCH mean of 7.0 X 10^{-3} ± 0.2 X 10^{-3} s^{-1} (mean ± SEM) (Fig. 2A). Eighteen percent (221/1236) of the pairs had significant blank response peaks which on average exceeded the CCH mean by 4.6 X 10^{-3} ± 0.1 X 10^{-3} s^{-1} (mean ± SEM) (Fig. 2B). Seventeen percent (209/1236) of the neuron pairs had significant peaks in response to both stimulus conditions and these neuron pairs were used for the subsequent analyses.

Correlation of CCH peak amplitudes, lags and widths

The relationship of spike-time correlation peak amplitudes for the two stimulus conditions was examined first. The CCH peak amplitudes from pairs in response to the preferred and the blank stimuli were strongly correlated (Fig. 3A; regression slope = 0.294; 95% confidence interval = ± 0.050; R^2 = 0.394; F =
132.3; \( P < 10^{-23} \) with a Pearson correlation coefficient of 0.623. Because studies have demonstrated links between CCH peaks and spike rate (Kruger and Aiple 1988; de la Rocha et al. 2007), we examined whether the correlated changes in geometric mean spike rate (GMSR) (Bair et al. 2001) for pairs between both conditions could account for the strong correlation observed between the CCH peak amplitudes. Similar to the previous reports, the spike-time correlation peaks were significantly but weakly correlated with the pairs’ GMSRs for both conditions (Fig. 3B, C; Preferred stimulus: Pearson correlation = 0.143; regression slope = 1 \( \times 10^{-4} \); 95% confidence interval = \( \pm 1 \times 10^{-4} \); \( R^2 = 0.021 \); \( F = 4.3 \); \( P < 0.05 \); Blank stimulus: Pearson correlation = 0.144; regression slope = 1 \( \times 10^{-4} \); 95% confidence interval = \( \pm 1 \times 10^{-4} \); \( R^2 = 0.021 \); \( F = 4.4 \); \( P < 0.05 \)). In addition, the GMSRs of the cell pairs were significantly correlated between the preferred and blank stimulus conditions (Fig. 3D; Pearson correlation = 0.310; regression slope = 0.091; 95% confidence interval = \( \pm 0.038 \); \( R^2 = 0.096 \); \( F = 22.0 \); \( P < 10^{-4} \)).

The degree to which changes in spike rate might account for the relationship observed between the CCH peaks from both conditions was examined next. The purpose was to determine whether the correlation between the preferred and blank stimulus CCH peak amplitudes was secondary to the correlation observed between the GMSRs for the two conditions. First, we observed that the difference between preferred and blank stimulus CCH peak amplitudes was not significantly correlated with the difference in GMSR for these conditions (Fig. 3E; Pearson correlation = 0.062; regression slope = 2 \( \times 10^{-5} \);
95% confidence interval = ± 2 X 10^{-5}; R^2 = 0.006; F = 0.81; P > 0.30). Second, using z-normalized values we statistically controlled for the effects of spike count on the correlation of CCH peaks between conditions using partial correlation analysis. This test suggests that even with differences in GMSR controlled, the CCH peak amplitudes for the two stimulus conditions were correlated with a Pearson correlation of 0.619, only 1.04% lower than without the GMSR controlled. These data, collectively, suggest that spike-time correlation amplitudes were highly correlated between the responses evoked by the preferred and the blank stimuli and that this relationship was largely independent of changes in spike rate.

FIGURE 3 ABOUT HERE

We next examined whether there were consistent differences in spike-time correlation strength for the two stimulus types (evoked vs. blank). For the 209 neuron pairs, CCHs to the blank stimulus had, on average, 38.5% lower peak amplitudes than CCHs to the preferred stimulus (5.9 X 10^{-3} ± 0.2 X 10^{-3} s^{-1} vs. 9.6 X 10^{-3} ± 0.3 X 10^{-3} s^{-1}; mean ± SEM; P < 10^{-23}; Wilcoxon signed-rank test). For these neuron pairs, the average difference between preferred and blank stimulus CCH amplitudes was 3.7 X 10^{-3} s^{-1} ± 0.2 X 10^{-3} s^{-1} (mean ± SEM), which was significantly different from 0 (P < 10^{-23}; Wilcoxon signed-rank test). However, a similar trend was observed with the neuron pairs’ GMSRs. The blank stimulus GMSRs were on average 56.4% lower than the preferred stimulus
GMSRs (5.01 ± 0.16 sp/s vs. 11.49 ± 0.55 sp/s; mean ± SEM; \( P < 10^{-23}; \) Wilcoxon signed-rank test) with a mean difference of 6.48 sp/s \( (P < 10^{-15}; \) Wilcoxon signed-rank test).

