The effect of natural vision on perception and V1 neural activity

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B.A., Psychology, University of California at Santa Cruz, 2009

THESIS

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This dissertation by James Niemeyer is accepted in its present form
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Curriculum Vitae

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Education

Current:
Brown University, Providence, RI
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Past:
University of California Santa Cruz, Santa Cruz, CA
B.A. in Psychology, Intensive Track, with Honors
Date of Graduation: June 13, 2009

Research Experience

Brown University, PhD research
Advisor: Michael Paradiso, 2010-2014 (Michael_Paradiso@Brown.edu)

- Research topic: PhD thesis on the effects of eye movements and natural scenes ("natural vision") on primary visual cortex processing and perception. I have implanted electrode arrays in V1 of three monkeys and trained each on a visual psychophysics detection task. The overall goal is to understand how visual responses in V1 and perception are affected in naturalistic viewing paradigms compared to the less natural conditions commonly used in vision research. Further, these experiments allow us to compare perceptual effects with neuronal effects seen in the task.

National Institutes of Health, Summer 2009
Summer graduate school rotation (via Brown-NIH partnership program)
Working in lab of Bruce Cumming in Laboratory of Sensory Motor Research (NEI, NIH) (bgc@lsr.nei.nih.gov)

- Performed single unit recordings in Middle Temporal (MT) visual cortex of macaque monkeys trained in a visual motion discrimination task. The experiment was created to understand the top-down effects on choice probabilities (CPs) and examine whether significant CPs are a result of a feedback decision made by the animal or a sensory-driven effect.

University of Rochester, Summer, 2008

Summer undergraduate research fellowship (REU fellowship)
Working in lab of Greg DeAngelis (gdeangelis@cvs.rochester.edu)

- Spent time divided between single unit recordings in macaque V3a, shadowing a post-doc (Akiyuki Anzai, currently a staff scientist), and creating a Matlab model of population responses of dorsal medial superior temporal (MSTd) neurons. The model was used to determine whether a combination of two general cell types in MSTd, called "congruent" and "opposite" cells, could provide a readout of object motion in the visual scene during vestibular and visual input into monkey MSTd. The model showed that a population of these MSTd cells is capable of producing a response that allows for simple decoding of object motion in the presence of visual motion, in the form of optic flow, and vestibular motion.

Undergraduate Research Assistant, Visual Psychophysics Lab, 2006-2009.
University of California Santa Cruz
Principal Investigator: Eugene Switkes (gene@chemistry.ucsc.edu)

- Aided in data collection, analysis, and programming experiments using Glass patterns to study psychophysical effects of temporal and chromatic changes to these patterns on global motion processing. Also spent time translating Mathematica data analysis software into Matlab scripts.

Undergraduate Research Assistant, Cognitive Modeling Lab
University of California Santa Cruz
From June 2007 to January 2009
Principal Investigator: Travis Seymour (nogard@ucsc.edu)

- Aided in creation and implementation of a human plan encoding experiment, where subjects explored a computerized virtual environment and were forced to solve previously-posed problems using non-conventional ("creative") solutions. The goal was to measure individual creativity of participants and correlate these values with performance on the task.

Research Presentations

Conference Presentation:
"Natural vision effects on contrast sensitivity and their correlation with macaque V1 activity"
James Niemeyer, Michael Paradiso
Vision Sciences Society conference, May 17, 2014

"Visual perception in a complex world: how natural conditions affect visual function", NSGP Retreat presentation, Aug 28, 2014

Brown Neuroscience ("In House") Departmental Presentations:
"Eye movement signals in visual cortex", May 17, 2011
"Effects of saccades on perception and V1 coding", April 24, 2012
"Effects of eye movements on V1 neural activity and perception", Dec 11, 2012

"V1 neural responses and perceptual sensitivity to stimuli are reduced after eye movements" Sept 24, 2013
"Changes in V1 neural activity and perception in 'natural vison'", Dec 16, 2014

Research Posters

"Changes in perception and neural activity associated with natural vision"
James Niemeyer, Michael Paradiso
Mind/Brain Research symposium, Brown University, March 25, 2015

"Natural vision effects on V1 activity and contrast sensitivity"
James Niemeyer, Michael Paradiso
Society for Neuroscience conference, Nov 17, 2014

"Effects of eye movements on perception and neuronal responses"
James Niemeyer, Michael Paradiso
Mind/Brain Research symposium, Brown University, March 25, 2014

"V1 responses and perceptual sensitivity to stimuli are reduced after saccades"
James Niemeyer, Michael Paradiso
Society for Neuroscience conference, Nov 13, 2013

"V1 Local Field Potential Activity around Saccade Times"
James Niemeyer
NIH-Brown Program Retreat, Woods Hole, MA, April 15, 2012

"Effects of eye movements on visual processing"
James Niemeyer, Michael Paradiso
NSGP (Brown) Retreat, August 30, 2012

"Effects of eye movements on early visual processing"
(Electronic Poster Presentation)
James Niemeyer
Center for Vision Research (Brown Institute for Brain Science) Anniversary event, Nov 9, 2012

"Can Self-Motion and Object Motion be Dissociated by MSTd Neurons?"
James E. Niemeyer[1] and Gregory C. DeAngelis[2]
[1] University of California Santa Cruz, CA [2] Dept. of Brain and Cognitive Sciences, Center For Visual Science, University of Rochester, NY
Presented at poster session held for undergraduate research fellows at the University of Rochester, July 30th 2008

"Solving Goals in a Virtual Environment: The Effects of Context and Creativity"
Dylan Dean, James Niemeyer, Colin Pollock, Jenni Werkmann, Deborah Siegel, Travis

Seymour
University of California, Santa Cruz
Presented at the Stanford Undergraduate Research Conference, May 17th, 2008

Fellowships/Honors/Awards

EEG Neural Decoding Competition, Second Place.
Brown University Neural Decoding Competition, 2013. Hosted by Michael Frank and Anne Collins (Brown University).
The task was to decode human subjects' feature-based attention (to color or shape of visual stimuli) using 124-channel EEG data.

- Applied a support vector machine classifier to the neural data, using EEG bandpower across electrodes in three different frequency bands to attain significant classification performance.

Graduate Research Fellowship – Interdisciplinary Vision Training Program. National Institutes of Health (NIH/NEI) T32. PI: Michael Paradiso
Funding years 2010-2014

Undergraduate Research Fellowship, Center for Visual Science, University of Rochester, New York
Program Dates: May 2008 to August 2008

Undergraduate Research Grant, University of California Santa Cruz
Received April 2008
For: Funding assistance for presentation of research at the Stanford Undergraduate Psychology Conference in May 2008
Provided by the Psychology Department at UC Santa Cruz

Student Employee Recognition Award, University of California Santa Cruz
Received June 2006 and again in June 2007
For: Recognition of work done as a student employee at UC Santa Cruz

Teaching Experience

Teaching Assistant, Neural Systems (BIO 1030), Fall 2010
Professor: David Sheinberg

Relevant Graduate Coursework

Advanced Systems Neuroscience (Neur 2050)
Neuroanatomy (Neur 1650)
Advanced Molecular/Cellular Neurobiology (Neur 2030)
Advanced Molecular/Cellular Neurobiology II (Neur 2040)
Computational Vision (CLPS 1520)

Principles in Experimental Surgery (Biol 2140)
Biostatistics and Data Analysis (PHP 2510)
Multivariate Statistical Techniques (CLPS 2908)

Acknowledgements

I wasn't counting, but just calculated that I've spent exactly 2,105 days in graduate school at the time of finishing my thesis last night (March 25, 2015). Over the course of that time I've received help, direct and indirect, from countless people and some other primates. I won't thank everyone individually here. However, there are a few names that belong in this thesis as much as my own.

