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Neural correlates of behavior and stimulus sensitivity of individual neurons and population responses in the primary visual cortex

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Neural correlates of behavior and stimulus sensitivity of individual neurons and population responses in the primary visual cortex

by

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Neural correlates of behavior and stimulus sensitivity of individual neurons and population responses in the primary visual cortex

Christopher Russell Palmer, Ph.D.
The University of Texas at Austin, 2009
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The overall goals of this dissertation were 1) to understand the role that neurons in primate primary visual cortex (V1) play in the detection of small visual stimuli, and 2) to understand the quantitative relationship between the responses of individual neurons and neural population responses in V1. These goals were addressed in experiments with awake, behaving macaque monkeys using electrophysiological and imaging techniques. Initially, I employed ideal observer models to assess V1 neural detection sensitivity in a reaction-time visual detection task and found it to be comparable to the monkey’s detection sensitivity. Using the same detection task, I found weak, but significant, correlations between V1 neural activity and the trial-by-trial behavior of monkeys (choice and reaction time). The conclusion of these studies is that the monkey’s behavior in the detection task was likely mediated by large neural populations. Voltage-sensitive dye imaging (VSDI) is a powerful imaging technique that is well suited for assessing the link between the activity of large neural populations and behavior. VSDI measures changes in membrane potential over a cortical area of 1-2 cm² with high spatial and temporal
resolutions. Using position tuning experiments with VSDI and electrophysiology, I described the relatively unknown quantitative relationships between spiking activity, the local field potential, and VSDI. These relationships were well captured by non-linear transfer functions. Lastly, these experiments also revealed important new findings about the representation of visual space by populations of neurons in V1. In particular, we resolved a long standing debate regarding the size of the cortical point image (CPI), the area of cortex activated by a single point stimulus. We found that the CPI is constant across eccentricity in parafoveal V1, suggesting that each point in space activates an approximately equivalent amount of cortical tissue. In conclusion, the results and analyses described in this dissertation contribute to our understanding of the role that neural populations in V1 play in mediating visual detection, reveal important properties of the representation of visual space by populations of neurons in V1, and provide the first analysis of the quantitative relationship between VSDI and electrophysiological signals.
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<tr>
<td>C₅₀</td>
<td>contrast threshold</td>
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<tr>
<td>CMF</td>
<td>cortical magnification factor</td>
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<td>CP</td>
<td>choice probability</td>
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<tr>
<td>CPD</td>
<td>cycles per degree</td>
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<td>CPI</td>
<td>cortical point image</td>
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<td>CR</td>
<td>correct reject</td>
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<tr>
<td>CRF</td>
<td>contrast response function</td>
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<td>EEG</td>
<td>electroencephalography</td>
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<td>FA</td>
<td>false alarm</td>
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<td>FEF</td>
<td>frontal eye fields</td>
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<td>FFT</td>
<td>fast Fourier transform</td>
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<tr>
<td>fMRI</td>
<td>functional magnetic resonance imaging</td>
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<td>LFP</td>
<td>local field potential</td>
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<td>LIP</td>
<td>lateral intraparietal cortex</td>
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<td>MMRT</td>
<td>minimal motor response time</td>
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<td>MST</td>
<td>medial superior temporal cortex</td>
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<td>MT</td>
<td>medial temporal cortex</td>
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<td>MU</td>
<td>multi-unit</td>
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<td>PPM</td>
<td>posterior probability model</td>
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<td>PET</td>
<td>positron emission tomography</td>
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<tr>
<td>pRF</td>
<td>population receptive field</td>
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<tr>
<td>PSTH</td>
<td>peri-stimulus time histogram</td>
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<tr>
<td>PT</td>
<td>position tuning</td>
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<td>RF</td>
<td>receptive field</td>
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<td>RIM</td>
<td>running integrator model</td>
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<tr>
<td>RMS</td>
<td>root mean square</td>
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<tr>
<td>ROC</td>
<td>receiver operating characteristic</td>
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<td>RS</td>
<td>response spread</td>
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<tr>
<td>RT</td>
<td>reaction time</td>
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<tr>
<td>S₂</td>
<td>secondary somatosensory cortex</td>
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<tr>
<td>SF</td>
<td>spatial frequency</td>
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<tr>
<td>SIM</td>
<td>simple integrator model</td>
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<tr>
<td>SU</td>
<td>single unit</td>
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<tr>
<td>TF</td>
<td>transfer function</td>
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<tr>
<td>V₁</td>
<td>primary visual cortex</td>
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<tr>
<td>V₂</td>
<td>secondary visual cortex</td>
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<tr>
<td>VIP</td>
<td>ventral intraparietal cortex</td>
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<tr>
<td>VSDI</td>
<td>voltage-sensitive dye imaging</td>
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<td>WHH</td>
<td>width at half height</td>
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Chapter 1: General Introduction

This thesis is comprised of seven chapters, including this introduction chapter and a short conclusion chapter. The other chapters are formatted like individual research papers, each with its own Abstract, Introduction, Methods, Results, Discussion, and Conclusion sections. I started by describing the sensitivity of macaque primary visual cortex (V1) neurons in a visual detection task (Chapter 2). In Chapter 3, I assessed neural sensitivity of V1 neurons using dynamic integration models which may improve performance relative to the fixed integration models used in Chapter 2, and which were used to estimate reaction times of neurons that were compared to the monkey’s actual reaction times. In Chapter 4, I investigated neural correlates of behavior, both choice and reaction time, in V1 neurons. Chapter 5 dealt with a comparison of the response properties of single neurons and multi-unit recordings (from small groups of neurons). In Chapter 6, I used position tuning experiments to derive sets of transfer functions describing the relationships between voltage sensitive dye imaging (VSDI) and electrophysiological responses. The position tuning experiments also yielded important results about key properties of the representation of visual space by populations of neurons in V1.

1.1 Detection sensitivity of neurons in primary visual cortex

The first step to understanding the role of neurons in macaque area V1 in perception was to assess neural sensitivity to simple visual stimuli. In Chapter 2, I described a study in which monkeys performed a simple reaction-time visual detection
task and assessed neural sensitivity with an ideal observer model. The monkey had relatively short reaction times, resulting in short, behaviorally relevant stimulus presentation and neural integration times. This is an improvement over previous attempts to characterize neural sensitivity where long, fixed neural integration times may have overestimated neural sensitivity.

The link between the activity of cortical neurons and both perception and behavior has been a central topic of interest for neuroscientists over the past few decades. Numerous studies have provided detailed descriptions of the response of neurons to environmental stimuli. Initially, in the 1960s and 1970s, the focus of research was to determine which neurons were optimally driven by various types of stimuli. Electrophysiological techniques allowed the experimenter to derive the tuning characteristics of single neurons for a large array of stimulus features (spatial and temporal frequency, motion, color, size, contrast, position, etc). Neurons that preferred a narrow portion of the parameter space of a given stimulus feature were said to be selective for (or well tuned to) that feature. Neurons in the auditory cortex were found to be selective for frequency, pitch, and loudness (see Schreiner et al., 2000 for review). Neurons in the somatosensory cortex were found to be selectively driven by stimuli that vibrated over narrow bands of frequencies (Talbot et al., 1968; Mountcastle et al., 1969). Neurons throughout the many visual cortical areas were found to be selective for motion (Hubel and Wiesel, 1962; Dubner and Zeki, 1971), orientation (Hubel and Wiesel, 1962; Henry et al., 1974), binocular disparity (Barlow et al., 1967), spatial frequency (Schiller et al., 1976), and other stimulus features.
In an attempt to go beyond knowing what type of stimulus will drive a neuron (and how narrowly or broadly neurons are tuned), the past two decades have seen sensory physiologists become more systematic with regard to investigating the functional role of cortical neurons in behavioral responses. Of course, stimulus selectivity and sensitivity are most important in the context of behavioral responses. An organism requires reasonable perceptual selectivity for any number of tasks in daily life (i.e. eat the red fruit, but not the not-yet-ripe green fruit; run away quickly when chased by a quick predator, but conserve energy and trot away from a slower predator). Neurons in separate, distinct cortical areas may be selective for (or well tuned to) the same stimulus feature (i.e. V1, V2, and V4 are all selective for orientation, spatial frequency, and color), but it may be the case that the neurons of one cortical area are more likely to influence or drive a behavior in response to a particular stimulus than neurons in another cortical area.

Using carefully selected perceptual tasks has been the key to determining to what extent the responses of a given group of neurons make a contribution to a given behavior. In general, a convincing test of a neuron’s role in driving a behavior requires the experimenter to present a subject with a simple stimulus which will then elicit a simple behavior. The activity of the neuron should be modulated by variations in some stimulus feature as well as be correlated with the subject’s behavioral responses. An example of a simple stimulus is the Gabor patch (used in all of the studies in this dissertation). The Gabor patch is a sinusoidal grating in a Gaussian envelope and has several features which the experimenter can manipulate such as spatial position, size, spatial frequency, temporal frequency (if set to flashing), orientation, contrast, color of the two portions of
the grating (black and white, green and red, etc.), movement direction or velocity, and phase of the grating. Generally all of the features are set to fixed values (corresponding to the neuron’s preferred tuning characteristics) except for one, which the experimenter will systematically vary to modulate neural response and/or subject behavior, which is often characterized with simple binary decisions (e.g. “go”/ “no go”; look left / look right).

A typical experiment will require the subject to view a simple stimulus that varies along one dimension (e.g. orientation) and classify the stimulus somehow (e.g. tilted more or less than 90 degrees) by producing one of two behaviors (i.e. move eyes to the right or left). In this way it is possible to measure not only how sensitive the neuron is to the stimulus (e.g. orientation tuning width), but also how well an outside observer could perform the simple behavioral task just by examining the record of the neuron’s spiking activity for each trial. The outside observer is often referred to as an ideal observer because it can describe the maximum, or ideal, performance possible in the task given the set of neural responses (see Geisler (1989) for a review). The performance of the ideal observer is usually reported relative to the performance of the animal performing the task (i.e. the neuron is less/more sensitive than the animal), though it is also possible to measure the sensitivity of the neuron even if the monkey is not required to produce a behavior in response to the stimulus. Indeed, several studies in a number of visual areas have shown the sensitivity of the subject (a macaque monkey in all of these examples) to be comparable to the average sensitivity of single neurons (Britten et al., 1992; Celebrini and Newsome, 1994; Croner and Albright, 1999; Hernandez et al., 2000; Uka and
DeAngelis, 2003) or the sensitivity of the most sensitive neurons (Vogels and Orban, 1990; Prince et al., 2000; Osborne et al., 2004; Liu and Newsome, 2005; Purushothaman and Bradley, 2005).

One factor that nearly all of the studies mentioned above have in common was that the stimulus was presented for a fairly long time only after which the monkeys were allowed to execute their behavioral decision. One study used 500 ms presentation durations and most of the others used 2000 ms, and spiking activity was integrated throughout these periods. Though many of the tasks in those studies were difficult and required the monkeys to perform near their perceptual threshold, the monkey’s psychophysical performance on many of the tasks could have reached a steady level even if the stimulus presentation times were reduced to 500 ms or less. The most likely effect of using such long stimulus presentation and sensory integration times was that the subjects may not have used the entire duration to make their decision, whereas the ideal observer counting up spikes certainly did use the entire duration. The ultimate result was that neural performance would appear to be artificially high relative to that of the subject. In fact the only study of this type that allowed the subject to respond as soon as it had made a decision is from Cook and Maunsell (2002). Unlike the several studies mentioned above, they found that the average sensitivities of MT and VIP neurons were well below that of the subject. It has yet to be shown that neural sensitivity can be comparable to the subject’s behavioral sensitivity in a reaction time task that uses behaviorally relevant stimulus presentation/neural integration intervals.
At first glance it may be surprising that any individual neuron (on average) could be as sensitive (or perform as well as) the subject in a perceptual task, even a very simple task. If just one neuron can do so well, should it not be the case that two or three or one hundred equally sensitive neurons working together would perform much better? For example, for independent neurons, the signal to noise ratio should theoretically increase as the square root of the number of neurons in the pool. A couple of well documented factors suggest reasons why this is not the case. First of all, when signals from multiple neurons are pooled they are not pooled independently. That is, stimulus related signals as well as common sources of noise are both pooled. The variability (i.e. noise) in the stimulus driven responses between neighboring cortical neurons is weakly correlated (Zohary et al., 1994). Therefore, a significant portion of the variability cannot be averaged out when pooling. This sets a limit on the maximum gain that can be attained by combining the signals of even large groups of neurons. In addition there are other potential reasons why neurons could appear to be so sensitive relative to the monkey. First, most studies assessing neural sensitivity are undertaken using nearly ideal conditions for the neuron, creating a potential bias favoring high neural sensitivity. When setting up a perceptual task, researchers will choose a stimulus that maximally activates the neuron(s) under study, whereas, in general, the subject has no special affinity for the stimulus chosen because the subject’s entire sensory apparatus is tuned for a very wide range of multiple stimulus features. Secondly, the activity of neurons in one cortical area may not be faithfully transmitted through all of the brain areas that are activated en route to a decision being made and executed. That is, high stimulus
sensitivity observed in “early” visual areas like V1 and V2 (or even “later” visual areas like V4 or MT) may be degraded as signals related to the stimulus are passed downstream to (and processed in) decision/motor execution areas.

My goal for the first part of this dissertation, discussed in Chapter 2, was to assess the detection sensitivity of V1 neurons relative to the detection sensitivity of the subject (a macaque monkey) in a visual detection task. Though V1 has been subjected to intense scrutiny over the years, few studies have measured the neural sensitivity of V1 neurons using an ideal observer whose performance could be compared to the monkey’s behavioral performance. In addition, the detection task that the monkeys in this study performed was a reaction time task, where stimulus presentation duration and sensory integration duration were controlled by the monkey’s reaction time. I used a reaction time task hoping to improve on the conventional methodology of most previous single unit stimulus sensitivity studies by attempting to determine neural sensitivity over behaviorally relevant intervals.

1.2 Dynamic integrator models

To assess V1 neural activity recorded during the reaction-time visual detection task described in this dissertation, two general types of ideal observer models were used (a fixed integration model and a dynamic integration model). A fixed integration model with two parameters (a latency variable and a pre-motor execution delay variable) was used for the bulk of the analysis in Chapter 2. In Chapter 3, I discussed three types of dynamic integration models: a simple integrator model; a running integrator model; and
a more complex model that dynamically computed posterior probabilities about the presence or absence of the stimulus.

In Chapter 2, I showed that the assumed motor delay between the decision and movement initiation and the integration duration can significantly impact the observed neural sensitivity. Another important characteristic of an ideal observer model that can critically alter the observed neural sensitivity is the exact means of reading out the spike code. On each trial, spikes can be counted and simply summed or averaged over the entire stimulus presentation interval to assay neural activity. In addition, spikes can be “forgotten” about at a certain rate (usually defined by the tau of an exponential function) as time goes by in the trial. Dynamic ideal observer models (where the integration interval, or the tau of the integrator memory, is free to change) are sometimes preferred for their flexibility and biological plausibility (see Ratcliff and Smith, 2004 for review).

The dynamic models I employed in Chapter 3 served two purposes. First, I wanted to test whether a dynamic integrator model produced higher neural sensitivity than the fixed integrator model, and if so, by how much, and what would that reveal about the two classes of model in general. Second, a dynamic model could be used to generate neural “reaction times” for each trial that could be compared directly with the monkey’s own reaction times for those trials. This additional piece of knowledge may shed light on the link between the activity of V1 neurons and the monkey’s behavior. That is, a high correlation between neural “reaction times” (generated by a realistic dynamic model) and monkey reaction times would suggest that V1 neurons play a
prominent role in driving the behavior observed in the monkey performing the detection task.

1.3 Neural correlates of behavior in primary visual cortex

Ideal observer analyses can be used to assess sensitivity of neurons to a stimulus, but they are limited in what they can tell us about the role of a given brain area in the production of a stimulus driven behavioral response. In Chapter 4, I searched for neural correlates of behavior in macaque area V1 by comparing the variability in neural responses to variability in two aspects of the monkey’s behavior in the visual detection task: choice and reaction time.

Though neurons in a given visual area may be highly sensitive to a certain class of stimuli, it may well be the case that these neurons have minimal impact on behavior driven by those stimuli. Further studies need to be undertaken to determine the role a given visual area plays in generating behavior. There are at least three ways to infer that cortical neurons actually play a causal role in behavior: micro-stimulation, ablation studies, and choice probability analysis.

Neurons in sensory areas can be stimulated directly with micro-stimulation (through the same electrode used to record action potentials from single neurons) during a perceptual task with the intention to alter perception and hence the subsequent behavior. If the neurons being stimulated actually influence behavioral decisions in the task, then changes in behavioral performance (Salzman et al., 1990; Salzman et al., 1992; Celebrini and Newsome, 1995; Ditterich et al., 2003; Moore and Armstrong, 2003; Nichols and
Newsome, 2002; Hanks et al., 2006) or time to decision (Ditterich et al., 2003) may be observed and can be correlated to some aspect of the micro-stimulation such as the strength or timing. Cortical neurons can alternatively be ablated, physically or chemically (see Rorden and Karnath, 2004 for review), or temporarily disabled via chemical (Newsome et al., 1985), thermal (Ponce et al., 2008), optical (Szobota et al., 2007) or genetic (Tan et al., 2006; Smear et al., 2007) methods. Observable behavioral deficits can then reasonably be attributed to neurons from the area which has been disabled. The argument can be stronger if the behavior returns back to baseline after the functionality of the temporarily disabled neurons has been restored. The third way to attribute a behavioral function to cortical neurons is to find significant correlations in the variability in neural activity with the subject’s behavioral variability on a trial-by-trial basis.

Perceptual tasks where the subject is forced to make a binary decision (such as go/no go, or move left/move right) in response to a visual stimulus can be useful in revealing a link between behavior and neural activity. Stimuli that are ambiguous, or weakly informative, can cause behavioral variability from trial to trial, even though the stimulus is identical in every trial. If a neuron in a given cortical area is thought to contribute to driving a particular behavior, then the trial-by-trial variability in the activity of the neuron responding to an identical stimulus should be correlated to the trial-by-trial variability in that behavior. It is important to use a stimulus that optimally drives the cortical area. For example, Britten et al. (1996) used a field of coherently moving dots to activate macaque MT, an area thought to be dedicated to the processing of visual motion; using stimuli that
only varied in color, for example, may not have produced any neural correlates of behavior in MT. They manipulated the level of coherence amongst the movement of the dots (ranging from 100% down to 0% coherence, but fixed within a trial), and the monkeys reported the direction of the coherently moving dots. They found weak but significant trial-by-trial correlations (termed choice probability) between neural activity and the choices reported by the monkeys (dots moving left or dots moving right), even for the condition where the coherence was 0%. Choice probability is a measure of the probability with which an ideal observer could predict the subject’s behavioral choices based on the neural activity in single trials. Significant choice probability has been found in many brain areas (MST - Celebrini and Newsome, 1994; MT - Britten et al., 1996; Dodd et al., 2001; Cook and Maunsell, 2002; Uka and DeAngelis, 2004; Purushothaman and Bradley, 2005; LIP - Shadlen and Newsome, 2001; Roitman and Shadlen, 2002; S2 - de Lafuente and Romo, 2005; V2 - Nienborg and Cumming, 2006). Importantly, significant choice probability has not been found in individual neurons in V1 (Nienborg and Cumming, 2006) or in primary somatosensory (S1) cortex (de Lafuente and Romo, 2005), though significant neural correlates of behavior have been found at the level of population responses in human V1 measured with fMRI (Ress and Heeger, 2003).

Chapter 4 describes the first observation of significant choice probability in individual neurons and small groups of neurons in area V1. As part of my analysis, I also described the dynamics of the rise of the choice probability above chance levels (which was not possible with the poor temporal resolution of the fMRI signal in the Ress and Heeger (2003) study). Knowing the dynamics of the choice probability allows
conclusions to be drawn about whether choice related neural signals are generated in the area of interest (as would be suggested by quickly rising choice probability) or whether the choice related signals could possibly be attributed to feedback from an area further downstream (as would be suggested by choice probability that rose to significance relatively late in the trial, close to the time of the saccade).

Another important aspect of the monkey’s behavior in the visual detection task employed in this dissertation was the speed with which decisions were made. Monkeys were free to react to the stimulus as soon as they detected it, and a large range of reaction times (RTs) were observed. Analyzing the variability in RT could provide another link between neural activity and behavior. If V1 neurons were contributing to driving behavioral responses, then the build up of neural activity should be correlated with RT. Previously, the activity of two visual areas (MT and VIP) has been shown to co-vary with RT (Cook and Maunsell, 2002). The results of Cook and Maunsell (2002) suggested that the variability in the latency of saccades was at least partially accounted for by variability in sensory cortical neurons. This contradicted the conclusion based on recordings from the frontal eye fields made by Thompson et al. (1996) which suggested that saccade variability was due primarily to variability in the motor response preparation stage. The final goal of the research described in Chapter 4 was to examine whether neural activity in V1 accounted for some of the variability in the monkey’s RTs in the visual detection task.
1.4 The relationship between single neurons and multi-unit activity

Of particular interest throughout this dissertation was the outcome of pooling the activity of populations of neurons. In Chapter 5, I focused on two methods to compare the activity of single neurons to that of small groups of neurons (multi-unit activity).

Multi-unit (MU) recordings using a single microelectrode can measure the spiking activity of up to dozens of individual neurons near the electrode tip. In Chapter 2, I reported that MU neural performance was comparable to single unit (SU) performance. Similar observations have been made in other visual areas as well (Liu and Newsome, 2003; Liu and Newsome, 2005; Stark and Abeles, 2007). Also, in Chapter 3, MU was shown to display significant choice probability (ability to predict subject’s choices based on neural responses during the stimulus presentation period) comparable to that of SU. Liu and Newsome (2005) also found SU and MU in area MT to have similar choice probability. The results from Chapters 2 and 3, as well as previous research, suggest much similarity between SU and MU in terms of stimulus sensitivity. In Chapter 5, I attempted to examine the relationship between the SU and MU signals in a more quantitative way.

The first part of this chapter addresses an important question regarding the pooling of neural activity. Is there a minimum number of neurons that when pooled can fully account for the performance of the monkey? Shadlen et al. (1996) attempted to answer this question using a model to account for psychophysical performance, choice probability, and the level of correlation between individual MT neurons (found by Zohary et al. (1994) to be ~0.12). Their analysis suggested that psychophysical
performance could best be accounted for by averaging over pools of at least ~100 neurons. As part of Chapter 5, I discussed a very simple model whereby the activity of up to 33 simulated independent and similarly tuned single neurons was summed and the performance of these simulated pools was assessed with the detection task. For this model I assumed total independence of the neurons (i.e. no weak correlation among neurons as described by Zohary et al., 1994) to describe the maximum improvement that can be observed with pooling.

In the second part of Chapter 5, I tested the hypothesis that the activity of a typical MU cluster was equivalent to the sum of the SU we recorded from in Chapter 2. I used three means of quantifying the SU and MU activity. I examined the contrast threshold of SU and MU to get a sense of the relative sensitivity of each type of measurement. Next, I examined the signal to noise ratio. If the activity of SU is combined linearly, then the MU baseline should equal the sum of the SU baseline and the MU stimulus related activity (i.e. the signal) should equal the sum of the signals from all of its constituent SU. Finally, I computed the average Fano factor for all the SU and MU. The Fano factor is the variance to mean ratio, and ranges from 0.75 to 1.5 (Geisler and Albrecht, 1997; Shadlen & Newsome, 1998; Tolhurst et al., 1983). As the stimulus intensity changes, the Fano factor generally remains constant. Assuming that MU are merely the sum of several independent SU, and that MU do not have a significant non-neural source (i.e. electrical noise), SU and MU should have the same Fano factor. As discussed in Chapter 5, if the SU were correlated, the MU Fano factor would increase linearly with the number of SU contributing to the MU, at a rate proportional to the level
of SU correlation. Overall, the results of Chapter 5 suggest that MU are consistent with
the sum of several weakly correlated SU, most of which are weakly tuned to the stimulus.
In the next chapter I compared both SU and MU to another technique for measuring the
activity of neural population activity, optical imaging with voltage sensitive dyes.

1.5 Spatial spread of V1 population responses and the non-linear relationship
between voltage-sensitive dye imaging and electrophysiological signals

Though optical imaging with voltage sensitive dyes (VSDI) has been used to
make important observations about neural population responses for at least two decades,
the relationship between VSDI and more commonly employed electrophysiological
measurements is poorly understood. In Chapter 6, I addressed the relationship between
the spiking activity of the average SU (as well as MU activity and the local field potential
(LFP)) and VSDI signals in the context of a position tuning experiment. The position
tuning experiment also revealed measurements of three key properties describing the
representation of visual space in V1: the cortical point image (CPI), the cortical
magnification factor (CMF), and the population receptive field (pRF). CPI, CMF, and
pRF were measured over a range of eccentricities and their relationships to one another
were analyzed in detail.

MU and LFP provide two rather different measures of population activity. The
relationship between SU and MU was discussed in detail in Chapter 5. The LFP is
thought to reflect slow wave modulations in neural activity such as synaptic potentials,
voltage-dependent membrane oscillations, and spike after-potentials across 0.5-3 mm of
cortex and it is composed of extracellular voltage fluctuations that are both inhibitory and excitatory in nature (Mitzdorf, 1987; see Logothetis, 2003, 2008 for review). Recently, studies measuring LFP have shown a link between neural activity and stimulus perception (Fries et al., 2002; Pesaran et al., 2002; Siegel and Konig, 2003; Gail et al., 2004; Henrie and Shapley, 2005; Rickert et al., 2005; Scherberger et al., 2005; Kreiman et al., 2006). An analogue of choice probability has been found to be significant in area MT with LFP recordings for frequencies above 40 Hz (Liu and Newsome, 2006). Also, several groups have observed a differential selectivity to specific features of visual stimuli in the gamma band range (typically defined as 30-90 Hz) of the LFP, relative to the lower frequencies (Gray and Singer, 1989; Frien and Eckhorn, 2000; Frien et al., 2000; Fries et al., 2002; Siegel and Konig, 2003; Kayser and Konig, 2004; Henrie and Shapley, 2005; Wilke et al., 2006; Womelsdorf et al., 2006, Belitski et al., 2008). LFP also appears to be a better indicator of the functional magnetic resonance imaging (fMRI) blood oxygen level dependent (BOLD) signal than spiking activity (Logothetis et al., 2001), opening up the possibility of using LFP recordings to speculate about various aspects of the BOLD signal.

There are several imaging techniques that enable imaging of neural populations of at least the same size as those supposedly comprising the LFP signal (0.5 – 3 mm of cortex, Logothetis et al., 2008) such as functional magnetic resonance imaging (fMRI), optical imaging of intrinsic signals, and positron emission topography (PET). However, there are limitations to these techniques (primarily poor spatial or temporal resolutions) which make them ill suited for studies in an area like V1 dealing with both the perceptual
sensitivity of large neural populations and the link between behavior of the subject and population neural activity.

Among current techniques for imaging large cortical populations, VSDI can be particularly useful for studying links between behavior and neural activity. VSDI measures precise changes in membrane potential that are well correlated with intracellular recordings (Tasaki and Warashina, 1976; Petersen et al., 2003). The VSDI signal reflects the activity of axons, dendrites, and cell bodies, and to some extent glia cells (Konnerth and Orkand, 1986). The VSDI signal is linearly related to membrane surface area, and as such, primarily reflects the activity of dendrites, as the sum of dendritic membrane area is many times larger than that of cell bodies and axons. VSDI has high spatial and temporal resolution (see Grinvald and Hildesheim, 2004 for a review), making VSDI a very useful tool for assessing real time dynamics of large neural populations (potential imaging area greater than 15 X 15 mm²). Several previously unobserved phenomenon have been brought to light or confirmed with VSDI including: the velocity (Grinvald et al., 1984; Orbach et al., 1985; Grinvald et al., 1994) and spatial extent of the spread of cortical activity (Grinvald et al., 1994); a measure of the how the spread of activity over cortex is related to the strength of microstimulation (Seidemann, et al., 2002; Slovin et al., 2003); a description of the spatio-temporal characteristics of on-going (spontaneous) cortical activity (Arieli et al., 1995, Tsodyks et al., 1999) and its usefulness in predicting stimulus evoked activity under certain circumstances (Arieli et al., 1996) and the spike train of a single neuron under other circumstances (Tsodyks et al., 1999); the dynamics of orientation selectivity (Sharon and Grinvald, 2002); the
visualization of the neural basis of the “line motion” illusion (Jancke et al., 2004); the development of a sensory map in rat barrel cortex (Petersen et al., 2004); and the performance of a neural population relative to an awake, behaving monkey in a near threshold perceptual task (Chen et al., 2006, 2008).

Surprisingly little work has been done to describe the relationship between the VSDI technique and what has traditionally been the standard measure of neural activity, the spiking activity of the single unit. Grinvald et al. (1994), Jancke et al. (2004), and Sharon et al. (2007) reported that spiking activity comprises a very small portion of the VSDI response, and that most of the spread of the VSDI response across the cortex is driven by subthreshold activity. These studies were limited in that spiking activity was only sparsely spatially sampled. Berger et al. (2007) reported similar results using VSDI and calcium sensitive dye imaging (which is a reasonable proxy for suprathreshold spiking activity) in rat barrel cortex. Arieli et al. (1995) and Tsodyks et al. (1999) described the spiking activity/VSDI relationship in terms of temporal correlations. However they used either a single strong, unchanging stimulus or no stimulus at all (when measuring spontaneous activity) to derive their findings. It remains unclear whether the relationship between the average spiking activity and the average VSDI signal is constant across a range of values of a given stimulus feature (size, contrast, position, etc).

For each experiment in Chapter 6, we recorded electrophysiological and/or VSDI signals while fixating monkeys were presented with stimuli at five to eight positions, spanning a distance from the receptive field center out to a position that no longer drove
neural activity above baseline. The electrophysiology/VSDI relationship was represented by a set of non-linear transfer functions that provided a means to estimate how much average spiking activity or LFP (relative to the maximal response) to expect given a certain level of stimulus-driven VSDI response (relative to its maximal response). The transfer functions indicate that only when the VSDI signal reaches 25-40% of its maximum do the electrophysiology signals exceeded 10% of their maximum. Additionally, the position tuning data lent itself to a thorough investigation of the representation of visual space by populations of neurons in V1.

V1 retinotopy has been examined extensively using electrophysiological techniques. However, because those techniques are limited by very sparse cortical sampling, a number of questions remain unresolved. In Chapter 6, I used VSDI to directly measure three facets of V1 representations of visual space: the cortical point image (CPI), the cortical magnification factor (CMF), and the population receptive field (pRF). CPI, CMF, and pRF were measured over a range of eccentricities and their relationships to one another were evaluated in detail.

VSDI is very well suited to resolve an open question about whether the amount of cortex used to process a single point in visual space, referred to as the CPI, changes across the visual field. Until imaging techniques came along that could actually visualize the spread of activity over the cortical surface, all estimates of the CPI were calculated from RF size and CMF measurements that were derived from electrophysiology studies. For example, consider a group of neighboring neurons whose population RF (pRF) center is at 3 degrees eccentricity and is located in an area of cortex where the CMF is ~3
mm/deg. If the space constant of the pRF is 0.8 deg, then a single point stimulus placed in the center of these neurons’ pRF will elicit a spread of activity with a space constant of 2.4 mm in the cortex. This distance is the response spread (RS) which in this case, because the stimulus is not a point, is not quite equal to the CPI. In fact, all previous estimates of the CPI are really just estimates of the response spread (RS) because they do not account for the size of the stimulus. The RS depends both on the stimulus size and on the CPI. Therefore to obtain the CPI (as I did for this chapter), the effect of the stimulus had to first be removed from the RS.

Grinvald et al. (1994) measured the RS directly with VSDI using (1 deg) gratings, and found it to be anisotropic. At eccentricities of 6 to 8 degrees the RS was 2.7 mm along the axis parallel to the V1/V2 border (corresponding to the vertical meridian) and 1.5 mm along the axis perpendicular to the V1/V2 border (corresponding to the horizontal meridian). For their study the RS was defined as the distance at which the mean VSDI response to the stimulus drops to $1/e^{th}$ (approximately 36%) of its maximum amplitude. Slovin et al. (2002) measured the RS to a stimulus almost identical (both were 1 degree gratings at 100% contrast) to that used by Grinvald et al. (1994), but located much more centrally (~3.2 degrees eccentricity compared to 6-8 degrees eccentricity). Slovin et al.’s (2002) values of 6.7 mm parallel to and 5.2 mm perpendicular to the V1/V2 border are larger than those of Grinvald et al. (1994) by a factor of 2-3. For their study the RS was defined as the width at half height (WHH) of the mean VSDI response to the stimulus. VSDI measurements of the RS by Chen et al. (2006) estimated it to be 2.2 mm and 1.54 mm along the axis parallel and perpendicular,
respectively, to the V1/V2 border. For their study, the RS was defined as one standard deviation of a 2-D Gaussian function fit to the mean stimulus related VSDI response. However, the stimulus Chen et al. (2006) used was a Gabor patch ($\sigma = 0.33$ deg) with 25% contrast. The degree of anisotropy found in the three studies measurements of the VSDI RS corresponds well to the anisotropy ratio found in estimates of the CMF (Daniel and Whitteridge, 1961; Van Essen et al., 1984; Tootell et al., 1988; Blasdel and Campbell, 2001; Yang et al., 2007), though there seems to be considerable individual variability in macaque retinotopy (Van Essen et al., 1984; Yang et al., 2007).