To control for spike rates, the CCHs measured for the two conditions were divided into groups based on similar GMSRs (2 - 16 sp/s in 2 sec intervals) and the peak amplitudes were compared within each group for the two different stimulus conditions (Fig. 4). Thus, in each case preferred and blank stimulus CCHs of similar GMSR were compared. For six of the seven groups tested, the CCH peaks for the blank stimulus had lower mean amplitudes than the CCH peaks for the preferred stimulus. The mean difference between the peak amplitudes for the two conditions was \( 3.0 \times 10^{-3} \pm 0.6 \times 10^{-3} \) s\(^{-1} \) (mean ± SEM; \( P < 0.005; \) Wilcoxon signed-rank test), which represents the difference in preferred and blank stimulus amplitudes with spike rate controlled. This value was 31% of the average CCH peak amplitude seen for the preferred stimulus.

FIGURE 4 ABOUT HERE

The correlation of CCH peak lags was examined next for both stimulus conditions. Similar to other studies examining spike-time correlations for pairs of neurons in the same visual area, the peaks for both conditions generally occurred with near 0 msec lag (0.41 ± 0.19 msec; mean ± SEM) (Kruger and Aiple 1988; Gray et al. 1989; Nowak et al. 1999; Bair et al. 2001; Samonds and Bonds 2005; Kohn and Smith 2005). The lags of the CCH peaks obtained for the
preferred and blank stimuli were highly correlated (Fig. 5A; Pearson correlation = 0.740; regression slope = 0.68; 95% confidence interval = ± 0.08; $R^2 = 0.553; F = 250.1; P < 10^{-23}$). For the neuron pairs examined, the CCH peak lags obtained for the blank stimulus were on average not different from the lags obtained for the preferred stimulus (0.41 ± 0.18 msec vs. 0.42 ± 0.19 msec; mean ± SEM; $P > 0.50$; Student t-test). The mean difference in lag between the preferred and blank stimulus peaks of each pair was 0.003 ± 0.132 msec (mean ± SEM), not different from 0 msec ($P > 0.80$; Wilcoxon signed-rank test). Thus, the CCH peak lags were strongly correlated with no consistent difference in peak position between the two conditions.

CCH widths also were strongly correlated for the two conditions (Fig. 5B; Pearson correlation = 0.543; regression slope = 0.49; 95% confidence interval = ± 0.10; $R^2 = 0.294; F = 86.6; P < 10^{-23}$). When examined for the 209 neuron pairs, the CCHs were 14.5% wider in response to the blank stimulus compared to those evoked by the preferred stimulus (16.77 ± 0.42 msec vs. 14.65 ± 0.46 msec; mean ± SEM; $P < 0.001$; Wilcoxon signed-rank test). When preferred stimulus CCH widths were subtracted from blank stimulus CCH widths for the same neuron pairs, the average difference was 2.14 ± 0.06 msec (mean ± SEM), which was significantly different from 0 msec ($P < 10^{-4}$; Wilcoxon signed-rank test). To test whether this difference could have been due to changes in spike
rate, we examined the correlation of CCH width with spike rate for the two stimuli. Figures 5 C and D show that CCH widths were not significantly correlated with the spike rates for either condition (Blank stimulus: Pearson correlation = 0.059; regression slope = 0.155; 95% confidence interval = ± 0.356; \( R^2 = 0.004; F = 0.73; P > 0.4 \); Preferred stimulus: Pearson correlation = -0.064; regression slope = -0.054; 95% confidence interval = ± 0.113; \( R^2 = 0.004; F = 0.86; P > 0.3 \)), suggesting that the broader CCHs seen in response to the blank stimulus were not an artifact of changes in spike rate.