I started out in science as a psychology student at UCSC. By my second year I had already regretted that choice of major, but found a psychobiology teacher named Eugene Switkes that began me on the path that puts me in front of this thesis document today. Switkes was a chemistry professor who also had a history with visual system studies (a combination of interests that confuses me still), and was willing to take me on as an undergraduate research assistant even though I knew absolutely nothing about computer programming or psychophysics or vision or really anything else that could be useful in a research lab. I fiddled in Matlab, converted Mathetmatica code, ran psychophysics experiments on myself, followed him to science presentations, and learned about MBDKL color space. My time with Switkes at Santa Cruz gave me both an appreciation for science and a good baseline for what to expect in terms of work required to achieve anything in science. He kept me consistently confused, curious, and excited, and that really hasn't changed in nine years. Switkes also told me about, and then wrote me a recommendation letter for, a summer research internship at the University of Rochester, where I worked for a faculty member there named Greg DeAngelis.

DeAngelis runs a monkey neurophysiology lab, and he let me do everything. I spent that summer learning about eye coil surgeries, doing single-unit recordings with his research associate Akiyuki Anzai (Aki), and most importantly, learning to use neural models. I spent half the summer trying to understand my research project, but have a very vivid memory of a midnight conversation with DeAngelis during which I finally understood, fully, what I was trying to model. Since that time Matlab has been my go-to tool for everything. DeAngelis gave me a full picture of what it takes to work in a neurophysiology lab and also an introduction to the tools that I'd use throughout my time in graduate school.

By the end of that summer in Rochester, I was committed to doing a PhD in neuroscience. After some fake deliberation I chose to enroll in the Brown-NIH partnership program, and nine days after receiving my B.A. I was working for Bruce Cumming at the NIH. He might be surprised if he ever finds out I put him in my acknowledgements section, but he played a big role in shaping what I aspire to be like in science. He's on top of everything. Every component of the lab work, whether it's monkey handling, surgery, unit recording, data fitting, data plotting, statistics, is managed by Cumming himself. To this day I've never met someone who was so willing to avoid delegating work to others, and I see a lot of merit in being fully knowledgeable about every component of the research. His style impressed me, and really set me up for future work in a physiology lab.

At Brown, I rotated with Michael Paradiso, and chose to stay here. The lab felt like a real lab to me – there were post docs, undergrad students, technicians, and the whole group felt like a family. Paradiso took an approach that allowed me to learn essentially anything I needed to in order to do well in neuroscience. I got surgery

experience, took courses on visual system models, learned about signal processing, learned to replace PCI cards in about 30 seconds, learned to troubleshoot infrared eye tracker problems, and trained animals completely from scratch on psychophysics tasks. All the while, as I developed these skill sets, Paradiso also stayed down-to-earth: we talked about football, ski slopes, ice slopes, and interesting science studies regardless of whether they had any pertinence to our work. Joining this lab worked well for me, and I'd do it again without hesitation.

Finally, Aaron Gregoire's name belongs in this document. Aaron is our lab manager and lab technician, but those titles don't come anywhere close to capturing his importance in the lab. Aaron taught me how to work with animals. I trained my dog to high-five when I was in high school and thought I was cool for that, but Aaron taught me how to train a macaque to perform a two-alternative-forced-choice task around guided saccades for a couple drops of Juicy Juice. We don't use our water restriction protocol in this lab because we don't need to. Aaron's proven that careful behavioral shaping obviates the need to deprive our animals of fluid to get them to perform tasks. The result of that is our monkeys are well trained, hard workers, who aren't combative toward human experimenters. Using his techniques, I was able to train multiple animals on the psychophysics tasks presented here. Without Aaron's guidance I wouldn't have succeeded in collecting any of my data. Aaron also kept me sane throughout my time at Brown. I can be high-strung and a little serious at times in lab, but his constant willingness to talk opinions on music, Mexican food, Tequila, and Netflix, always helped in keeping me grounded. He was always available to help and chat, almost acting as my therapist at times, all while giving me the tools to successfully and humanely work with nonhuman research subjects.

For the sake of displaying professionalism I've intentionally kept my acknowledgements section limited to a few people who have played the biggest roles in shaping my PhD path and career aspirations to this point in my life; however, when I click "Upload Dissertation File" I'll feel guilty if I don't at least mention that I've had an incredibly great and supportive group of friends and family since starting graduate school. My siblings (Michael, Sarah, Travis), their kids (Braden, Reed, Chase, Penelope, Timothy), my parents, my classmates, and other friends have all been hugely important to me – their support, love, and friendship were more crucial to this dissertation than the mentors listed above. Thanks guys.

Dedication

Charlotte and Victor Niemeyer, my parents, absolutely deserve the dedication of this thesis document for being not only great parents but also life role models, and playing more of a part in my last 28 years than anyone else.

Addendum Acknowledgements

(sketches by Aaron):

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General Introduction

Visual system neurophysiology began in the middle of the 20th century (Barlow, 1953; Hubel & Wiesel, 1959), and has led to a general understanding of not only visual system function, but also to an understanding of how the brain processes, stores, and utilizes information. Further, the visual system served as a starting point for the study of other perceptual systems: humans today have an intricate knowledge of auditory, olfactory, tactile, and gustatory perception that were all relatively mysterious 70 years ago. By probing the visual system, scientists learned that individual units of brain activity, called action potentials or spikes, from individual neurons, carried important information about visual stimuli being presented to living organisms. This simple technique has been employed in many other brain regions of many different animal species, and scientists today have learned much about non-perceptual systems as well. For example, neuronal activity has been extensively studied in motor processing areas of the brain, language areas, and even decision-making circuitry of higher-order mammals. This probe-and-observe technique of studying brain activity has even led to better understanding of non-human perceptual systems such as magnetoreception in birds and insects, infra-red processing by pit vipers, lateral line sensation in fish, and pheromone communication in a mix of other species. In short, the visual system proved to be an important starting point for understanding information processing within the brain.