Electrophysiology studies by both Dow et al. (1981) and Van Essen et al. (1984) suggest that the RS (again, closely related to the CPI for stimuli that are smaller than the (p)RF) is substantially larger foveally than parafoveally. The estimate from Van Essen et al. (1984) dropped by a factor of four within the range of 2 to 5 degrees eccentricity, but then leveled out somewhat between 5 and 80 degrees eccentricity, whereas the estimates from Dow et al. (1981) claim that the size of the RS/CPI drops at a constant rate out to the far periphery. Alternatively, in electrophysiology studies by Hubel and Wiesel in macaque (1974) and Albus in cat (1975) it was suggested that the RS/CPI remains constant across eccentricity. The VSDI study described in Chapter 6 was the first to directly measure the CPI and its level of anisotropy over a range of parafoveal eccentricities (1.89-4.45 degrees). The results indicate that the CPI does not change significantly with eccentricity. The implication of this important result about a fundamental property of cortical organization is that each point in visual space is represented by an equivalent amount of cortex.
Whereas the CPI is a measure of the area of cortex used to process a single point in visual space, the population receptive field (pRF) is a measure of the area of visual space processed by a population of neurons in a small cortical region. We measured the pRF over the same range of eccentricities as we used to measure the CPI. Like the CPI, it was necessary to remove the effect of the stimulus from the estimate of the pRF. The size of the population of neurons contributing to the VSDI pRF numbers in the tens of thousands. Even though there is considerable overlap of the RF of the individual neurons in that population, there is a significant scatter in their RF center and size. Therefore, we would expect the pRF (by virtue of being composed of neurons with significant scatter in RF size and center) to be larger than the average SU RF.

RF size of SU and MU increases with distance from the fovea by at least an order of magnitude (Dow et al., 1981). The reason for this is that the density of retinal ganglion cells is maximal in the fovea, and falls off by at least an order of magnitude in the far periphery (Rolls and Cowey, 1970). Consequently, the amount of cortical tissue representing foveal vision is very large relative to peripheral vision. The change in visual space representation as a function of eccentricity can be tracked with the cortical magnification factor (CMF). CMF is defined as the distance between any two points in the visual cortex divided by the distance between the two corresponding points in visual space, and is reported in units of mm/deg. CMF generally changes with eccentricity according to a power function having an exponent of ~ -1. This result has been confirmed with electrophysiology (Dow et al., 1981; Van Essen et al., 1984), deoxyglucose autoradiography (Tootell et al., 1988), cytochrome oxidase staining of the
representation of angioscotomas (Adams and Horton, 2003), and VSDI (Yang et al., 2007).

As mentioned above, multiplying the CMF times the (p)RF size reveals the CPI (the extent to which neural activity driven by a single point stimulus will spread over the surface of the visual cortex). Also, as mentioned above, the shape of the CPI is anisotropic. The CMF measured parallel to the V1/V2 border has also been reported to be larger than the CMF measured perpendicular to the V1/V2 border, by an amount that is roughly matched by the CPI anisotropy. If the CPI and CMF anisotropy are not exactly matched, the relationship between the CPI, CMF, and pRF would predict that the pRF is also anisotropic to a degree that would roughly balance the anisotropy in the CPI and CMF. To confirm this prediction about anisotropy, we measured CMF, CPI, and pRF with stimuli arranged in horizontal configurations (roughly corresponding to a cortical representation mapped perpendicular to the V1/V2 border) as well as with vertical stimulus configurations (roughly corresponding to a cortical representation mapped parallel to the V1/V2 border). Also, because the CMF decreases with eccentricity, if the pRF is symmetrical, the CPI would be expected to be somewhat asymmetric (larger measured towards the fovea) along an axis parallel to the V1/V2 border (corresponding to the iso-polar direction). To confirm this prediction about asymmetry, we made separate measurements of the CPI and pRF towards the fovea and towards the periphery.

Our results indicate that CPI, CMF, and pRF all have some degree of vertical/horizontal anisotropy, which approximately balances out in accord with the
known relationship amongst them. We also found significant asymmetry in the CPI (larger towards the fovea) and in the pRF (smaller towards the fovea).

Together, the results from the second part of Chapter 6 indicate that each point in visual space is represented by an equivalent area of cortex, resolving a long standing controversy about a key principle of how the cortex is organized, and illuminate important details of V1 cortical representation of visual space that have not been observed previously.
Chapter 2: Linking Neural and Behavioral Performance in a Reaction-Time Visual Detection Task Using a Fixed Integration Model

Abstract
Perceptual decisions are likely to be based on signals that are provided by populations of neurons in early sensory cortical areas. How these neural responses are combined across neurons and over time to mediate behavior is unknown. To study the link between neural responses and perceptual decisions, we recorded the activity of single units (SU) and multiple units (MU) in the primary visual cortex (V1) of monkeys while they performed a reaction-time visual detection task. We then determined how well the target could be detected from these neural signals. We found that, on average, the detection sensitivities supported by SU and MU in V1 are comparable with the detection sensitivity of the monkey even when considering neural responses during brief temporal intervals (median duration 137 ms) that ended shortly before the monkey’s reaction time. However, we observed systematic differences between the overall shape of the neurometric functions and the monkey’s psychometric functions. Our results suggest that the activity of a large population of V1 neurons is combined sub-optimally by subsequent processing stages to mediate behavioral performance in visual detection tasks.
Introduction

Stimuli in the environment elicit neural responses that are distributed over large populations of neurons in early sensory cortical areas. These distributed signals must then be read out, or decoded, by subsequent processing stages, in order to mediate behavior. The nature of this decoding process, and in particular, the identity and number of neurons that contribute to a given percept and the way signals from these neurons are combined to mediate behavior, are unknown.

Hypotheses regarding the number of neurons that contribute to perception range from a handful of neurons to many thousands of neurons (for review, see Parker and Newsome, 1998). In several prior studies, the sensitivity of the subject was found to be comparable to the average sensitivity of single neurons (Britten et al., 1992; Celebrini and Newsome, 1994; Croner and Albright, 1999; Hernandez et al., 2000; Uka and DeAngelis, 2003) or the sensitivity of the most selective neurons (Vogels and Orban, 1990; Prince et al., 2000; Osborne et al., 2004; Liu and Newsome, 2005; Purushothaman and Bradley, 2005). However, even when the sensitivity of neurons compared favorably with the sensitivity of the monkey, the trial-to-trial correlations between single unit (SU) activity and behavioral choices were found to be weak (e.g., Britten et al., 1996), suggesting that perceptual decisions are based on a large number of neurons (Shadlen et al., 1996).

The current study examines the link between activity of primary visual cortex (V1) neurons and behavioral performance in a visual detection task. Determining the
nature and quality of the signals carried by individual V1 neurons is a prerequisite for understanding how these signals might be combined to guide behavior. A central goal of the current study was therefore to characterize the detection performance of single V1 neurons. In addition, since perceptual decisions are likely to be based on signals from multiple neurons, we determined the detection performance of multi-unit (MU) activity for comparison with both SU and monkey detection performance. In contrast to most previous studies in which neuronal and behavioral performances were compared over a fixed and typically long stimulus presentation interval, in the current study we examined neural responses over a brief interval that ended shortly prior to the monkey’s reaction time (RT), ensuring a more realistic comparison between neural and behavioral performances.

Specifically, we addressed two primary questions: (1) how much task related information is carried by V1 neurons, (2) how similar is the performance of simple models that base their decisions on the activity of V1 neurons to the monkeys’ performance.

**Materials and Methods**

**Subjects and surgery**

Three monkeys (Macaque mulatta) were used in this study. Monkeys underwent two surgical procedures. In the first procedure, a head-restraining device was implanted and two custom-designed recording chambers were positioned over the skull above V1 in both hemispheres. Following a recovery period, the animal went through an extensive
period of training on the visual detection task. Animals were trained using standard operant conditioning techniques where water and juice were used as positive rewards. During training and recording sessions (2-5 hours long) each animal was seated comfortably in a primate chair with its head restrained. Once the animal reached a stable level of performance on the task, a second surgery was performed to prepare the monkey for optical and electrophysiological recordings. In this surgery, a cranial window was opened and the dura was resected and replaced by a transparent artificial dura (Arieli et al., 2002). Within several weeks following this surgical procedure, the animal’s dura healed and formed a tight seal around a silicone ring extending out from the artificial dura, leaving a central region clear for optical and electrophysiological recordings. The chamber was covered by a transparent plastic cover with a small hole plugged by a rubber gasket.

The animals used in this study were also used in voltage sensitive dye (VSD) imaging experiments (e.g., Chen et al., 2006). Some electrophysiological recordings were conducted simultaneously with the imaging experiments but most were conducted in separate sessions. We did not find significant differences in behavioral or neural performance between experiments in which electrophysiological recordings were conducted separately or simultaneously with VSD imaging. In addition, we did not observe any systematic changes in neuronal or behavioral sensitivities as a function of the number of VSD imaging sessions conducted prior to the electrophysiological recordings. These results suggest that VSD imaging does not have a short-term or a long-term effect on behavioral and neuronal detection sensitivities.
All surgical procedures were carried out under deep anesthesia, using strictly sterile techniques, in a dedicated surgical suite. All procedures were approved by the University of Texas Institutional Animal Care and Use Committee and conformed to NIH standards.

**Task and visual stimulus**

Each trial began when the animal achieved fixation in a small window (< 2° full width) around a 0.1° X 0.1° central fixation point displayed against a uniform gray background (Fig. 2.1A, left panel). Following the initial fixation period, the fixation point dimmed (Fig. 2.1A, middle panel). In the target-absent trials (50% of trials), the monkey had to maintain gaze on the fixation point for an additional 1200 ms to receive the reward. In the target-present trials (50% of trials) the monkey was rewarded for making a saccade to the location of the Gabor target. The Gabor target appeared 300 ms after the dimming of the fixation point (Fig. 2.1A, fourth panel) and was removed 300 ms later or upon the monkey detecting the target. To get the reward, the monkey had to make a saccadic eye movement to the target within 600 ms of its onset (but at least 70 ms after target onset), and maintain gaze on the target location for 300 ms.

The parameters of the Gabor patch were adjusted to match the preferred parameters of the recorded SU or multi units (mean eccentricity: 4.23°, range across blocks: 2.0° to 9.2°; mean σ of Gabor patch: 0.37°, range: 0.167° to 0.667°; mean spatial frequency: 1.90 cpd (cycle per degree), range: 0.62 cpd to 4.37 cpd; orientation: no orientation bias seen). These parameters were not changed within a block of trials. Four
to seven contrast levels (minimum 2% up to maximum 50%) were used for the target, encompassing the animal’s detection threshold. Within a block of trials, target-present trials at different contrasts were randomly interleaved with an equal number of target-absent trials.

Figure 2.1
Figure 2.1. Visual detection task. **A,** Monkey initially shifted gaze to a fixation point at the center of the screen. Fixation point then dimmed. Three hundred milliseconds later a target could appear in the periphery. The monkey was allowed to make a saccade to the target location as soon as it had detected the target. Three hundred milliseconds later the target was extinguished, but the monkey could still make a saccade to the target for another 300 ms. **B,** Time line for computing mean firing rates and spike counts. Mean firing rates and spike counts were computed over a period starting 36 ms after target onset and ending 20 ms before the monkey’s saccade to the target [allowing for motor preparation (Motor Prep.) time] or 200 ms [maximal (max) integration time] after target onset, whichever came first. In this example, the rate/count was computed over just the light gray bar. The dark gray bar shows the overlap between the maximal integration interval and the motor preparation interval (black bar). **C,** Psychometric function describing how often the monkey reported the presence of the Gabor target as a function of the contrast of the target. The solid line is the best-fit Weibull function (see Materials and Methods). The dashed vertical line indicates the monkey’s threshold. Note that threshold is defined as the contrast at which performance is 75% correct combined across target-present and target-absent trials. Because the false alarm rate in this experiment was close zero, threshold is the contrast at which the hit rate is ~50%. The horizontal error bar is a 95% confidence interval of the threshold based on a bootstrap analysis (see Materials and Methods). The overall accuracy of the monkey in this experiment is indicated in the figure. Prob., Probability.

Visual stimuli were presented on a gamma-corrected high-end 21” color display at a fixed mean luminance of 30 cd/m². The display subtended 20.5° x 15.4° at a viewing distance of 108 cm, had a pixel resolution of 1024 x 768, 30-bit color depth, and a refresh rate of 100Hz.

**Electrophysiology**

A tungsten microelectrode (0.5-1.5 MΩ, FHC) ensheathed in a protective metal guide tube was lowered to just above V1 through a rubber gasket positioned within a transparent plastic cover sealing the recording chamber. Once the guide tube penetrated the rubber gasket, we advanced the electrode until it extended out from the guide tube by 3-5 mm, and then locked it in place. We then advanced the electrode through the
artificial dura with a hydraulic microdrive (Narishige, Tokyo, Japan) until a single neuron and/or a cluster of MU was isolated. A dual slope/height window discriminator (Bak Electronics, Germantown, MD) was used to isolate spikes from single neurons. A second independent window was used to accept spikes from several neurons, so MU activity could be recorded concurrently with SU activity.

When recording SU and MU simultaneously, spikes from the SU channel were excluded from the events of the multiunit channel. Across experiments, the slope and the delay of the slope/height window discriminator were manually adjusted to maximize the chance of detecting spikes. We used the lower threshold of the height window to control the rate of acceptance of a voltage deflection as multiunit events. The position of this criterion is arbitrary. A high criterion is likely to lead to acceptance of spikes from a small number of single neurons that are near the tip of the electrode. A lower criterion is likely to lead to acceptance of spikes from a larger number of neurons, but potentially also some voltage deflections that are not due to action potentials.

After isolation, we qualitatively analyzed the receptive field (RF) properties of the recorded neuron(s). If recording from both an SU and MU cluster simultaneously, the stimulus was modified to maximize the single neuron responses. This was done using a custom software package (courtesy of G. DeAngelis) that allowed interactive variation of the parameters (location, size, orientation, and spatial frequency) of a sinusoidal grating while monitoring neural responses. Based on the initial analysis of the receptive field properties, we performed a further quantitative assessment using a sine-wave grating presented for 300 ms for a minimum of 5 trials per condition to identify the neuron(s)’
Figure 2.2. Parameters of Gabor target as a function of target eccentricity.  

A, Sigma of Gabor target at various target eccentricities. Solid line is the best-fit regression line, with Pearson correlation ($r$) and its significance values ($p$) noted.  

B, Bandwidth as a function of eccentricity.  

C, Spatial frequency as a function of target eccentricity.
preferred orientation. At some of the sites, we also quantitatively assessed the preferred size (at a fixed spatial frequency of 3 cpd) and then spatial frequency (with size fixed at the preferred value) of the recorded neuron(s). To assess the preferred size and spatial frequency, a block of trials with Gabor patches of various sizes or spatial frequencies was run. The smallest size or lowest spatial frequency that gave the maximal response was used for the target detection block. In general the size increased and the spatial frequency decreased with increased receptive field eccentricity (Fig. 2.2). Bandwidth did not change systematically across eccentricity.

**Analysis of behavioral data**

For a target-present trial, the trial was scored a hit if the monkey made an eye movement to the target within the specified time frame (70 ms to 600 ms after target onset), and the trial was scored a miss if the monkey failed to shift its gaze out of the fixation window. For target-absent trials, the trial was scored a correct rejection if the monkey maintained fixation for the entire length of the trial. The trial was scored a false alarm if the monkey moved its gaze towards the target location. If the animal made a saccade outside of the specified time frame, or made a saccade to a non-target location, the trial was immediately aborted and not used for behavioral or neurophysiological analysis. RTs for hits and false alarms were denoted as the duration of the interval between target onset and the time at which the monkey’s gaze first left the fixation window (en route to the target location).
Behavioral performance was fitted using maximum likelihood estimation by a modified cumulative Weibull function (Green and Swets, 1966):

**Equation 2.1:** \[ P(C) = 1 - (1 - \gamma) \cdot e^{-(C/\alpha)^\beta} \]

where \( P(C) \) is the probability that the subject would report that the target was present as a function of target contrast \( C \), \( \alpha \) and \( \beta \) are the offset and slope terms respectively and \( \gamma \) is the false alarm rate. The detection threshold \( (T) \) was defined as the target contrast at which the monkey was 75% accurate taking into account both the hit and the false alarm rates. The overall accuracy was defined as the rate at which the monkey correctly performed the task across all of the trials: \( \text{accuracy} = \frac{\#\text{hits} + \#\text{correct rejects}}{\#\text{total trials}} \).

Behavior monitoring and data acquisition were performed by a PC running software for real-time neurophysiological recordings from alert animals (Tempo, Reflective Computing, St. Louis, USA). This computer interfaced with an infrared eye-tracker (Dr. Bouis, Karlsruhe, Germany) for high quality analog eye position monitoring. Eye position signals were sampled with 16 bit resolution at 250 Hz. Electrophysiological signals were sampled at 1 KHz. The data acquisition computer also interfaced with the system used to acquire electrophysiological data (Bak Electronics, Mount Airy, USA). In addition, this computer controlled a dedicated PC with a high-end graphics card that was used for stimulus presentation.
**Analysis of physiological data**

**Integration period**

Neural responses were integrated during a short period that started 36 ms after stimulus onset and ended at variable times depending on the monkey’s RT (Fig. 2.1B). We selected 36 ms for the beginning of the integration period because it was approximately the shortest latency of the response to high contrast targets. The default maximal time for the integration interval was 200 ms after stimulus onset. However, if the RT for a trial was less than 220 ms, the integration period ended 20 ms before the monkey initiated the saccade to the target. We ended the integration period 20 ms before the saccade to allow for sufficient time between the formation of a decision and the monkey’s actual eye movement. We refer to this 20 ms period as the minimal motor response time (MMRT). We also considered other possible values of MMRT and maximal integration time. In addition, we compared results obtained with variable integration times with results obtained with a fixed integration time.

**Jackknife procedure**

We used a jackknife procedure to ensure that we did not over-estimate the performance of the ideal observer (see Results). In this procedure, a separate analysis was performed for each of the n trials in an experiment. For each trial, an optimal criterion was established based on the remaining n-1 trials. The criterion was then applied to the spike count/rate value from the single excluded trial. The trial was classified as correct if the spike count/rate exceeded the criterion for a target-present trial, or if it was below the
criterion for a target-absent trial. This procedure was repeated for every trial in an experiment to obtain the neurometric function.

**Bootstrap analysis**

We performed two types of bootstrap tests. In the first test, we determined whether a single parameter (overall accuracy, $T$, $\beta$, or $\gamma$) was significantly different between two functions (psychometric and neurometric). In the second, more stringent, test, we asked whether the overall shapes of the two functions were significantly different, taking into account all the parameters of the neurometric and psychometric functions simultaneously.

To generate new bootstrap samples for the behavioral or the neural performance, each point on the neurometric and psychometric functions was replaced by drawing a random number from a binomial distribution with parameters $n$ and $p$, where $n$ is the number of trials and $p$ is the proportion of trials in which the subject reported that the target was present for that contrast level. The new data points were then fitted with the modified Weibull function to give new estimates for overall accuracy, $T$, $\beta$ and $\gamma$. This procedure was repeated 1,000 times to give distributions of estimates for each parameter. To determine if a given parameter was significantly different between the two functions, the 1,000 bootstrap samples from each function were paired, and the distribution of the differences between them was computed. The $p$-value was estimated as the proportion of the differences that fell below zero (if the median difference was positive), or above zero (if the median difference was negative).
To determine whether the overall shapes of the two functions were significantly different, we combined the three parameters used to describe the neurometric and psychometric functions ($T$, $\beta$, and $\gamma$) into a single variable using linear discriminant analysis (Duda et al., 2001). We then measured the distance (in units of $d'$) between these two distributions. To determine the statistical significance of this distance, we replaced the second function with another binomial draw from the values of the first function. We then used the same method to compute the distance between these two functions. We repeated this analysis 1000 times, to obtain a ‘null’ distribution of distances. The $p$-value for the distance between the two original functions was computed as the proportion of distances in the null distribution that exceeded the measured distance.

To find the criterion that minimizes the difference between the neurometric and psychometric functions, we used the procedure described above to compute $d'$ between the neurometric and psychometric functions for each possible criterion and selected the criterion that minimized $d'$.

**Analysis of eye movements**

We investigated the effects of four indicators of eye movements during the period in which neural responses were averaged: (1) average distance from the fixation point, (2) average distance from the target, (3) average velocity, and (4) maximal instantaneous velocity. The average distances are the mean distance between the center of gaze and the fixation point or the target location during the integration period. The average velocity is the overall distance the eye moved during the integration period divided by its duration.
Instantaneous velocity is the maximum instantaneous velocity of the eye during the integration period.

To determine if eye movements affect the relative neural and behavioral sensitivities, we split each experiment in half, and computed overall accuracy for the half containing the trials with the lower-than-median eye movement values and the half with the higher-than-median eye movement values for each of the four indicators (see Table 2.1). Ten experiments were excluded from this analysis because splitting the data to two halves left too few trials to evaluate the model’s and the monkey’s performances.

**Neuron database**

The results here are based on 62 MU recordings and 33 MU recordings. SU/MU recordings had to meet three criteria in order to be included in our analysis: (1) minimum of 8 repetitions per condition; (2) overall behavioral accuracy within 70%-95% (so that we could reliably estimate the parameters of the psychometric function); (3) stable baseline neural activity across the entire block (discussed below). Of the 55 single neurons that were initially screened, 22 were excluded because isolation was not maintained for long enough to collect a minimum of 8 repetitions per condition. All of the original 78 multi-unit experiments resulted in 8 repetitions per condition. Four experiments were excluded based on the behavioral accuracy falling outside of the accepted range. In addition, the recordings of 12 multi-unit experiments were found to be unstable over time.
To assess the stability of the multi-unit responses across a block of trials, baseline activity for each trial was computed as the spike rate in the 300 ms interval before the fixation point dimmed. Baseline activity was averaged over bins of 10 consecutive trials. Then the trial order was randomly shuffled, and again baseline activity was averaged over bins of 10 consecutive trials. This was done 1,000 times to obtain 95% confidence intervals on the baseline measurement. If a significant number of the original data points (bins of 10 trials) fell outside of the 95% confidence interval, then the block was considered unstable and removed from the database. We used the binomial distribution to determine how many times the data had to fall outside of the 95% confidence interval to be considered significantly unstable.

Table 2.1 – Effect of eye movements on neural and behavioral accuracies

<table>
<thead>
<tr>
<th></th>
<th>50% best</th>
<th>50% worst</th>
<th>Mean Difference</th>
<th>p-value t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Accuracy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>monkey</td>
<td>mean distance from fixation</td>
<td>79.25%</td>
<td>78.50%</td>
<td>0.75%</td>
</tr>
<tr>
<td></td>
<td>mean distance from target</td>
<td>78.45%</td>
<td>79.44%</td>
<td>-0.99%</td>
</tr>
<tr>
<td></td>
<td>mean velocity</td>
<td>78.84%</td>
<td>78.83%</td>
<td>0.01%</td>
</tr>
<tr>
<td></td>
<td>instant. velocity</td>
<td>78.77%</td>
<td>79.15%</td>
<td>-0.38%</td>
</tr>
<tr>
<td>model</td>
<td>mean distance from fixation</td>
<td>74.55%</td>
<td>71.90%</td>
<td>2.65%</td>
</tr>
<tr>
<td></td>
<td>mean distance from target</td>
<td>74.34%</td>
<td>72.54%</td>
<td>1.80%</td>
</tr>
<tr>
<td></td>
<td>mean velocity</td>
<td>73.71%</td>
<td>73.00%</td>
<td>0.71%</td>
</tr>
<tr>
<td></td>
<td>instant. velocity</td>
<td>73.77%</td>
<td>72.41%</td>
<td>1.36%</td>
</tr>
</tbody>
</table>
Results

Monkeys were trained to detect a small, oriented visual target and indicate target presence by shifting gaze to the target location as soon as it was detected (Fig. 2.1A). The target appeared in half of the trials. In the remaining target-absent trials, the monkey was rewarded for maintaining fixation. Target contrast was randomly selected from several contrast levels spanning the monkey’s detection threshold.

While the monkey performed the detection task, we used extracellular recording techniques to measure the activity of SU and MU in V1. The results reported here are based on recordings from 33 SU and 62 MU sites in five hemispheres of three monkeys. To maximize the probability that the recorded neurons would contribute to performance in the task, at each recording site, the stimulus was tailored to match the preferred stimulus parameters of the recorded neuron(s) (see Materials and Methods).

We started our analysis by assessing the behavioral sensitivity of the monkey and comparing it with the detection sensitivity that can be supported by the activity of SU and MU in V1. Next, we compared the shapes of the neurometric and psychometric functions.

Assessing behavioral detection sensitivity

Figure 2.1C shows the behavioral performance of the monkey in one experiment. Each point represents the proportion of trials in which the monkey indicated that the target was present as a function of target contrast. Target contrast of zero represents the half of the trials in which the target was absent. Performance was fitted with a psychometric function (solid black line) derived from a modified Weibull function (Quick, 1974) (see
Materials and Methods). We assessed the detection sensitivity of the monkey with two measures: detection threshold ($T$), which was defined as the target contrast at which performance was 75% correct (combined across target-present and target-absent trials), and overall accuracy (overall percent correct across a block of trials). The monkey’s detection threshold in this experiment is depicted with a vertical dashed line (Fig. 2.1C).

The time it took the monkey to initiate a saccade to the location of the target depended on the target contrast. Figure 2.3A shows the mean RT of the three monkeys at different target contrasts collapsed across all experiments. As target contrast was lowered, average RTs became significantly longer (significance test for regression slope, $p = 0.008$). These results suggest that longer durations are required to reach perceptual decisions regarding the presence of the target at lower target contrasts.

Interestingly, the average RT in target-absent trials (false alarms) was shorter than the average RT at low target contrasts. This difference, however, was due to the fact that in many experiments the monkey made almost no false alarms, and in those experiments RTs tended to be longer. In fact, in the subset of experiments with false alarm rates of above 15%, RTs were very short even at the lowest target contrasts (Fig. 2.3B). In this subset of the experiments, average RTs were indistinguishable in false alarms and in target-present conditions with hit rates comparable to the false alarm rates (paired $t$-test $p$ value = 0.74; $n = 18$). These results suggest that in some experiments the monkey tended to make fast saccades to the target location even in the absence of sufficient sensory evidence. Such “fast guesses” could explain the drop in the average RT in false alarms trials.
Figure 2.3. Mean RTs. A, Mean RTs as a function of target contrast collapsed across all experiments (n = 74). Data points are in the middle of the bin. B, Mean RTs for blocks where the false alarm rate was above 15% (n = 21). RTs at target contrast equal to zero correspond to false alarm trials. Target contrast bins are (0, 2-3, 4-6, 7-10, 11-15, 16-20, 21+). Solid line represents best linear fit of mean RT as a function of log contrast in target-present trials. Error bars are SEM across experiments.

“Fast guesses” could lead to a drop in the monkey’s detection sensitivity. This effect, however, appears to be small. In the two animals with significant false alarm rates, behavioral thresholds in experiments with above the median false alarm rates were not significantly different from behavioral thresholds in experiments with below the median false alarm rates (paired t-test, p > 0.1 for both monkeys). Dynamic integrator models also show signs of “fast guessing” (Chapter 3) and suggest that “fast guesses” may
actually not be guesses, but rather are caused by strong fluctuations in neural activity in the early part of the trial.

Target eccentricities varied across sites from ~2 to ~9º. Across our data set as a whole, behavioral detection thresholds tended to increase with stimulus eccentricity (Fig. 2.4A). This was true despite the fact that the parameters of the visual target were matched to the preferred parameters of the neuron(s) at the recording site, and therefore increased in size and decreased in spatial frequency with increasing eccentricities (Fig. 2.2).

To compare the monkey’s detection sensitivity with the detection sensitivity of SU and MU in V1, we next used an ideal observer analysis that allowed us to evaluate the neural responses with the same metrics used to describe the monkey’s performance.

*Ideal observer analysis of neural detection sensitivity*

We used the responses of one SU site and one MU site as example experiments (Fig. 2.5). Both SU and MU responses in the example experiments increased monotonically with target contrast. We used a simple model based on signal detection theory (Green and Swets, 1966) to quantify the detection sensitivity that could be supported by these neural signals. Specifically, the model allowed spiking activity in single trials to be converted into decisions about the presence or the absence of the target.

Neural responses of SU or MU sites were first integrated over a short temporal window (median duration, 137 ms) that started 36 ms after stimulus onset and ended either 20 ms before the onset of the monkey’s saccadic response, allowing for a minimal motor response time (MMRT), or 200 ms after stimulus onset, whichever occurred first (Fig. 2.1B) (see Materials and Methods).
Figure 2.4. The relationship between target eccentricity and behavioral and neuronal detection thresholds. A, Scatter plot of behavioral thresholds as a function of target eccentricity. Because the target parameters were matched to the preferred parameters of the recorded V1 neuron(s), the size of the target increased with eccentricity and the spatial frequency decreased with eccentricity (Fig. 2.2). B, Scatter plot of neural detection thresholds for the rate model vs. target eccentricity. C, Scatter plot of the ratio of neural over behavioral detection thresholds vs. target eccentricity. Black data points are MU, gray data points are SU. Black lines show the best-fit linear regressions for the MU data and the gray lines show the best-fit linear regression for the SU data. The Pearson correlation coefficient $r$ and its significance value $p$ are indicated in each panel for SU and MU separately. Contr., Contrast.
We initially considered two models for detecting the target from the neural responses in single trials. The first model (summation) used the raw integrated responses to detect the target. In the second model (rate), the integrated responses in each trial were divided by the duration of the integration interval (which varied from trial to trial) in order to obtain an average spike/event rate.

**Figure 2.5**

**Figure 2.5.** Peri-stimulus time histograms from two representative recording sites. *A*, SU. *B*, MU. Neural responses were averaged over repetitions (*n* = 10 for each target contrast; *n* = 50 for target-absent trials). Bin size is 25 ms and data points lie in the middle of the bin period. Vertical blue lines denote stimulus onset (time 0) and offset (time 300 ms). For conditions with at least 4 hits, colored arrows indicate the median RT. Horizontal black lines denote typical times of neural integration. Key shows target contrasts; 0% contrast = target-absent trials. SU and MU recordings are from different sites. sp, spikes.

Spike counts and spike rates were compiled into separate histograms for each target contrast (Fig. 2.6A-*B*, summation; Fig. 2.6C-*D*, rate), with target-present trials
shown as filled bars alongside distributions of an equivalent number of target-absent trials (empty bars). There was almost no overlap between the spike count and spike rate distributions in target-present and target-absent trials at the highest target contrast (top panels, Fig. 2.6A-D). As the target contrast was lowered, significant overlap was seen.

Our primary goal here was to compare the neural sensitivity implied by the distributions in Figure 2.6A-D with the behavioral sensitivity of the monkey. A common measure of the detection sensitivity implied by two distributions is the area under the receiver operating characteristic (ROC) curve (Green and Swets, 1966). This measure, however, cannot be applied to the distributions in Figure 2.6A-D because in our task, the monkey did not know in advance what would be the contrast of the target. Computing a separate ROC value for each contrast is equivalent to allowing the observer to select a different criterion at each contrast. In our task, however, the monkey has to adopt a single criterion that would apply to all target contrasts. We can find the optimal single criterion for the distributions in Figure 2.6A-D by comparing the combined distribution of responses to all target contrasts with the distribution of responses in all target-absent trials (bottom panels in Figs. 2.6A-D). The ideal observer model used a criterion (dashed vertical lines, Fig. 2.6A-D) that minimized the total number of errors (misses plus false alarms). Once the optimal criterion had been selected, it was used to determine what percentage of trials the model would classify as target-present (Fig. 2.6E-F, gray symbols) for each target contrast. The same modified Weibull function that was used to fit the monkey’s behavioral data was used to fit the neural data and construct neurometric functions for the two models (Fig. 2.6E-F, gray curves). From these neurometric
functions we computed the detection threshold and the overall accuracy for the summation and rate models.

Figure 2.6
Figure 2.6. Response distributions and neurometric/psychometric functions. **A**, Distributions of spike counts for target-present trials (filled bars) and target-absent trials (open bars) from the SU recording session shown in Figure 2.5**A**. Spikes were counted during the integration period described in Fig. 2.1**B**. **B**, MU spike counts from the recording session shown in Figure 2.5**B**. Dashed vertical lines in **A** and **B** are optimal criteria for the summation model. **C**, **D**, Same as **A** and **B** but for spike rates rather than spike counts. **E**, **F**, Comparison of the monkey’s performance with that of the count and rate models that base their decisions on the neural responses in single trials. Each point represents the probability that the observer (monkey or model) would indicate the presence of the target. **E**, SU neurometric and psychometric functions (same experiment as Figures 2.5**A**). **F**, MU neurometric and psychometric functions (same experiment as Figures 2.5**B**). Overall accuracy listed in each panel. Detection thresholds ($T$) are shown with thin vertical lines. Error bars show 95% confidence intervals for threshold (horizontal) and false alarm rate (vertical). Prob., Probability.