As mentioned earlier, use of jitter correction has different effects on events correlated over shorter vs. longer time scales. This may differentially influence the computation of CCH widths for preferred and blank stimulus conditions. To test the effect the correction method had on the comparison of CCH widths for the two stimulus conditions, we first compared the widths of CCHs computed using a jitter window of 100 msec instead of 50 msec. Even with this jitter window, the blank CCHs were 9.4% broader than the preferred stimulus CCHs (17.79 ± 0.51 msec vs. 16.26 ± 0.47 msec; mean ± SEM; \( P < 0.01 \); Wilcoxon signed-rank test). As an additional control, we also compared CCHs measured with shuffle correction. These CCHs also were broader, by 14.6%, for the blank compared to the preferred stimulus condition (Fig. S6; 22.84 ± 0.62 msec vs. 19.93 ± 0.55 msec; mean ± SEM; \( P < 0.001 \); Wilcoxon signed-rank test).

We also asked if the spike-time correlations seen with the blank isoluminant screen might be explained by excitation caused by the luminance (73 cd/mm²) or refresh rate of the screen (120 Hz). Significant spike-time
correlations were detected for the dark condition and these CCH peaks were strongly correlated with the CCHs for the blank stimulus (Fig. S7), showing that the spike-time correlations seen between the blank and grating stimuli were not induced by factors specific to the luminance level or refresh rate of the screen. The dark CCHs also were highly correlated with the CCHs for the preferred stimulus (Fig. S8).

Relationship to relative orientation preference and receptive field overlap

Several previous studies have suggested that spike-time correlation peaks depend on the relative orientation preference and the receptive field overlap of the neurons in the pair (Engel et al. 1990; Gray et al. 1989; Kohn and Smith 2005; Samonds et al. 2004; Schwartz and Bolz 1991; Ts’o et al. 1986). To further examine the spike-time correlations evoked by preferred and blank stimuli, we next determined whether the correlations for both conditions showed a similar dependence on orientation preference or receptive field overlap between the cell pairs.

To test the effect of orientation tuning on the spike-time correlations, we correlated CCH peak amplitude with the difference in each neuron’s orientation preference (Fig. 6A). CCH peak amplitudes showed a significant correlation with similarity in orientation preference for both the preferred (Pearson correlation = 0.403; regression slope = 1 X 10^{-4}; 95% confidence interval = ± 5 X 10^{-5}; R^2 = 0.162; F = 40.3; P < 1 X 10^{-4}) and blank stimuli (Pearson correlation = 0.239; regression slope = 3 X 10^{-5}; 95% confidence interval = ± 2 X 10^{-4}; R^2 = 0.060; F =
Although the strong spike-time correlations observed among pairs preferring similar orientations in response to the preferred stimulus could have been due to a higher spike rate given our testing method (see Materials and Methods), this explanation would not account for the same pattern observed for the pairs in response to the blank stimulus. Additionally, the difference in average peak CCH amplitude for the preferred vs. blank stimuli was significantly correlated with similarity in orientation preference (Pearson correlation = 0.199; regression slope = $1 \times 10^{-5}$; 95% confidence interval = ± $5 \times 10^{-6}$; $R^2 = 0.040$; $F = 9.3$; $P < 0.01$). Thus preferred stimulus CCH amplitudes deviated from the spontaneous amplitudes most when both neurons were driven well by the stimulus. This difference in CCH peak amplitude was also correlated with similarity in orientation preference even when GMSR was controlled with partial correlation analysis (Pearson correlation = 0.192; 3.5% lower than without GMSR controlled). This result suggests that it is not only the presence of the drifting grating that correlates spike times, but also its orientation relative to the preferred orientations of the neurons in the pair.