However, even after 55 years of study, there are many remaining questions about visual system neurophysiology. For example, due to the common lab practices of studying the visual system, neuroscientists have a weak understanding of how the visual

system functions in natural, real-world conditions. The classic method for examining cortical neurons of the occipital cortex (visual cortex) involves forcing an anesthetized or awake animal to fixate on a specific point of a dimly lit display screen in a dimly lit experiment room while visual stimuli are flashed on and off. The reason for requiring steady fixation in these experiments is that neurophysiologists typically believe that neuronal receptive fields (RFs) are retinotopically fixed, and thus eye movements would confound experiments of responses to stimuli within RFs. The reason for using dimly lit display screens is that contrast of visual stimuli is known to affect neuronal responses, so presenting a bright stimulus on a dark screen is more likely to produce good neural responses during experiments; this same fact is what justifies using dimly lit experiment rooms as well. The reason for flashing stimuli on and off is that the visual system responds well to fast changes, and therefore flashed stimuli evoke better neural responses than slowly-appearing ones.

A large majority of visual system experiments are performed in these conditions, which has led to much of our understanding of cortical processing. Unfortunately, this understanding is limited to the conditions in which visual system studies are carried out. The conditions used are intentionally deprived: stimuli are presented in the absence of rapid eye movements (saccades) against low-luminance lighting conditions. The conditions that the visual system encounters in the real world, during natural vision, is quite different: frequent saccades create constantly-changing retinal input in visual cortex, and the visual world is much more complex than dimly lit display screens. In addition, visual stimuli in the real world are rarely flashed on – saccadic eye movements bring stimuli onto the retina. Thus, the types of stimuli utilized by experimenters to elicit

strong neural responses do not accurately represent the types of stimuli that the typical human visual system encounters.

If we assume that the goal of visual system neurophysiology is to understand neuronal function in the human brain then clearly the common methods of studying the system are not sufficient to achieve the goal. Neuroscientists have performed in-depth studies of basic brain function, but we've generally neglected some of the most important components of vision. Specifically, we've avoided including saccadic eye movements and visual scene complexity in our experiments.

This leaves open the question of how visual function, both neural and perceptual, may appear different in more naturalistic contexts. The primary topic of this dissertation revolves around that question. I wish to know how neuronal activity and perception are different in more natural conditions that involve eye movements on complex scene backgrounds compared with less natural conditions that mimic the typical method of studying the brain.

Background

Eye movements in vision

There are various types of eye movements that serve multiple purposes. However, there are two main functions of eye movements: fixation and tracking of objects (Palmer, 1999). Fixation of objects is the very first step in visual processing, and thus is a crucial component of natural vision. The most common mechanism to produce a new fixation is

a ballistic eye movement, or saccade, from one point in visual space to another. This act is usually performed for the purpose of bringing a point of interest in space onto the fovea of the retina. By foveating an object an observer is employing the highest level of acuity that the retina can offer, and because much of the visual system is devoted to the processing of retinal inputs from the fovea, the act of saccading is an important one.

Saccades are not only useful for viewing items of interest in the visual world, but are also necessary for vision: an experiment first performed in 1945 showed that when stabilizing an image on the retina, by use of a specialized contact lens, the image would disappear (Ditchburn & Ginsborg, 1952; Pritchard, 1961). The mechanism responsible for this effect is adaptation to the stimulus by visually sensitive cells. By being presented with an unchanging stimulus, neurons that have receptive fields covering this stimulus become generally less responsive (Kohn, 2007). Thus, one effect of saccades on the visual system is to simply keep the system responsive.

Visual search is another key function of eye movements. Human observers make 2-3 saccades per second (Ross et al., 2001; though this finding depends on the task of the observers: Yarbus, 1967), with typical fixations lasting only a few hundred milliseconds (Palmer 1a, 1999). It has been demonstrated that when freely moving observers are equipped with eye trackers, their common daily motions, such as hand and arm movements, are tightly preceded by eye movements (Land et al., 1998). Between their uses in reading to discriminating fine details during exploration of a scene, saccadic eye movements are constantly employed.

The importance of studying 'natural' vision

Due to saccades, retinal inputs to the brain change drastically at about 2-3Hz, leaving only a few hundred milliseconds for the brain to process a visual scene during fixations. If saccade durations are taken into consideration, then these fixation periods would be even shorter. This means that visual system computations must occur quickly and be capable of changing quickly between different fixations as well. However, as stated above, experimenters frequently ignore eye movements during their studies. Therefore, this important component of natural vision is rarely examined.

Another important component of natural vision is scene complexity. Light levels, spatial frequency content, color, and motion, are all things that can vary substantially across space and time in the visual world. A good example is one that humans encounter very frequently: sitting indoors, humans are frequently adapted to moderate light levels, but with a single saccade bringing fixation on a window to the outside world then we may rapidly adjust the average luminance of the scene. This drastic change occurs in as little time as it takes to perform an eye movement – tens of milliseconds in some cases. Therefore, the spatiotemporal variables of the world (including eye movements) comprise an important component of natural vision.

A quick look at the previous 10 issues from the Journal of Vision, Journal of Neuroscience, and Journal of Neurophysiology (dating back from January 19, 2015) shows that 247 articles were published on the general topic of "Vision" from these 30 issues. Of these 247 articles, the summed number of studies performed that involved saccades or complex visual scenes totals 37. This small sample gives us a rough estimate: about 85% of visual system studies are performed in the absence of eye

movements or complex scene backgrounds. Furthermore, the remaining 15% are not necessarily concerned with "natural" vision, but are frequently geared to study a specific component of vision (such as sparseness of responses to natural scene images, or saccade metrics during visual search).

Due to the frequency of saccades and changes in complex scenes during normal viewing conditions, it is likely that these factors play a role in how the visual cortex processes information from the retina. However, it is clear that this role is not typically studied in vision experiments. A major goal of the following experiment is to illustrate some facets of visual processing that are typically ignored in classic studies of the field. To achieve this, we've designed a research paradigm in which we compare less and more natural viewing conditions. Specifically, we define "natural" conditions as ones that involve saccadic eye movements and complex scene backgrounds.

Effects of saccades on V1 responses

Saccadic effects on visual cortical responses were first examined in 1954 (Green, 1957). Green's initial EEG study showed a quick positive voltage change, a lambda wave, occurring over occipital cortex immediately after fast eye movements. Subsequently, other studies have demonstrated saccadic effects on cortical responses in BOLD activity (Bodis-Wollner et al., 2002), LFPs (Feldman and Cohen, 1968), and single-unit spiking responses (Gee et al., 2010; Reppas et al., 2002). These studies were all performed for the purpose of examining eye movement effects during non-changing visual stimulation, and they show that eye movements affect neural activity of the visual system.

In one project performed in our lab, I trained monkeys to make guided saccades from peripheral fixation points to a central fixation point. This task was performed on a homogenous grey background CRT display. Below, to demonstrate saccadic effects on V1 activity, I plot the average LFP shape from a V1 recording during this task.