To ensure that we did not overestimate the neuron(s)’ detection sensitivity, the analysis was performed for each trial separately using a jackknife procedure (Efron and Tibshirani, 1993) (see Materials and Methods).

Similar to the behavioral thresholds, neural detection thresholds were correlated with stimulus eccentricity (Fig. 2.4**B**) for both SU and MU. As stimulus eccentricity increased, neural detection threshold also tended to increase. This is somewhat surprising since the parameters of the visual target were matched to the preferred parameters of the recorded neuron(s). The ratios of the neural to behavioral thresholds were not significantly correlated with eccentricity (Fig. 2.4**C**), indicating that eccentricity had similar effects on neural and behavioral sensitivity in our data set.

**Comparing neural and behavioral detection sensitivities**

In the example SU site, the performance of both models was comparable to that of the monkey (overall accuracy of summation model, 80%; rate model, 82%; monkey, 83%).


In the example MU site, the summation model performed significantly worse than the monkey (overall accuracy of summation model, 67% vs. monkey, 79%; bootstrap test, p = 0.008). The performance of the rate model, on the other hand, was comparable to that of the monkey (overall accuracy, 78%).

Across our data set, the summation model was significantly less accurate than the monkey (Table 2.2). This was true whether the neural performance was based on SU or MU. The average accuracy of the rate model, on the other hand, was not significantly different from the average accuracy of the monkey (Table 2.2 and Fig. 2.7A) for both SU and MU.

**Table 2.2 – Quantitative comparison of the psychometric functions with the ideal-observer neurometric functions**

<table>
<thead>
<tr>
<th></th>
<th>Physiology Mean (SEM)</th>
<th>Behavior Mean (SEM)</th>
<th>p-value t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy (% correct)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>75.66% (1.26%)</td>
<td>78.62% (1.11%)</td>
<td>p = 0.082</td>
</tr>
<tr>
<td>summation model (SU)</td>
<td>72.31% (1.18%)</td>
<td>78.62% (1.11%)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>76.83% (1.01%)</td>
<td>78.53% (0.75%)</td>
<td>p = 0.177</td>
</tr>
<tr>
<td>summation model (MU)</td>
<td>69.41% (1.52%)</td>
<td>78.53% (0.75%)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>Threshold (T)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>7.29% (0.70%)</td>
<td>6.10% (0.69%)</td>
<td>p = 0.231</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>7.46% (0.41%)</td>
<td>6.21% (0.36%)</td>
<td>p = 0.046</td>
</tr>
<tr>
<td><strong>Slope (β)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>3.87 (0.68)</td>
<td>8.43 (0.64)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>4.22 (0.60)</td>
<td>9.18 (0.76)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>False Alarm Rate (γ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>4.56% (1.16%)</td>
<td>8.13% (1.44%)</td>
<td>p = 0.058</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>10.26% (1.18%)</td>
<td>9.75% (1.25%)</td>
<td>p = 0.768</td>
</tr>
</tbody>
</table>
Figure 2.7. Scatter plots of the parameters of monkey’s psychometric functions vs. the parameters of the neurometric function for the rate model.  

**A**, Overall accuracy.  

**B**, Detection threshold ($T$).  

**C**, Slope ($\beta$).  

**D**, False alarm rate (FA; $\gamma$).  

Filled data points indicate experiments in which a bootstrap test found a significant difference in a parameter value between the monkey and the neuron(s).  

MU – gray squares ($n = 62$); SU – black triangles ($n = 33$).  

Histograms show the ratio of the values for each parameter, neuron(s)/monkey.  

To compute the ratio in **D**, at sites in which the monkey’s false alarm rate was equal to zero it was arbitrarily set to 1%.  

The filled gray histograms are for MU and the black outline histograms for SU.  

Arrows (gray-MU; black-SU) indicate median ratio.  

Asterisks indicate significant difference between the model and the monkey based on a paired *t*-test.  

Diagonal lines are unity lines, not fits to the data.
Additional analysis (discussed below) indicated that the accuracy of the summation model could not be significantly improved by integrating neural responses over shorter or longer intervals. These results demonstrate that a model that bases its decisions on spike counts of SU or MU in V1 is relatively inefficient and is inconsistent with the monkey’s performance in the detection task. The rate model, however, showed an average detection sensitivity that was comparable to that of the monkey. We therefore proceeded to quantitatively compare the shape of the neurometric functions of the rate model with the shape of the psychometric functions.

In the example experiments, the detection thresholds of the rate model \( T = 5.0\% \) in the SU site, \( T = 6.62\% \) in the MU site) were also comparable to the monkey’s detection thresholds \( T = 5.2\% \) in the SU site, \( T = 7.25\% \) in the MU site). Across all experiments, average detection thresholds were slightly lower for the monkey than for the rate model for both SU and MU (Table 2.2 and Fig. 2.7B).

Behavioral and neural thresholds varied somewhat between the three monkeys. In particular, one monkey had significantly lower neural and behavioral thresholds than the other two animals, probably because of the lower eccentricities of the recording sites in this animal (Table 2.3).

**Table 2.3 – Threshold and stimulus parameters per monkey**

<table>
<thead>
<tr>
<th>Monkey</th>
<th>mean behavioral threshold (SEM)</th>
<th>mean neural threshold (SEM)</th>
<th>target eccentricity (SEM)</th>
<th>target sigma (SEM)</th>
<th>target bandwidth (SEM)</th>
<th>target spatial frequency (cpd) (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R (n = 32 sites)</td>
<td>7.61 (0.66)</td>
<td>9.35 (0.63)</td>
<td>5.39 (0.21)</td>
<td>0.411 (0.02)</td>
<td>1.23 (0.09)</td>
<td>1.32 (0.07)</td>
</tr>
<tr>
<td>P (n = 8 sites)</td>
<td>7.64 (0.64)</td>
<td>8.21 (1.01)</td>
<td>4.98 (0.50)</td>
<td>0.412 (0.04)</td>
<td>1.03 (0.13)</td>
<td>1.62 (0.20)</td>
</tr>
<tr>
<td>B (n = 34 sites)</td>
<td>4.49 (0.24)</td>
<td>6.31 (0.61)</td>
<td>3.28 (0.26)</td>
<td>0.279 (0.01)</td>
<td>0.99 (0.08)</td>
<td>2.46 (0.17)</td>
</tr>
</tbody>
</table>
In the 21 experiments where both SU and MU were recorded simultaneously from the same microelectrode, there was no significant difference between SU and MU in overall accuracy and threshold under the rate model (Table 2.4). The quantitative relationship between SU and MU activity is further analyzed in Chapter 5.

Our finding that the detection sensitivities of SU and MU in V1 using the rate model were comparable to the monkey’s detection sensitivity demonstrates that V1 neurons are highly sensitive to stimuli near detection threshold even when using brief, behaviorally relevant, integration periods. In addition, it also shows that detection sensitivity of SU is comparable to that of MU.

**Table 2.4 – Comparison of neurometric functions for SU and MU recorded simultaneously**

<table>
<thead>
<tr>
<th></th>
<th>Single Unit Mean (SEM)</th>
<th>Multi-unit Mean (SEM)</th>
<th>p-value t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy</strong> (% correct)</td>
<td>rate model</td>
<td>74.39% (1.65%)</td>
<td>77.57% (1.45%)</td>
</tr>
<tr>
<td><strong>Threshold</strong> (T)</td>
<td>rate model</td>
<td>7.28% (0.90%)</td>
<td>6.07% (0.67%)</td>
</tr>
<tr>
<td><strong>Slope</strong> (β)</td>
<td>rate model</td>
<td>4.29 (1.00)</td>
<td>5.08 (1.08)</td>
</tr>
<tr>
<td><strong>False Alarm Rate</strong> (γ)</td>
<td>rate model</td>
<td>5.64% (1.71%)</td>
<td>12.41% (2.45%)</td>
</tr>
</tbody>
</table>

* note: SU & MU (n=21)

**Quantitative comparison of neurometric and psychometric functions**

Although the overall accuracies and thresholds of the monkey and the rate model were comparable in the experiments depicted in Figures 2.5 and 2.6, there were significant
differences in the shapes of the Neurometric and psychometric functions. In the SU recording site (Fig. 2.6E), the slope ($\beta$) of the neurometric function for the rate model was significantly shallower than the slope of the psychometric function ($p = 0.012$, bootstrap test) (see Materials and Methods). In the MU recording site (Fig. 2.6F), the neural false alarm rate ($\gamma$) of the rate model was significantly higher than the monkey’s false alarm rate ($p = 0.022$, bootstrap test).

Across our data set, we found systematic differences between the shapes of the psychometric and the neurometric functions (Table 2.2). Most notably, the average slopes of the neurometric functions tended to be significantly lower than those for the monkey (Table 2.2 and Fig. 2.7C), showing that task difficulty affects neural and behavioral performances differently. These results indicate that the average performance of an ideal observer model that bases its decision on the spike rate of a SU or a small pool of neurons in V1, though highly sensitive, is inconsistent with the behavioral performance of the monkey.

An additional difference between the neurometric and psychometric functions is that for many of the SU sites the neurometric function had a lower false alarm rate than the monkey (Fig. 2.7D). The reason for this low false alarm rate is simple. For many SU, in the vast majority of target-absent trials the neuron did not fire at all during the short integration interval (e.g., Fig. 2.6A). Since the ideal observer had to use a criterion that was larger than zero, the false alarm rate of the ideal observer was typically very low. Because the level of baseline activity was much higher for MU sites, a rate model that
based its decisions on MU activity had an average false alarm rate comparable to that of the monkey (Table 2.2 and Fig. 2.7D).

Similar results were obtained in a site-by-site bootstrap analysis that compared the overall shape of the neurometric and psychometric functions (simultaneously taking into account $T$, $\beta$ and $\gamma$, see Materials and Methods). In the majority of the SU sites (26/33) and MU sites (51/62) the psychometric and neurometric functions were found to be significantly different.

The models that we considered so far used the optimal criterion to separate target-present and target-absent trials. In reality, the monkey may not be able to use the optimal criterion to perform the detection task. We therefore determined whether suboptimal criteria could provide a significantly better match between the psychometric and neurometric functions. For each SU and MU site, we varied the detection criterion and found the criterion that produced a neurometric function that was most consistent with the psychometric function (see Materials and Methods). We then compared the average parameters of the psychometric function with the average parameters of these new neurometric functions (Table 2.5).

For the SU and MU sites, the neurometric functions were still significantly shallower on average than the psychometric functions even when using the criterion that minimized the difference between the neurometric and psychometric functions at each site. Furthermore, the accuracies of the model were now significantly lower on average than the accuracies of the monkey (Table 2.5).
Table 2.5 – Comparison of the psychometric functions with the neurometric functions that are most consistent with behavior

<table>
<thead>
<tr>
<th></th>
<th>Physiology Mean (SEM)</th>
<th>Behavior Mean (SEM)</th>
<th>p-value t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>73.94% (0.99%)</td>
<td>78.62% (1.11%)</td>
<td>p = 0.003</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>75.03% (0.90%)</td>
<td>78.53% (0.75%)</td>
<td>p = 0.004</td>
</tr>
<tr>
<td><strong>Threshold (T)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>7.26% (0.83%)</td>
<td>6.10% (0.69%)</td>
<td>p = 0.291</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>7.64% (0.45%)</td>
<td>6.21% (0.36%)</td>
<td>p = 0.016</td>
</tr>
<tr>
<td><strong>Slope (β)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>4.69 (0.75)</td>
<td>8.43 (0.64)</td>
<td>p = 0.003</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>4.01 (0.43)</td>
<td>9.18 (0.76)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>False Alarm Rate (γ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rate model (SU)</td>
<td>8.41% (1.61%)</td>
<td>8.13% (1.44%)</td>
<td>p = 0.897</td>
</tr>
<tr>
<td>rate model (MU)</td>
<td>15.64% (1.80%)</td>
<td>9.75% (1.25%)</td>
<td>p = 0.009</td>
</tr>
</tbody>
</table>

The most consistent difference between the neurometric and psychometric functions was the steeper slopes of the psychometric functions. For the vast majority of the SU (30/33) and the MU (45/62) sites, no criterion (optimal or suboptimal) could be found that would produce a neurometric function with an equal or steeper slope and an equal or lower threshold than those of the monkey.

Overall, our results demonstrate significant inconsistencies between neural and behavioral performances when using models that base their decisions on spike counts or spike rates of SU or multi-units in V1. In general, the performance of models based on MU activity was more similar to the performance of the monkey (Tables 2.2, 2.4, 2.5). These results suggest that perceptual performance in our detection task is based on signals provided by a larger and/or a more distributed population of neurons than the ones recorded by our MU signals.
Figure 2.8

A

B

C

D

E

F

G

H

- SUA Overall Accuracy (%)
- MUA Overall Accuracy (%)
- SUA Threshold
- MUA Threshold

Ax: Max Integration Time (ms)
Bx: MMRT (ms)
Figure 2.8. Effect of varying the integration period parameters on accuracy and threshold. Mean accuracy as a function of the maximal integration time (50 ms up to 450 ms) for SU recordings A, and for the MU recordings B. Mean threshold as a function of the maximal integration time for SU, C and for MU D. Mean accuracy as a function of MMRT (0 ms up to 60 ms) for SU E and for MU F. Mean threshold as a function of MMRT for SU G and for MU H. In A, B, E, and F, the MMRT was fixed at 20 ms. In C, D, G and H, the MMRT was fixed at 200 ms. Solid horizontal lines indicate the mean accuracy or threshold for the monkey and the dashed lines indicate the corresponding SEM. Asterisks indicate data points where the overall accuracy (threshold) was significantly lower (higher) than the monkey based on a t-test. Error bars are SEM. Max, Maximum; contr., contrast; SUA, single-unit activity; MUA, multi-unit activity.

Effect of varying integration period parameters

To test the robustness of our results, we evaluated the performance of the rate and summation models using various values for the maximal integration time and minimal motor response time (MMRT). Although there was a slight improvement in the average accuracy of the rate and summation (count) models based on SU activity when using a maximal integration time longer than 200 ms (Fig. 2.8 A), the improvement was not significant. The rate model based on the MU activity also did not improve significantly for maximal integration times above 200 ms (Fig. 2.8 B). In contrast, the accuracy of the summation model based on the MU activity peaked for a maximal integration time of ~150 ms and dropped for longer or shorter values. Thresholds for the rate model based on SU and MU sites were very high for low maximal integration times, and did not decrease much beyond a maximal integration time of 200 ms (Fig. 2.8 C, D).

When higher MMRT values (30 to 60 ms) were used, overall accuracy of both models decreased significantly (Fig. 2.8 E, F), with the summation model performing consistently worse than the rate model, and threshold increased significantly (Fig. 2.8 G,
Most of this decrease in performance for longer MMRT came from the high contrast target conditions (usually 25% target contrast), where the model in many blocks performed well below 100% and sometimes worse than at lower target contrasts.

Because RTs were very short on high contrast trials (Fig. 2.3), assuming a long MMRT left extremely short intervals for the evaluation of neural signals in such trials, which led to decreases in performance.

Because many of the monkey’s RTs were shorter than 200 ms, it was often the case that target-absent trials had longer integration periods than target-present trials. To exclude any potential bias because of this variable integration time, we repeated our analyses using a fixed integration period of 200 ms (regardless of the monkey’s saccade time). The neurometric functions remain almost identical under this analysis (Table 2.6),

| Table 2.6 – Quantitative comparison of the psychometric functions with the ideal-observer neurometric functions (Fixed Integration Time – 200ms) |
|-------------------------------------------------|------------------------------|------------------------------|-----------------------------|
|                                                  | Physiology Mean (SEM) | Behavior Mean (SEM) | p-value t-test |
| Accuracy (% correct)                             | Rate model (SU)    | Rate model (MU)     | Rate model (SU)    | Rate model (MU)     |
| summation model (SU)                             | 76.25% (1.30%)    | 78.62% (1.11%)    | p = 0.17          |
| summation model (MU)                             | 77.82% (1.02%)    | 78.53% (0.75%)    | p = 0.575         |
| Threshold (T)                                    | Rate model (SU)    | Rate model (MU)     | Rate model (SU)    | Rate model (MU)     |
| rate model (SU)                                  | 7.02% (0.70%)     | 6.10% (0.69%)     | p = 0.355         |
| rate model (MU)                                  | 6.90% (0.41%)     | 6.21% (0.36%)     | p = 0.211         |
| Slope (β)                                        | Rate model (SU)    | Rate model (MU)     | Rate model (SU)    | Rate model (MU)     |
| rate model (SU)                                  | 3.48 (0.36)       | 8.43 (0.64)       | p < 0.001         |
| rate model (MU)                                  | 5.10 (0.50)       | 9.18 (0.76)       | p < 0.001         |
| False Alarm Rate (γ)                             | Rate model (SU)    | Rate model (MU)     | Rate model (SU)    | Rate model (MU)     |
| rate model (SU)                                  | 6.82% (1.41%)     | 8.13% (1.44%)     | p = 0.519         |
| rate model (MU)                                  | 10.36% (1.15%)    | 9.75% (1.25%)     | p = 0.722         |
demonstrating that our results are not systematically biased by the variable integration duration.

The differences in the performance between the summation and the rate models were more pronounced for the MU data than for the SU data (Table 2.2), particularly for longer integration times (Fig. 2.8A,B). Because the integration durations tended to be short in target-present trials and longer in target-absent trials, the additional integration time reduced the separability between spike counts from target-present and target-absent trials but had little effect on the rate model. The MU responses were more sensitive to this reduced separability because the relative differences between the evoked response and the baseline response were much smaller for the MU responses than for the SU responses (see analysis of the quantitative relationship between SU and MU responses, Chapter 5).

Possible effect of eye movements

Small eye movements within the fixation window (microsaccades and drifts) could have affected our detection sensitivity measurements. Eye movements could cause the stimulus to move outside of the receptive field of the recorded neuron(s). This could lead to a decrement in the neural performance and could bias the comparison of neuronal and behavioral detection sensitivities if the monkey could effectively integrate signals from different eye positions. To rule out this possibility, for each experiment we used a simple test to capture the effect (if any) of small, fixational eye movements during the integration period. We investigated four indicators of eye movements (see Materials and
Methods). For each indicator we recalculated the overall accuracies of the monkey and the rate model for half of the trials with the best fixation during the integration period and half of the trials with the worst fixation. Both the monkey and the rate model performed slightly better on the best fixation trials across all four indicators (Table 2.1), but these differences were not significant. These results indicate that small eye movements during the integration period are not likely to have influenced our result.

**Discussion**

The primary goal of this study was to compare neuronal and behavioral performances in a reaction-time visual detection task. We found that SU and MU in V1 have detection sensitivities comparable to those of the monkey even when evaluating neural responses over brief intervals that ended shortly before the monkey’s RT. However, we observed significant inconsistencies between the shapes of the neurometric and psychometric functions. We conclude that, though highly sensitive, spike rates of SU and MU in V1 are insufficient to account for the monkey’s behavioral performance. Instead, our results suggest that a large pool of V1 neurons is needed to account for the behavior of the monkey in this task.

**Comparison of neuronal and behavioral detection sensitivities**

Our finding that the detection sensitivity of single V1 neurons was comparable to that of the monkey is consistent with several previous studies (Britten et al., 1992; Celebrini and Newsome, 1994; Croner and Albright, 1999; Hernandez et al., 2000; Uka and DeAngelis,
2003; Heuer and Britten, 2004), but not with other studies in which the sensitivity of single neurons was found to be significantly lower than the sensitivity of the subject (Vogels and Orban, 1990; Prince et al., 2000; Osborne et al., 2004; Liu and Newsome, 2005; Purushothaman and Bradley, 2005); (for review, see Parker and Newsome, 1998; Romo and Salinas, 2001; Born and Bradley, 2005). Such differences across studies suggest that the relationship between neural and behavioral sensitivities depends on the exact nature of the perceptual task.

Most prior studies that compared neural and behavioral sensitivities used fixed and long integration times. This may have introduced a bias in favor of neural sensitivity since the subject may have effectively used a shorter integration period. In fact, in the only other study in which neural and behavioral sensitivities were compared while monkeys performed a reaction-time detection task, single neurons were found to be significantly less sensitive than the monkey (Cook and Maunsell, 2002). Here we demonstrate that V1 neurons are highly sensitive to low-contrast visual targets even when evaluated during extremely short integration times.

The behavioral thresholds measured in the current study were significantly higher than in previous detection studies in humans (e.g., Rovamo et al., 1978; Petrov and McKee, 2006) and monkeys (e.g., Merigan et al., 1991). The most likely source for these differences in threshold is stimulus size. Detection thresholds are known to decrease significantly as target size is increased (e.g., Robson and Graham, 1981). Other factors that could have contributed to the higher detection threshold reported here are: (1) our task included significant uncertainty regarding target contrast; (2) our task is a reaction-
time task, and stimuli were briefly presented; (3) our definition of threshold incorporates the false alarm rate; and (4) the parameters of the Gabor patch were adjusted to match the preferred properties of the recorded neuron(s) and therefore varied significantly from day to day. Importantly, factors 1-3 also affected the performance of the models that detect the target from the neural responses, making the comparison of neuronal and behavioral performance valid.

**Choice of temporal parameters**

We found that neuronal sensitivity does not increase significantly when using maximal integration times beyond 200 ms (Fig. 2.8A), suggesting that the majority of the useful signals of the neurons occur rapidly. This result is consistent with findings from single neurons in areas V1 (Muller et al., 2001; Frazor et al., 2004) and MT (Uka and DeAngelis, 2003; Osborne et al., 2004), and from psychophysical studies in monkeys (Uka and DeAngelis, 2003) and in humans (Ludwig et al., 2005).

The monkeys’ RTs in our detection task increased with decreasing target contrast but were, overall, very short (Fig. 2.3) and were sometimes consistent with express saccades (Fischer and Boch, 1983; Rohrer and Sparks, 1993). We believe that RTs were short because (1) the monkeys were highly trained, (2) the target was always in the same location, and (3) the monkeys were cued as to when to expect the onset of the target. Therefore, the monkeys were able to start preparing an eye movement in advance, and execute it shortly after enough evidence regarding the presence of the target had been accumulated.
Quantitative comparison of the shapes of neurometric and psychometric functions

We found that the neurometric functions were, on average, significantly shallower than the monkey’s psychometric functions. There are multiple ways in which the neurometric functions could be steepened through further processing. For example, uncertainty in later stages as to which V1 neurons to read out could lead to significant steepening of the neurometric functions (Pelli, 1985). Similarly, a subsequent processing stage with a high threshold could steepen the neurometric function. Note, however, that any subsequent mechanism that leads to steepening of the neurometric functions has to do so by reducing performance at low target contrasts and is therefore suboptimal in terms of its detection performance. Consequently, to achieve overall performance comparable to that of the monkey while steepening the neurometric function, such a mechanism must operate on signals that are significantly more sensitive than the monkey to start with. Our current results suggest that such signals could be provided by large populations of V1 neurons. In fact, taking into account the large numbers of V1 neurons that are active in response to small visual targets (e.g., Grinvald et al., 1994; Chen et al., 2006), the high detection sensitivity of single neurons reported here, and the relatively weak correlations observed between pairs of neurons in the cortex (e.g., Gawne and Richmond, 1993; Zohary et al., 1994), it is evident that V1 population responses, if pooled optimally, should be significantly more sensitive than the monkey in the detection task. In support of this possibility, our lab recently reported that the activity of large populations of V1 neurons measured with voltage sensitive dye imaging is consistently more sensitive than the monkey in the same detection task (Chen et al., 2006).
Conclusions

We used ideal observer analysis to demonstrate that the detection sensitivities of SU and MU in V1 neurons are comparable to those of the monkey, but only when examining spike rate, not spike count. However, we found systematic differences in the neurometric and psychometric curves that were constructed to describe the monkey and the neurons’ overall performance in the detection task. Together, our results are consistent with the hypothesis that neural responses from large populations of V1 neurons are combined sub-optimally by subsequent processing stages to mediate behavioral performance in visual detection tasks. Understanding the nature of the inefficiencies that lead to the observed behavioral performance is an important goal for future experiments.
Chapter 3: Linking Neural and Behavioral Performance in a Reaction-Time Visual Detection Task Using Dynamic Integration Models

Abstract

Neurons in sensory areas such as the primary visual cortex (area V1) respond to stimuli with high temporal precision. Thus, ideal observer models that can track neural responses dynamically may be able to reveal important properties of the encoding and decoding of information along neural circuits. Here we recorded single neurons and small groups of neurons (multi-units) in macaque V1 while the monkey was engaged in a reaction-time (RT) visual detection task. We used three ideal observer models to analyze neural responses on a millisecond by millisecond basis in order to determine if and when a decision criterion regarding the presence or absence of a visual target had been surpassed. The detection sensitivity (as well as the RT) of each model was compared to the detection sensitivity (and RT) of the monkey in the visual detection task. We obtained five primary results: 1) no dynamic model was able to match the detection sensitivity of the monkey; 2) the dynamic model which used neural responses to calculate the posterior probability of the presence of the target had higher detection sensitivity than the dynamic models that simply compared the accumulated neural response (over the whole trial or over a relatively short running window) to a decision criterion; 3) the neural responses contributing to the models’ detection decisions were concentrated at the beginning of the trial; 4) the RTs of the dynamic models were significantly correlated with the RTs of the monkey on a trial by trial basis; 5) the mean RT of the monkey increased as target contrast was lowered at a rate that was higher than that seen with the
mean RT predicted by the dynamic models. Overall, the detection sensitivity of the
dynamic models was worse than the monkey (and the model from Chapter 2 which
integrated signals over fixed time intervals), but the RTs they generated provided
potentially useful insights regarding the dynamics of behavioral decision making.

Introduction

In Chapter 2, we compared the sensitivity of monkeys in a reaction-time visual detection
task to neural sensitivity in area V1. Single unit (SU) and multi-unit (MU) sensitivity
were found to be comparable to the monkey’s sensitivity in the detection task though
there were systematic differences in the neurometric and psychometric curves describing
the neural and behavioral performance. The sensitivity of a much larger population of
V1 neurons, as measured by voltage-sensitive dye imaging (VSDI), was found to
significantly exceed the sensitivity of the monkey (Chen et al., 2006). Both the Chapter 2
study and Chen et al. (2006) assessed neural responses over fixed time intervals (an
average duration of ~140 ms) starting shortly after target onset. To illustrate how
information relevant to the detection task can evolve over time, Chen et al. (2008) used
an optimal dynamic pooling model to assess the VSDI signals from V1. This model had
significantly lower “reaction times” than the monkey and a higher detection sensitivity
than both the monkey and the fixed integrator model from Chen et al. (2006) (similar to
the model used in Chapter 2). The optimal dynamic pooling model combined a
whitening filter (to reduce substantial temporal correlations in the VSDI signal) with the
continuously updated computation of the posterior probability of the presence of the
target. A simpler integrator model (also employing a whitening operation) performed nearly as well as the optimal model in both accuracy and speed. In this chapter, the SU and MU responses were subjected to both a simple integrator model (as well as a running integrator model) and a posterior probability model. Using the exact same set of data from Chapter 2, we looked at how accuracy (i.e. detection sensitivity) of the neurons is affected by the type of model used and how the RTs of the dynamic models compared to the actual RTs of the monkey.

**Materials and Methods**

*Subjects and surgery* (See chapter 2)

*Task and visual stimulus* (See chapter 2)

*Electrophysiology* (See chapter 2)

*Analysis of behavioral data* (See chapter 2)

*Neuron database* (See chapter 2)

*Analysis of eye movements* (See chapter 2)

*Analysis of physiological data*

*Jackknife procedure* (See Chapter 2)

All models were subject to a jackknife procedure similar to that used for the fixed integrator models in Chapter 2.

*Bootstrap analysis* (See Chapter 2)
**Simple integrator model**

The simple integrator model (SIM) was the most basic of the dynamic models constructed to examine the SU and MU responses (spike counts) in the visual detection task. In this model, the number of spikes was continuously integrated starting at the point of the average spiking latency (36 ms after target onset). The mean integrated response to the blank, or target-absent, trials was subtracted from the integrated response of each trial (both target-present and target-absent trials). Neural responses were integrated up until the end of each trial. For the trials in which the monkey reported the presence of a target (“hit” and “false alarm” trials), the end of the trial was the monkey’s RT minus 20 ms (corresponding to the minimal motor response time, MMRT; see Chapter 2). For the trials in which the monkey did not report the presence of a target (“miss” or “correct reject” trials), the trial ended 600 ms after the onset of the target.

If the integrated neural response (minus the mean blank response) exceeded a decision criterion before the end of the trial, the model considered the trial a target-present trial (i.e. a “hit”, if the trial was actually a target-present trial, or a “false alarm”, if the trial was actually a target-absent trial), and the time at which the criterion was exceeded was the model’s RT for that trial. If the integrated response failed to exceed the criterion before the end of the trial, the trial was considered a target-absent trial (i.e. a “miss” if the trial was actually a target-present trial, or a “correct reject” if the trial was actually a target-absent trial). The overall accuracy (hits and correct rejects divided by the total number of trials) of the SIM was evaluated at each of 50 levels of the decision criterion (minimum criterion value = max integrated neural response/50; maximum
criterion value = max integrated response). The criterion (called the optimal decision criterion) yielding the maximum overall accuracy (i.e. detection sensitivity) was then used to evaluate the probability of reporting the target (PT) for each target contrast (target-absent trials = 0% contrast trials). We fit the PT values for each contrast with a modified Weibull function (see Chapter 2) to generate neurometric functions describing the model’s decision “behavior” in the detection task.

**Running integrator model**

The running integrator model (RIM) was similar to the SIM in almost all respects; the main difference being that a short running window (we tested several lengths between 20 and 100 ms) was used to integrate neural activity. Like the SIM, the optimal decision criterion (yielding the highest overall accuracy) was then used to evaluate PT for each target contrast, which we used to construct neurometric functions.

**Posterior probability model**

Like the SIM and RIM, the posterior probability model (PPM) analyzed the integrated SU and MU responses, but it did so in a more sophisticated way. The PPM computed the posterior probability at each time \( t \) that the target was present, given the integrated neural response up to time \( t \) (minus the mean blank response up to time \( t \)). If at any time \( t \) the posterior probability of the trial being a target-present trial exceeded a criterion, the posterior ideal observer reported “target present”, in which case time \( t \) was the RT for that trial. If at time \( t \) the criterion was not exceeded, the neural responses
continued to be integrated and the posterior probability recalculated for the next time period. Also, like the SIM and RIM, the PPM did not start evaluating neural responses until 36 ms after target onset.

Assuming that the integrated neural response $\Sigma R(t)$ at time $t$ was independent across trials and was normally distributed, Bayes’ rule could be used to compute the posterior probability for each trial type $i$:

$$\text{Equation 3.1 : } p(i \mid \Sigma R(t)) = \frac{\text{prior}_i \cdot \text{norm}(\Sigma R(t); \mu_i(t), \sigma_i(t))}{\sum_{j=1}^{n} \text{prior}_j \cdot \text{norm}(\Sigma R(t); \mu_j(t), \sigma_j(t))}$$

where $\mu_i(t)$ and $\sigma_i(t)$ are the mean and SD of $\Sigma R(t)$ for each target contrast $i$ ($i=1...n$ trial types) at time $t$, $\text{norm}(\Sigma R(t); \mu_i(t), \sigma_i(t))$ is the normal distribution with mean $\mu_i(t)$ and SD $\sigma_i(t)$ evaluated at $\Sigma R(t)$, and prior is the prior probability of trial type $i$.

The overall accuracy for all of the trials was computed for each of 49 decision criteria (posterior probability equal to 0.51 to 1.0 in increments of 0.01). Like the SIM and RIM, the optimal decision criterion was then used to evaluate PT for each target contrast, from which we constructed neurometric functions.

**Results**

The detection sensitivity of the monkey was compared to the detection sensitivity of SU and MU in V1 as defined by three types of dynamic ideal observer models. We found the RIM and PPM to have significantly higher detection sensitivities than the SIM, but significantly lower detection sensitivity than the monkey. We also compared parameters
defining neurometric and psychometric functions (slope, detection threshold, and false alarm rate). Also, we compared the RTs of the monkeys to the RTs of the dynamic models. There was a high level of trial-by-trial correlation between the monkey’s actual RTs and those of the models. Finally, upon fitting the mean RT data for the monkey and the models with linear functions, we discovered a component of the RT that may be dependent on task difficulty.