FIGURE 6 ABOUT HERE

Next, the effect of receptive field overlap on the spike-time correlations for both conditions was examined (Fig. 6B). CCH amplitude showed a significant correlation with receptive field overlap for both the preferred (Pearson correlation = 0.381; regression slope = $1 \times 10^{-4}$; 95% confidence interval = ± $1 \times 10^{-5}$; $R^2 = 0.04$).
0.145; $F = 21.1; P < 1 \times 10^{-4}$) and blank stimuli (Pearson correlation = 0.21; regression slope = $3 \times 10^{-5}$; 95% confidence interval = $\pm 2 \times 10^{-5}$; $R^2 = 0.048; F = 9.1; P < 0.01$). Thus, both evoked and blank spike-time correlations are affected by the degree to which neurons in a pair share receptive field space and orientation preference.

**Discussion**

In this study we asked whether spike-time correlations seen in pairs of primate V1 neurons that are driven by a moving grating of preferred orientation were similar or different from the correlations seen between these same cell pairs when responding spontaneously to a blank stimulus or to no stimulus. Strong correlations were observed between these conditions in the amplitudes, lags and widths of their CCHs. These relationships were strongest for cell pairs whose receptive fields overlapped and that preferred a similar orientation. Below we consider the significance of these key findings in light of results published by others.

**Comparison with previous studies**

Although a number of investigations have detected significant spike-time correlations in spontaneous cortical activity, results reported have been conflicting. In some cases spike-time correlations were shown to be as strong or stronger for the spontaneous than for the preferred stimulus condition (Bair et al. 2001; Cardoso D'Oliveira et al. 2000). In other cases, investigators have
reported the reverse, namely that correlations were weaker in the blank condition (Maldonado et al. 2000, 2008; Nowak et al. 1999; Kohn and Smith 2005). One difference between the current study and others is that we controlled for spike-time correlations caused by spike counts using a more conservative approach, the jitter correction method. This difference is important because the jitter correction method takes into consideration the trial by trial covariation in neuron spike counts and therefore is a more reliable correction technique than the more commonly used shuffle corrector (Aertsen et al. 1989). By using the jitter correction we were able to examine spike-time correlations without the influence of loosely-correlated events. Removing such events is important because slow cortical oscillations in activity have been heavily documented in resting and anesthetized brains (Vincent et al. 2007; for review see Faisal et al. 2008).

Another difference between the current study and previous studies is that we directly compared the blank stimulus responses of cell pairs that had overlapping receptive fields and preferred the same orientations with those that did not. This distinction was not made in other studies (Bair et al. 2001; Cardoso D’Oliveira et al. 2000; Maldonado et al. 2000, 2008; Nowak et al. 1999; Kohn and Smith 2005). Visual cortex spike-time correlations are significantly stronger for preferred compared to non-preferred stimuli (Gray et al. 1989; Kohn and Smith 2005; Samonds et al. 2004; Zhou et al. 2008). This difference could also account for our finding that spike-time correlations for cell pairs in response to their preferred stimulus were significantly stronger than those evoked by the blank stimulus. Regardless, our study demonstrates that spike-time correlations under
blank stimulus conditions show a strong similarity to those under preferred stimulus conditions. So why is this so?

 Sources of spike-time correlation

That the underlying circuitry of the visual cortex promotes spike-time correlations is not very surprising considering the important role that these correlations appear to play during normal cortical development. In the developing brain, waves of spontaneous correlated firing have been observed among retinal ganglion cells specific to each eye and this patterned activity helps properly guide the development of these cells’ axons into a laminar pattern within their thalamic targets (Ramoa et al. 1988; Stellwagen and Shatz 2002; Vislay-Meltzer et al. 2006). Cells that fire together tend to wire together, a relationship mediated by the NMDA receptor (Constantine-Patton and Cline 1998; Vislay-Meltzer et al. 2006). Disruption of the correlated activity, or of the activity of this receptor, severely perturbs the normal development of the visual cortex (Kleshevnikov et al. 1997; Volgushev et al. 1997; Voronin et al. 1996).

Several features of the cortical circuit have been implicated in correlating spikes. Gap junctions correlate neuronal spike times and their knockout in the mouse reduces this correlation (Christie et al. 2006). Both feedforward (Alonso et al. 1996; Castelo-Branco et al. 1998) and feedback (Silito et al. 1994) pathways have properties that correlate spike-times among functionally-related populations of neurons. In addition, specific subsets of neurons, such as
interneurons (Nomura et al. 2003; Merriam et al. 2005), astrocytes (Fellin et al. 2004) and layer 5 “chattering cells” (Gray and McCormick 1996) have been implicated in generating spike-time correlations. Even when retina (Trong and Rieke 2008) and cortex (Reyes et al. 2003) are removed and examined in vitro without the influences of visual stimuli or other brain areas, strong spike-time correlations are detected.