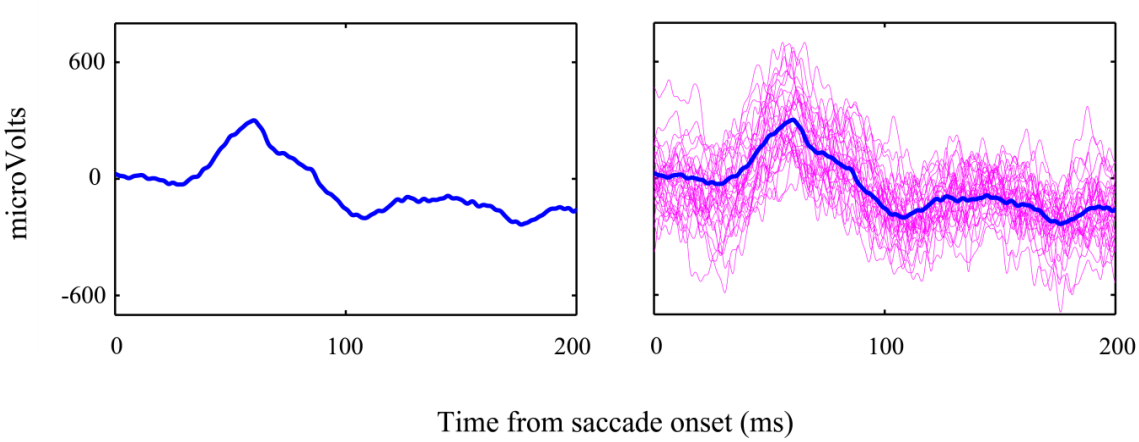

Figure 1 Average LFP V1 neural activity aligned to saccade onset (time=0ms). First panel: A single recording channel's LFP activity was averaged over 55 separate saccades from a 7-degree peripheral fixation target to a central target. The grey display background did not change luminance during the trials, leaving the channel's receptive field stimulated by the same stimulus before, during, and after the saccade. Second Panel: 25 of the saccade trials from the left panel figure are shown in magenta traces, with their average shown in blue. Individual trials were included in this panel to show the variation in LFP shapes after saccades. Though there is variation in the LFP shapes in individual trials, there is still an obvious change in the LFP after a 7-degree saccade begins.

A clear saccade-related response profile can be seen in Figure 1. This profile is apparent in individual traces shown in the second panel of the figure: after about 50ms from saccade onset there is an increase in voltage potential from the V1 electrode, followed by a dip in the voltage about 100ms post-saccade. Because the visual stimulus at the receptive field location is identical during the trial, we can argue that any activity changes observed are caused by the saccadic eye movement. However, it should also be

noted that stimulus motion in the far periphery can also affect responses within receptive fields (the so-called "periphery effect", detailed by McIlwain, 1964); such effects are ignored in Figure 1, which is presented here simply to demonstrate that eye movements can influence V1 activity even while receptive field stimulation is held constant.

Natural scenes and their effects on V1 activity

The presence of eye movements is not the only difference between real-world vision and how vision is studied in laboratory settings. The visual stimuli that eyes encounter in nature are very different from the stimuli presented in most experiments. Stimuli produced for typical V1 studies often consist of simple sine-wave gratings with spatial frequencies set by experimenters. These gratings are structured to give strong responses from neurons in V1, but are not commonly found in nature. In the natural world, the Fourier power spectra of scenes often follow the 1/f rule, where the power within the image falls off inversely with spatial frequency (Field, 1987; Parraga et al., 1998). This law holds across various categories of natural images (Torralba & Oliva, 2003). Though scenes are almost always dominated by extremely low spatial frequencies, the stimuli used to probe visual neurophysiology are usually set to the preferences of individual cells.

Figure 2 shows the different power spectra for a typical probe stimulus and a single natural scene image. This figure demonstrates that natural scenes contain power across many spatial frequencies, while sine-wave gratings do not. In fact, by their own

construction, sine-wave gratings typically have their spectral power contained within a set spatial frequency.

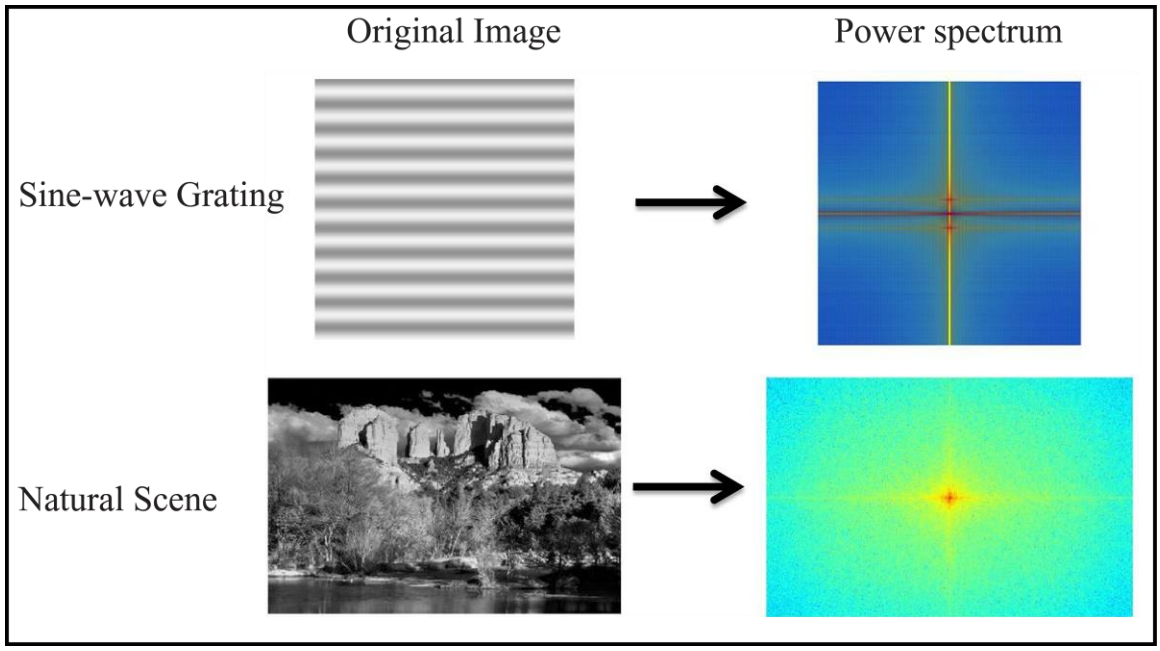

Figure 2 shows two original greyscale images, a sine-wave grating and a natural image, and their respective Fourier power spectrums. In the power spectrum images warmer color is associated with higher power, relative within-image. The center origin of the power spectrum images represents the lowest possible spatial frequency.

As stated previously, there are benefits to using sine-wave gratings in neurophysiology experiments, and I would not claim that they are an "incorrect" stimulus to use. In many studies it is necessary to reduce the number of variables between conditions in order to examine specific effects. However, the motivation for most of the research described in this document comes from the fact that visual studies almost always fail to examine effects that may arise during more natural conditions. Figure 2 shows that

spatial frequency content of stimuli is frequently restricted to narrow bands, often single bands, which is vastly different from the types of stimuli that enter receptive fields during real-world viewing.