**Assessing behavioral detection sensitivity**

Figure 2.1C (as well as Fig 3.4, black curve) shows the typical behavioral performance of the monkey in the visual detection experiment. Chapter 2 gives details about how the monkey’s psychometric function was constructed. Briefly, each point on the curve represents the probability (PT) that the monkey reported that the target was present as a function of target contrast. Target contrast of 0% represents the half of the trials in which the target was absent. PT were fitted with a psychometric function derived from a modified Weibull function (Quick, 1974) (see Chapter 2). In Chapter 2, we assessed the detection sensitivity of the monkey with two measures: detection threshold (T), which was defined as the target contrast at which performance was 75% correct (combined across target-present and target-absent trials), and overall accuracy (overall percent correct across a block of trials). The monkey’s detection threshold in the example experiment from Chapter 2 is depicted with a vertical dashed line (Fig. 2.1C). For this chapter, we focused primarily on the overall accuracy as a proxy for detection sensitivity.
The time it took the monkey to initiate a saccade to the location of the target (i.e. the monkey’s RT) depended on the target contrast (Fig. 2.2A). As target contrast was lowered, average RT became significantly longer. These results suggest that longer durations are required for the monkey to reach perceptual decisions regarding the presence of the target at lower target contrasts.

**Simple integrator model**

Spikes recorded from SU and MU were integrated starting 36 ms after stimulus onset to yield the trial’s integrated time course. Figure 3.1 shows mean integrated time courses (colored solid lines) with SD (dashed colored lines) that were computed for trials from each of the target contrast conditions from one example MU site. Time courses extend as long as the longest RT from each condition. The mean time course of the target-absent trials (Fig. 3.1, grey solid line) was subtracted from all of the conditions. Median RTs are shown as ticks along the upper horizontal axis. The SIM sets an optimal decision criterion (Fig. 3.1, black dashed line) on the integrated responses to yield a target-absent/target-present choice for each trial. The time at which the optimal decision criterion was reached was the RT for that trial (either for “hits” or “false alarms”). The time course of a single trial (12% contrast) is depicted with a thick green line. The time course of this trial does cross the decision criterion, and since it was a target-present trial, the trial was classified as a “hit”. The model’s RT for this example trial is indicated by the vertical red line, and the monkey’s RT for that same trial is indicated by the black vertical line. All of the trial outcomes (“hit”, “miss”, “false alarm”, and “correct reject”)
Figure 3.1. Simple Integrator Model. Mean integrated spike counts for 6 target-present conditions (solid colored curves) and the target-absent (blank) condition (solid grey curve) from one MU site. The mean blank was subtracted from all conditions. Thin dashed lines are SD. Horizontal dashed line is the optimal decision criterion. Thick green curve is the integrated response (minus mean blank) for one 12% contrast trial. The point the green curve crosses the optimal decision criterion is the model’s RT (red vertical line) for that trial. The black vertical line is the monkey’s RT for that trial. Colored ticks along the top abscissa show median RTs for the target-present conditions and the target-absent condition (i.e. median false alarm RT).

went into determining the overall accuracy rate (“hits” and “correct rejects” divided by the total number of trials) of the SIM for the block (74.3%), which was significantly lower than the overall accuracy of the monkey for this block (81.8%). Significance within individual experiments was determined with the bootstrap procedure described in Chapter 2.
The optimal decision criterion was used to evaluate the model’s PT for each condition (6 target-present conditions, and 1 target-absent condition) yielding a neurometric function (blue curve, Fig. 3.4), which is shown alongside the psychometric function (black curve) describing the monkey’s performance in the task.

The primary reason for this model’s poor performance (relative to the monkey and the other models described in this chapter and the previous chapter) in this experiment and across all experiments, is its high number of false alarms. Because spikes accumulate over the entire course of each trial, target-absent trials end up with a large number of spikes by the end of the trial (600 ms). In addition, the variability in the mean accumulated response for each condition also increased throughout the trial. Notice how the SD of the time courses for each contrast condition in Figure 3.1 increased at a relatively constant rate throughout the trial. Also note that the mean plus SD of the target-absent time course almost reached the level of the criterion threshold by the end of the trial. The increase in the variability over time makes the target-present and target-absent response distributions less distinct, lowering the detection sensitivity. To deal with the increase in the mean and SD of the response late in the target absent trials, the SIM model had to use a higher criterion to avoid a high false alarm rate. However, a high criterion would mean that the spike counts in many target-present trials (especially ones with short RT) would not cross the criterion, further decreasing the performance of the model.
Running integrator model

Figure 3.2 shows mean integrated time courses (with SD) for each contrast condition computed with a 45 ms running window. Integrated response at time \( t \) is computed from \( t-45 \) ms to time \( t \). All of the conventions are the same as in Figure 3.1. The overall accuracy for this model was 78.6% (comparable to that of the monkey), and the neurometric function (red curve) can be seen in Figure 3.4. Of all the lengths for the running window tested (20-100 ms, in 1 ms increments), a window length of 45 ms was found to result in the highest mean overall accuracy (computed over 33 SU and 62 MU). Therefore, only RIM using 45 ms running windows was used for the remaining analyses, and all mention of the RIM from this point forward implies RIM with a 45 ms long window.

The RIM has a higher overall accuracy than the SIM (for this experiment and across all experiments). As mentioned above, the SIM performs poorly because the mean and SD of the integrated responses increase throughout the trial, leading to target-absent trials with large spike counts and many false alarms, or alternatively, many misses at high target contrast (which generally had the shortest RT). The advantage of the RIM is that it uses a running window which prevents the accumulation of spikes over long durations. The implication of this is that the mean and SD of the RIM target-absent time course (Fig. 3.2, dashed grey lines) are relatively constant, resulting in fewer false alarms and allowing a lower decision criterion to be used.
Figure 3.2. Running Integrator Model. Mean integrated spike counts for the same MU site seen in Figure 3.1. The mean integrated spike counts were computed with a running 45 ms window for 6 target-present conditions (solid colored curves) and the target-absent (blank) condition (solid grey curve), which has been subtracted from all conditions. Thin dashed lines are SD (for clarity, shown only for the blank and 25% contrast conditions). Spike counts were integrated starting at 36 ms after target onset, but because this model used a running 45 ms window, the point on each time course plotted at 81 ms represents the integrated response from 36-81 ms, which is the first point that the model analyzes. Horizontal dashed line is the optimal decision criterion. Thick green curve is the integrated response (minus mean blank) for one 12% contrast trial. The time at which the green curve crosses the optimal decision criterion is the model’s RT (red vertical line) for that trial. The black vertical line is the monkey’s RT for that same trial. Colored ticks along the top abscissa show median RT for the target-present conditions and the target-absent condition (i.e. median false alarm RT).
**Posterior probability model**

The PPM computed the posterior probability at each time \( t \) that the target was present given the integrated neural response up to time \( t \) and the prior probability of each condition (see Materials and Methods). For the block depicted in Figure 3.3 (same block from Fig. 3.1 and 3.2), there are 7 trial types: one target-absent (half of the trials in a block) and six target-present at different target contrasts (the other half of the trials in the block). Therefore, the prior probability of the target-absent condition is 0.5, and 0.0833 for each of the different target-present conditions. Figure 3.3 depicts one target-present trial. The sum of the posterior probabilities (Fig. 3.3, thick blue curve) for the individual target-present conditions (Fig. 3.3, thin colored curves) exceeded the decision criterion (Fig. 3.3, thick horizontal black line) at 84 ms, the model’s RT (Fig. 3.3, vertical red line) for that trial. As with the SIM and RIM, all of the trial outcomes from each trial were assembled into a neurometric curve (Fig. 3.4, green curve) and an overall accuracy rate (80.9%), which was comparable to that of the monkey.

**Performance of dynamic models**

Figure 3.4 shows the behavioral performance of the monkey in the visual detection task with a psychometric function (black curve) for the experiment depicted in Figure 3.1-3.3, displayed alongside neurometric curves for the three dynamic models mentioned above. In this typical MU example, the monkey had a higher overall accuracy (shown in the figure legend) than that of the SIM (significantly higher), the RIM (not significantly higher), and the PPM (not significantly higher). Across all the experiments (33 SU and
Figure 3.3. Posterior probability time courses for one trial (12% contrast) from the same MU site seen in Figure 3.1-2. Time courses describing the posterior probability that the target was present are represented by the thin colored lines. The thick purple line shows the sum of all the target-present conditions (thin lines). The thick grey line shows the posterior probability for the target-absent (blank) condition. Horizontal dashed line is the optimal decision criterion. The point the thick purple (target-present) curve crosses the optimal decision criterion is the model’s RT (red vertical line) for that trial. The black vertical line is the monkey’s RT for that trial. Red ticks along the top abscissa show timing of individual spikes within the trial.

62 MU), the monkey had a significantly higher detection sensitivity (paired t-tests) than the SIM, RIM and PPM (collapsed across SU and MU, Fig. 3.5A). Additionally, the psychometric functions had significantly steeper slopes (Fig. 3.5B), significantly lower thresholds (Fig. 3.5C), and significantly lower false alarm rates (Fig. 3.5D) in comparison to the neurometric functions of each of the dynamic models (paired t-tests).
Figure 3.4. Neurometric and psychometric curves for one MU site. Neurometric curves (SIM – blue; RIM – red; PPM – green) and psychometric curve for the MU experiment depicted in Figure 3.1-3. Overall accuracy is listed in key.

The mean SIM detection sensitivity was significantly lower than the mean RIM and PPM detection sensitivities (paired *t*-tests). Due to its poor detection sensitivity, we did not use the SIM for any further analyses. Also, as mentioned above, we only used the RIM with the 45 ms integration window in further analyses, as it gave the highest performance among all the running integration windows.

The average detection sensitivities of both the RIM and PPM were lower than the average detection sensitivity of the fixed integrator model (i.e. the rate model) from Chapter 2 (but not significantly so, paired *t*-tests). The neurometric functions of the fixed
integrator model also had, on average, slopes that were significantly steeper than the RIM and PPM and false alarm rates that were significantly lower than the RIM and PPM.

Mean detection thresholds were comparable for all three models (paired *t*-tests).

**Figure 3.5**

![Figure 3.5](image)

**Figure 3.5.** Mean neurometric and psychometric function parameters. *A* mean overall accuracy of monkey (M), SIM (S), RIM (with 20 ms, 30 ms, 40 ms, 45 ms, 50 ms, 60 ms, and 70 ms windows), and PPM (P). *B* Mean slope of neurometric/psychometric functions. *C* Mean contrast threshold. *D* Mean false alarm rate. Error bars are SEM.
RIM and PPM reaction times

One key aspect of the dynamic models is that they can make predictions about when there is sufficient information about the stimulus on a given trial to reliably detect the target. These predictions can be compared to the monkey’s actual RT. By definition, the model’s RT would always be a minimum of 20 ms shorter than the monkey (due to the MMRT we assumed), hence we added the 20 ms MMRT to the model’s RT before we made any comparisons between monkey and model RT.

Figure 3.6

Figure 3.6. Mean monkey and model RT for one MU experiment. Mean RT from one MU experiment (same as depicted in Fig. 3.1-4) as a function of target contrast for monkey (black), RIM (red), and PPM (green). RTs at target contrast = 0% correspond to false alarm RT. Solid lines represent best linear fits of mean RT (not including the false alarm RT) as a function of log contrast in target-present trials. Error bars are SEM across trials.
Figure 3.6 shows the RTs for the example experiment depicted in Figure 3.1-3.3. Mean RTs (with SEM) for the monkey (black points), the RIM (red points), and the PPM (green points) are shown as a function of contrast. The points at 0% contrast are the RT of the false alarms. The monkey made very few false alarms, and missed all of the trials at the lowest contrast (4% contrast). Note that the mean false alarm RTs for the monkey and the PPM are lower than the mean hit RTs for the lowest contrast (see below for a discussion about short false alarms). Slopes of linear functions fit to each set of mean RTs (excluding the false alarm RTs) were used to describe the rate at which RT changed with contrast.

Figure 3.7 shows RT across all 95 experiments (collapsed over SU and MU experiments), binned into 6 contrast groups. It is important to note that the mean RT shown in Figure 3.6-7 come from a subset of trials where for each and every trial the monkey, the RIM, and the PPM all scored a “hit”. This way a true comparison can be made between the monkey and model RT (as well as between just the RIM and PPM RT). When the monkey and the models reported that the target was present, the mean RTs from the monkey were on average significantly higher (paired t-tests) than those predicted by the models (with the added 20 ms MMRT).

Note that, like the example experiment in Figure 3.6, the mean false alarm RTs for the monkey and the models were lower than the mean hit RTs for the lowest contrast bin. Linear functions fit to each set of mean RTs (again, excluding the false alarm RTs) reveal that the mean RTs of the monkey increased with decreasing contrast at
approximately twice the rate of the change in the mean model RTs (monkey slope = -71 ms; RIM slope = -33 ms; PPM slope = -45 ms).

Differences between mean RT for the RIM and PPM at each bin were significant (paired t-tests). The shorter RT for the RIM can be explained by the fact that the RIM had a higher false alarm rate than the PPM. This meant that the detection criterion was

Figure 3.7

![Figure 3.7](image)

**Figure 3.7.** Mean monkey and model RT for all SU and MU experiments. Mean RTs across all 95 experiments, collapsed across SU (n = 33) and MU (n = 62), as a function of target contrast. Data points are in the middle of the bin. Target contrast bins are (0, 2-3, 4-6, 7-10, 11-15, 16-20, 21+). RTs at target contrast equal to zero correspond to false alarm trials. Solid lines represent best linear fit of mean RT as a function of log contrast in target-present trials (points at 0% contrast (mean false alarm RT) are excluded from linear fits) for monkey (black – slope = -71 ms), RIM (red – slope = -33 ms), and PPM (green – slope = -45 ms). Error bars are SEM across experiments.
relatively lower for the RIM than the PPM. Integrated responses (or posterior probability) will cross a relatively lower decision criterion sooner than a relatively higher decision criterion, hence the shorter mean RTs for the RIM.

It is possible that the significant differences in mean monkey and model RT come from the fact that the detection sensitivity (i.e. overall accuracy) of the neurons is significantly worse, on average, than that of the monkey (Fig. 3.5A). That is, poor neural detection sensitivity may have also produced estimates of RT for the models that are significantly different at each target contrast from those of the monkey (as seen in Fig. 3.7). Therefore, we repeated the comparison of monkey and model RT for a subset of experiments where the monkey and models had similar (i.e. not significantly different) detection sensitivity, which we identified using the bootstrap test described in Chapter 2. The subset of experiments with comparable performance for the monkey and the RIM (unfilled circles, Fig. 3.8A) and for the monkey and the PPM (unfilled circles, Fig. 3.8B) make up roughly half (53/95 for RIM and 49/95 for PPM) of the total number of experiments. Figure 3.9 shows RTs (again, collapsed over SU and MU experiments and binned into 6 contrast groups) across the subset of experiments with comparable monkey and model detection sensitivity (Fig. 3.9A – RIM; Fig. 3.9B – PPM). It appears that there is very little difference in the model’s RT for the full set of experiments vs. the subset of experiments with comparable detection sensitivity, so the difference between monkey and model average RT cannot be explained by differences in monkey and model detection sensitivity.
Figure 3.8. Mean monkey and model overall accuracy. Mean overall accuracy of the monkey vs. A the RIM and B the PPM. Lines through data are unity lines. Filled points represent significant difference between monkey and model overall accuracy (see Results).

As mentioned above, RTs for the RIM and PPM were consistently shorter than the monkey’s RTs, even after accounting for the MMRT. It would be reasonable to expect that the average RT for the models would be merely offset from those of the monkey by a constant duration that represents the additional neural transmission and saccade execution times (e.g. our 20 ms MMRT, which is likely an underestimate). However, as the target contrast decreases, the RTs for the monkey in the example experiment increased at a rate significantly faster (permutation test) than the RTs predicted by the RIM and PPM (Fig. 3.6). The slope of a line fitted to the mean monkey RT data was also significantly higher (permutation test) than that of both models (Fig. 3.7). The result suggests that there may be a component of the monkey’s RT (related to decision making processes or planning/execution of the saccade to the target) that is dependent on the difficulty of the task or the timing of the signal coming out of V1. The
fitted lines did not include the false alarm RTs, because we believe the false alarm RTs were artificially short due to the high incidence of “early errors”. “Early errors” on target-absent trials may have occurred due to transient clustering of spikes in the first 30-100ms of the trial. This clustering of spikes was capable of almost instantly triggering the models’ decision criteria to respond that the trial contained a target, causing a false alarm. In Chapter 2, we assumed that the high incidence of very short false alarms indicated that the monkey was engaging in “fast guessing” due to an internal bias, but the models in this chapter suggest that those short false alarm RTs may in fact be driven by early fluctuations in neural activity within early sensory areas resulting in honest errors.

Figure 3.9

Figure 3.9. Mean monkey and model RT for a subset of experiments with comparable monkey and model overall accuracy. Mean RT as a function of target contrast collapsed across all SU and MU experiments where monkey and model overall accuracy (i.e. detection sensitivity) was not significantly different (see Fig. 3.8). Data points are in the middle of the bin. Target contrast bins are (0, 2-3, 4-6, 7-10, 11-15, 16-20, 21+). Mean RT at 0% contrast corresponds to RT on false alarm trials. Solid lines represent best linear fit of mean RT as a function of log contrast in target-present trials for monkey (black – slope = -70 ms), RIM (red – slope = -31 ms), and PPM (green – slope = -41 ms). Error bars are SEM across experiments.
**Trial-by-trial correlation between monkey’s RT and models’ RT**

In addition to comparing the mean for the monkey and the dynamic models, we also examined how well the monkey’s RTs could be predicted by the two dynamic models on a per trial basis. To do this, we computed the correlation between z-normalized monkey and model RT. Within a given experiment, we z-normalized RT for the monkey within each contrast condition separately, and did the same for each set of the model’s RT. This was done separately for the RIM and PPM. We then grouped all the z-scores for all the trials in a given experiment and computed the correlation between the monkey and model z-scored RTs. For the example experiment used in Figure 3.1-4,6, we found a highly significant correlation.

**Figure 3.10**

(A) Correlation between monkey and model RT for one MU experiment.  
Correlation between z-scored RT predicted by the RIM model and the RT of the monkey in the corresponding trials. These RT come from the example experiment used in Figure 3.1-4,6. RT are z-normalized within each contrast condition separately. The line is the best linear fit to the data. The correlation value and the correlation significance (r and p) are listed in the panel.  
(B) Same as (A), correlation between PPM and monkey RT.
significant correlation between the monkey RT and each of the model’s predicted RT (RIM - Pearson correlation co-efficient $r = 0.30, p < 0.001$; PPM - Pearson correlation co-efficient $r = 0.39, p < 0.001$) (Fig. 3.10). We only included in this analysis trials in which the monkey and the model both scored a “hit”, and hence both had a RT value for the trial. For example, in this experiment (Fig. 3.10), the monkey did not score a “hit” on any of the 4% contrast targets; therefore there are no z-scores for the 4% contrast.

We repeated this analysis across all 95 SU and MU experiments. For each experiment, we first z-normalized the RTs within each contrast condition separately, then combined all the trials together (across all experiments), and finally computed the monkey/model RT correlation (Fig. 3.11), which was highly significant for both dynamic models (RIM $r = 0.27, p < 0.001$, for ~2700 trials; PPM $r = 0.23, p < 0.001$, for ~2650 trials). This indicates that variability in the model’s RTs is correlated with the variability in the monkey’s RTs. This is evidence that V1 neurons likely contributed to the timing of the decision to initiate the saccades in the detection task. In Chapter 4, I further investigated the contribution of V1 neurons to the behavior of the monkey by examining the correlation between the variability in the activity of V1 neurons and variability in both the monkey’s RTs as well as behavioral choices.
Figure 3.11. Correlation between monkey and model RT for all experiments. A Correlation between z-scored RTs predicted by the RIM model and the RTs of the monkey in the corresponding trials for all 95 SU and MU experiments. Within each experiment, RTs are z-normalized within each contrast condition separately. The line is the best linear fit to the data. The correlation value and the correlation significance (r and p) are listed in the panel. B same as a, correlation between PPM and monkey RT.

Discussion

Ideal observer models that dynamically computed integrated spiking activity (or posterior probability of the presence of the target), which can be compared to an optimal decision criterion had, on average, significantly lower detection sensitivities than the monkey in the visual detection task. Also, despite having more flexibility as to when to make decisions, none of the dynamic models had significantly higher detection sensitivities than the fixed integrator model from Chapter 2 (i.e. the rate model). This was due primarily to the dynamic model’s high false alarm rate caused by vulnerability to the increased variability in the integrated responses in the late part of the trial (SIM) and the large fluctuations in the variability in the integrated responses at the start of the trial (RIM and PPM). However, these dynamic models were valuable for being able to
indicate the moment when there was sufficient information in V1 about the stimulus on a
given trial to reliably detect the target which can be compared to the monkey’s actual RT.
We found that both dynamic models (RIM and PPM) predicted RTs that were on average
significantly shorter than, yet highly correlated with (on a trial-by-trial basis), the
monkey’s RT. Finally, we observed a small difference in the rate at which the RTs of the
monkey and the RTs of the models decreased with target contrast, suggesting that RT
may be partially dependent on the difficulty of the task or extrastriate processing.

**Comparison of dynamic integrator models with fixed integrator model**

*Simple Integrator Model*

It was obvious that the SIM was the weakest of the three models used to evaluate
neural detection sensitivity. The main weakness of the SIM was that it suffered from too
many false alarms. This greatly decreased the overall accuracy of the model. The fixed
integrator model from Chapter 2 (the one that computed spike rate, not spike count), on
the other hand, had a moderate false alarm rate (not significantly different than that of the
monkey). This was possible due to the following reasons (which are all related to the fact
that the fixed integrator model computed spike rate, via normalization by the integration
period). For trials (evaluated with the fixed integrator model) when the monkey
responded early, well before 200 ms (usually on mid to high contrast trials), the low
number of accumulated spikes was normalized by a correspondingly small integration
duration to yield a high spike rate. Yet on longer trials lasting ~200 ms (dominated by
the target-absent trials), the total number of spikes (which may have actually been
moderately high) was normalized by a correspondingly long integration duration (max 200 ms) to give a low spike rate. This facet of the model actually lead to high separability of the target-present and target-absent neural response (spike rate) distributions. The wide separation in the distributions gave the model the freedom to use a relatively high criterion to separate those distributions, which yielded a low false alarm rate.

On the other hand, we did not compute the spike rate for the SIM, but merely counted the accumulated number of spikes. For trials when the monkey responded early, well before 200 ms (usually on mid to high contrast trials), the low number of accumulated spikes required a relatively low threshold if most of the high contrast trials were to be classified as target-present trials by the model. On longer trials, lasting up to 600 ms (dominated by target-absent trials), as time went by in the trial the SD of the accumulated number of spikes continued to increase, creating less separation between the target-present and target-absent accumulated spike count distributions. For these trials the criterion needed to be high to avoid a flood of (mostly late) false alarms.

The compromise between a low threshold for the short, high contrast target-present trials and the longer target-absent trials was a decision criterion that still gave a quite high false alarm rate (note how the mean plus SD of the target-absent condition in Fig. 3.1 almost reaches the decision criterion), and hence a low overall accuracy rate (since half of the trials are target-absent trials).

In general, the SIM, as well as the RIM and PPM, may actually be handicapped (relative to the fixed integrator model) by examining neural responses from the entire 600
ms period that we gave the monkey to perform the detection task on each trial. Our results from Chapter 2 (Fig. 2.8) indicate that the majority of the stimulus related neural responses occur within a short time after the onset of the stimulus. Findings from single neurons in areas V1 (Muller et al., 2001; Frazor et al., 2004) and MT (Uka and DeAngelis, 2003; Osborne et al., 2004), as well as from psychophysical studies in monkeys (Uka and DeAngelis, 2003) and in humans (Ludwig et al., 2005) confirm this notion. In addition, Chen et al. (2008) used the voltage-sensitive dye imaging (VSDI) signal to assess V1 neural population detection sensitivity (in a task similar to the one used in this chapter). Though the time course of the VSDI signal was not transient, the experimenters were able to use a whitening filter to minimize the considerable effect of temporal correlations in the VSDI signal. The whitening operation emphasized transient responses because most of the power in the noise of the VSDI signal is at the low temporal frequencies. Therefore, the whitening operation effectively made the initial part of the trial (dominated by the transient responses) far more informative (in terms of d’, or signal to noise ratio) than the latter part of the trial.

Running Integrator Model

The RIM, by virtue of having a shorter “memory” than the SIM, was able to avoid the excessive accumulation of spikes in the target-absent trials that caused the SIM to incur such a high level of false alarms (notice the relatively constant SD in the RIM time courses, Fig. 3.2, vs. the SD that increased throughout the trial for the SIM, Fig. 3.1). For this reason, the RIM performed quite well relative to the SIM. We suspect that the
optimal running window length was 45 ms because this was long enough to observe a noticeable difference in spiking activity in target-present and target-absent trials, but not so long that the target-present and target-absent spike distributions began to overlap due to the increase in the variability in the number of accumulated spikes we saw for the SIM. Keeping the variability in the accumulated spike count low was the key for the RIM to maintain a decision criterion low enough to prevent a high false alarm rate.

*Posterior Probability Model*

The PPM and RIM did not have significantly different detection sensitivities, consistent with the VSDI results of Chen et al. (2008), which used the same visual detection task and utilized quite similar ideal observer models. However, it is rather surprising that the PPM does not perform better than the fixed integrator model due to the extra information we gave to the model. The reason the PPM does not do better is because it was also plagued by a false alarm rate that was higher than the fixed integrator model. The false alarms of the PPM tended to occur very early in the trial. The overlap in the distributions of the mean responses of the target-present and target-absent conditions in the first ~50 ms after stimulus onset was quite high (Fig. 3.1) and any transient clustering of spikes in this part of a target-absent trial sent the posterior probability that the trial contained a target shooting up almost instantly, causing a false alarm. Note that this did not happen with the VSDI data because the SD of the VSDI signal is pretty much constant throughout the trial (see Chen et al., 2008; Fig. 5B). The fixed integrator model from Chapter 2 was relatively immune to these fluctuations in
instantaneous firing rate during the first part of the trial because it computed the rate based on the entire integration interval.

**RIM and PPM reaction times**

The dynamic model’s RT signifies the moment that the neural signal crosses the decision threshold. If the triggering of a decision set off a stereotyped saccadic response, then it would be reasonable to expect that the difference between the time the decision threshold was reached and the execution of the monkey’s saccade should be the same for all contrasts. However, what we observed was that at high target contrasts (> 21%) the differences between the mean monkey and model RTs were ~85 ms and ~105 ms (for the PPM and RIM, respectively), whereas the offsets at the lowest contrast bin (2-3%) were ~140 ms and ~190 ms (for the PPM and RIM, respectively). This suggests that as the task became harder (via a reduction in target contrast), there was an additional period of time between the “decision” coming out of V1 (i.e. decision threshold being crossed) and the execution of the saccade. Perhaps this additional time represents a cost built into the system to ensure reliability when there is relative uncertainty in the signal (i.e. the decision threshold is reached late into the trial, as is the case for low contrast trials). Perhaps the additional time represents a lack of vigilance during longer trials on the part of the monkey relative to the model (which by definition never falters in its vigilance).

Another possible interpretation is based on the notion, put forth as a conclusion of the results from Chapter 2, that large populations of neurons are necessary to mediate the perceptual decision process. High contrast targets likely activate larger populations of
neurons than do low contrast targets. If a large population of neurons is signaling the presence of the target, then downstream decision and motor areas may be activated more quickly than in the case where smaller populations are signaling the presence of the target. This type of situation would lead to the observed discrepancy between the offsets in the model’s predicted RT and the monkey’s actual RT for low and high contrast conditions.

The significant trial-by-trial correlations we observed in the variability of the monkey and model RTs may indicate that V1 neurons play some role in determining the timing of the execution of the monkey’s decision. In the next chapter, I further examined whether variability in the same set of V1 neurons contributed to the timing of the choice in the detection task (by computing the correlation between variability in V1 activity and the monkey’s RT on a trial-by-trial basis). In addition, I sought to determine if the variability in V1 was also correlated to the choice itself (target present vs. target absent) via a calculation of choice probability (i.e. the correlation between variability in V1 activity and the monkey’s choice on a trial-by-trial basis).

Together the detection sensitivity and reaction time results from the three models suggest three implications for the decoding of stimulus related signals in the brain: 1) the majority of the relevant stimulus related neural responses occur within a short time after the onset of the stimulus; 2) any decoding system that fails to regularly purge its “memory” (every 45 ms was optimal for our RIM) is subject to the accumulation of noise which can drastically lower stimulus sensitivity; 3) decisions made when the task is
difficult may be relatively delayed (as illustrated by the differences we saw in the monkey and model RT slopes) due to any number of downstream inefficiencies.

**Conclusions**

Though they had lower detection sensitivities than the monkey, and were more prone to false alarms than the fixed integrator model from Chapter 2, the dynamic integrator models provided reasonable estimates of V1 neurons’ RTs, which could be compared to the monkey’s RTs. Significant trial-by-trial correlation between variability in monkey and neural RTs suggests that V1 neurons contributed to the timing of the initiation of the saccade to the target in the detection task. Also, comparisons of the relative rates with which the mean RT increased as target contrast decreased suggest the existence of a decision mechanism beyond area V1 that may have been partially dependent on the difficulty of the detection task.
Chapter 4: Neural correlates of choice and reaction time in V1

Abstract

Perceptual decisions are driven by stimulus related signals that are initially processed in early sensory cortical areas. Performing a task at or near perceptual threshold creates variability in behavior which must be accounted for by variability in neural activity. A key question is how much of the variability in behavior is due to variability in the sensory related signals and how much is due to variability in decision or motor related signals in the brain. Another key question, which will be the focus of this study, is how much does the activity of individual neurons or small groups of neurons contribute to the co-variation that exists between behavior and neural activity within early sensory areas. Correlations between the outcomes of a simple behavioral task and the firing rate of individual cortical neurons on a trial-by-trial basis have suggested at least minor roles for several cortical areas (i.e. V2, MT, MST, VIP, and LIP) in the decision making process leading up to the motor execution of a behavior. Though neural correlates of behavior have been observed in large neural populations in human V1 using fMRI, few attempts have been made (all of them unsuccessful) to find trial-by-trial correlations, referred to as choice probability (CP), between behavior and the activity of individual primary visual cortex (V1) neurons, or any other primary sensory cortical area for that matter. Here we report the first observation of significant CP in area V1 for single neurons, as well as for multi-unit sites (MU) and the local field potential (LFP), using a reaction-time visual detection task. The detection task we used had equal numbers of trials where a target was
present (behavioral outcome “hit” or “miss”) and trials where a target was absent (behavioral outcome “correct reject” or a “false alarm”). CP for target-present trials (i.e. difference in neural responses between “hits” and “misses”) was significantly higher than for target-absent trials (i.e. difference in neural responses between “false alarms” and “correct rejects”). Also, CP for the target-present trials became significant earlier than for target-absent trials (for which only MU and LFP showed significant CP). LFP showed frequency band dependent variations in CP, which were roughly the same for target-present and target-absent trials. Correlations between spiking activity and reaction time (another important aspect of behavior), which had previously been observed in areas MT and VIP, were also observed in area V1, further strengthening the notion that V1 neurons contribute to decision making processes.

Introduction

We all make decisions based primarily on input from the environment. Some decisions are difficult to make (or take longer to make) because sensory stimuli may be at or just above perceptual threshold, resulting in variable behavior, despite zero variability in the stimulus. Sensory physiologists can measure the variability in the neural responses of different brain areas to the same near-threshold stimuli across multiple presentations. If, on average, the variability in the responses of neurons in some part of the brain is highly correlated with variability in the organism’s behavior, this is strong evidence that this part of the brain plays an important role in driving that behavior. In motor areas, such as primary motor cortex or the frontal eye fields which control eye movements, these
correlations could theoretically be very high (i.e. greater than 0.9), depending on the exact manner in which signals are combined to generate behavior. Choice probability (CP) has been observed in multiple extrastriate areas (medial superior temporal area (MST) - Celebrini and Newsome, 1994; Cook and Maunsell, 2002; medial temporal area (MT) - Britten et al., 1996; Dodd et al., 2001; Uka and DeAngelis, 2004; Purushothaman and Bradley, 2005; lateral intraparietal area (LIP) - Shadlen and Newsome, 2001; Roitman and Shadlen, 2002; ventral intraparietal area (VIP) - Cook and Maunsell, 2002; ventral premotor cortex (VPC) - Romo et al., 2004; secondary somatosensory cortex (S2) - de Lafuente and Romo, 2005; secondary visual cortex (V2) - Nienborg and Cumming, 2006).