Nevertheless, evoked responses from a preferred stimulus generate greater correlation than is seen under the blank or no stimulus conditions suggesting that stimulus properties must be taken into account even when the role of spike counts can be ruled out. Obviously stimuli cannot generate responses without an underlying cortical architecture, which makes it difficult to separate the relative influences of both stimulus and circuitry particularly given the tight coupling in the visual system. Feedforward pathways from the retina are in a good position, however, to modulate early cortical spike-time correlations. Cells in retina, LGN and V1 have strongly correlated spike times that could be related to properties of the stimulus (Dan et al. 1998; Meister et al. 1995; Pillow et al. 2008; Samonds et al. 2004; Zhou et al. 2008). In addition, correlated spikes among neurons in retina and LGN are more effective at eliciting spikes in their higher area targets than spikes not correlated in time (Alonso et al. 1996; Singer and Bedworth 1973). Thus, appropriate stimulus features may add to the correlation of spike times that reflect underlying circuitry.

*Functional implications*
Neuronal response amplitudes exhibit large trial-to-trial fluctuations (Bair et al. 2001; Kohn and Smith 2005; Zohary et al. 1994; for review see Ermentrout et al. 2008; Faisal et al. 2008). Two processes that have been heavily implicated in this variability are the initial state of a neuron or circuit, and noise present in the signal (for review see Ermentrout et al. 2008; Faisal et al. 2008). Our data support the idea that, like other neuronal response properties (Chiu et al. 2002; Fiser et al. 2004; Haider et al. 2007; Kenet et al. 2003), spike-time correlations present during spontaneous cortical activity are strongly related to the spike-time correlations evoked by a preferred stimulus. What remains to be determined, however, is what influence this ongoing activity has on the output of the system. Because the spike-time-correlations we observed for the preferred stimulus were similar to, albeit stronger than, the correlations evoked by the blank stimulus, it could be argued that the stimulus-evoked spike-time correlations are simply a reflection of background activity and not involved in coding per se especially given the relative rarity of spike-time correlations.

Alternatively, it can be argued that ongoing cortical activity is required for proper cortical coding. Activating neurons is a metabolically expensive process and maintaining a proper level of neuron activity is essential for normal brain function (Lennie, 2003). The brain may have evolved the ability to use noise to keep neurons near their firing thresholds (For review see Faisal et al. 2008). To the detriment of some of the information in the signals, the ongoing activity would ensure propagation of weaker signals, those that would otherwise not yield downstream responses. In fact, correlated spikes have been suggested to yield
supralinear responses in the neurons onto which they converge (Alonso et al. 1996; Azouz 2005; Bruno and Sakmann 2006; Castelo-branco et al. 1998).

Given that our spike times correlated to a significantly greater degree than expected by chance for the blank stimulus, it is likely the spike-time correlations have an impact on the responsiveness of the circuit during normal viewing conditions. If two neurons are tuned to different orientations, for example, our study and others show that it is difficult to generate significant spike-time correlations (Gray et al. 1989; Kohn and Smith 2005; Samonds et al. 2004; Zhou et al. 2008). Even when summed with the spontaneous correlations, these spikes may not have an influence on downstream spiking. Neurons tuned to similar orientations, however, will produce strong spike-time correlations in response to the preferred stimulus and, when summed with the strong correlations already present in spontaneous activity, may have a pronounced effect on downstream neuron responses.

Clearly, much remains to be determined to understand the potential roles of these spike-time correlations in visual processing. Since neurons have specific responses to correlated spike times during development and in adulthood (Alonso et al. 1996; Bruno and Sakmann 2006; Castelo-branco et al. 1998; Fujisawa et al. 2008; Kleshevnikov et al. 1997; Volgushev et al. 1997; Voronin et al. 1996), it is possible that the brain has evolved sparse coding mechanisms to utilize correlated spikes as information-rich codes that efficiently propagate through the visual hierarchy (Lennie, 2003; Pillow et al., 2008; Vinje
and Gallant, 2000; Weliky et al. 2003). It remains to be determined, however, whether this information can be propagated usefully beyond V1.