The utility of studying natural scenes' effects on vision was first brought up after Barlow (1961) put forth the principle of redundancy reduction. Much of the sensory world, particularly the visible world, contains redundant information. For example, the Fourier spectrum of the natural scene in Figure 2 will look very similar to many other natural scenes due to the 1/f law (Torralba & Oliva, 2003). This similarity should not necessarily be needed for encoding visual stimuli, assuming that the mammalian brain has evolved to efficiently process vision (Barlow, 1961; Olshausen & Field, 1997). In fact, experimental evidence exists for this type of decorrelation (often termed "whitening") has been found in the visual system (Atick & Redlich, 1992; Dan et al, 1996). In simple terms, the visual system does not need to pay attention to the redundancy of images that are represented as correlated responses on the retina.

In a single-unit V1 study, David et al. (2004) showed that when nonlinearity of responses is taken into account during model fitting, visual responses to natural stimuli are predicted twice as accurately as reduced sine-wave grating stimuli. Specifically, during natural movie stimulation, the temporal component of the V1 responses displayed late inhibition relative to the temporal component of the responses to grating stimuli. Similarly, the spatial tuning of the cells was different between these two stimulus types. These findings show that neural activity is different between responses to artificial versus more natural visual input, and this response difference could have implications for the manner in which we study cortical activity.

Adaptation and natural scene viewing

Visual adaptation is a phenomenon where the perception of a stimulus is affected by previously viewed stimuli (Kohn, 2007). For example, when a high contrast grating is viewed for a long time (on the scale of many seconds or minutes), then another grating stimulus viewed immediately afterwards will appear to be of lower contrast than it actually is. This form of adaptation is specific to the luminance, orientation, and spatial frequency of the stimuli used (Movshon & Lennie, 1979; Gilinksy, 1968; Blakemore & Campbell, 1969a).

Contrast adaptation is different from traditional light adaptation, and is a specific form of adaptation where contrast sensitivity is affected in a pattern-specific fashion. In contrast adaptation, the perceived contrast of a stimulus is reduced after prolonged viewing of a higher contrast stimulus with similar orientation/spatial frequency. Even the adapting stimulus appears lower in contrast with a sufficient viewing duration (Blakemore & Campbell, 1969a). The effects of this show interocular transfer, suggesting that adaptation is not restricted to the retina and depends at least partially on cortical responses (Blakemore & Campbell, 1969b). Thus, it isn't surprising that this perceptual phenomenon has a clear neuronal correlate in striate cortex (as well as other visual regions): if an adapting stimulus and test stimulus are similar, then V1 cell responses to the test stimulus will be weaker compared to conditions in which adaptation did not occur (Maffei et al., 1973; Giaschi et al., 1993; Vautin & Berkley, 1977). This effect is clear in both simple and complex V1 cells (Albrecht et al., 1982). The average reported duration

of this effect from studies is about 20s (Sanchez-Vives et al., 2000), but this depends on the contrasts tested and the duration of the adaptation (Movshon & Lennie, 1979; Albrecht et al., 1982).

Because adaptation is commonly studied in very artificial situations in which adapting stimuli are presented for many seconds or minutes at fixation, it is often viewed as a type of neuro-plasticity (Kohn, 2007). This is an accurate description, as neural responses are plastic in the sense that they depend on previously viewed stimuli. However, contrast adaptation can occur in less than 1s (Baccus & Meister, 2002; Priebe et al., 2002). This has led to the belief that contrast adaptation may occur during normal visual fixations. In one study by Muller et al. (1999), it was found that complex cells in V1 can display adaptation effects within a few hundred milliseconds, and that this adaptation could increase stimulus discriminability during short fixations periods. Their finding was one of the earliest to show that neural adaptation can occur quickly and may be employed by the visual system during natural vision.

Humans viewing natural scenes will fixate on scene components for variable time periods that range from less than 50ms to over 1 second. In one study, the average fixation length during these conditions was reported to be 330ms (Henderson & Hollingworth, 1999). Thus, saccadic eye movements are made a few times per second, though this effect depends on the task of the viewer (Yarbus, 1967). If fixation durations are on the order of a few hundred milliseconds, and adaptation is known to occur within this time period, then the visual system is likely experiencing adaptation effects at every individual fixation. This is a significant claim about visual system function, but it is commonly ignored during experiments.

Contrast Sensitivity

The ability to see edges, luminance contrast, is arguably the most important step in visual form processing. Without seeing object borders, organisms would have less than a vague idea of the items (e.g., structure, food, predators) in their environments. While form-less vision works for some invertebrates like worms and snails, most mammals are dependent on their visual system's ability to detect and process luminance contrast. Seeing differences in light and dark is especially helpful in low-light situations such as navigating through one's home at night or driving in dim conditions. Without sensitivity to changes in luminance, the human visual system would be relatively useless.

Like visual acuity, contrast sensitivity is an important measure of human perceptual ability. In fact, visual acuity is a form of contrast sensitivity, but restricted to a single stimulus size (Moseley & Hill, 1994). Ophthalmologists use it to diagnose various vision disorders such as glaucoma (Arden & Jacobson, 1978), retinitis pigmentosa (Hyvarinen et al., 1981), strabismic amplyopia (Hess & Howell, 1977), and even multiple sclerosis (Regan et al., 1977). Meanwhile, researchers use contrast sensitivity as a metric of visual ability to compare between different experimental conditions. A standard method of measurement is to present various sine-wave gratings that vary in contrast and wave-length (wave-length that appears as bar width in 2D sine waves). At individual wavelengths a person will be tested to find the amount of luminance change needed for that individual to detect the presence of the grating. In experimental settings we often utilize a two-alternative forced-choice (2AFC) task, where

research subjects must pick which of two grating stimuli has higher contrast (or is more detectable). The experimenter finds the threshold contrast needed for the subject to report perceiving that grating stimulus a certain percent of the time and the inverse of this threshold is called the contrast sensitivity value. There are a range of tests used in clinical settings, but it is generally agreed that a 2AFC grating task provides the best measure of contrast sensitivity (Moseley & Hill, 1994; Blackwell, 1952).

Contrast sensitivity varies across different spatial frequencies. At extremely low spatial frequencies a high amount of contrast is needed for an observer to detect changes in luminance. The same is true for very high spatial frequencies. Thus, contrast sensitivity is often measured as a function over a range of spatial frequencies. The general shape of these functions in humans is an inverted-U, where the best sensitivity observers experience is usually around 3cpd (Arden, 1978).

In summary

Saccadic effects on V1, contrast adaptation, spatial frequency content of natural images, and contrast sensitivity were discussed in the previous sections. These are all important components of what I will call "natural vision" in this document, and the experiments and data shown in this thesis are all a next-step in understanding the function of these components during visual processing. In short, the main goal of this thesis is to examine how adding "naturalness" in experiments can change visual perception and cortical activity. We hope to understand how the visual system functions in the real world, and how this is different from the way it is typically studied in laboratory studies.