In the visual motion pathway, CP has been shown to increase along the visual hierarchy from area MT to areas MST, VIP and LIP. It is not clear, however, whether CP always increases along a visual pathway. Alternatively, CP may be maximal at the area that contains signals that are most appropriate to guide behavior, irrespective of where this area is located in the visual hierarchy. Importantly, though Ress and Heeger (2003) observed neural correlates of behavior in human V1 using fMRI, prior studies have failed to observe significant CP in individual neurons within the first stages of cortical sensory processing (de Lafuente and Romo, 2005; Nienborg and Cumming, 2006). The activity of some visual areas has been shown to co-vary with reaction times (RT) as well (Cook and Maunsell, 2002). However, these links to behavior have not yet been observed in primary visual cortex or any other primary sensory area.
We trained three macaque monkeys to perform a simple reaction-time visual
detection task. We observed variability in the response of single neurons (single units,
SU), small groups of neurons (multi-units, MU), and the local field potential (LFP) in
macaque primary visual cortex (area V1) that co-varies with behavior (both in terms of
choices and reaction times). Importantly, this is the first time CP and RT-spike
correlations have been reported in neurons in V1 or any primary sensory area. This result
indicates that stimulus representations in early sensory areas contribute significantly to
variation in behavior, even at the level of single neurons and small groups of neurons.

Materials and Methods

Subjects and surgery  (See chapter 2)

Task and visual stimulus  (See chapter 2)

Electrophysiology  (See chapter 2)

Analysis of behavioral data  (See chapter 2)

Neuron database  (See chapter 2)

All of the data for this study comes from the detection experiment described in Chapter 2.
those results were based on 62 MU recordings and 33 SU recordings. The selection
criteria for those recordings are described in the Materials and Methods section of
Chapter 2. For the CP analysis, we selected only experiments where there were contrast
conditions with at least 3 hits and 3 misses (for the target-present CP) or at least 3 false
alarms and 3 correct rejects (for the target-absent CP). Out of the 62 MU and 33 SU
recordings used in Chapter 2, our selection criterion left 46 MU and 25 SU recording
sites for the target-present CP analysis and 32 MU and 17 SU recording sites for the target-absent CP analysis. For each of the MU and SU recordings we also attempted to record the local field potential (LFP). Using the criteria mentioned in Chapter 2 (and the criteria listed above in this chapter) left us with 58 LFP recording sites for the target-present CP analysis and 40 LFP recording sites for the target-absent CP analysis.

**Analysis of choice probability**

We performed a separate choice probability (CP) analysis for target-present trials (hits vs. misses) and for target-absent trials (correct rejects vs. false alarms). For a given contrast, firing rates in all trials (irrespective of behavior) were first converted into z-scores. Z-score values were then combined across contrasts to form two distributions for the two possible behaviors (e.g. hits vs. misses). CP values were computed for each site as the area under the receiver operating characteristic (ROC) curve (Green and Swets, 1966) describing these two combined distributions. To equate the integration times of hits and misses (see Chapter 2 for a description of how integration times were determined for each hit trial), misses were randomly assigned integration times from the distribution of RTs on the hit trials from the same contrast condition. This procedure was repeated 1000 times, and the mean CP was reported for each site. The same method was used for the target-absent condition (correct rejects were assigned false alarm integration times). Significance of the CP was assessed using a permutation test (Britten et al., 1996).
Choice probability time courses

Time courses of the CP were derived to illustrate how the CP evolved over the course of the trial. We constructed time courses by computing CP for discrete time intervals throughout the trial. CP was computed within a short integration window (we used windows of various length between 25 ms and 100 ms); in figures in this chapter the CP was always plotted at the end of the bin (e.g. a point at 50 ms depicted the CP computed over the interval from 0 to 50 ms after target onset). The integration window was moved over the data every 10 ms or 25 ms starting 225 ms before target onset and ending 275 ms after target onset to obtain a full time course covering both pre and post stimulus time periods. Error bars in all time course figures represent SEM across sites and target contrasts.

Local field potential

The LFP, recorded simultaneously with the same metal microelectrodes we used to record SU and MU, is a measure of synaptic potentials, voltage dependent membrane oscillations, and after-polarizations across swaths of cortex 0.5-3 mm wide (Logothetis, 2008). LFP, being a time dependent signal, can be decomposed into various frequency bands. Typically, 200 Hz to 250 Hz is the high frequency cutoff for what defines the LFP signal (Kreiman et al., 2006; Liu and Newsome, 2006; Stark and Abeles, 2007; Belitski et al., 2008; Goense and Logothetis, 2008). For the initial LFP analyses in this chapter, the LFP response was defined as the amplitude (square root of power) of the power spectrum of the LFP in the 1-200 Hz frequency range (computed with fast Fourier
transform, FFT, for individual trials during the integration period; see above for details about the integration period). In the subsequent analyses, LFP was defined as the amplitude of the power spectrum of the LFP computed over smaller frequency bands (40 Hz wide).

To assess LFP stability (see Methods and Materials in Chapter 2) and construct time courses of the LFP signal to visually compare with SU and MU peri-stimulus time histograms (PSTHs), we computed the root mean square (RMS) of the raw LFP for each trial, then found the average root mean square (RMS) per condition. RMS in each trial is defined as:

\[ RMS = \sqrt{\frac{\sum LFP^2}{t^2}} \]

where \( t \) is the time (ms) over which the RMS is being computed. The RMS for each trial was computed over a 700 ms period surrounding target onset, and the RMS for each trial was averaged across each contrast condition to derive the LFP PSTHs. The PSTH for each contrast condition was normalized to the peak of the maximum contrast condition.

**Analysis of eye movements**

One possible source of the co-variation between neural responses and behavior (which could mistakenly be considered CP) could be eye movements during the trial. To rule out eye movements as a source of correlation between the variability in neural responses and behavior we investigated the effects of four indicators of eye movements during the period in which neural responses were averaged: (1) average distance from the fixation
point, (2) average distance from the target, (3) average velocity, and (4) maximal instantaneous velocity. The average distances are the mean distance between the center of gaze and the fixation point or the target location during the integration period. The average velocity is the overall distance the eye moved during the integration period divided by its duration. Instantaneous velocity is the maximum instantaneous velocity of the eye during the integration period. To examine the potential contribution of eye movements to choice probabilities, we determined whether neural responses were significantly correlated with the four eye movement indicators.

**Reaction time – spike correlation analysis**

For every experiment, the reaction times (RT) and spikes from trials from each contrast condition were analyzed separately. This analysis was only performed on “hit” trials. Spikes were integrated over 100 ms windows for each trial in a given contrast condition. For each 100 ms window, the integrated spike counts were then z-transformed using the mean and SD of all the trials in that contrast condition. The same procedure was used for z-transforming all of the RTs for trials from a given contrast condition. It was often the case in this analysis that a trial would end (because of a saccade to the target made by the monkey) in the middle of a 100 ms window (especially for trials with short RT). When this happened, we excluded that trial from the RT-spike correlation analysis for that 100 ms period. This prevented contamination of the correlation by spiking activity that was potentially related to the saccade. In fact we also excluded trials that ended 20 ms prior to the end of the integration window to be on the safe side. This 20 ms buffer, which we
called the minimal motor response time (MMRT), was discussed thoroughly in Chapter 2.

RT-spike correlations for each experiment were computed by combining all of the z-transformed spike counts and z-transformed RTs from each condition within an experiment. The RT-spike correlations were then averaged across experiments at each time point to yield a single mean RT-spike correlation time course. We found that the mean RT-spike correlation time courses for SU and MU were similar, so for all figures and analyses, we combined SU and MU results. Error bars in all time course figures represent SEM across experiments.

**Results**

*Trial-to-trial co-variation between V1 activity and behavioral choices*

If V1 responses contribute to behavioral performance in the detection task, trial-to-trial variations in neural responses to identical visual stimuli should be correlated with trial-to-trial variations in the monkey’s behavior. The strength of these co-variations could provide useful information regarding the size of the neural population that contributes to behavior. Such co-variations, often termed choice probability (CP), have been observed in several brain areas (MST - Celebrini and Newsome, 1994; Cook and Maunsell, 2002; MT - Britten et al., 1996; Dodd et al., 2001; Uka and DeAngelis, 2004; Purushothaman and Bradley, 2005; LIP - Shadlen and Newsome, 2001; Roitman and Shadlen, 2002; VIP - Cook and Maunsell, 2002; VPC - Romo et al., 2004; S2 - de Lafuente and Romo, 2005;

**Choice Probability in Target-Present Trials**

Choice probability measures the probability with which an ideal observer could predict the behavioral outcome of the detection task based on the neural response in single trials. We separately analyzed the target-present trials (hits vs. misses) and the target-absent trials (false alarms vs. correct rejects). Figure 4.1A shows peri-stimulus time histograms (PSTHs) for 9 hits (green curve) and 20 misses (red curve) for a single contrast condition (5%) from one SU experiment. Figure 4.1B-C show hit vs. miss PSTHs for an example MU and LFP experiment, respectively. The CP value is listed in each panel. Overall, CP values for SU and MU were very similar, but slightly lower for LFP (Table 4.1). Paired *t*-tests reveal that CP values for LFP were significantly lower than MU (p-value = 0.039), but not SU (p-value = 0.853). Figure 4.2A shows a frequency histogram of CP values across all SU sites for target-present trials. Filled bars indicate sites for which the CP value is significantly different from 0.5 (based on a permutation test). Figure 4.2B-C shows CP values across all MU sites and LFP sites for target-present trials, respectively. The average CP values are significantly higher than 0.5 (SU average CP=0.6099, p<0.001, *t*-test; MU average CP=0.6236, p<0.0001, *t*-test; LFP average CP = 0.5634, p<0.001, *t*-test), indicating that the monkeys were more likely to report seeing the target on trials in which V1 responses were relatively high. These results demonstrate for the first time that trial-to-trial variability in the responses of SU,
MU, and LFP in V1 can be significantly correlated with the monkey’s perceptual decisions.

Figure 4.1

Figure 4.1. Peri-stimulus time histograms (PSTHs) for hit and miss trials in an example SU, MU, and LFP experiment. A, PSTH of “hit” (n = 9) and “miss” (n = 20) trials for one contrast condition (5% contrast) from one SU experiment. Vertical lines indicate target onset (0 ms) and target offset (300 ms). B, C, similar to A using an MU experiment (B, contrast = 6%) and an LFP experiment (C, contrast = 4%), where the responses are in units of normalized root mean square (RMS) of the LFP (see Materials and Methods for details of the RMS). PSTH bin size is 25 ms, with data plotted in the middle of the bin. CP values are listed in each panel.
Figure 4.2

**A** SU  
- Count  
- n = 25  
- CP = 0.6099  
- [Frequency histogram for SU with mean value indicated by an arrow and asterisks indicating significant difference from 0.5 based on a t-test.]

**B** MU  
- Count  
- n = 46  
- CP = 0.6236  
- [Frequency histogram for MU with mean value indicated by an arrow and asterisks indicating significant difference from 0.5 based on a t-test.]

**C** LFP  
- Count  
- n = 58  
- CP = 0.5684  
- [Frequency histogram for LFP with mean value indicated by an arrow and asterisks indicating significant difference from 0.5 based on a t-test.]

**Figure 4.2.** Frequency histograms of target-present CP values of V1 neurons. **A**, CP of SU. **B**, CP of MU. **C**, CP of LFP. Filled bars indicate sites with significant CP (permutation test, p<0.05). Arrows indicate mean value. Asterisks indicate significant difference from 0.5 based on a t-test.
Additionally, we computed a grand CP value for each measurement by first combining the z-scores of spike rates from all the trials within the same behavioral category across all sites and then computing a single CP value between the combined distributions. Grand CP values were close to the average CP across sites (Table 4.1), demonstrating the robustness of our results.

<table>
<thead>
<tr>
<th></th>
<th>Hits vs. misses</th>
<th>FA vs. CR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean CP (SEM)</td>
<td>t-test p-value</td>
</tr>
<tr>
<td>SU</td>
<td>0.6099 (0.031)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>MU</td>
<td>0.6236 (0.027)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>LFP</td>
<td>0.5634 (0.10)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>SU</td>
<td>0.5091 (0.210)</td>
<td>p = 0.669</td>
</tr>
<tr>
<td>MU</td>
<td>0.5212 (0.020)</td>
<td>p = 0.314</td>
</tr>
<tr>
<td>SU and MU</td>
<td>0.5217 (0.06)</td>
<td>p = 0.276</td>
</tr>
</tbody>
</table>

Several studies have shown that the gamma-band frequency activity of the LFP is more selective for specific stimulus features than lower band activity (Gray and Singer, 1989; Frien and Eckhorn, 2000; Frien et al., 2000; Fries et al., 2002; Siegel and Konig, 2003; Kayser and Konig, 2004; Henrie and Shapley, 2005; Wilke et al., 2006; Womelsdorf et al., 2006). Breaking down the LFP into 20 Hz bands using FFT analysis, we found that the amplitude of the power spectrum of the gamma-band range (40-100 Hz) did indeed have higher CP than that of the lower frequencies (<40 Hz) (Fig. 4.3). In fact, all bands except 1-20 Hz showed significant CP. CP peaked at the 60-80 Hz range, and remained high out to 200 Hz.
Figure 4.3. CP as a function of LFP frequency band for target-present trials. Mean and SEM of CP of target-present trials for LFP, which was broken into 20 Hz bands via fast Fourier transform (FFT). Asterisks indicate significant difference from 0.5 based on a t-test.

Extreme values of CP were due to relatively small numbers of trials at some sites. However, combining data from SU and MU, sites with low numbers of trials had roughly the same mean CP as sites with higher numbers of trials (Figure 4.4A). Additionally, we computed average CP values for 37 SU and MU sites in which CP was obtained for two contrasts. The average CP at the lower contrast trials (CP=0.626) was not significantly different from the average CP at the higher contrast trials (CP=0.596; paired t-test p=0.47). CP was also stable across conditions of varying difficulty, as measured by the probability with which the monkey detected the target (Fig 4.4B).
Figure 4.4. CP as a function of number of trials and task difficulty. A, Mean and SEM of CP as a function of the minimum (Min.) number of trials per outcome type (hits or misses). B, Mean and SEM of CP as a function of the probability (Prob.) of reporting that the target was present. In A and B, results are combined across SU and MU sites.

Choice probability time courses

To examine the possibility that the observed CP for the target-present trials was due to feedback related to the monkey’s decision, we computed the normalized time course of the CP. Figure 4.5A shows the normalized time course of the CP in target-present trials for the SU sites. Responses on hit trials were significantly higher than responses on misses from shortly after response onset. A similar result was obtained for the MU responses (4.5B) and LFP responses (not shown). These results rule out the possibility that the observed CP are due to feedback related to the monkey’s decision. Figure 4.6 shows a side-by-side comparison of the time courses of the CP for the SU, MU, and LFP relative to the time of target onset (vertical line at 0 ms in this and all subsequent CP time course figures).
Figure 4.5. PSTHs of normalized neural responses (left y-axis) and CP time courses (right y-axis) in target-present trials. Circles show mean normalized (Norm.) PSTHs of SU recordings for all of the hit trials (black) and for all the miss trials (cyan) that are used in the CP analysis. For each stimulus condition within each experiment, the hit and miss PSTHs were first normalized to the peak of the larger of the two PSTHs. Error bars represent SEM across sites and target contrasts. Each data point in the PSTH represents the accumulated response from the previous 50 ms. The time course of the CP (red) shows the average and SEM of CP in overlapping 50 ms time bins across all experiments and stimulus conditions contributing to the CP analysis. A, All trials from conditions with at least 3 hits and 3 misses (n = 25). C, Trials from lower contrast conditions with at least 3 hits and 3 misses (n = 14). E, Trials from higher contrast conditions with at least 3 hits and 3 misses (n = 14). B, D, F, Similar to A, C, E using MU recordings (B, n = 46; D, n = 23; F, n = 26). The three MU sites for which we obtained CP measurements for three contrast levels contributed two sets of normalized PSTHs each to F.
To determine if the amplitude and the time course of the CP depended on target contrast, we recomputed the normalized time courses at sites in which we obtained CP values for two or more target contrast levels. Normalized time courses were computed separately for the higher contrast trials (Figs. 4.5C-D for SU and MU, respectively) and for the lower contrasts trials (Figs. 4.5E-F for SU and MU, respectively). The normalized responses rose more rapidly at the higher contrast, as did the time course of the CP. CP for low contrast trials (both SU and MU), as well as SU high contrast trials, dropped significantly below 0.5 just after stimulus onset. The majority of the dip appears to be due to an increase in the activity during miss trials, as the hits time course near this time period remained flat. The increase in neural activity may actually lead to the trial being a miss, if the detection decision is mediated by a criterion that monitors the post-stimulus onset firing rate minus the pre-stimulus onset firing rate.

These time courses appear to be at odds with the result mentioned above which stated that on average low contrast trials actually had higher (but not significantly higher) CP than high contrast trials. It also appears to contradict the results shown in Figure 4.4B, which showed CP to be independent of probability that the monkey reported the target (which itself is highly related to target contrast). However, those previous results were based on CP computed with an integration window extending from shortly after the onset of the target until ~200 ms after the onset of the target, and thereby missed critical features of how CP evolves over time separately for different types of trials.

The time courses in Figures 4.5-6 all show CP calculated using an overlapping integration period of 50 ms. For the time courses to be useful in indicating the average
time point at which the CP starts to rise above chance and become significant (which can be helpful for discussions regarding the source of the CP), it may be helpful to use a narrower integration window. In addition, we wanted to observe the effect of using a broader window with the intention of maximizing the separation between hit- and miss-related neural activity. Therefore, we used integration window sizes of 25 ms, 75 ms, and 100 ms to compare to the 50 ms window for the SU (Fig. 4.7A). We also used more

Figure 4.6

Figure 4.6. CP time courses for SU, MU, and LFP target-present trials. Only trials from conditions with at least 3 hits and 3 misses were included. Each CP time course shows the average and SEM of CP in overlapping 50 ms time bins across all experiments and stimulus conditions contributing to the CP analysis. SU and MU time courses are identical to the time courses seen in the top panels of Figure 4.5. LFP CP time course is limited to frequency band 60-120 Hz, which showed the highest CP among various frequency bands of the LFP (see Figure 4.3).
frequent sampling (windows slid every 10 ms, compared to every 25 for Figs. 4.5-6) to obtain a comparison of the time courses on a fine scale. The point at which the CP rises above chance appears to be later when using a more temporally restricted window. The same trend exists for the MU (Fig 4.7B). Also, the maximum CP achieved with the shortest window falls well below that of the longest window, indicating that longer windows are more conducive to capturing more of the differences that exist in the hit and miss trials. These results suggest that when computing CP there is a tradeoff between the maximum magnitude that can be observed and the precision of the dynamics of the time course. When analyzing strong hit/miss differences in neural activity, short time windows can be used to get more accurate time courses. When hit/miss differences in

Figure 4.7

![Figure 4.7](image)

**Figure 4.7.** CP time courses for target-present trials using integration windows of various widths. *A*, The time course of the CP shows the average and SEM of CP in overlapping 25 ms (green), 50 ms (black), 75 ms (blue), and 100 ms time bins across all SU experiments and stimulus conditions contributing to the CP analysis. *B*, Similar to *A* for all MU experiments and stimulus conditions contributing to the CP analysis.
neural activity are weaker (as we will see below with the LFP frequency band analysis and the target-absent CP), longer integration windows may be helpful in determining whether hit/miss differences exist and whether they are significant.

As mentioned above, CP for the LFP was shown to depend on the frequency band analyzed (Fig. 4.3). As one might expect, the time courses of the various LFP bands were also quite different (Fig. 4.8). The integration window used to examine this issue was 100 ms wide, which, per the result demonstrated in Figure 4.7, better illustrated the difference in magnitude for the various bands. The lowest frequency band (1-40 Hz) had the shallowest time course and also the lowest maximum CP. The higher frequency bands had slightly steeper time courses and rose above chance at approximately the same time. The middle frequency band (81-120 Hz) had the largest maximum CP (significantly higher than the lowest frequency for most time points past 150 ms).

**Choice probability in target-absent trials**

In contrast to the significant CP values we observed in target-present trials (Fig. 4.2), CP values in target-absent trials (correct rejects vs. false alarms) were not significantly different from 0.5 for SU (Fig. 4.9A; average CP=0.5091, p=0.669, *t*-test) as well as for MU (Fig. 4.9B; average CP=0.5212, p=0.314, *t*-test) and LFP (Fig. 4.9C; average CP=0.5271, p=0.276, *t*-test). When breaking the LFP down into its component frequency bands, the results are mixed (Fig. 4.10). Some of the mid-range bands (i.e. gamma bands) showed significant CP, as did some of the higher bands.
Figure 4.8. CP time courses for various LFP frequency bands for target-present trials. The time course of the CP for five non-overlapping LFP frequency bands shows the average and SEM of CP in overlapping 100 ms time bins across all experiments and stimulus conditions contributing to the CP analysis.

The lack of significant CP in target-absent trials could be due to the relatively few number of false alarms made by the monkey (less than 5% of all trials) compared to the number of misses (which make up ~10% of the trials). Small numbers of false alarms could make it difficult to extract a meaningful difference in spiking activity especially in target-absent trials where the firing rates are quite low to begin with. Lack of significant CP could also suggest that other sources of noise downstream to V1 dominated behavioral variability in target-absent trials. This finding is consistent with the relatively short RTs observed for many false alarm trials (Chapter 2, Fig. 2.2 and Chapter 3, Fig. 3.7). Such short RTs suggest that in some of our experiments the monkeys had a
Figure 4.9. Frequency histograms of CP values of V1 neurons for target-absent trials. A, CP of SU. B, CP of MU. C, CP of LFP. Filled bars indicate sites with significant CP (permutation test, p<0.05). Arrows indicate mean values.
Figure 4.10. CP as a function of LFP frequency band for target-absent trials. Mean and SEM of CP of target-absent trials for LFP, which was broken into 20 Hz bands via a fast Fourier transform (FFT). Asterisks indicate significant difference from 0.5 based on a t-test.

significant rate of “early errors” (see Chapter 3 for a discussion of “early errors”) which we originally categorized as “fast guesses” (Chapter 2 for a discussion of “fast guesses”) thinking those trials were not based on sensory evidence (e.g., Carpenter and Williams, 1995). If a large portion of the false alarms were due to “early errors”, then there would be much less of a chance to uncover a correlation between the V1 responses and the monkey’s behavior on those trials.

However, a look at the time courses of the target-absent CP (Fig. 4.11, using 100 ms integration windows) revealed that in the later part of the trial the average CP actually did rise significantly above chance (at least for MU and the LFP). This is consistent with
the idea that “early errors” diluted the correlation between neural activity and choice during the first 100 ms or so of the trial, which is why the target-absent CP appeared to be so low (Figure 4.9) when calculated based on integration times starting shortly after “target onset” and ending, on average, ~150 ms later. Most of the “early errors” trials ended (and stopped contributing to the CP) by the time the target-absent CP time courses were becoming significantly greater than chance.

Figure 4.11 also shows a significant rise in the CP of the LFP starting ~50 ms before the time of target onset and ending ~50 ms after target onset, before rising up

Figure 4.11. CP time courses for SU, MU, and LFP target-absent trials. Only trials from conditions with at least 3 false alarms and 3 correct rejects were included. Each CP time course shows the average and SEM of CP in overlapping 50 ms time bins across all experiments and stimulus conditions contributing to the CP analysis. LFP CP time course is limited to frequency band 60-120 Hz, which showed the highest CP among various frequency bands of the LFP (see Figure 4.10).
again later in the trial at roughly the same time as the MU CP rises up. Even though this elevation occurs partially when the target was presented, it is most likely not related to the perception of a stimulus, considering how “early” the response is. This rather robust elevation may be an attention mechanism specific to the LFP (seen in the other LFP bands as well (Fig. 4.13), though most prominently in the 81 to 120 Hz band), though that does not explain why it is only present in the target-absent trials and not the target-present trials (Fig. 4.6). On the other hand, it may represent a pre-trial “go” bias (again, specific to the LFP) towards indicating the presence of the target. A possible reason we observed it for the target-absent trials and not target-present trials is that target-present trials had on average a significantly higher spike rate. If the “go” bias was relatively weak, the “go” bias may not have had much influence on high spike rate target-present trials, but may have had a noticeable influence on the low spike rate target-absent trials).

Figure 4.12

**Figure 4.12.** CP time courses for target-absent trials using integration windows of various widths.  
**A,** The time course of the CP shows the average and SEM of CP in overlapping 25 ms (green), 50 ms (black), 75 ms (blue), and 100 ms time bins across all SU experiments and stimulus conditions contributing to the CP analysis.  
**B,** Similar to **A** for all MU experiments and stimulus conditions contributing to the CP analysis.
Figure 4.12 shows the target-absent CP time courses separately for SU (Fig. 4.12A) and MU (Fig. 4.12B). Regardless of the size of the integration window, there was no point at which SU showed significant CP. For the MU, the onset of significant CP comes ~120 ms to ~180 ms after stimulus onset (depending on which size integration window is used). Therefore, the onset of the significant CP appears about 70 ms later in target-absent trials relative to target-present trials (see Fig. 4.7B; MU significant CP onset was between 50 and 110 ms, depending on the integration window used). All of the LFP bands showed significant CP at some point (Fig. 4.13), with the lowest frequency band being the slowest to rise above chance.

**Potential Effect of Eye Movements**

One potential caveat in the CP analysis is that the observed co-variation may be due to a common factor that separately influences neural responses and behavioral choices. If such a factor exists, it may not be appropriate to interpret significant CP as evidence that the measured neural responses directly contribute to behavior. One potential source for co-variations between neural responses and behavior are small fixation eye movements.

To rule out the possible contribution of eye movements to the observed CP values, we examined the relationship between four indicators of the eye movements (see Methods) and the firing rate of SU and MU. Combining data across all trials contributing
Figure 4.13. CP time courses for various LFP frequency bands for target-absent trials. The time course of the CP for five non-overlapping LFP frequency bands shows the average and SEM of CP in overlapping 100 ms time bins across all experiments and stimulus conditions contributing to the CP analysis.

to the CP analysis (by first converting firing rate values to z-scores), we did not find significant correlations between spike rates and any of the four eye movement indicators for either target-present trials or target-absent trials (all correlation coefficients were smaller than 0.01). Since eye movements do not account for variability in the neural response (at least based on our four measurements), they could not account for CP. We verified this by fitting a multiple linear regression to the neural responses as a function of the four eye movement parameters and then re-computing the grand CP values between the residual neural responses and behavior. As expected, the new CP values were essentially identical to the original grand CP values.
Correlation between CP and neural detection sensitivity

In this chapter we measured the neural correlate of behavioral choice (CP) and in Chapter 2 we measured the neural sensitivity (relative to the monkey’s overall sensitivity) to the stimulus. We wanted to know whether the neurons with high sensitivity to the stimulus also contributed more to the decision in the detection task and, therefore, whether they have higher CP. To address this issue we determined whether there was a correlation between CP and the neural detection sensitivity measurements from Chapter 2, but found no (Pearson) correlation between CP values and the ratio of neural to behavioral detection sensitivity (or accuracy) in target-present trials ($r = 0.124$, $p = 0.301$) and in target-absent trials ($r = 0.086$, $p = 0.391$).

Trial-to-trial co-variation between V1 activity and reaction times

RT in the detection task were widely distributed (Fig. 4.14), ranging between 75 and 600 ms, which was the maximum time we gave the monkey to make a saccade to indicate the presence of the target. RT, on average, decreased monotonically with increasing target contrast, as did the variability in RT (Chapter 2, Fig. 2.2). We already saw that choice variability was correlated with variability in the responses of V1 neurons. Could some of the variability in RT be accounted for by variability in the spiking activity of V1 neurons? We tested this with a careful analysis of RTs and spike counts from several intervals throughout the trial.

Figure 4.15 shows all of the z-transformed spike counts (from a 100 ms time period starting shortly after target onset) and RT for one example MU experiment. Spike
counts and RTs were z-transformed within each of the 5 contrast conditions separately. For Figure 4.15, spike counts were calculated during a 100 ms period, starting 60 ms after the onset of the target and ending 160 ms after the onset of the target. Some trials from this experiment had RTs lower than or equal to 140 ms (160 ms minus the 20 ms MMRT) and were therefore excluded (see Materials and Methods). For this MU example, the correlation between spike count and RT during the 100 ms integration window was significantly negative ($r=-0.362$; $p$-value $= 0.007$). This result indicates that, for this MU site, increased neural activity during this limited time window (60-160 ms post target onset) was significantly correlated with lower RT.

Figure 4.14

Figure 4.14. Histogram of RTs for all “hit” trials across all conditions and all experiments. The mean (and SD) of this distribution was 193 ms (81 ms) and the median was 185 ms.
To see whether this result holds for the rest of the data and over more time periods throughout the trial, we next combined the z-transformed spike counts and RTs (z-transformed within individual contrast conditions) over all the sites (combining all of the SU and MU due to their similar RT-spike correlations) to compute a grand RT-spike correlation. We computed the grand RT-spike correlation (Fig. 4.16) at several points in time relative to the time of target onset (vertical line at 0 ms in this and all subsequent RT-spike time course figures), ranging from 80 ms pre-target onset to 200 ms post-target onset. We did not compute the RT-spike correlation over the first ~200 ms for individual
sites, as we did with the CP analysis (Fig. 4.2 and Fig. 4.9). We felt that computing the RT-spike correlation over a fixed interval would not capture the more meaningful dynamics of the RT-spike relationship. Therefore we focused only on the time course of the RT-spike correlation.

Figure 4.16

![Graph](image)

**Figure 4.16.** Time course of correlation between spiking activity and RT. RTs for all hit trials from all SU and MU experiments were z-transformed (within individual contrast conditions from individual experiments) and correlated with z-transformed (within condition) spike counts integrated during overlapping 100 ms long windows. Trials with RTs lower than the high end of the integration window were excluded from that (and successive) bin(s). Data points are plotted at the end of the 100 ms window, and correlations were computed every 20 ms.

There was no noticeable RT-spike correlation prior to target onset, but we did observe a significant negative correlation starting at the time point ending at 100 ms (i.e.
the window from 0-100 ms). Blue points in Figure 4.16 (as well as Fig. 4.17-19) represent correlations that were found to be significantly different from 0 ($t$-test). The time course of the RT-spike correlation for the next several time points stayed significantly negative, peaking at the point ending at 180 ms ($r = -0.18$), and then becoming non-significant ~60-80 ms later.

Cook and Maunsell (2002) found RT-spike correlations in areas MT and VIP using a motion detection task. They observed that the magnitude of the correlation was dependent on the difficulty of the task, which was primarily driven by the stimulus strength (i.e. the coherence level of a field of moving dots). We wanted to know whether this result would be common to our V1 neurons using the contrast detection task. However, as mentioned above in the choice probability section, contrast is not the best indicator of difficulty in our task. We have two proxies for task difficulty: probability of reporting the target (PT) and reaction time (RT). We grouped the data into four categories. Trials from contrast conditions within individual experiments were split into groups based on whether the PT (or median RT) of the individual contrast condition was above or below the global median PT (0.7) or global median RT (186 ms). The global median PT and RT were computed over all of the contrast conditions in all of the experiments. The magnitude of the negative RT-spike correlations was larger for the more difficult contrast conditions (low PT and high RT) than for the easier trials (high PT and low RT) (Fig. 4.17). Additionally, the RT-spike correlations of the more difficult trials became significant slightly later than did the RT-spike correlations of the easier trials (by ~20-60 ms).
Using a large integration window (100 ms) to calculate the RT-spike correlation may cause imprecision in the estimate of the time course of the correlation. To investigate this possibility, we used three other shorter durations (25, 50, and 75 ms) for the integration window (Fig. 4.18). As mentioned above, we used shorter integration windows for the CP analysis as well (Fig. 4.7) and found a trade-off between the strength of the CP and precision in estimating the timing of its rise to significance. Using a quite short window (25 ms) for the CP analysis provided a better estimate of the true time course (which had the same general shape as the other time courses that used the longer
Figure 4.18. Time course of correlation between spiking activity and RT computed using 100 ms, 75 ms, 50 ms, and 25 ms integration windows. The correlations were computed in the same way as described for Figure 4.16 (except they were computed with different sized integration windows, which are listed in each panel).

On the other hand, Figure 4.18 shows that the RT-spike correlation time courses computed with short windows (25 ms and 50 ms) were rather noisy, though this result does suggest that the time at which RT-spike correlations become significant is earlier (by ~20-30 ms) than the time at which CP becomes significant.

Because we excluded trials from the RT-spike correlation for time periods when the trial had already ended (and hence a saccade to the target had already been executed), there are different populations of trials contributing to the data points in all of the time courses shown above. The dropping-out of trials with short RTs that is inevitable in the
later data points could have altered the shape of the time course in unknown ways. To address this potential confound, we re-analyzed the data excluding all trials from individual contrast conditions where even one trial had a RT less than 150 ms (Fig. 4.19, top) or less than 200 ms (Fig. 4.19, bottom). This allowed us to view the time courses with no drop-outs for any data point. The time courses appear to have the same general shape as in Figure 4.16, with the slope of the time course being shallower (and the

Figure 4.19

![Time course of correlation between spiking activity and RT computed after excluding any condition with a trial whose RT was lower than 150 ms or 200 ms. The correlations were computed in the same way as described for Figure 4.16. Top, Only trials from individual contrast conditions where all of the trials had RT greater than 150 ms were included. Bottom, Only trials from individual contrast conditions where all of the trials had RT greater than 200 ms were included.](image-url)
correlations reaching significance later) for the subset of trials with RT of 200 ms or shorter, as would be predicted by Figure 4.17.