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Figure legends

Fig. 1. Examples of CCHs for preferred and blank stimulus conditions. A. CCH in response to the preferred stimulus. B. CCH from the same neuron pair in response to the blank stimulus. The CCHs were corrected with the jitter correction method. Upon qualitative examination it was evident that whereas the lags were similar for these two CCHs, they had different amplitudes and widths. For this neuron pair, the blank stimulus CCH was lower in amplitude (0.0079 s\(^{-1}\) vs. 0.0134 s\(^{-1}\)) and broader in width (17.2 msec vs. 9.8 msec) than the preferred stimulus CCH. Blue - preferred stimulus CCH; Red - blank stimulus CCH.

Fig. 2. Detection of significant spike-time correlation peaks. A. Each point in the plot represents the CCH peak and mean (over range -100 to 100 msec) for one of the 1236 pairs used in the analysis. Twenty-two percent (273/1236) of the pairs had significant CCH peaks with an average difference in peak correlation and CCH mean of 7.0 \(\pm\) 0.2 \(\times\) \(10^{-3}\) s\(^{-1}\) (mean \(\pm\) SEM). Open black circles - all neuron pairs; Closed blue circles - pairs with significant preferred stimulus peaks. The plot in the upper right corner integrates the lower plot along the diagonal. This diagonal plot demonstrates what proportion of pairs had significant spike-time correlations relative to the total number of cell pairs. The plot’s x-axis represents peak correlation - mean correlation. White bars - all pairs; Blue bars - significant peaks in response to the preferred stimulus. B. Eighteen percent of the pairs (221/1236) had significant CCH peaks in response to the blank stimulus.
exceeding noise by $4.6 \times 10^{-3} \pm 0.1 \times 10^{-3}$ s$^{-1}$ (mean ± SEM). Open black circles - all neuron pairs; Closed red circles - pairs with significant blank stimulus peaks; White bars - all pairs; Red bars - significant peaks for the blank stimulus.

**Fig. 3.** Correlation of preferred stimulus and blank CCH peak amplitudes.  

A. Each point represents the CCH peak amplitudes for one of the 209 pairs that had significant spike-time correlation. The CCH peak amplitudes were strongly correlated for the preferred and blank stimuli (Pearson correlation = 0.623; regression slope = 0.294; 95% confidence interval = ± 0.040; $R^2 = 0.394$; $F = 132.3$; $P < 10^{-23}$).  

B. Preferred stimulus CCH peak amplitudes were correlated with the GMSRs of these pairs (Pearson correlation = 0.143; regression slope = $1.0 \times 10^{-4}$; 95% confidence interval = ± $4 \times 10^{-5}$; $R^2 = 0.021$; $F = 4.3$; $P < 0.05$).  

C. CCH amplitudes and GMSRs were also correlated for the blank condition (Pearson correlation = 0.144; regression slope = $1 \times 10^{-4}$; 95% confidence interval = ± $1 \times 10^{-4}$; $R^2 = 0.021$; $F = 4.4$; $P < 0.05$).  

D. Similarly the pairs’ GMSRs were significantly correlated between both stimulus conditions (Pearson correlation = 0.310; regression slope = 0.091; 95% confidence interval = ± 0.038; $R^2 = 0.096$; $F = 22.0$; $P < 10^{-4}$).  