To accomplish this, the experiments outlined here will incorporate saccadic eye movements over natural image backgrounds. The purpose of this is to mimic the frequent eye movements mammals typically make over scenes during natural visual conditions.

For the experiments presented, macaque monkeys were trained to perform saccadic eye movements to points presented on a CRT screen. Electrode arrays implanted on V1 of the animals allow us to measure the neural responses of individual neurons, as well as multi-unit activity and LFPs. At the same time that the neural recordings took place, the animals were performing either guided saccades between points on the screen or a behavioral task to measure contrast sensitivity. This approach allows us to examine neural function at the exact same time that an awake behaving primate is performing a perceptual task, which provides a picture of visual function as a whole.

Detailed information about the experiments and results will be presented below, but the important summary is as follows: saccades across natural scenes produce unique types of neural and perceptual responses in animals performing a contrast sensitivity task. This method of measuring neural activity and perception is rarely, if ever, used in visual system studies. Thus, the results from these experiments provide important insight into the normal, *natural*, workings of primate vision.

Flash-Saccade Experiment

Background

In the previous sections we've seen that there are multiple aspects of natural vision that may affect visual processing in ways that are not normally studied in lab experiments. For example, eye movements and quick-forming adaptation are both known to affect neural responses and perception. Because most visual system studies usually measure neural responses and perception to stimuli flashed on after a forced fixation period, the natural functioning of the visual system is ignored. The main goal of experiments presented here is to uncover how and why visual function is different in more natural conditions.

In an article published from the Paradiso lab in 2008, MacEvoy et al. performed a study with a similar goal. In those experiments, they measured single-unit V1 neural activity in four general conditions that ranged progressively between "natural" and "unnatural". In the most unnatural condition, a bar stimulus was flashed on a grey background. In another condition, a bar stimulus was present on the screen and an animal's eye movement brought the V1 receptive field to the bar's location. The remaining conditions were identical to the previous two, except that a natural scene image was present on the screen with the bar stimulus. Thus, the most unnatural condition contained a bar flash after a fixation on a grey screen, which is a common method of studying V1 neuronal responses. Meanwhile, the most natural condition contained an eye movement over a scene background, bringing an RF under study to an already-present bar stimulus on the screen.

A novel, interesting, result was discovered with their paradigm (MacEvoy et al., 2008): responses of single V1 units to stimuli were higher when a saccade on a natural scene brought the RF to an already-present bar stimulus. The figure below shows this finding.

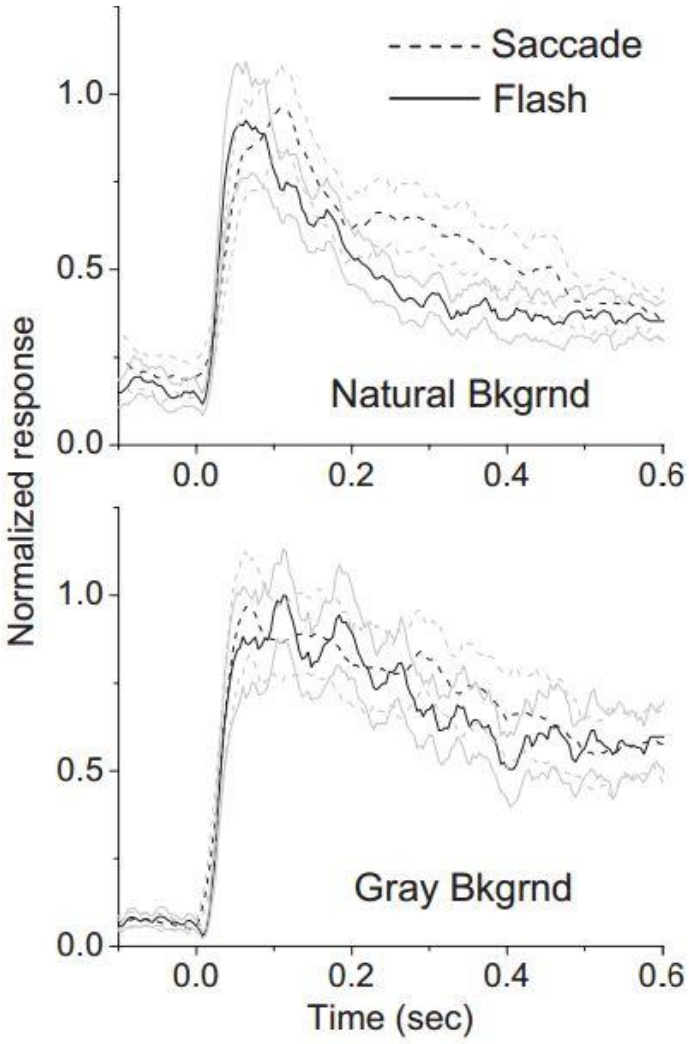

Figure 3 from MacEvoy et al., 2008 (their figure 5B) shows average normalized responses as a function of time from stimulus onset from 59 V1 neurons studied between natural scene background (top, "background" spelled as "bkgrnd") and grey background (bottom) conditions. In the dotted lines, a 5-degree saccade by the monkey brought the V1 RF to a bar stimulus that was present for 1500ms on a

natural scene background. Solid lines show response to a stimulus flashed on after a 500ms fixation period, and left in the RF also for 1500ms. Note that the response on the natural background was stronger after a saccade than after a forced fixation period of 500ms. Light-ish lines show SEM of responses.

The implication of this finding is that "natural" vision, in which saccades bring cortical RFs to stimuli already present in the world, produces stronger neural responses than the traditional laboratory method of flashing stimuli after forced fixation periods. However, a replication study was performed by Ruiz & Paradiso (2012), and a different result was obtained. The experimental paradigm was nearly identical in the 2012 study, except for some timing differences. The figure below shows the main result of that experiment:

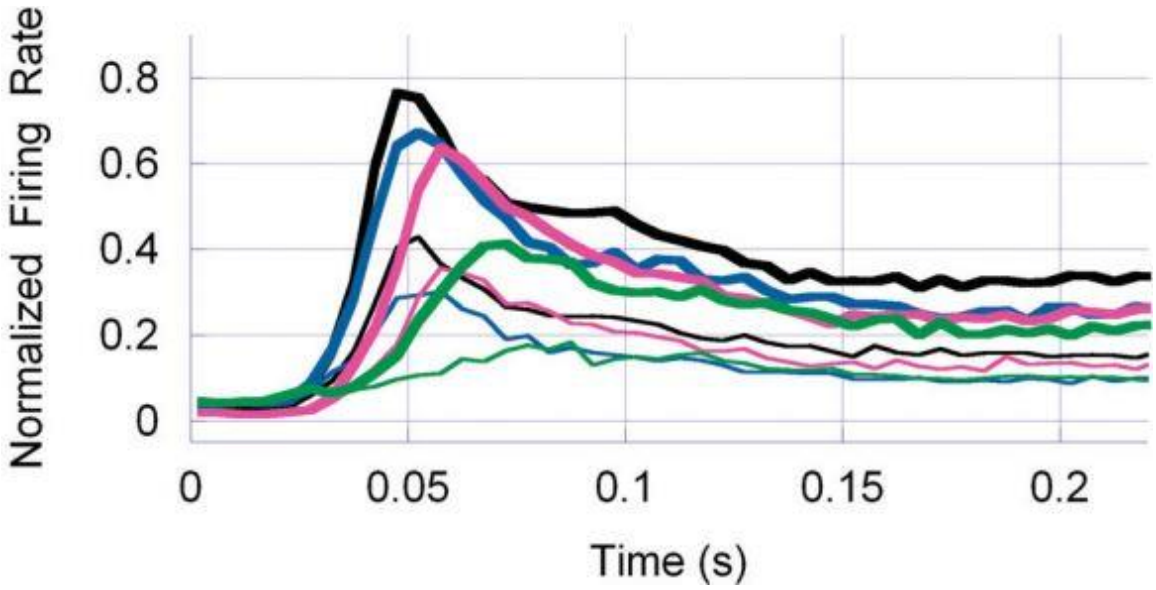

Figure 4 from Ruiz & Paradiso, 2012 (Figure 4C) shows average normalized responses as a function of time from stimulus onset from 74 V1 units in 4 main conditions. Thick lines represent average responses to stimuli of preferred orientation. Thin lines show average response to bar stimuli oriented 180 degrees off of preferred orientation. Black lines show response to bar stimuli flashed on a homogenously luminated grey background. Blue lines show response to bar stimuli flashed on a natural scene background. Magenta lines show response to stimuli brought into an RF with a saccadic eye movement on a grey background.

Green lines show the most natural condition: RFs are brought to an already-present bar stimulus on a natural scene background. The main finding from this figure is opposite to what was seen in the MacEvoy et al., 2008 study: saccades to stimuli reduced V1 responses.

This finding is not the same as what was seen in the 2008 study. Besides minor differences in the experimental paradigms, they are essentially the same except for the results. To reinforce the findings of the 2012 study, a follow-up perceptual experiment was also performed in humans. In those experiments, which have not yet been published, it was discovered that perceptual contrast sensitivity is reduced in more natural conditions, following the same progression as the reduction in V1 neuronal activity from that 2012 article. Below is a figure that summarizes the finding in those experiments.

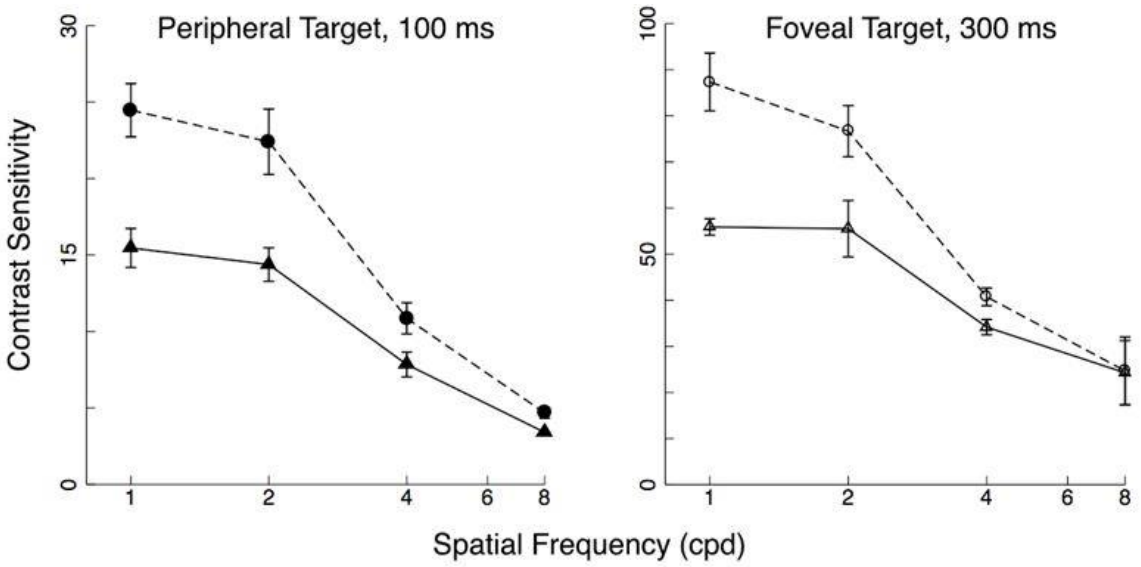

Figure 5 shows human contrast sensitivity functions averaged over a few subjects at four tested spatial frequencies. The left panel shows CS when a narrow gabor stimulus was presented peripherally, while the right panel shows results for a foveal target. Dotted lines show CS averaged between subjects after the target stimulus was flashed following a forced fixation period on a natural image background. Solid lines show the CS values when a stimulus was already present on the natural image background following a 5-degree saccade.

The above figure shows that saccades on natural scenes reduce human perceptual ability compared to conditions in which a stimulus is flashed after a fixation period. This psychophysical finding is directly parallel to what was seen in the neuronal data in Ruiz & Paradiso (2012). However, a neural finding from a few monkeys cannot be used as the sole evidence for a perceptual effect seen in humans. A next-step in showing that V1 response reduction in natural vision can lead to a reduction in perceptual sensitivity would be to perform recordings from V1 while simultaneously having an animal perform a contrast sensitivity task.

Also important and interesting, the CS difference is present even for stimuli that are foveated (second panel). Most V1 neurophysiology studies are performed in the periphery due to receptive field sizes being larger and thus less influenced by eye movements. This psychophysics finding shows that the effect that was observed in the neuronal data is not only occurring in peripheral receptive fields but may also be occurring in foveal neurons. This is important because contrast sensitivity in clinical settings is typically measured at fixation, not peripherally.

Another feature of the 2012 neuronal data is that there appears to be an interaction between saccades and natural scene backgrounds. In Figure 4, the green line indicating V1 responses after a saccade on a natural scene background is far below either of the conditions involving a saccade on a grey background or a flashed stimulus on an image background. Thus, there must be some combined effect of a saccade across a natural scene that causes this reduced neural response in natural vision.

The discrepancies between the 2008 and 2012 studies are problematic, and a major goal of the experiments below was to reconcile those findings. Another goal was to understand the interaction of saccades and image backgrounds that causes such a strong reduction in V1 neuronal activity. Most importantly, we set out to show that neural activity in V1 would display an effect similar to what is seen in perceptual data. In other words, we sought to replicate the above studies in conjunction with a behavioral measure of contrast sensitivity. To accomplish this, macaque monkeys were trained on a 2AFC contrast sensitivity task and then implanted with micro electrode arrays in V1. This allows for a full picture of neural function: both contrast sensitivity, an important low-level visual function, and V1 neural activity are measured concurrently.