**Relationship between choice probability and RT-spike correlations**

We have shown that the activity of V1 neurons is correlated with two aspects of the monkey’s behavior in the detection task: choice and reaction time. Is it the case that the neurons with high CP or high neural sensitivity (as calculated in Chapter 2) also have high RT-spike correlations?

Cook and Maunsell (2002) observed significant correlations between neuron sensitivity and RT-spike correlations for areas MT and VIP. In contrast, we found no significant correlation between the RT-spike correlations (for any time period) and CP or neural detection sensitivity from individual SU and/or MU sites in V1 (data not shown). However, looking at time courses of the RT-spike correlation for our V1 neurons, we did observe subtle differences between the time course for all of the trials in all sites and the time courses for subsets of the trials that came from sites where the CP was greater than 0.5 or 0.65 (Fig. 4.20). Over a short period from 30 ms to 100 ms after target onset there was a trend for trials from sites with high CP to have larger RT-spike correlations than trials from sites with lower CP.
Figure 4.20. Time course of correlation between spiking activity and RT separated based on choice probability. The correlations were computed in the same way as described for Figure 4.16. The time course for all trials from all experiments (red) is plotted along with time courses for just those trials from individual contrast conditions where choice probability (CP) was greater than 0.5 (green) and 0.65 (blue). To more clearly compare the dynamics of the time courses for these three data sets, correlations were computed every 1ms, using the standard 100 ms integration windows. For clarity, only the significant portions of the time courses were represented with colored points.

Discussion

Choice probability in V1

Choice probability (CP) has been observed in multiple extrastriate areas (MST - Celebrini and Newsome, 1994; Cook and Maunsell, 2002; MT - Britten et al., 1996; Dodd et al., 2001; Uka and DeAngelis, 2004; Purushothaman and Bradley, 2005; LIP - Shadlen and
Newsome, 2001; Roitman and Shadlen, 2002; VIP - Cook and Maunsell, 2002; VPC - Romo et al., 2004; S2 - de Lafuente and Romo, 2005; V2 - Nienborg and Cumming, 2006), but never in primary sensory cortex (de Lafuente and Romo, 2005; Nienborg and Cumming, 2006). There is some evidence that CP may increase along the visual hierarchy, though it may be the case that CP may be maximal at the area that contains the most appropriate goal directed signals. Here we show significant CP and RT-spike correlations in V1, demonstrating for the first time that in some tasks neural correlates of behavior can be observed in the earliest stages of cortical processing. Our study may have revealed significant neural correlates of behavior because V1 neurons seem to be ideally suited to provide relevant information in our detection task. Our result suggests that the mechanisms that link sensory representations to behavior are quite flexible and have the capacity to weight information based on its relevance to behavior, irrespective of where these signals are located in the visual pathway.

*Target-present and target-absent choice probability*

CP results in target-present trials (hits and misses) were quite robust. Significant CP was observed in all three measurements (SU, MU, and LFP) and rose above chance levels rather early (< 100 ms after target onset). Significant CP in target-absent trials (false alarms (FA) and correct rejects (CR)) was only seen for two of the measurements (MU and LFP) and rose above chance a full 70 ms after CP rose above chance in target-present trials. A likely explanation for the differences in the CP for target-present and target-absent trials is that there were many more miss trials than false alarm trials in each
of the experiments, providing a more robust estimate of differences in the neural activity of hits and misses than that which could possibly be seen in FA and CR.

**SU, MU, and LFP choice probability**

For the most part the SU, MU, and LFP we recorded from had (on average) quite similar CP. There were noticeable differences though, mostly between SU and MU/LFP. In general, the CP for SU was weaker than for MU and LFP, exhibited both in the decreased magnitude and the delayed onset of significant CP. CP for SU in the target-absent trials never reached significance at any point in the trial. Possible sources of difference between SU and MU/LFP may come from the fact that the overall signal of SU was quite low relative to MU and LFP. In general, the spiking activity of our V1 SU neurons was rather sparse. Mean baseline activity was less than 1 spike/second and mean maximum firing rate, in response to the high contrast target (either 25% or 50% contrast), was ~36 spikes/second. MU, on the other, had average baseline and maximum firing rates about 30 times and 4 times the average SU, respectively, and the LFP signal was inherently dense as it is a reflection of small changes in membrane voltage and not an all-or-nothing signal like the action potential. The sparseness of SU spikes may have made it difficult to tease apart differences between hit and miss trials in the relatively short intervals (40-165 ms) during which we integrated signals (for the case where we only looked at the first 200 ms after stimulus onset [Fig. 4.2]). Britten et al. (1996) showed that CP drops to chance for trials with very low firing rates. The effect of low firing rate may have been more pronounced for low contrast trials, where most of the behavioral
variability was concentrated and firing rates were very low, and for which CP does appear to be weaker than in higher contrast trials (Fig. 4.5C vs. 4.5D and 4.5E vs. 4.5F). Additionally, the fact that MU and LFP CP was higher than SU CP is consistent with the hypothesis that perceptual decisions are mediated by the activity of many neurons within a given sensory area.

Overall, CP for MU and LFP was quite similar. The magnitude and time course of MU CP was most comparable to that of the middle of the gamma-band (40-100 Hz) of the LFP for both target-present and target-absent trials. In fact, the middle of the gamma-band of the LFP had the strongest CP and steepest CP time course. This result is consistent with many previous studies that found that the gamma-band of the LFP showed higher selectivity for specific stimulus features than did lower LFP frequencies (Gray and Singer, 1989; Frien and Eckhorn, 2000; Frien et al., 2000; Fries et al., 2002; Siegel and Konig, 2003; Kayser and Konig, 2004; Henrie and Shapley, 2005; Liu and Newsome, 2006; Wilke et al., 2006; Womelsdorf et al., 2006). Liu and Newsome (2006) compared the stimulus selectivity of MU and LFP in area MT using a motion discrimination task. They found that MU and LFP tuning for speed and direction was highly correlated, especially for the LFP frequencies at and above the gamma-band. They also found an analogue of CP only for LFP frequencies at and above the gamma-band. The conclusion they drew from their results is that the gamma-band activity originates from local patches of cortex, perhaps on the spatial scale of cortical columns (within a few hundred micrometers of the electrode tip). A similar spatial scale has been postulated for MU activity (DeAngelis and Newsome, 1999; Liu and Newsome, 2003).
Choice probability time courses

The CP time courses show that choice related signals first appeared around 100 ms after stimulus onset (average RT of trials in the CP analysis was ~200 ms), consistent with the idea that bottom-up processes explain the CP. The time courses were quite flat in the pre-stimulus period, indicating that behavioral decisions were not based on pre-trial biases, but rather on within trial perceptual events (although see discussion above about possible pre-trial bias/attention in the LFP signal). In addition, we showed that the dynamics of the CP for SU and MU were quite similar. CP for low contrast trials (both SU and MU), as well as SU high contrast trials, inexplicably dipped significantly below 0.5 just after stimulus onset. The “hits” time course near this time period remained flat, whereas the “misses” time course increases, producing the dip in CP. Perhaps the increase in neural activity right near the beginning of the “miss” trials may be just a random increase in baseline activity. If the decision to “go”, or to indicate the detection of the target, were based on the magnitude of the difference between the baseline firing rate and the firing rate at some point after target onset (and not on an absolute firing rate threshold, for example), then trials in which there is a random increase in the baseline just prior to target onset may fail to trigger the “go” decision. More controlled studies would need to be made to address this speculation, however.

We also observed a trade-off between the magnitude of the CP signal and precision in its dynamics when using longer (100 ms – higher magnitude) and shorter (25 ms – increased precision) integration periods. Longer integration periods were useful
when attempting to tease out differences in otherwise similar CP time courses (i.e. LFP frequency band-dependent CP), whereas shorter integration periods were useful for comparing estimates of the time at which neural responses started to be related to choice.

Reaction time-spike correlation in V1

We found weak, but significant negative correlations between RTs and neural spike counts on a trial-by-trial basis. Like the results of Cook and Maunsell (2002), our results suggest that the variability in the latency of saccades is at least partially accounted for by variability in the responses of sensory cortical neurons, with some portion of the variability possibly coming from decision and/or motor areas (based on the difference between the monkey’s actual RT and our RT predictions from the dynamic integrator models, see Chapter 3). This contrasts the conclusion based on recordings from the frontal eye fields (FEF) made by Thompson et al. (1996) which stated that saccade variability was primarily due to variability in the motor response preparation stage. We can think of two differences between the Thompson et al. (1996) study and the studies described in this chapter and Cook and Maunsell (2002) that might explain the difference in conclusions. First, Cook and Maunsell (2002) point to the fact that they chose stimuli that maximized the firing of the neurons they recorded from, which were in sensory areas. We did this as well. Thompson et al. (1996) recorded from FEF, so they did not have the capacity to optimize stimulus parameters to the neurons they recorded. Second, there were differences in the task in each of the studies. We used a threshold detection task. Cook and Maunsell (2002) used a threshold motion detection task. Thompson et al.
(1996) used a pop-out visual search task, where, unlike our study, there is much more spatial variability in the eye movement component of the task.

The time course of the RT-spike correlation was similar to the time course of CP, though the RT-spike correlation reached significance ~20-30 ms earlier than the CP. This may have something to do with the richness of the variability in the RT relative to that found in the sparse, binary nature of the monkey’s detection “choices”. This notion of richness/sparseness of the variability in RT may have also contributed to observed differences in “easy” and “difficult” trials (not observed for CP). “Easy” trials were primarily defined by their brevity, and as seen in Figure 4.14, the RT distribution is quite skewed, so that there is more variability in RT above the median (186ms) than below.

Despite the general similarities in the RT-spike correlation and CP results, we did not find a significant relationship between the CP and RT-spike correlations, though we found slight differences between the RT-spike correlation time courses of trials from sites with and without high levels of CP. Also, we did not observe significant RT-spike correlations for target-absent trials, though we did for CP. Perhaps the RT-spike correlation analysis was not as robust as the CP analysis due to the possible inclusion of a relatively large number of “early errors”, which may have flooded the analysis with RTs that were not indicative of the time needed to make perception-based decisions.

**Conclusions**

In conclusion, we found significant CP in V1 for SU, MU, and LFP (with the gamma band frequencies showing the highest CP), making this the first observation of a neural
correlate of behavior in a primary sensory area. The time courses of the CP showed that CP rose above chance early in the trial, reducing the possibility that the entire source of the CP was feedback from downstream visual/decision areas. The target-present CP was higher than the target-absent CP. The target-present CP also reached significance earlier than the target-absent CP (only for MU and LFP, whereas the SU target-absent CP never became significant), possibly due to the inordinate influence of “early errors” on target-absent trials. We also found significant correlations between neural activity and another important aspect of behavior, reaction time. The time course of the reaction time – spike correlation was dependent on the difficulty of the task (harder trials had a larger magnitude correlation, though it took more time to reach significance). These results suggest that decisions can be made based on early sensory areas when these areas contain the most useful signals. This suggests that decision mechanisms are flexible and have the capacity to weight information based on its relevance to behavior, irrespective of where these signals are located in the visual pathway.
Chapter 5: The relationship between single neurons and multi-unit activity

Abstract

Single neuron electrophysiology has been used for decades as a tool to describe neural function. Multi-unit recordings (whereby a single microelectrode is used to record activity of a small groups of neurons) have some practical advantages (e.g., easier to maintain and less prone to cell size and cell type bias) over the much more ubiquitous single neuron recordings. However little is known about the relationship between single neuron and multi-unit recordings. Here we focused on two methods to compare the activity of single neurons to multi-unit activity. We compared the neural detection sensitivity of Monte-Carlo simulations of pools of up to 33 independent single neurons from the primary visual cortex of macaque monkeys in a visual detection task to the neural performance of multi-unit recordings, as well as to the monkey’s behavioral performance. We find that eight independent, similarly tuned single neurons are sufficient to account for the detection sensitivity of the average multi-unit site. We also quantitatively compared single unit recordings to multi-unit recordings (in terms of signal to noise ratio, mean to variance ratio, and contrast threshold) in order to test the hypothesis that the activity of multi-units is the sum of groups of single neurons. We conclude that multi-units are composed of several single units, most of which were weakly tuned to the stimulus.
Introduction

Much of our knowledge about the function of various areas of the brain comes from studying electrical activity of neurons, the basic signaling units in the brain.

Traditionally, neural activity from individual neurons, recorded one at a time, is averaged or otherwise grouped together to describe a particular brain area’s response to a stimulus or involvement in a motor behavior. More sophisticated methods of combining, or pooling, the responses of single neurons have been used to indicate the minimum number of neurons necessary to perform some neural function (i.e. execution of a motor behavior or detection of a stimulus). Shadlen et al. (1996) reported that a pool of about at least 100 neurons (in area MT) was required to account for the psychophysical performance of a monkey in a visual discrimination task. The model that Shadlen et al. (1996) developed accounted for the correlation between the variability (i.e. noise) in the stimulus driven responses between neighboring cortical neurons (~0.12, Zohary et al., 1994). The correlated noise means that a significant portion of the variability cannot be averaged out when pooling, setting a limit on the benefit of combining the signals of large groups of neurons. Another study, which did not account for the inter-neuronal correlation, claimed that psychophysical performance could be accounted for by much smaller pools of neurons (Tolhurst et al., 1983). A third study suggested that even simple pools of 2000 or more neurons could not account for psychophysical performance, though the task used was fine perceptual discrimination (Purushothaman and Bradley, 2005).

Despite their ubiquitous nature, single unit (SU) recordings have a number of drawbacks, such as cell size bias (Towe and Harding, 1970) and cell type bias (towards
large pyramidal cells) (Stone, 1973) and the difficulty of maintaining a recording for long periods of time (Kreiman et al., 2006; Stark and Abeles, 2007). Also it can be very time consuming to sample a region of the brain one neuron at a time. Multi-unit (MU) recordings, whereby the activity of small groups of neurons is recorded at once by a single microelectrode, offer an alternative to single unit recordings. Since the electrode in a MU recording is placed in a general area to pick up a number of cells, there may be less cell type bias in MU recordings. Also the electrode is not placed right up against a particular neuron (often needed to record the relatively small neurons in area V1), so it is less likely to penetrate and kill the neuron, which is a common problem in maintaining SU recordings long enough to adequately characterize the neuron’s responses. MU recordings have now been used in many studies in lieu of SU (van Essen et al., 1984; Gray and Singer, 1989). However, the relationship between SU and MU has not been examined quantitatively.

With MU recordings, the activity of several neurons is being combined. Do the combined stimulus related signals of these neurons outweigh their combined baseline noise? MU have been reported to have sensitivity to visual stimuli that is comparable to SU (this dissertation, Chapter 2; Liu and Newsome, 2003; Liu and Newsome, 2005; Stark and Abeles, 2007), suggesting that merely grouping neurons is not improving sensitivity, but it is unclear why that would be the case.

In this chapter I focus on quantitatively comparing the responses of SU and MU from the visual detection task (described in Chapter 2). First we employed a Monte Carlo analysis of independently tuned SU to simulate pools of up to 33 neurons, and compared
the performance of the pools in the visual detection task to the performance of the average MU site, as well as to the performance of the monkey. We then tested the hypothesis that MU responses are equivalent to the linear sum of SU responses.

**Materials and Methods**

*Subjects and surgery* (See chapter 2)

*Task and visual stimulus* (See chapter 2)

*Analysis of behavioral data* (See chapter 2)

*Neuron database* (See chapter 2)

*Analysis of eye movements* (See Chapter 2)

**Electrophysiology**

A tungsten microelectrode (0.5-1.5 MΩ, FHC) ensheathed in a protective metal guide tube was lowered to just above V1 through a rubber gasket positioned within a transparent plastic cover sealing the recording chamber. Once the guide tube penetrated the rubber gasket, we advanced the electrode until it extended out from the guide tube by 3-5 mm, and then locked it in place. We then advanced the electrode through the artificial dura with a hydraulic microdrive (Narishige, Tokyo, Japan) until a single neuron and/or a cluster of MU was isolated. A dual slope/height window discriminator (Bak Electronics, Germantown, MD) was used to isolate spikes from single neurons. A second independent window was used to accept spikes from several neurons, so MU activity could be recorded concurrently with SU activity.
One of the goals of the current study was to examine the effect of pool size on neural performance in the detection task. We therefore varied the level of the lower criterion of the height window across experiments, aiming to sample multiunit sites with a wide range of pool sizes. Because the number of neurons that contribute to the MU activity is likely to be related to the level of baseline (spontaneous) MU activity, we adjusted the criterion to obtain different levels of baseline MU activity at different recording sites. Across our data set, the range of MU baseline firing rates was ~1.2 events/sec to ~160 events/sec. The SU baseline firing rates obtained in our study ranged from ~0.11 spikes/sec to ~3.67 spikes/sec with the median SU baseline firing rate at 1.70 spikes/sec.

When recording SU and MU simultaneously, spikes from the SU channel were excluded from the events of the multiunit channel. Across experiments, the slope and the delay of the slope/height window discriminator were manually adjusted to maximize the chance of detecting spikes. We used the lower threshold of the height window to control the rate of acceptance of a voltage deflection as multiunit events. The position of this criterion is arbitrary. A high criterion is likely to lead to acceptance of spikes from a small number of single neurons that are near the tip of the electrode. A lower criterion is likely to lead to acceptance of spikes from a larger number of neurons, but potentially also some voltage deflections that are not due to action potentials.

After isolation, we qualitatively analyzed the receptive field (RF) properties of the recorded neuron(s). If recording from both an SU and MU cluster simultaneously, the stimulus was modified to maximize the single neuron responses. This was done using a
custom software package (courtesy of G. DeAngelis) that allowed interactive variation of the parameters (location, size, orientation, and spatial frequency) of a sinusoidal grating while monitoring neural responses. Based on the initial analysis of the receptive field properties, we performed a further quantitative assessment using a sine-wave grating presented for 300 ms for a minimum of 5 trials per condition to identify the neuron(s)’ preferred orientation. At some of the sites, we also quantitatively assessed the preferred size (at a fixed spatial frequency of 3 cpd) and then spatial frequency (with size fixed at the preferred value) of the recorded neuron(s). To assess the preferred size and spatial frequency, a block of trials with Gabor patches of various sizes or spatial frequencies was run. The smallest size or lowest spatial frequency that gave the maximal response was used for the target detection block. In general the size increased and the spatial frequency decreased with increased receptive field eccentricity (Fig. 2.2). Bandwidth did not change systematically across eccentricity.

**Analysis of physiological data**

**Integration period**

Neural responses were integrated during a short period that started 36 ms after stimulus onset and ended at variable times depending on the monkey’s RT (Fig. 2.1B). We selected 36 ms for the beginning of the integration period because it was approximately the shortest latency of the response to high contrast targets. The default maximal time for the integration interval was 200 ms after stimulus onset. However, if
the RT for a trial was less than 220 ms, the integration period ended 20 ms before the monkey initiated the saccade to the target.

**Monte Carlo Analysis of Independent Single Units**

We simulated the performance of a pool of independent, similarly tuned, SU in the visual detection task using a simple Monte Carlo analysis. To simulate a pool of \( N \) units, \( N \) SU were randomly chosen (with replacement) from the set of recorded single neurons. To simulate a single trial, the response of each neuron was randomly selected from the responses of the neuron at that contrast, and the pooled response on that trial was computed as the sum of the responses from the \( N \) neurons. Each simulated experiment included 20 trials for each of 5 target contrast and 100 blank trials. We then computed the neurometric function from these simulated pooled neural responses and extracted the fitted parameters of the neurometric function. These steps were repeated 100 times with different random pools of the same size, and the mean (and SD) of the parameters for the neurometric functions was noted. The above steps were repeated for pool sizes of two neurons up to 33 neurons.

**Results**

**Monte Carlo Analysis of Independent Single Units**

We performed a simple Monte Carlo analysis to examine how the shape of the neurometric function changes as a function of the size of a pool of independent, similarly tuned SU (see Materials and Methods). The performances of simulated pools of different
sizes were compared with the average performance of the monkey (solid horizontal lines, Fig. 5.1A-D). As the size of the pool increased, the accuracy of the pooled response became higher and the threshold became lower, exceeding the monkey’s detection sensitivity for pools of eight or more neurons (Fig. 5.1A,B). False alarm rates initially increased but then decreased to a level lower than that of the monkey at large pool sizes. In the range of five to seven pooled SU, the average accuracy, threshold and false alarm rate for the pooled responses were all comparable to those of the monkey, yet the slope of the neurometric function remained lower than the slope of the monkey’s psychometric function. In fact there was no pool size for which the slopes could be matched. Possible ways in which the neurometric function could be steepened were mentioned in the Discussion section of Chapter 2.

The dashed horizontal lines in Fig. 5.1A-D show the average parameters of the neurometric functions based on MU responses. The average detection sensitivity of the MU responses was significantly lower than the predicted detection sensitivity based on simulations of pools eight or more independent and similarly tuned SU. Additional analysis of the quantitative relationship between SU and MU responses described below revealed some possible sources for this discrepancy.

**Quantitative comparison of single unit and multi-unit responses**

Our results indicate that MU in V1 have detection sensitivities that are not significantly different from single V1 neurons (Table 2.4). It is somewhat surprising that MU were not more sensitive than SU. The results of our simple Monte Carlo simulation (Fig. 5.1)
demonstrate that a pool of eight or more independent and similarly tuned single neurons would be significantly more sensitive than a typical MU cluster (and the monkey).

Similarly, a simple calculation shows that it is enough to sum responses from two

Figure 5.1

A

B

C

D

Figure 5.1. Monte Carlo simulations of the performance of summed independent SU as a function of the number of neurons in the pool. A, Expected accuracy (percent correct). B, Expected threshold. C, Expected slope. D, Expected false alarm rate. Each data point is the mean of 100 random combinations (with replacement) of SU from our data set. Error bars are SD. Solid lines are the mean values for the monkey’s behavior during the 33 SU recordings. Dashed lines are the mean values for the 62 MU recordings. The point at n = 1 is the average value for the SU.
neurons that have comparable detection sensitivities and are weakly correlated to obtain a pooled performance that is more sensitive than each neuron on its own (Chen et al., 2006; their Fig 3.a]. These theoretical considerations and the results of our simulations suggest that the detection sensitivities of the MU responses should have increased as the number of neurons that contributed to the MU signal increased. In fact, we found just the opposite (Fig. 5.2). Sites with high baseline rates, which were likely to combine signals from many SU, tended to be less sensitive to the target than sites with lower baseline rates.

Figure 5.2

![Image](image.png)

**Figure 5.2.** Neural threshold of MU sites as a function of baseline firing rate. The solid line is a best-fit regression line, with Pearson correlation coefficient $r$ and its significance value $p$ noted. contr., contrast.

There are at least three ways in which the detection sensitivity of the MU responses could be degraded relative to the detection sensitivity predicted by our Monte Carlo simulations (Fig. 5.1). First, V1 neurons are selective to multiple parameters of the
visual stimulus, and therefore, a significant fraction of the neurons that contribute to the 
MU activity may carry little or no signal regarding the target (e.g., neurons for which the 
stimulus was in the null phase or neurons that are tuned to higher spatial frequencies; 
Geisler and Albrecht, 1992; DeAngelis et al., 1999). Such non-selective responses would 
add to the baseline MU response and to its response variability and therefore reduce its 
detection sensitivity. A second possibility is that the SU that contribute to the MU signal 
are highly correlated, and that these correlations reduce the benefit that can be attained by 
summing the responses from multiple neighboring single neurons. Finally, it is possible 
that additional sources of noise that are not due to SU spikes contribute to the MU 
response and degrade its sensitivity. By evaluating the quantitative relationship between 
the SU and MU responses, we provide (below) an initial attempt to examine each of these 
possibilities.

To explore the possibility that non-selective neurons contribute to the MU 
responses, we compared the average baseline and evoked MU responses with those 
expected by summation of SU from our data set. For each SU and MU site, we computed 
the average number of spikes during the 200 ms following the time of stimulus onset at 
each contrast level. These responses were then fitted with a Naka-Rashton contrast 
response function of the form:

Equation 5.1: \[ R(C) = R_{\text{min}} + (R_{\text{max}} - R_{\text{min}}) \frac{C^n}{C^n + C_{50}^n} \]

where \( C \) is the target contrast, \( R(C) \) is the average number of spikes at contrast \( C \), \( R_{\text{min}} \) 
and \( R_{\text{max}} \) are the baseline and maximal response respectively, \( C_{50} \) is the half saturation
contrast and \( n \) is an exponent. In general, this function provided an excellent fit to the data, accounting for more than 95% of the variance for 28 of the 33 SU and 55 of the 62 MU sites.

Figure 5.3

**Figure 5.3.** Comparison of contrast response function parameters for SU and MU. Mean response as a function of contrast was fitted for each SU and MU site using a Naka-Rashton contrast response function (see Results). **A**, Histogram of \( R_{\text{max}} \) values. Open bars – SU; filled bars – MU. Gray arrow indicates median value for SU; black arrow indicates median value for MU. **B**, Histogram of \( R_{\text{min}} \) values. **C**, Histogram of the exponent \( n \). **D**, Histogram of half saturation constant \( C_{50} \). **B-D**, Same conventions as in **A**.
As expected, baseline and maximal response were much higher for MU than for SU (median $R_{\text{max}}$, 6.72 for SU and 30.84 for MU; median $R_{\text{min}}$, 0.17 for SU and 4.54 for MU; Fig. 5.3A,B). On the other hand, contrast response functions for SU and for MU were similar in terms of their exponent and half saturation (median $n$, 3.81 for SU and 3.08 for MU; median $C_{50}$, 8.45 for SU and 8.38 for MU; Fig. 5.3C,D).

If MU activity is the sum of the response of multiple SU that are all similarly tuned, as more SU are added to the MU pool, we would expect both the baseline response $R_{\text{min}}$ and the selective response $R_{\text{max}} - R_{\text{min}}$ to increase at a similar rate. If, on the other hand, some of the SU that contribute to the MU signal are only weakly tuned to the target, those neurons would contribute to the baseline response but would add little to the selective response. Under the assumption that the MU signals are the sum of the responses of multiple SU, we can estimate the expected total number of SU that contribute to each MU pool, $N_T$, by dividing the $R_{\text{min}}$ for each MU site with the average $R_{\text{min}}$ of all the SU sites. Similarly, we can estimate the equivalent number of SU that could account for the selective component of the MU response, $N_S$, by dividing the selective response of the MU site with the average selective response of all the SU sites.

To determine the contribution of selective SU to the MU pool, we examined the relationship between $N_S$ and $N_T$ for all the MU sites. Figure 5.4A shows a scatter plot of $N_S$ vs. $N_T$ for each of the MU sites. Surprisingly, the number of equivalent selective SU does not exceed 9 even though $N_T$ can be as high as a 100. Furthermore, while there is a lot of variability in $N_S$, the average $N_S$ saturates at a value $\sim$4. In other words, only...
Figure 5.4

**Figure 5.4.** Relationship between MU activity and SU activity. 

**A.** Scatter plot of the equivalent number of selective SU, $N_S$, that can account for the selective MU response vs. the expected total number of SU, $N_T$, that contribute to the baseline MU response (see Results for details). Gray circles – SU; black circles – MU. Solid curve – fit to the observed MU data with a saturating function.

**B.** Scatter plot of $N_S$ over $N_T$ as a function of $N_T$. Same conventions as in **A**. Solid curve derived from the curve in **A**.

4 SU from our data set are sufficient, on average, to account for the selective response of MU sites with baseline activity that corresponds to as many as 100 single neurons.

To further examine the relationship between $N_S$ and $N_T$, Figure 5.4B shows the ratio of $N_S$ to $N_T$ as a function of $N_T$. As $N_T$ increased, the ratio of $N_S$ to $N_T$ dropped dramatically, reaching a mean value of 0.5 at $N_T$ of ~5 and values well below 0.1 for $N_T$ above 40. These surprising results demonstrate that a large portion of the MU
response was not selective to the target even at low baselines. As the baseline was increased, the fraction of the MU response that was selective to the target became negligible. This selective MU response could have been mediated by a small number of neurons with selectivity comparable to the average SU in our data set or by a larger number of less selective neurons.

Figure 5.4 demonstrates that MU activity in our task is inconsistent with the sum of the responses of similarly tuned selective SU. These results imply that as the threshold of the window discriminator was lowered, most of the events that were detected by the window discriminator were not coming from selective neurons.

We are left with two options. Either these events represent spikes of neurons that were not tuned or were only weakly tuned to the target, or alternatively, these events came from sources other than SU spikes. One potential way to distinguish between these two possibilities is to examine the response variability of the SU and MU signals. The variability in the spike count of single neurons in a short interval is known to be proportional to the mean, with the proportionality constant (also known as Fano factor) in the range of 1.2-1.6 (e.g., Tolhurst et al., 1983; Geisler and Albrecht, 1997). If a large portion of the MU responses was coming from sources that are not SU spikes, it seems unlikely that these sources would obey the same variance to mean ratio as the SU.

To compare the Fano factor of the SU and MU responses, for each SU and MU site we fitted a linear regression to the relationship between the variance to the mean across all contrasts and took the slope of the regression line to be the SU or MU site Fano factor. The histograms in the right panel of Figure 5.5 show the distributions of the Fano factors...
of the MU and the SU responses. As with SU, the variance of the MU responses was proportional to the mean over a wide range of baselines with comparable Fano factors for SU and MU sites. This result is consistent with the hypothesis that the MU responses are indeed the sum of spiking activity of many SU.

Figure 5.5

Figure 5.5. Fano factors (variance-to-mean ratios) for SU and for MU sites. Left, Scatter plot of Fano factor of SU (gray circles) and MU (black circles) as a function of $N_T$. Dashed lines indicate the expected relationship between the MU Fano factor and $N_T$ under different assumption regarding the correlation $r$ between the SU that contribute to the MU signals. Solid black line – best fit linear regression for the relationship between the MU Fano factor and $N_T$. The slope of this curve corresponds to a weak correlation between the SU that contribute to the MU signal (see Results for more details). Right, Histogram of Fano factor for SU (open bars) and MU (filled bars). Gray arrow indicates the mean Fano factor for the SU sites; black arrow indicates the mean Fano factor for the MU sites. The average Fano factor for the MU was slightly higher than that for the SU (mean SU, 1.34; mean MU, 1.74, $t$-test, $P=0.055$).
To explore the possibility that the SU that contribute to the MU response are correlated, and that these correlations lead to further reduction in the sensitivity of the MU responses, we examined the relationship between the Fano factor and the baseline of the MU responses. If the MU responses are the sum of \( N \) independent, identical SU responses, the MU Fano factor, \( F_N \), should be the same as the Fano factor of the SU. If, on the other hand, the MU signal is the sum of identical SU that are correlated with a correlation coefficient \( r \), it is easy to show that the expected Fano factor for the MU responses would be equal to:

\[
F_N = F_1 + F_1 (N - 1)r
\]

where \( F_1 \) is the SU Fano factor. In other words, if the neurons in the pool that contribute to the MU response are correlated, the Fano factor of the MU response should increase linearly with \( N \), with a slope equal to \( rF_1 \).

Figure 5.5 shows a scatter plot of the Fano factors for the SU and MU sites as a function of \( N_T \). The average Fano factor of the SU (1.34) is comparable to values obtained in previous studies (e.g., Tolhurst et al., 1983; Geisler and Albrecht, 1997). The average Fano factor of the MU sites is somewhat higher (1.74; \( t \)-test, \( p = 0.055 \) between the SU and MU). The higher average Fano factor for the MU sites was due to the increase in the Fano factor for higher values of \( N_T \). The best-fitting regression line for the Fano factor of the MU sites is indicated by the black curve. The slope of this curve corresponds
to a very low correlation value of $r = 0.011$, suggesting that the SU responses that contribute to the MU responses are only weakly correlated.

**Discussion**

*Monte Carlo Analysis of Independent Single Units*

A simple Monte Carlo simulation revealed that the pooled responses of at least 8 independent (i.e. not correlated) SU are needed to be significantly more sensitive than the average MU site. This result may be stimulus specific. For example, a moving stimulus or a stimulus that contains more spatial frequencies could potentially generate more selective responses from the same population of neurons within a MU site, meaning that a larger pool of independent SU would be needed to achieve significantly higher stimulus sensitivity than the average MU site.

*Quantitative comparison of single unit and multi-unit responses*

We found that multi-units in V1 have detection sensitivities that are comparable to the detection sensitivities of single V1 neurons (Chapter 2), consistent with previous findings in area MT (Liu and Newsome, 2003, 2005). A closer examination of SU and MU responses revealed several interesting results. SU and MU have similar contrast thresholds ($C_{50}$) (suggesting that non-selective SU are contributing to MU) and similar response variability (Fano factor) (confirming that MU are indeed comprised of SU, and not non-neural sources of electrical activity). Only ~4 of our SU were sufficient to account for the selective responses of the majority of the MU, even though the baseline
activity of some of the MU was equivalent to the baseline of up to 100 SU. This part of the analysis may explain our finding that as MU baseline activity increased (presumably an indication of a larger number of contributing SU) MU sensitivity actually decreases (Fig 5.2).