E. The difference in CCH amplitude for the preferred and blank stimulus CCH amplitudes was not significantly correlated with the difference in GMSRs for the two conditions (Pearson correlation = 0.062; regression slope = $2 \times 10^{-5}$; 95% confidence interval = ± $2 \times 10^{-5}$; $R^2 = 0.006$; $F = 0.81$; $P > 0.30$), suggesting that the correlation of CCH amplitudes was independent of changes in spike count.
**Fig. 4.** CCH peak amplitudes for preferred vs. blank stimuli with GMSR controlled. The pairs were divided into seven groups based on GMSR ranging from 2 to 16 sp/s in 2 sp/s intervals. Each point in the lower plot represents the average CCH amplitude for all preferred stimulus pairs with GMSR at a given range and average CCH amplitude for all blank stimulus pairs with GMSR at the same range. Six of the seven groups tested had CCH peaks to the blank stimulus that were, on average, lower in mean amplitude than the CCH peaks in response to the preferred stimulus. The diagonal plot displays the distribution of the differences obtained from subtracting the blank CCH amplitudes from the preferred stimulus CCH amplitudes. The x-axis of this plot represents preferred stimulus CCH amplitude - blank stimulus CCH amplitude. The mean difference between the preferred and blank stimulus CCH peak amplitudes for these groups was significant, $3.0 \times 10^{-3} \pm 0.6 \times 10^{-3} \text{s}^{-1}$ (mean ± SEM; $P < 0.005$; Wilcoxon signed-rank test), which accounted for 31% of the spike-time correlations observed for the preferred stimulus. This analysis included 145 preferred stimulus CCHs and 209 blank stimulus CCHs.

**Fig. 5.** Correlation of CCH peak lags and widths, at half-height, for preferred and blank stimuli.  
**A.** The lags of the CCH peaks were strongly correlated between preferred and blank stimulus conditions (Pearson correlation = 0.740; regression slope = 0.68; 95% confidence interval = ± 0.08; $R^2 = 0.553$; $F = 250.1$; $P < 10^{-23}$).  
**B.** CCH widths were strongly correlated between the two stimulus conditions
(Pearson correlation = 0.543; regression slope = 0.49; 95% confidence interval = ± 0.10; R² = 0.294; F = 86.6; P < 10⁻²³). C. In response to the blank stimulus, spike rate and width at half-height were not significantly correlated (Pearson correlation = 0.059; regression slope = 0.155; 95% confidence interval = ± 0.356; R² = 0.004; F = 0.73; P > 0.4). D. The same was observed for the preferred stimulus (Pearson correlation = - 0.064; regression slope = - 0.054; 95% confidence interval = ± 0.113; R² = 0.004; F = 0.86; P > 0.3), suggesting that the broader blank CCHs were not an artifact of decreased spike rate.

**Fig. 6.** Spike-time correlations for preferred and blank stimuli in relationship to orientation tuning and receptive field overlap. A. CCH peak amplitudes were significantly correlated with similarity in orientation preference for both the preferred (Pearson correlation = 0.403; regression slope = 1 X 10⁻⁴; 95% confidence interval = ± 5 X 10⁻⁵; R² = 0.162; F = 40.3; P < 1 X 10⁻⁴) and blank stimuli (Pearson correlation = 0.239; regression slope = 3 X 10⁻⁵; 95% confidence interval = ± 2 X 10⁻⁴; R² = 0.060; F = 12.6; P < 0.01). On the x-axis, the group labeled 0° contains pairs that differed in preferred orientation 0° and 10°, the group labeled 20° contains pairs differing in preferred orientation by 20° and 30°, etc. B. The relative receptive field overlap of the neurons in the pair was determined by measuring the percentage of each receptive field overlapped by the other field and averaging the two percentages for both neurons. The 50% group contains all pairs that had relative receptive field overlap greater than 25% and less than or equal to 50%. The same holds for the other groups designated
on the x-axis. CCH amplitude was significantly correlated with receptive field overlap for both the preferred (Pearson correlation = 0.381; regression slope = $1 \times 10^{-4}$; 95% confidence interval = ± $1 \times 10^{-5}$; $R^2 = 0.145$; $F = 21.1$; $P < 1 \times 10^{-4}$) and blank stimuli (Pearson correlation = 0.21; regression slope = $3 \times 10^{-5}$; 95% confidence interval = ± $2 \times 10^{-5}$; $R^2 = 0.048$; $F = 9.1$; $P < 0.01$). Preferred stimulus - solid line; Blank stimulus - dashed line.
Supplemental Figure 3

Stimulus block 1

Neuron 1:

Stimulus block 5

Neuron 2:

µV

0

-20

-40

-60

0 500 1000

Time (µsec)

0 500 1000

Time (µsec)
Supplemental Figure 4

The figure shows three separate panels, each representing a different condition labeled as 'Preferred stim.' and 'Blank stim.'.

1. For the first panel, the x-axis represents 'Stimulus block' ranging from 1 to 5. The y-axis denotes the 'Spike rate (sp/s)' ranging from 0 to 30. Each data point is marked with a diamond (blue) indicating 'Preferred stim.' with a significance level of $P > 0.30$.

2. The second panel also plots the spike rate against stimulus block, this time with a $P > 0.40$ significance level for the 'Preferred stim.' data points.

3. The third panel follows the same layout with a $P > 0.30$ significance level for 'Preferred stim.' and $P > 0.10$ for 'Blank stim.'
Supplemental figure 5

A

Preferred stimulus CCH amplitude (s⁻¹)

Blank CCH amplitude (s⁻¹)

$R^2 = 0.202 \quad F = 313.4 \quad P < 10^{-23}$

B

Blank CCH amplitude (s⁻¹)

Difference in orientation preference (deg.)

- Preferred stimulus
- Blank stimulus
Supplemental Figure 7

A

Dark CCH amplitude (s^-1)

Blank stimulus CCH amplitude (s^-1)

R^2 = 0.558  F = 195.5  P < 10^{-23}

B

Dark CCH lag (msec)

Blank stimulus CCH lag (msec)

R^2 = 0.516  F = 165.2  P < 10^{-23}

C

Dark CCH width (msec)

Blank stimulus CCH width (msec)

R^2 = 0.606  F = 238.7  P < 10^{-23}
Supplemental Figure 8

A

Dark CCH amplitude (s⁻¹)

Preferred stimulus CCH amplitude (s⁻¹)

R² = 0.310     F = 69.6     P < 10⁻²³

B

Dark CCH lag (msec)

Preferred stimulus CCH lag (msec)

R² = 0.369     F = 90.7     P < 10⁻²³

C

Dark CCH width (msec)

Preferred stimulus CCH width (msec)

R² = 0.342     F = 80.4     P < 10⁻²³
Figure 1
Figure 2

A

B

All pairs

Significant pref. stimulus peaks

Significant blank stimulus peaks
Figure 3

A

$R^2 = 0.39 \quad F = 132.3 \quad P < 10^{-23}$

Blank CCH amplitude (s$^{-1}$) vs. Preferred stimulus CCH amplitude (s$^{-1}$)

B

$R^2 = 0.02 \quad F = 4.3 \quad P < 0.05$

Blank CCH amplitude (s$^{-1}$) vs. Blank GMSR (sp/s)

C

$R^2 = 0.02 \quad F = 4.4 \quad P < 0.05$

Preferred stim CCH amp vs. Preferred stim GMSR (sp/s)

D

$R^2 = 0.10 \quad F = 22.0 \quad P < 10^{-4}$

Pref - blank CCH difference (s$^{-1}$) vs. Pref - blank GMSR difference (sp/s)

E

$R^2 = 0.01 \quad F = 0.81 \quad P > 0.30$

Pref - blank CCH difference (s$^{-1}$) vs. Pref - blank GMSR difference (sp/s)
Figure 5

A. Blank CCH lag (msec) vs. Pref. stim. CCH lag (msec)

$R^2 = 0.55$  $F = 250.1$  $P < 10^{-23}$

B. Blank CCH width (msec) vs. Pref. stimulus CCH width (msec)

$R^2 = 0.295$  $F = 86.59$  $P < 10^{-23}$

C. Blank CCH width (msec) vs. Blank GMSR (sp/s)

$R^2 = 0.004$  $F = 0.73$  $P > 0.4$

D. Pref. stimulus CCH width (msec) vs. Pref. stimulus GMSR (sp/s)

$R^2 = 0.004$  $F = 0.86$  $P > 0.3$
Figure 6

A

CCH peak amplitude (s^{-1})

Preferred stimulus
Blank stimulus

0 20 40 60 80
Difference in orientation preference (deg.)

B

Receptive field overlap (%)

0 25 50 75 100