**Conclusions**

A simple Monte Carlo analysis showed that the average MU site could not be composed of more than about eight independent, similarly tuned SU. This number is similar to the average number of neurons (four) we found was sufficient to account for the stimulus selective response of MU. Overall, we conclude that MU responses are consistent with the summation of several SU, most of which are not selective to the stimulus used. Clearly, more work is needed in order to determine unequivocally the nature of the MU signal and its relationship to SU responses. In addition, it remains to be seen to what extent the relationship between SU and MU activity observed here would hold for other types of stimuli and in other cortical areas.
Abstract

Even the most localized sensory stimuli are likely to be encoded by large populations of neurons in early sensory cortical areas. Thus, to understand sensory encoding and decoding, it is essential to characterize neural population responses. Population responses can be studied at high spatial and temporal resolutions by voltage-sensitive dye imaging (VSDI). However, the relationship between VSDI signals, which measure changes in membrane potentials, and more traditional electrophysiological signals, is poorly understood. In this study, we first characterized the properties of VSDI signals measured in primary visual cortex (V1) of awake, behaving monkeys in response to small oriented visual stimuli that varied in position, and then compared the VSDI signals with single-unit (SU), multi-unit (MU) and local field potentials (LFP) responses to the same stimuli.

We found that: 1) while population receptive field (pRF) size increased with eccentricity, cortical point image (CPI) size remained roughly constant, suggesting, contrary to some previous reports, that each point in visual space is processed by a fairly constant neural population in parafoveal V1; 2) Cortical magnification factor (CMF), CPI, and the population receptive field (pRF) were anisotropic and CPI and pRF were spatially asymmetric; 3) transfer functions (TF) describing the quantitative relationship between VSDI and the electrophysiological signals are well captured by steep power functions. Specifically, spiking and LFP activity exceeded 10% of their maximum only when VSDI
signals exceeded 40% and 25% of their maximum, respectively. A key open question is whether these TFs also apply across other stimulus dimensions.

**Introduction**

Measurements of cortical population responses are essential for understanding the encoding and decoding of sensory stimuli in the mammalian cortex. Population responses can be measured with a variety of techniques, at various spatial and temporal scales. Two local measurements of population responses that can be assessed with a standard extracellular microelectrode are the spiking activity of small groups of neurons (multi-units, MU) and the local field potential (LFP). Voltage-sensitive dye imaging (VSDI) can provide a more efficient, parallel measure of population responses over a large field of view (typically 1-2 cm²). VSDI can directly measure changes in the membrane potential of local cortical populations with high spatial and temporal resolutions. Surprisingly little work has been done to describe the quantitative relationship between the VSDI signal and the more standard extracellular electrophysiological signals. A primary goal of the current study was to address this deficiency.

Our first goal in this study was to characterize the spatial profile of the population responses in macaque primary visual cortex (V1) in response to small oriented stimuli using VSDI and three electrophysiological signals (single unit (SU) activity, MU activity, and the LFP). The spatial profile of the cortical response to a small visual stimulus is closely related to the cortical point image (CPI; McIlwain, 1986), which is the cortical
region that responds to a point stimulus, and to the population receptive field (pRF), which is the combined receptive field of a local population of neurons (see Results section below for a more detailed discussion of the relationship between these properties).

Previous studies of the representation of visual space at the level of neural populations in V1 have used either electrophysiology (Hubel and Wiesel (1974); Dow et al., 1981; Van Essen et al., 1984) or VSDI (Grinvald et al., 1994; Slovin et al., 2002; Chen et al., 2006; Sit et al., 2008) to characterize the spatial profile of V1 population activity. No study, however, did so using both electrophysiology and VSDI in the same animals and using identical stimuli, making comparisons between the spatial response profiles derived by these two techniques difficult.

The impact of stimulus eccentricity on the CPI in V1 has only been measured (indirectly) with electrophysiology. However, these measurements have led to conflicting conclusions, with Dow et al. (1981) and Van Essen et al. (1984) suggesting that the CPI changes dramatically just outside the fovea (~2-5 degrees), and Hubel and Wiesel (1974) suggesting that it remains roughly constant. VSDI can be used to directly measure the entire spatial response profile from which the CPI can be derived (see Results), making it ideally suited to resolve this longstanding controversy.

Our second goal was to use the measurements of the spatial response profile in V1 to quantify the relationship between spiking activity (SU and MU), LFP and VSDI. These relationships can be described by transfer functions (TFs) that provide a means to
estimate how much average stimulus-driven spiking activity or field potential to expect given a certain level of stimulus-driven VSDI response.

Using VSDI, we made several important discoveries regarding the representation of visual space at the level of neural populations in V1. We found that the CPI is fairly constant across eccentricity in parafoveal V1, suggesting that each point in space is represented by a fixed amount of cortical tissue. We also discovered unexpected anisotropy in the pRF and asymmetry in the CPI and pRF.

Finally, by comparing the spread of activity obtained by VSDI and electrophysiology, we found that the quantitative relationships between the VSDI and electrophysiological signals are well captured by steep power functions, with spiking and LFP activity exceeding 10% of their maximum only when VSDI signals exceed 40% and 25% of their maximum, respectively.

**Materials and Methods**

*Subjects and surgery*

Four monkeys (*Macaca mulatta*) were used in this study. Surgical procedures for VSDI and electrophysiological recordings from behaving monkeys have been described in detail elsewhere (Chen et al., 2006; Chapter 2 of this dissertation). All surgical procedures were performed under deep anesthesia, using strictly sterile techniques, in a dedicated surgical suite. 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 animal achieved fixation in a small window (<2° full width) around a 0.1 X 0.1° central fixation point displayed against a uniform gray background. Following initial fixation, a Gabor patch (a sinusoidal grating in a Gaussian envelope) was presented parafoveally. V1 neural activity was assessed with electrophysiological and/or optical imaging techniques. The Gabor patch was presented 2 to 4 times for 200 ms at 2 Hz (200 ms on, 300 ms off). The monkey received a reward at the end of the final stimulus presentation provided it did not break fixation.

The position of the Gabor patch varied pseudo-randomly from trial to trial among a total of 5 to 8 positions (extending from receptive field (RF) center, or the center of the imaging chamber in the case of the VSDI experiments, to a peripheral location that elicited a response indistinguishable from the baseline). In different experiments stimulus position was changed along horizontal, vertical, or iso-eccentric directions. The contrast of the Gabor patch was always 100% and it was always in sine phase. In electrophysiological recordings (and in combined (n = 2) electrophysiology and VSDI sessions) the orientation, spatial frequency and starting position of the Gabor patch were adjusted to match the preferred parameters of the recorded SU or MU (mean RF eccentricity, 2.82°; range across experiments, 1.98 – 4.27°; mean spatial frequency, 2.73 cycles per degree (cpd); range, 1.99 – 4.19 cpd; no orientation bias seen), while the sigma of the Gabor patch was kept constant at 0.167°. In VSDI experiments, only the position of the Gabor patch varied across experiments (mean eccentricity, 2.62°; range across experiments, 1.89 – 4.45°); the sigma of the Gabor patch was kept at 0.167° and the
spatial frequency at 2.76 cpd. These parameters were not changed within a block of trials.

Visual stimuli were presented on a gamma-corrected high-end 21 inch color display at a fixed mean luminance of 30 cd/m². The display subtended 20.5 X 15.4° at a viewing distance of 108 cm, had a pixel resolution of 1024 X 768, had 30-bit color depth, and had a refresh rate of 100 Hz.

Electrophysiology (see Chapter 2)

Voltage sensitive dye imaging

The experimental techniques for optical imaging with VSDI in awake, behaving monkeys have been described elsewhere (Seidemann et al., 2002; Slovin et al., 2002; Arieli et al., 2002). Briefly, in the current study we used the voltage sensitive dyes RH1838 or RH1691 (Shoham et al., 1999), and a high speed camera (Imager 3001, Optical Imaging), to image any changes in membrane potentials in an area of up to 14.4 x 14.4 mm² over the occipital lobe of macaque monkeys. The camera collected 512x512 pixels at 110 Hz and the pixel size was ~28 x 28 microns².

Behavior monitoring and data acquisition

Behavior monitoring and data acquisition were performed by a PC 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. Electrophysiological signals were sampled at 1 kHz. The data acquisition computer also interfaced with the systems used to acquire electrophysiological data (Bak Electronics, Mount Airy, MD) and optical imaging data (Optical Imaging, New York). In addition, this computer controlled a dedicated PC with a high-end graphics card that was used for stimulus presentation.

Experiment database

The results are based on 23 SU recordings, 33 MU recordings, 30 LFP recordings, and 11 VSDI recordings (two of which were performed simultaneously with electrophysiology). All electrophysiological recordings had to meet three criteria to be included in our analysis: (1) minimum of eight repetitions per condition; (2) stable baseline neural activity across the entire block (discussed below); (3) fitting index ($R^2$) of the position tuning (PT) functions > 0.9 (see below for descriptions of PT functions).

Of the 34 single neurons that were initially screened for this study, 6 were excluded because isolation was not maintained for long enough to collect a minimum of eight repetitions per condition. All of the 36 MU and 36 LFP recordings resulted in eight repetitions per condition. 3 SU, 1 MU, and 3 LFP were excluded because of poor PT function fits to the data. In addition 2 SU, 2 MU, and 3 LFP were excluded due to instability in the baseline of the recording.
Stability of SU, MU, and LFP responses across a block of trials was assessed with the following method. Baseline activity for each trial was computed as the spike rate in the 300 ms interval before stimulus onset. LFP baseline activity was computed as the root mean square (RMS) (see below) for the same 300 ms pre-stimulus interval. Baseline activity was averaged over bins of 10 consecutive trials. Then, the trial order was randomly shuffled, and again, baseline activity was averaged over bins of 10 consecutive trials. This was done 1000 times to obtain 95% confidence intervals on the baseline measurement. If a significant number of the original data points (bins of 10 trials) fell outside of the 95% confidence interval (as assessed by a binomial test), then baseline was considered unstable and the block was excluded from analysis.

**Analysis of electrophysiological data**

SU and MU responses (spikes) were integrated from 36 ms after stimulus onset to 36 ms after stimulus offset, for a total of 200 ms. Integrated responses for a given trial were averaged across 2-4 stimulus presentations. Most of the LFP analysis was initiated by computing the amplitude of the power spectrum (square root of power) within a range of 1 to 200 Hz using the fast Fourier transform (FFT) for the same 200 ms time period described above. For some position tuning analyses, to assess whether our results were frequency dependent, we computed the amplitude of the power spectrum of the LFP within five 40 Hz wide bands.

To assess LFP stability and construct peri-stimulus time histograms (PSTHs) of the LFP signal to visually compare with SU and MU PSTHs, we computed the root mean
square (RMS) of the raw LFP for each trial, then computed the mean RMS per condition. RMS in each trial is defined as:

$$\text{Equation 6.1: } \text{RMS} = \sqrt{\frac{\sum LFP^2}{t^2}}$$

where $t$ is the time over which the RMS is being computed.

**Analysis of the voltage sensitive dye imaging**

VSDI analysis followed six steps: (i) normalize fractional change in signal across all trials (ii) anchored (subtracted) the responses in each block by the average response in the 100 ms interval prior to response onset; (iii) averaged the VSDI response during the integration period (36-236ms after stimulus onset); (iv) removed outlier trials (see below) from each block, usually less than 1% of trials; (v) fitted the averaged VSDI response with a 2-D Gaussian function and (vi) removed the fitted DC component.

Effective pixel size (after 8 X 8 binning) was ~250 microns. Steps i-iii were done independently for each 8 X 8 binned pixel. Outliers (step iv) were trials whose response during the integration period was 5 SD from the mean integrated response across all trials. Generally outliers were caused by excessive movements by the animal.

Anchoring (step ii) was helpful for eliminating the effect of uneven illumination in the recording chamber or uneven dye penetration, and for eliminating the effect of slow drift in the VSDI response across trials. All data analysis was performed in Matlab (Mathworks).
**Power function bootstrap significance test**

The changes in cortical magnification factor (CMF) and RF size with eccentricity have been shown to be well fitted by power functions (Van Essen et al., 1984). We therefore used power functions ($Y = B \times X^N$, where $X$ is eccentricity, $B$ is a scale factor) to fit the variations in CMF, CPI size, and (p)RF size as a function of eccentricity. For cases where we fitted separate power functions to multiple sets of similar data, we forced the power function exponent to be similar for each set of data (see Materials and Methods).

We used a simple bootstrap procedure to determine if the exponent was significantly different from zero. For each data set (e.g. pRF size as a function of eccentricity), we randomly shuffled the pRF size values amongst all of the eccentricity values and fitted the shuffled data with a power function to obtain a null distribution of exponents ($n = 1000$). The exponent of the power function fit to the original data set was considered significant if it fell outside of the 95% confidence interval of the null distribution of exponents.

**Results**

The overarching goals of the current study were twofold: First, to characterize the spatial profile of V1 population responses to small localized visual stimuli using VSDI and extracellular electrophysiology (single unit spiking activity (SU), multiple unit spiking activity (MU) and local field potentials (LFP)); Second, by comparing the spread of activity obtained by the different techniques, our goal was to determine the quantitative relationship between these different signals.
Because the spread of activity within the retinotopic map in V1 is largely determined by the contrast of the stimulus (Chen et al., 2006), in the current study we focused on the millimeter-scale envelope of the population response and the contrast envelope of the Gabor stimulus. The finer scale modulations at the columnar level will be addressed in future studies.

Consider the spread of activity in response to a small, localized stimulus in a patch of cortex in the dorsal portion of macaque V1 such as the one shown in Figure 6.1B. V1 contains a topographic map of visual space, with disproportional representation of the center of gaze (fovea). As one moves from the representation of the fovea in dorsolateral V1 towards the representation of the periphery (increasing the eccentricity in visual space), receptive fields (RFs) of V1 neurons become larger, and the cortical magnification factor (CMF; the distance in cortex that corresponds to a given distance in visual space) decreases, the latter changing approximately by a power law (Van Essen et al., 1984; Tootell et al., 1988; Adams and Horton, 2004).

At any given location in V1, there is significant heterogeneity in the size of RFs (Van Essen et al. 1985; Snodderly and Gur, 1995; Jones et al., 2001; Levitt and Lund, 2002). In addition, there is significant scatter in RF centers (Sanderson, 1971; Hubel and Wiesel, 1974). Thus, the population RF (pRF), which is the combined RF of a local population of V1 neurons (such as the ones contributing to MU signals or to the response in a single VSDI pixel), is likely to be larger than the average RF of the SU at that location. Because, as discussed below, the pRF plays an important role in shaping the response profile in V1, central goals of the current study were to characterize pRFs at
different eccentricities in V1 and to compare the pRFs obtained with electrophysiology and VSDI.

The spatial profile of the V1 population response to a stimulus depends on two components; first, the stimulus itself, and second, the pRF. The pRF has an important effect on the response profile, particularly for small stimuli, because neurons that fall outside of the direct mapping of the stimulus to the cortex still respond to the stimulus as long as it overlaps their RF. Mathematically, under a linearity assumption that is approximately true for small local stimuli, the spatial spread of the response is equivalent to filtering the projection of the stimulus to the cortex (the stimulus multiplied by the local CMF) with the projection of the pRF to the cortex (the pRF multiplied by the local CMF). This second term is the cortical point image (CPI; see McIlwain, 1986 for discussion), which measures the cortical response profile to a point stimulus. The CPI captures a fundamental feature of cortical representation - it describes the cortical population that processes a given point in visual space. Another central goal of the current study is to characterize the CPI at different eccentricities with electrophysiology and VSDI and to compare the CPIs obtained by these different techniques.

If the visual stimulus has a Gaussian contrast envelope (e.g., Gabor patch), and under the assumptions that the pRF is also Gaussian and that the CMF is approximately constant within the activated region, the response profile in V1 will also be a Gaussian with space constant $\sigma_R$ (in mm) given by the following equation:

\[
\text{Equation 6.2:} \quad \sigma_R = \sqrt{(\sigma_{st} \cdot CMF)^2 + (\sigma_{rf} \cdot CMF)^2}
\]
where $\sigma_{st}$ is the space constant of the stimulus and $\sigma_{pf}$ is the space constant of the pRF. The first term under the square root captures the contribution of the stimulus to response spread. The second term under the square root captures the contribution of the pRF to response spread, which will dominate $\sigma_e$ when the stimulus is smaller than the pRF. Importantly, this simple analysis implies that irrespective of how small and localized a visual stimulus is, the response in the cortex has a minimal spread that is determined by the size of the CPI (the product of the pRF size ($\sigma_{pf}$) and the CMF).

While it is well established that the RF size of V1 neurons increases with eccentricity and CMF decreases with eccentricity, there are conflicting reports regarding whether CPI changes systematically with eccentricity or remains relatively constant. While some have argued that the CPI remains roughly constant across the visual field, implying that each point in visual space is processed by a roughly constant sized neural population in primate V1 irrespective of eccentricity (Hubel and Wiesel, 1974), others have argued that there is significant variation in the CPI in parafoveal V1 (Dow et al., 1981; Van Essen et al., 1984).

The Results section is divided into three parts. In the first part, we characterized the CPI by directly measuring the 2-D spatial profile of the response using VSDI. Specifically, we asked whether the size of the CPI depends on eccentricity or remains roughly constant in parafoveal V1 (eccentricities of 1.9-4.45 deg). In the second part, we characterized the pRF as measured by VSDI and electrophysiology. We did this by measuring the response at a single location in V1 as a function of the position of a small visual stimulus (Gabor patch). In the first and second parts we also examined in more
detail the shapes of the CPI and the pRF and looked for possible anisotropies and asymmetries. Finally, in the third part, we compared the shapes of the pRFs obtained by VSDI and electrophysiology (SU, MU, and LFP), and derived transfer functions that quantitatively described the relationship between these different signals.

**Direct measurement of the CPI with VSDI**

Because VSDI allowed us to directly measure the entire 2-D spatial profile of the response to small, local stimuli within a range of parafoveal eccentricities, our first goal was to characterize the CPI using VSDI and determine its dependency on eccentricity. However, as discussed above (Eq. 6.2), the response profile is also 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, after removing the contribution of the stimulus to the spatial response spread.

**CMF depends on eccentricity and direction**

VSDI allowed us to directly measure the cortical population response to stimuli that fall within a limited region of the visual field. The patches of cortex that we imaged represent a wedge-shaped region in visual space extending from an eccentricity of 1.9° to 4.45° (degrees of visual angle), and representing directions about the visual axis between 270° to 330° (angular degrees). Predictably, as we varied the position of the stimulus within this region, the population response moved systematically across the surface of the cortex. The rate at which the VSDI response moved across the cortex relative to the rate
at which the position of the stimulus was varied in visual space was determined by the CMF.

Figure 6.1 shows VSDI population responses to varying stimulus position from a typical experiment. The positions of the stimuli in this experiment were varied along a horizontal line (Fig. 6.1A). The VSDI response maps for each stimulus position are shown in Figure 6.1B. Each VSDI response map was fitted with a 2-D Gaussian function (see Methods; dashed ellipsoid in each panel shows the 1-sigma contour of the 2-D Gaussian fit). As the stimulus moved towards the vertical meridian, the center of the response noticeably moves from the medial posterior corner of the imaging area to the anterior lateral corner. We computed the CMF by finding the distance between the centers of the fitted VSDI responses (indicated by the 1.25 X 1.25 mm² colored squares in Fig. 6.1B) to pairs of neighboring stimuli, then dividing that cortical distance by the distance between the corresponding pair of stimuli in visual space. The 7 estimates of CMF are plotted in Figure 6.1C at the point equidistant between the neighboring stimuli in each pair. While the individual values of the CMF were quite noisy, there was a significant trend for the CMF to increase with decreasing eccentricity. To illustrate the change in the CMF, the center of the response to the stimulus at (-3.25,-1.95; pink square) was added to the panel labeled (-2.25,-1.95) and the center of the response to the stimulus at (-3.25,-1.95; blue square) was added to the panel labeled (-0.75,-1.95). In both cases, the stimuli are 1 degree apart, but the center of the cortical representations are further apart for the pair of stimuli closer to the fovea, indicative of a CMF that decreases
Figure 6.1. V1 spatial response profile measured with VSDI. A Left, stimulus coordinates in degrees of visual angle. Concentric lines are shown in 1 deg eccentricity increments. ‘x’ at (0,0) indicates fixation point. Blue rectangle corresponds to blue arc in b showing the approximate spatial representation of the various stimulus positions in the cortex. The arrow and red line also correspond to b to indicate how visual space is represented in the cortex. B Top, image of cortical vasculature with scale and landmark information. Red rectangle indicates the 10 X 10 mm$^2$ region of interest (ROI) for the response maps below. Bottom, spatial distribution of response amplitudes for different stimulus positions. 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 one standard deviation of the 2-D Gaussian function used to fit the VSD response maps. Colored squares (1.25 mm X 1.25 mm$^2$) in each panel denote the center of the 2-D Gaussian function. The pink square added to the panel labeled (-2.25,-1.95) and the blue square added to the panel labeled (-0.75,-1.95) are used to illustrate the CMF (see text). All of the squares representing the centers of the 2-D Gaussian functions are shown in the bottom right panel to further illustrate the CMF. C CMF as a function of eccentricity. Black curve is a power function fit to data. D Size of the CPI as a function of eccentricity roughly parallel (squares, fit with power function, solid curve) and perpendicular (diamonds, fit with power function, dashed curve) 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. Solid line denotes 0 degrees difference and dashed line denotes the mean orientation difference from line parallel to V1/V2 border.

with eccentricity. The CMF data were fit with a simple two parameter power function (see Materials and Methods). In this example experiment, which is typical of all the experiments, the CMF decreased significantly with eccentricity (bootstrap test; see Materials and Methods).

Figure 6.2A summarizes our CMF measurements across the 11 VSDI experiments. Across seven experiments where we used a horizontal stimulus configuration (black symbols), the CMF varied almost by a factor of two from the most foveal location (eccentricity of ~2 deg) to our most peripheral location (eccentricity of ~4 deg). A similar change in the CMF as a function of eccentricity was measured in the four experiments with the vertical configuration (red symbols). However, at each eccentricity
the CMF along the vertical direction was significantly larger (by a factor of 1.59) than the CMF along the horizontal direction, revealing significant anisotropy in the CMF along these two directions. This result is consistent with previous reports of anisotropy in the representation of visual space near the V1/V2 border, with the direction parallel to the V1/V2 border (approximately consistent with the vertical configuration) having significantly larger CMF than the direction normal to the V1/V2 border (roughly corresponding to the horizontal configuration) (Van Essen et al., 1984; Dow et al., 1985; Tootell et al., 1988; Blasdel and Campbell, 2001; Adams and Horton, 2003; Yang et al., 2007). The exponent of the power functions describing CMF as a function of eccentricity (-0.82) is comparable to the exponent measured by Tootell et al. (1988), but smaller than those measured by Van Essen et al. (1984) and Adams and Horton (2003), perhaps because these last two studies measured the CMF over a much larger range of eccentricities.

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 roughly constant across eccentricity and is significantly anisotropic, asymmetric._

To derive the CPI, VSDI responses for each stimulus position were first fit with a 2-D Gaussian function. To capture potential anisotropies in the spatial response profiles, we used separate parameters for sigma major, sigma minor, and orientation of the 2-D Gaussian function (see Materials and Methods). The spatial response profiles were noticeably anisotropic. In the experiment illustrated in Figure 6.1, the mean sigma major
was 2.01 mm and the mean sigma minor was 1.55 mm. By removing the contribution of
the direct projection of the stimulus from the response profile (Eq. 6.2), we derived
estimates for the CPI along the major and minor directions (Fig. 6.1D). Because the
direct projection of the stimulus (the product of the stimulus size with the local CMF
equal ~ 0.5 mm) was much smaller than the response spread, the CPIs were almost
identical to the spatial response profile values. CPI\textsubscript{major} (mean = 1.99 mm, SD = 0.22) was
1.30 times larger, on average, than CPI\textsubscript{minor} (mean = 1.53 mm, SD = 0.17). Importantly,
though there are slight decreases in CPI\textsubscript{major} and CPI\textsubscript{minor} with eccentricity, these
decreases were not significant.

As expected from the anisotropy in the CMF, the orientation of the major axis of
the CPI was almost parallel to the V1/V2 border (Fig. 6.1E; mean orientation difference =
-8.5°; SD = 9.9°).

Figure 6.2 summarizes the results from all 11 VSDI experiments. Across all
experiments the major axis tended to be oriented parallel to the V1/V2 border (Fig. 6.2B;
mean orientation relative to border = -14.5°, SD = 16.6°, for all stimuli with a
CPI\textsubscript{major}/CPI\textsubscript{minor} ratio > 1.1). The mean (and SD) of the CPI was 1.94 mm (0.24) and 1.39
mm (0.18) in the direction approximately parallel (CPI\textsubscript{major}, Fig. 6.2C) and perpendicular
(CPI\textsubscript{minor}, Fig. 6.2D) to the V1/V2 border, respectively. Importantly, despite large
changes in CMF over the same range of eccentricities (Fig. 6.2A), there was no
significant change in the size of the CPI as a function of eccentricity, providing direct
evidence that the CPI is approximately constant in parafoveal V1. This is consistent with
findings by Hubel and Wiesel (1974) and is inconsistent with the findings of Dow et al.
Figure 6.2. Summary of VSDI spatial response profile measurements. A Summary of the cortical magnification factor (CMF) as a function of eccentricity for stimuli varying in position in either a horizontal or vertical (black/red) configuration. Power functions are used to fit each set of data. Asterisks indicate that the power functions are significantly decreasing. Significance is determined by the fact that the power functions fall outside of 95% CI on the null distribution of bootstrapped power functions (grey and pink shaded areas) (see Materials and Methods for details of bootstrap power function significance test). B Summary of the orientation (relative to a line parallel to V1/V2 border) of the major axis of the CPI as a function of eccentricity for stimuli varying in position in either a horizontal or vertical (black/red) configuration. Solid line denotes an orientation of 0 degrees and dashed line denotes the mean orientation relative to a line parallel to V1/V2 border. C,D Summary of the size of the CPI as a function of eccentricity for stimuli varying in position in either a horizontal or vertical (black/red) configuration along the major axis (C) and minor axis (D) of the 2-D Gaussian function used to fit the response maps in Figure 6.1B. One power function is used to fit both sets of data in C,D. Grey shaded areas show null distribution of bootstrapped power functions.
(1981) and Van Essen et al. (1984) who reported significant changes in the CPI in the same eccentricity range. This important result implies that each point in the visual field is monitored by a relatively constant number of neurons in V1. Furthermore, it shows that this minimal population is extremely large, spanning ~6x8 mm of cortex in V1.

It is possible that the large CPI obtained with VSDI is due to the strong sub-threshold component of the VSDI signals. A central goal of our study was therefore to estimate the CPI based on spiking activity and LFP as measured by electrophysiology and compare these estimates with the ones obtained with VSDI. The results of this comparison are described later.

The average anisotropy factor for the CPI (\(CPI_{\text{major}}/CPI_{\text{minor}}\)) was 1.40 while the average anisotropy factor for the CMF (V/H ratio = 1.59) was larger. Part of this difference could be because the vertical and horizontal directions are only approximately similar to major and minor directions of the CPI. Notice in Figure 6.1B that as the stimulus is moved in a horizontal direction the position of the spatial response profile does not drop off in a straight line perpendicular from the V1/V2 border, as would be expected if the horizontal direction was a perfect approximation of CPI minor. Also note in Figure 6.3C that as the stimulus is moved in a vertical direction the position of the spatial response profile moves in a straight line nearly (but not perfectly) parallel to the V1/V2 border.

Additionally, because CPI is the product of the pRF and the CMF, it is possible that anisotropy in the pRF contributes to this difference. In other words, it is possible that the pRF in the horizontal direction is larger than in the vertical direction, thus leading to
anisotropy that is smaller for the CPI than for the CMF. This possibility is tested in the next section.

Because CMF decreases with eccentricity, if the pRF is symmetric with respect to the directions towards and away from the fovea, CPI should be larger towards the fovea (due to larger CMF) and smaller towards the periphery (due to smaller CMF). To test for such asymmetry in the CPI, we collapsed the VSDI response maps (e.g. Fig. 6.1B) along the $\sigma_{\text{major}}$ direction, and then fitted the 1-D slices with two half 1-D Gaussian functions. We only tested along $\sigma_{\text{major}}$ because the direction along the V1/V2 border (roughly parallel to $\sigma_{\text{major}}$) is closer to the fovea-periphery direction (iso-polar) while the direction roughly parallel to $\sigma_{\text{minor}}$ is closer to the iso-eccentric direction, meaning that there is less difference in eccentricity between the two halves (foveal and peripheral) in $\sigma_{\text{minor}}$ than in $\sigma_{\text{major}}$.

We found significant asymmetry along CPI$_{\text{major}}$, in the direction of our prediction (mean towards fovea = 2.16 mm, SD = 0.41; mean towards periphery = 1.75 mm, SD = 0.44, paired $t$-test p-value < 0.001, $n = 62$ sites). In the next section we used the VSDI measurements to test the symmetry of the pRF.

In summary, using direct measurements of the population response profile with VSDI we found that the CPI is roughly constant across eccentricity, despite large changes in the CMF. The implication of this result is that every point in the visual field has equal coverage, which is the brain devotes equal computational power to each point in space, at least in parafoveal V1. This key result resolves a controversy amongst previous electrophysiological studies. In addition, we found significant anisotropy in the CPI, but
less than that measured in the CMF, suggesting the difference in the anisotropy of the CPI and the CMF will be present in the pRF. Finally, we found that the CPI along its major axis is significantly larger towards the fovea than towards the periphery. In the next section, we used VSDI and electrophysiology to characterize the pRF, and tested the predictions from this section about anisotropy in the pRF. We then compared pRF measurements obtained with VSDI with the ones obtained by electrophysiology to quantitatively describe the relationship between VSDI and electrophysiological signals.

**Characterizing V1 (p)RFs with VSDI and electrophysiology**

The population receptive field (pRF) is the area of visual space that activates a local population of neurons. Our goal in this section was to characterize the pRF with both VSDI and electrophysiology, examining its size and shape. The pRF was estimated by measuring the fall off in activity of a local population of neurons as the stimulus was presented at different locations in visual space. In each experiment the stimulus position was varied along horizontal, vertical, or iso-eccentric directions (electrophysiology experiments only), and moved either in one direction (most electrophysiology experiments) or in both directions from the center of the (p)RF of the recorded neuron(s). We fit the amplitudes of the neural response as a function of stimulus distance from the (p)RF center with 1-D Gaussian functions, which we refer to as position tuning (PT) functions, the sigmas of which are the space constants. To test predictions about the shape of the pRF based on observations of anisotropy in the CPI and to examine possible asymmetry in the pRF, we measured the space constant separately for horizontal and
vertical stimulus configurations, and for directions towards and away from the fovea (relative to the center of the pRF). Analogous to our analysis of the spatial profile of the responses in V1, removing the effect of stimulus size from the PT space constant was necessary to derive the pRF size (see below).

*VSDI pRF depends on eccentricity and is significantly anisotropic and asymmetric*

Figure 6.3 shows how the VSDI pRF was estimated with PT functions using an example where the stimuli were in a vertical configuration (Fig. 6.3A). To compute the PT function for the VSDI responses, we first selected a 1.25 X 1.25 mm² integration area (e.g. red square, 1.25 mm X 1.25 mm², in top left panel of Fig. 6.3C) centered at the peak of the cortical response to one stimulus position, and then integrated the cortical response at that same fixed 1.25 X 1.25 mm² location (red square) during the presentations of the stimuli at the remaining n – 1 positions (seen in the other panels of Fig. 6.3C). The center of the peak cortical response was defined as the center of a 2-D Gaussian function fit to the mean cortical response for each stimulus position. The amplitudes of the integrated responses as a function of the distance of the stimulus from the center location, plotted in the top left panel of Figure 6.3D (red circles), were then fit with a 1-D Gaussian position tuning (PT) function. The fall off in VSDI amplitude for stimuli at each of the other spatial locations (PT functions plotted in the remaining panels of Fig. 6.3D) was measured by integrating the VSDI response within the center of each response map (other colored squares in Fig. 6.3C) in turn.
Figure 6.3
**Figure 6.3.** V1 pRF size measured with VSDI. A Stimulus coordinates in degrees of visual angle. Concentric lines are shown in 1 deg eccentricity increments. Blue rectangle corresponds to blue arc in b showing the approximate spatial representation of the various stimulus positions in the cortex. The arrow and red line also correspond to b to indicate how visual space is represented in the cortex. B pRF size as a function of eccentricity, measured towards the fovea (circles, fit with power function, solid curve) and towards the periphery (triangles, fit with power function, dashed curve). C Spatial distribution of response amplitudes for different stimulus positions (see Fig. 6.1B for details). All of the squares representing the centers of the 2-D Gaussian functions are shown in the bottom right response map to illustrate spatial representation vertical configuration of stimuli. D Response amplitude (ΔF/F%) as a function of stimulus displacement relative to the point closest to the vertical meridian (-0.5, -1.95 in this case). Response amplitudes for each panel come from spatially integrating, in turn, each response map within the location of the response centers (colored squares) for each stimulus position. Data are fit with two half 1-D Gaussian functions, one for points moving towards the fovea (relative to location listed at top of each panel) and one for points moving towards the periphery. Colors correspond to colors used in c.

Intuitively, the PT function should depend not only on the size of the neural population receptive field (pRF) but also on the stimulus size; for the same pRF size, if the stimulus is large, the PT function will have a larger sigma than if the stimulus is small. Mathematically, the PT function is equal to convolving the stimulus with the pRF. Therefore, to obtain the sigma of the pRF (or the RF for SU data), we removed the effect of stimulus size using the following equation:

**Equation 6.3:**  \[ \sigma_{RF} = \sqrt{\sigma_{PT}^2 - \sigma_{ST}^2} \]

where \( \sigma_{PT} \) is the sigma of the PT function and \( \sigma_{ST} \) is the sigma of the Gabor stimulus (always 0.16 deg). This method was repeated for each stimulus position to obtain multiple estimates of the pRF size. The same method was used for estimating the (p)RF size in the electrophysiology data (see below).
We observed asymmetry in the CPI (it is larger towards the fovea). To test for asymmetry in the pRF, we fit the VSDI responses in each panel of Figure 6.3D with one or a pair of half 1-D Gaussian functions, i.e. position tuning (PT) functions. When fitting with a pair of PT functions, the first PT function was used to fit all of the points moving towards the fovea, relative to the location listed at the top of each panel in Figure 6.3D. A second PT function was used to fit points moving towards the periphery. We did not consider PT functions with less than 2 points on the flank to be reliable. Therefore, some of the sets of VSDI response amplitudes in Figure 6.3D, corresponding to the two most foveal and two most peripheral stimuli, were only fit with one PT function.

The space constants (sigmas) of the valid PT functions were plugged into Equation 6.3 (which removed the almost negligible effect of stimulus size) to give the actual sizes of the pRFs (e.g. the sigma of the most peripheral stimulus (-1.00, -3.00) in Fig. 6.3D was 0.50 deg, and the pRF was calculated to be 0.48 deg). We fit each set of pRF sizes (measured towards the fovea (circles) and towards the periphery (triangles)) with a power function (using a common exponent for both functions, allowing only the scale factors to vary) (Fig. 6.3B). The pRF size increased with eccentricity (common power function exponent = 1.69). The pRF measured towards the periphery was larger than it was measured towards the fovea in the two positions that we had data for both.
Figure 6.4. Summary of VSDI pRF size. Summary of the pRF size as a function of eccentricity for stimuli moving in a horizontal/vertical (black/red) configuration towards the fovea/periphery (circles/triangles) with power functions (all having the same exponent, but different scale factors) fitting each set of data. Asterisks indicate that the power functions are significantly increasing (see Materials and Methods for details of bootstrap power function significance test).

A summary of the pRF sizes as a function of eccentricity for all of the VSDI experiments is shown in Figure 6.4. Because we were testing for asymmetry in the pRF, we separated foveal and peripheral pRF estimates using different symbols. Also, given that the CMF showed significant vertical/horizontal anisotropy, and that the anisotropy was larger than that found in the CPI, we expected some anisotropy in the pRF. Therefore we used different colors to distinguish horizontal and vertical stimulus configurations.
Because there was no evidence of inter-monkey differences in the size of the pRF, we did not differentiate by monkey as we did for CMF and CPI (Fig. 6.2A,C,D).

For the cases where we could estimate pRF in the vertically positioned stimuli both towards the fovea and towards the periphery, pRF sizes measured towards the fovea (VF) (mean = 0.400 deg, SD = 0.074) were significantly different (paired t-test p-value = 0.010) than pRF sizes measured towards the periphery (VP) (mean = 0.512 deg, SD = 0.154). We did not test for asymmetry in the horizontally positioned stimuli for the same reason we did not measure asymmetry along the minor axis of the CPI; the vertical direction is closer to fovea-periphery direction (iso-polar) while the horizontal direction is closer to the iso-eccentric direction, meaning that there is less difference in eccentricity between the two halves in the horizontal configuration than in the vertical configuration.

As expected, the pRF showed significant horizontal vs. vertical anisotropy. pRF sizes for horizontally positioned stimuli (combined across the direction towards and away from the fovea; mean = 0.624; SD = 0.119) were significantly larger than pRF sizes in the vertical direction (mean = 0.451; SD = 0.123; non paired t-test p-value < 0.001). We made this comparison only within 2.0 to 3.5 degrees eccentricity (range of overlap in horizontal and vertical data). The anisotropy ratio (V/H) is 0.722. This result confirms the prediction (see CPI results section above) that the pRF would be larger for the horizontal stimulus configurations, roughly balancing out the difference in the CPI and CMF anisotropies we observed (see Table 6.1).
Each set of pRF sizes (HF, HP, VF, and VP) was fit with a power function. All four power functions were fit with a common exponent (0.58, see Materials and Methods) and a scale factor value that was allowed to vary. Scale factor values were: HF = 0.38; HP = 0.37; VF = 0.24; and VP = 0.27. There was a significant increase in the pRF size as a function of eccentricity for each type of data (bootstrap test on power function exponents), inconsistent with the electrophysiology results of Van Essen et al. (1984).

Table 6.1: Anisotropy in CPI, CMF, and pRF

<table>
<thead>
<tr>
<th></th>
<th>CPI(^{1,2}) mean (SD)</th>
<th>CMF(^3)</th>
<th>pRF(^{1,2}) mean (SD)</th>
<th>CMF * pRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hor. minor</td>
<td>1.39 mm (0.18)</td>
<td>2.47 mm/deg</td>
<td>0.62 deg (0.12)</td>
<td>1.53 mm</td>
</tr>
<tr>
<td>Vert. major</td>
<td>1.94 mm (0.24)</td>
<td>3.92 mm/deg</td>
<td>0.45 deg (0.12)</td>
<td>1.76 mm</td>
</tr>
<tr>
<td>Ratio V/H</td>
<td>1.40</td>
<td>1.58</td>
<td>0.72</td>
<td>1.14</td>
</tr>
</tbody>
</table>

1 Symmetric fits only
2 All values are means for stimuli within the range of 2.0 and 3.5 degrees eccentricity
3 CMF value at midpoint between 2.0 and 3.5 deg. (taken from power functions in Fig. 6.24)

To summarize the VSDI pRF findings: 1) the pRF is significantly dependent on eccentricity, counterbalancing the effect of eccentricity on the CMF such that the CPI remains roughly independent of eccentricity; 2) pRF size is larger in the horizontal stimulus configuration than in the vertical stimulus configuration, consistent with the fact that the anisotropy observed in the CMF is larger than that in the CPI; 3) pRF size is asymmetric (larger when measured towards periphery than towards fovea).

We next measured p(RF) for SU, MU, and LFP to compare to the VSDI pRF and (in the following section) to derive transfer functions that quantitatively describe the relationship between VSDI and electrophysiological signals.
**Electrophysiology derived (p)RFs**

(p)RF sizes for electrophysiology signals were measured with a method very similar to the method used for finding pRF sizes for the VSDI data. PSTHs from one typical experiment where SU, MU, LFP, and VSDI were recorded simultaneously can be seen in Figure 6.5A-C. The RF center (optimized for the SU) in this experiment was (0.5, -2.5), and the stimulus configuration was horizontal. Predictably, neural responses decreased as the stimulus was moved away from the center of the RF. Figure 6.5D shows the mean integrated response at each position for SU, MU, and LFP with the response to the blank condition subtracted from each mean response, and each mean response was then normalized by the mean response amplitude at the (p)RF center. For this example experiment (as well as all but 4 electrophysiology experiments), all of the stimulus positions relative to the (p)RF center were in the direction towards the periphery. Therefore, for all of the analyses comparing electrophysiology and VSDI signals, we did not do separate PT function fits for stimuli towards the fovea and towards the periphery as we did for the VSDI experiments. The (p)RF sizes (with stimulus size removed per Eq. 6.3, as was done for the VSDI data) were SU = 0.20 deg, MU = 0.27 deg, and LFP = 0.33 deg. Normalized VSDI response amplitudes (generated by finding the center of the response map for just the stimulus positioned in the center of the SU RF) as a function of stimulus position are included in Figure 6.5D (pRF size = 0.58 deg).
Figure 6.5. Spatial response spread measured with electrophysiology and VSDI. **A** Peri-stimulus Time Histogram (PSTH) for SU responses. Neural responses were averaged over repetitions (n = 10) and stimulus presentations per trial (n = 2). Bin size is 25 ms, and data points lie in the middle of the bin period. Vertical dashed lines denote stimulus onset (time = 0 ms) and offset (time = 200 ms). Shading indicates the integration period (36-236 ms). The key shows the horizontal coordinate of stimulus position relative to RF center (0.5, -2.1). PSTHs for **B** multiunit and **C** normalized RMS of the LFP signal are from the same experiment as **A**. **D** Normalized response amplitudes for each stimulus position fit with 1-D Gaussian functions for SU, MU, LFP, and VSDI (also from same experiment). The VSDI Gaussian function is derived from the response map of the stimulus located at the RF center (0.5, 2.1) of the electrophysiological responses. The RF sizes (space constants (sigmas) of the Gaussian functions minus the effect of stimulus size; see text for details) are listed in the key. Error bars are SEM. Dashed lines indicate SEM of the blank condition for each measure.

In many experiments, two or three electrophysiological measurements were made simultaneously. When LFP was recorded simultaneously with SU and/or MU, the LFP pRF size was significantly larger than both the SU RF size (n = 17, LFP mean = 0.480 deg, SU mean = 0.380 deg, paired *t*-test *p*-value = 0.002) and MU pRF size (n = 18, LFP
mean = 0.485 deg, MU mean = 0.401 deg, paired t-test p-value = 0.018). When SU and MU were recorded simultaneously, there was no significant difference in their (p)RF sizes (n = 16, SU mean = 0.424 deg, MU mean = 0.470 deg, paired t-test p-value = 0.20).

In principle, low frequency LFP signals should travel further through cortical tissue. Therefore, the pRF size of the low frequency component of the LFP should be larger than that of the higher frequency components. To test whether the LFP pRF size was dependent on the specific frequency of the LFP signal, we found the amplitude (square root of power) of the LFP response for five 40 Hz bands (1-40 Hz; 41-80 Hz; 81-120 Hz; 121-160 Hz; 161-200 Hz) using FFT. However, we found no significant differences (paired t-tests) in the pRF sizes of any of the 40 Hz bands. Our result is actually consistent with the results of Logothetis et al. (2007) who showed that spatial propagation is independent of the frequency of the LFP signal.

We used our measurements of the electrophysiology (p)RF to compute estimates of the CPI. (p)RF sizes for stimuli in a vertical (horizontal) configuration were multiplied by CMFV (CMFH), at the appropriate eccentricity (based on the VSDI-derived CMF power functions in Fig. 6.2A), to yield estimates of CPImajor (CPIminor). All of the CPIminor data came from a small range of eccentricities (2.35 – 2.75 degrees). In comparing CPImajor and CPIminor, we used a subset of the CPImajor data that came from the same range. Electrophysiology estimates of CPImajor were: SU - mean = 1.01 mm, SD = 0.40, n = 7; MU - mean = 1.12 mm, SD = 0.59, n = 9; LFP - mean = 1.18 mm, SD = 0.32, n = 6. Electrophysiology estimates of CPIminor were: SU - mean = 0.62 mm, SD = 0.29, n = 3; MU - mean = 0.73 mm, SD = 0.35, n = 3; LFP - mean = 1.14 mm, SD =
0.36, n = 4. CPI\textsubscript{major} vs. CPI\textsubscript{minor} anisotropy ratios were 1.63, 1.53, and 1.23 for SU, MU, and LFP, respectively.

**Quantitative relationship between VSDI and electrophysiological signals**

A comparison of VSDI pRF and electrophysiology (p)RF sizes is shown in Figure 6.6.

Figure 6.6 shows the (p)RF sizes for SU, MU, and LFP for all of the experiments (collapsed over stimulus configuration type) plotted with the pRF sizes of the VSDI (from Fig. 6.4, also collapsed over stimulus configuration type). Because we did not do

![Figure 6.6](image)

**Figure 6.6.** Summary of (p)RF sizes. Summary of (p)RF size as a function of eccentricity for VSDI (black points), SU (red points), MU (blue points) and LFP (green points). Data are collapsed across stimulus configuration. Power functions (all having the same exponent, see Materials and Methods) are used to fit each set of data.
separate towards-fovea/towards-periphery PT function fits for the electrophysiology data, we used just one PT function (full 1-D Gaussian functions, assuming symmetry) to derive the (p)RF size for each stimulus for this analysis. Though the range of (p)RF centers of the electrophysiology data was 1.89 to 5.1 degrees, only (p)RF data from within the range of 1.89 to 3.15 degrees eccentricity was used in this analysis. This smaller eccentricity range was used because it contained a sufficient amount of data for each type of measurement. Power functions were used to fit the VSDI, SU, MU, and LFP (p)RF sizes within 1.89 to 3.15 degrees eccentricity. A common exponent was used for each power function (see Materials and Methods), and the scale factor was allowed to vary. The common exponent was 0.81. Like the size of the VSDI pRF, the sizes of the (p)RF of SU, MU, and LFP increased significantly with eccentricity, inconsistent with Van Essen et al. (1984). The ratio of the scale factors of the power functions defined the ratio of the typical VSDI pRF size to the typical electrophysiology (p)RF sizes in a way that was independent of eccentricity. The electrophysiology power function scale factors (normalized by the VSDI power function scale factor) are plotted in Figure 6.7A. The space constants of SU and MU (p)RFs are ~40% smaller than those for the VSDI pRF. The space constant of the LFP pRF falls in between, and is ~20% larger than the space constants of SU/MU (p)RF and ~25% smaller than the space constant of the VSDI pRF. These results are the first known quantitative comparison of the VSDI and electrophysiological signals. We next used these differences in (p)RF size to derive the transfer functions between VSDI and electrophysiology.
Figure 6.7. Aggregate position tuning and transfer functions. A Scale factors of electrophysiology pRF power functions (normalized to the VSDI pRF power function scale factor). B Aggregate position tuning (PT) functions based on the ratio of scale factors in A. C PT transfer functions providing the % electrophysiology response (relative to the max response) as a function of % VSDI (relative to its max response) derived by plotting aggregate electrophysiology PT functions against the aggregate VSDI PT function.
Transfer functions

The relationship between the VSDI and electrophysiology (p)RFs is illustrated in Figure 6.7B which shows the normalized average (p)RFs. Figure 6.7C shows the TFs between the VSDI response and each of the electrophysiology responses, derived from the normalized (p)RF curves in Figure 6.7B. Because each aggregate PT function was assumed to be a Gaussian function and because the ratio of two Gaussian functions is a power function, each TF could be described with a power function whose exponent was equal to the square of the ratio of the space constants for each pair of neural signals (VSDI/SU, for example) (see Table 6.2 for aggregate PT function sigma ratios and TF exponents).

Table 6.2 - Ratio of VSDI and Electrophysiology (p)RF sigmas and TF exponents

<table>
<thead>
<tr>
<th></th>
<th>ratio $\sigma_{\text{Ephys.}} : \sigma_{\text{VSDI}}$</th>
<th>TF exponent</th>
</tr>
</thead>
<tbody>
<tr>
<td>SU</td>
<td>0.61</td>
<td>2.70</td>
</tr>
<tr>
<td>MU</td>
<td>0.62</td>
<td>2.55</td>
</tr>
<tr>
<td>LFP</td>
<td>0.76</td>
<td>1.70</td>
</tr>
</tbody>
</table>

The TFs show that significant VSDI activity can be observed before significant spiking activity can be measured. Specifically, spiking and LFP activity reached 10% of their maximum only when VSDI signals exceeded 40% and 25% of their maximum, respectively. Importantly, these TFs can now be used to make quantitative predictions about the response of the SU, MU, or LFP based on the VSDI response.
Discussion

The primary goals of this chapter were: 1) to characterize the size and shape of the cortical point image (CPI), and determine if it changes with eccentricity; 2) to characterize the size and shape of the population receptive field (pRF); and 3) to construct transfer functions (TFs) to describe the relationship between VSDI and electrophysiology responses. We found that, across a range of parafoveal eccentricities, CPI size remains constant, whereas the cortical magnification factor (CMF) decreases significantly and pRF size increases significantly. We found significant anisotropy in the CPI (larger along the vertical meridian) and slightly larger anisotropy (also significant) in the CMF (larger along the vertical meridian) that was roughly balanced out by significant anisotropy in the pRF (larger along the horizontal meridian). We also found the CPI to be asymmetric (significantly larger towards the fovea), as well as the pRF (significantly larger towards the periphery). The average SU and MU (p)RF was ~40% smaller than the VSDI pRF and the average LFP pRF was ~25% smaller than the VSDI pRF. Finally, TFs derived from aggregate VSDI and electrophysiology PT functions showed spiking and LFP activity exceeded ~10% of their maximum only when VSDI signals exceeded ~40% and ~25% of their maximum, respectively.

Cortical point image

We found that the area of cortex activated by a point stimulus, the CPI, was constant across eccentricity, indicating that each location in space has equal coverage (i.e. activates an equivalent amount of cortical machinery). Previous attempts to measure the
CPI have failed to account for the scatter in the cortical response due to the size of the stimulus. However, it was possible to compare our CPI size measurements with the spatial response profile, or response spread (RS), measured by Chen et al. (2006), since their stimulus size (Gabor stimulus $\sigma = 0.33$ deg) was negligible relative to the size of the RS. In general, our CPI size measurements were comparable with their data, as were our estimates of anisotropy. Other groups that have measured the CPI with VSDI used stimuli that were ~6 times larger than the stimuli we used (Grinvald et al., (1994) and Slovin et al., (2002)), and since their RS measurements were dominated by the direct projection of the stimulus, it was not possible to compare our results to theirs.

Before the technology existed to measure the CPI or RS directly with optical imaging methods, the CPI was computed by multiplying RF size (from SU or MU) times the CMF. RF size and CMF at various eccentricities were obtained via multiple electrode penetrations, even large numbers of which still grossly under sampled the cortical surface. Regardless, Hubel and Wiesel (1974) and Albus (1975, working with cats) claimed that the CPI is constant across eccentricity, whereas Dow et al. (1980) and Van Essen et al. (1984) claimed that CPI decreases with eccentricity especially just outside the fovea (2-5 degrees eccentricity). We are the first to directly measure the size of the CPI over a range of eccentricities (finding it to be fairly constant between 1.89 to 4.45 degrees), allowing us to definitively resolve the discrepancy between the electrophysiology studies mentioned above.

The fact that we were able to observe a drop in CMF by a factor of ~2 over the range of 1.89-4.45 degrees eccentricity suggests that the VSDI method is indeed a
sensitive measurement of V1 retinotopy, and suggests that we did not fail to observe a
change in CPI with eccentricity due to poor measurement sensitivity.

Our estimates of the CPI based on the electrophysiological signals were ~40%
(SU and MU) and ~25% (LFP) smaller than the size of the CPI measured directly from
population responses using VSDI. We suspect that the large difference is due to the
strong subthreshold component of the VSDI. The LFP based CPI estimates were larger
than both the SU and MU, most likely also due to the subthreshold component within the
LFP signal. Though it may seem surprising that the LFP CPI is closer in size to that of
the SU and MU than that of the VSDI signal, Katzner et al. (2009) have shown the spread
of LFP signals to be much more limited than previous estimates have proposed.

When exploring the relationship between the CPI, the CMF and the pRF, we
made the assumption that $\text{CPI}_{\text{major}}$ could be paired with (and calculated from) $pRF_V$ and
$CMF_V$ because varying stimulus position along a line parallel to the vertical meridian
made the CPI move roughly parallel to the V1/V2 border. Likewise, we assumed
$\text{CPI}_{\text{minor}}$ could be compared with (and calculated from) $pRF_H$ and $CMF_H$. However, the
error in mapping the horizontal meridian to a line perpendicular to the V1/V2 border is
likely larger than the error in mapping the vertical meridian to a line parallel to the V1/V2
border (see bottom right response maps in Fig. 6.1B and Figure 6.3C). This weak
assumption may explain why some of the calculations of CPI do not more closely match
the observed CPI values (see Table 6.1). It may also account for some of the differences
in the CPI measured with VSDI and electrophysiology.
**Population receptive field size**

The population receptive field (pRF) is the area of visual space that activates a local population of neurons (in our case neurons within a 1.25 X 1.25 mm$^2$ region of cortex). The size of the integration window was chosen to be just large enough to obtain a relatively noise free estimate of cortical response. However, the sigma of the 2-D Gaussian used to fit the mean cortical response was not dependent on the size of the integration window.

**Asymmetry in CPI**

Since the CMF decreases with eccentricity, points equidistant in visual space correspond to points on the cortex that are further away from each other as you move towards the fovea, and also to points on the cortex that are closer as you move towards the periphery. Therefore, we predicted that the CPI should be asymmetric (larger measured towards the fovea than towards the periphery). Consistent with our prediction was the result that the CPI was asymmetric along its major axis (roughly parallel to the V1/V2 border, which itself is parallel to the iso-polar axis in V1). As far as the pRF goes, it could either be symmetric or asymmetric, so long as the relationship amongst CPI, CMF, and pRF (CPI = CMF*pRF) was balanced. Indeed, when we measured the pRF for experiments with vertical stimulus configurations (which unlike horizontal stimulus configurations, mapped to the cortex in a roughly iso-polar direction, maximizing the difference in eccentricity between fovea and periphery) the pRF was asymmetric. This is the first
reported observation of asymmetry found in the CPI and pRF, and reflects the effect of
the change in CMF over relatively short distances across the cortex in V1.

**Transfer functions**

Aggregate position tuning (PT) functions were used to construct non-linear transfer
functions (TF) that were used to quantitatively describe the relationship between VSDI
and SU, MU, and LFP responses. Previously, Grinvald et al. (1994), Jancke et al. (2004),
and Sharon et al. (2007) reported that spiking activity comprised a very small portion of
the VSDI response, and that most of the spread of the VSDI response across the cortex
was driven by subthreshold activity. These studies were limited in that spiking activity
was only sparsely sampled. Berger et al. (2007) reported a similar observation, though,
using VSDI and calcium sensitive dye imaging (which is a reasonable proxy for
suprathreshold spiking activity) in rat barrel cortex. Arieli et al. (1995) and Tsodyks et
al., (1999) described the spiking activity/VSDI relationship in terms of temporal
correlations. However they used either a single strong, unchanging stimulus or no
stimulus at all (Arieli et al. (1995) examined spontaneous activity) to derive their
findings. None of these studies examined whether the relationship between spikes and
the VSDI signal is constant across a range of values of a given stimulus feature (such as
position).

Our TFs provided a means to estimate how much average spiking activity or field
potential (relative to the maximal response) to expect given a certain level of stimulus-
driven VSDI response (relative to its maximal response). Importantly, the TFs reveal that
VSDI responses reach 40% or 25% of their maximum before spiking activity or the LFP rises above its baseline levels, respectively. This suggests that a significant amount of the VSDI signal is strictly sub-threshold in nature. Previous studies that have measured VSDI and SU simultaneously (Grinvald et al., 1994; Jancke et al., 2004; Sharon et al., 2007) have suggested that VSDI responses reached upwards of 50-90% before SU responses were observed. However, those studies did not explicitly try to quantify the VSDI/electrophysiology relationship, and generally had very few SU samples. Future experiments will be necessary to obtain TF using other stimulus manipulations (e.g., size, contrast, spatial frequency), as it is an open question whether a single non-linear transfer function could be used to predict the average spiking population response from the average VSDI response, or whether each stimulus dimension requires its own TF. Also, performing more experiments where electrophysiology and VSDI are done simultaneously should provide more robust TF.

**Conclusions**

The position tuning experiments yielded transfer functions that quantitatively described the relationship between VSDI and SU, MU, and the LFP. The position tuning TF showed noticeable differences between the VSDI and electrophysiological signals. Specifically, spiking and LFP activity exceeded 10% of their maximum only when VSDI signals exceeded 40% and 25% of their maximum, respectively. A key open question is whether these TFs also apply across other stimulus dimensions.
The position tuning experiment also revealed important findings with regard to how visual stimuli are represented in parafoveal V1. We found that the size of the CPI measured with VSDI is roughly constant across eccentricity, implying that each point in visual space is processed by an equivalent amount of cortical tissue in area V1. Changes in the CMF as a function of eccentricity were roughly balanced by changes in the size of the pRF, as predicted given a constant CPI. The anisotropies in CMF, CPI, and pRF also roughly balanced each other out. The VSDI signal was also sensitive enough to measure small, but significant, asymmetry in the size of the CPI and pRF. This asymmetry, which has not been observed previously, is likely due to the significant increase in CMF with eccentricity. Overall, the ability to directly measure the CMF, CPI, and pRF over a large portion of V1 at a high spatial resolution with VSDI produced important results about the principles of neural organization in a sensory cortical population.
Chapter 7: Conclusion

*Neural correlates of behavior and stimulus sensitivity*

The experiments in Chapters 2-4 of this dissertation were geared towards understanding the role that neurons in V1 play in representing visual stimuli and mediating behavioral responses based on visual stimuli. The research in those chapters presents strong evidence that V1 neural activity (from individual neurons and small groups of neurons) plays an important role in mediating behavioral performance in visual detection tasks.

First, we found that V1 neurons are highly sensitive to visual stimuli. In fact, the overall detection sensitivity of SU and MU was comparable to that of the monkey. Second, we found that the variability of SU and MU activity was significantly correlated on a trial-by-trial basis with variability in both choices and reaction times of the monkey in the detection task. This was the first observation of significant choice probability (CP) and reaction time correlation in individual V1 neurons, as well as the first significant neuronal/behavioral correlations observed in individual neurons from any primary sensory area. The mean CP for V1 neurons (mean SU CP = 0.60, mean MU CP = 0.62) in this task was on the high end of CP observed previously in other visual areas like medial superior temporal area (MST - Celebrini and Newsome, 1994; Cook and Maunsell, 2002) and medial temporal area, (MT - Britten et al., 1996; Dodd et al., 2001; Uka and DeAngelis, 2004; Purushothaman and Bradley, 2005). The high CP we observed may be due to the fact that the stimulus used in this study was better suited for V1 neurons than stimuli in other studies were suited for their respective areas of interest.
There were several indicators, however, that task related information processed by individual neurons (as well as small groups of neurons), was quite limited. A mean CP of ~0.60 is still relatively weak, leaving a lot of variability in behavior that is unaccounted for. Also there was a noticeable disconnect between how well neurons were correlated with both the choice and reaction-time aspects of the behavior in the detection task. Neurons with a high CP showed only a slightly higher RT-spike correlation. We also failed to see a correlation between CP and detection sensitivity (relative to the monkey’s detection sensitivity) amongst the V1 neurons. In addition, there were, on average, systematic differences in the psychometric and neurometric functions describing the behavior of the monkey and the model, respectively, in the detection task. That is, three important aspects of the monkey’s behavior (e.g. rate at which sensitivity to stimulus changed with contrast, false alarm rate, contrast threshold) could not be accounted for by SU and MU activity. Finally, the reaction time predictions produced by the dynamic integrator models (though significantly correlated with the monkey’s actual reaction time) were indicative of extra-striate processing that was dependent on task difficulty that is likely driven more by population responses rather than individual neurons.

Overall, the results of the visual detection experiments suggest that stimulus sensitivity and stimulus driven behavior are likely mediated by large populations of neurons.
Single neuron vs. population responses

Single unit recordings have traditionally been the primary tool for assessing neural activity. However, there is accumulating evidence suggesting that sensory encoding and decoding occurs on the scale of large neural populations. The focus of Chapters 5 and 6 was to compare the activity of SU to neural populations of various size: small groups (a handful to dozens) of neurons (MU); local field potential (LFP, membrane potential of neurons in a 0.5-3mm radius); and large populations of neurons measured with voltage-sensitive dye imaging (VSDI).

The comparison of SU and MU was inspired by the results of Chapter 2, where we found no significant difference in the mean detection sensitivities of SU and MU in V1. We were curious as to how increasing the size of the neural pool would not result in higher neural sensitivity. Therefore, in Chapter 5, we compared SU and MU along three parameters: signal to noise ratio; Fano factor; and contrast threshold (C50). Our conclusion was that MU were made up of several weakly correlated SU, most of which were not well tuned to the stimulus. The overall similarity in the results of the detection task, and the analyses in Chapter 5, coupled with some practical advantages of MU over SU (MU are easier to maintain and less prone to cell size and cell type bias) as well as a higher firing rate for MU (which I suggested in the discussion section of Chapter 4 may have been a reason choice probability was higher for MU than SU), make a compelling case for the expanded use of MU recordings, especially for longer term recordings where SU tend to fail at some point.
The LFP we measured also had higher target-absent choice probability than the average SU. In addition, the receptive fields (RF) measured with LFP signals were significantly larger than both the average SU and MU RF. We expected to observe the largest RF sizes for the lowest LFP frequencies (lower frequency signals should theoretically travel further through biological tissue), but we did not see any frequency dependence in the LFP RF size, consistent with signal propagation results from Logothetis et al., (2007).

The transfer functions (TF) between VSDI and electrophysiological signals in the position tuning experiment were highly non-linear. The transfer functions are useful for making predictions about how much MU activity (for example) to expect, relative to the maximum possible MU response, given a certain amount of VSDI activity, relative to its maximum. An important observation was that LFP and spiking activity only reached 10% of their maximum response by the time the VSDI signal reached 25% and 40% of its maximum, respectively. However these results may be limited not only to the stimulus manipulation (our preliminary results suggest that contrast and position tuning yield very different TF; more experiments in one or two more monkeys are needed to verify contrast TF results), but also limited to area V1 (area MT, with its much higher average SU firing rate, may yield entirely different TF), and possibly limited to short stimulus presentation and integration intervals. VSDI time courses are quite different from those of SU PSTHs; the former have long plateaus that drop slowly, while the latter tend to be much more transient. The exact shape of the TF may depend on the timing of signal integration.
The position tuning experiment in Chapter 6 also revealed important findings with regard to how visual stimuli are represented in parafoveal V1. The size of the CPI was found to be relatively stable over eccentricity, implying that each point in visual space is processed by an equivalent amount of cortical tissue in area V1. This result is not due to lack of measurement sensitivity with the VSDI, as we observed significant changes in both CMF and pRF as a function of eccentricity, as well as small, but significant anisotropies and asymmetries in the CPI and pRF.

For most of the experiments performed in the lab, we prefer to do optical imaging in parafoveal V1, as we did for this experiment. Even though the recording chamber is ~14 X 14 mm (and the accessible area of cortex ~10 X 10 mm), the range of visual space we could study was limited to an area close to the fovea. However, our recording chamber did cover the range of eccentricities (~2-5 degrees) relevant to the controversy about the size of the CPI.

Concluding remarks

There were a number of key contributions to the field of sensory neurophysiology described in this dissertation. The study of neural correlates of behavior and stimulus sensitivity in a reaction-time visual detection task showed that individual neurons and small groups of neurons in V1 can be as sensitive to a visual stimulus as the monkey. This result is important because few studies have shown V1 neurons to have stimulus sensitivity comparable to behavioral sensitivity, and also few studies in any brain area have examined the stimulus sensitivity of multi-unit activity. Also, no other study has
shown the neural and behavioral sensitivity of cortical sensory neurons to be comparable when neural signals were evaluated for extremely short integration durations that were largely determined by the monkey’s reaction time. We also showed for the first time that individual neurons and small groups of neurons in V1 have significant choice probability and reaction-time/spike correlations. Our results are the first known report of choice probability from individual neurons or small groups of neurons in a primary sensory area. The comparison of single neuron and population level responses in V1 also revealed important findings. We performed a quantitative analysis of the relationship between single units and multi-unit clusters which indicated that multi-unit activity is comprised of several weakly correlated single neurons, most of which are weakly tuned to the stimulus. The activity of single neurons (as well as multi-units and the local field potential) was also quantitatively compared to population responses in V1 (measured by VSDI) through experiments focusing on the characterization of the spatial profile of cortical responses. We derived transfer functions to describe the quantitative relationship between VSDI and the electrophysiological signals. The transfer functions were well captured by steep power functions. These experiments also led to the first known report of asymmetry in the CPI (it was larger measured towards the fovea than towards the periphery). Most importantly, we were able to show that each point in visual space is processed by an equivalent population of neurons in area V1, resolving a long-standing controversy. Overall, the direct measurements of the CMF, CPI, and pRF over a large portion of parafoveal V1 with VSDI produced important results about the principles of neural organization in a sensory cortical population.
Bibliography


Vita

Christopher Russell Palmer was born in Denver, Colorado on September 17, 1975. He is the only son of Mary Ann and Russell Palmer. After graduating from Horizon High School in Scottsdale, Arizona in 1993, he earned Bachelor’s degrees in Psychology in 1997 and Biology in 1999 from Northern Arizona University. He worked for two years as a research associate at the Stein Institute for Research on Aging at the University of California at San Diego before entering the Institute for Neuroscience doctoral program and the Center for Perceptual Systems at the University of Texas at Austin in 2002.

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