Experimental Paradigm

Goal

To uncover the effects of adding naturalness in experiments and to answer the specific questions about visual function, an experimental paradigm needed to be used that allowed for simultaneous perceptual and neurophysiological measurement. Thus, we created a 2AFC task and trained monkeys to detect the location of gabor stimuli on a natural scene background. While the monkeys performed this detection task, the contrast and spatial frequency of the gabor targets was adjusted either across trials or recording sessions. At the same time, neural activity from V1 RFs was measured in response to these stimuli.

Paradigm

Three monkeys were trained on this task (Figure 6). A gabor stimulus was presented at one of two locations on a natural scene background and the animal indicated at which location the gabor appeared. Behavioral and neuronal data were collected simultaneously.

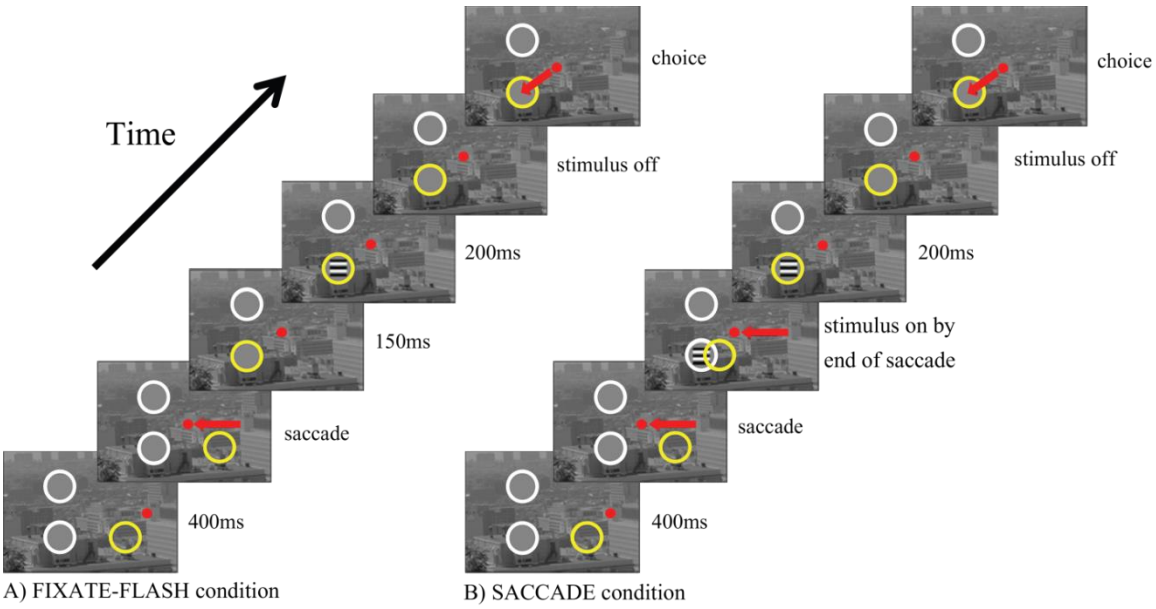

Figure 6 demonstrates the experimental paradigm used in this study. There were two general conditions, FIX-FLASH (A), and SACCADE (B) – occasionally in this text the phrases FIX-FLASH, Fixate-flash, and FIXATE-FLASH will be used interchangeably, and occasionally SACCADE and Saccade will be used interchangeably. An identical grey-scale natural scene background, taken from the van Hateran natural image database (van Hateren & van der Schaaf, 1998), was used in both conditions. Yellow circles represent hypothetical V1 RFs. Grey patches were set to the same luminance as the average of the natural scene background. White circles around the patches were not actually present during the experiment: they are used here just to highlight the grey patch regions. Also, the target stimulus shown in this diagram is more of a square wave grating than the actual gabor stimuli used in the experiments. Note that the only difference between conditions is the time at which the stimulus appears in the RF: in the FIX-FLASH condition, a 150ms hold period presents the RF with a homogenous grey patch. In the SACCADE condition, the RF travels from natural image background directly to the stimulus on its grey buffer patch. Also not shown is the fact that in half of the trials the stimulus appeared in the upper visual field (on the buffer patch in the upper left quadrant) for the purpose of creating a 2AFC task. In those trials the RFs were not stimulated by the gabor, but neural data was still recorded.

Trials began with the presentation of a red spot (0.3 degrees in diameter) located 7 degrees to the right of the screen center. For the trial to proceed, the animal had to acquire this first fixation point within 2s and hold fixation for 400ms. After 300ms, a second red fixation point appeared at the center of the screen (i.e. 7 degrees to the left of the first point) and the first fixation point was extinguished. The animal was required to initiate a saccade to the second fixation point within 200ms, and this saccade was forced to be completed within 80ms. These values forced the saccade latency to be under

200ms, but after training the animals typically initiated this saccade in 100-150ms (presumably because they learned the timing at which the saccade target would appear), and the saccade durations were usually under 40ms. If any timing rules were violated the trial would abort immediately. A trial would also be aborted if the animal moved its eyes more than 0.8 deg from the first fixation point or the saccade target after acquiring it. In the vicinity of the second fixation point were two small circular grey patches that had the same mean luminance as the background image and were overlaid on the image. One of these "buffer patches" was below and to the left of the fixation point on the visual display and would encompass the receptive field of one neuron after the saccade (electrode arrays in all animals were placed such that receptive fields were in the lower left visual quadrant). The other buffer patch was at an equal eccentricity superior to the fixation point. At some time relative to the saccade used to acquire the second fixation point, a gabor stimulus appeared in the upper or lower buffer patch. The orientation and spatial frequency of the gabor stimulus were optimized for each recording session. The buffer patch ensured that only the gabor stimulus, and not the natural scene background, stimulated the classical receptive field (RF). In half of the trials the stimulus was presented at the RF location and in the other half of the trials the stimulus was presented at the other location. The location of the stimulus and the type of condition (FIX-FLASH or SACCADE) were randomized.

In the FIX-FLASH condition, the gabor stimulus was flashed on 150 ms after the second fixation point was acquired. Thus, the animal acquired the second fixation point and held fixation for 150ms with only the grey buffer patch covering the RF; only after this delay was the gabor presented at one of the two stimulus locations. On the other

hand, in SACCADE conditions, the gabor was presented *during* the saccade used to acquire the second fixation point**.** The 1kHz eye tracker detected the onset of the saccade in order to accomplish this: a position-based signal that was sampled every millisecond was used to determine when the animal left the fixation window (eye position signals were usually calibrated multiple times during recording sessions). After the saccade was detected, the eye tracker signal was used to turn on the stimulus such that the gabor stimulus was presented during the saccade period. Thus, the saccade took the receptive field onto the already-present gabor stimulus (and grey buffer patch). A photodiode system, sampling at 10kHz, was used to verify that the stimuli actually appeared before the eye movement ended. This was important because these 7-degree saccades usually only lasted about 35ms (and a screen refresh requires at least 8.3ms). An added benefit of the photodiode system was that it verified the control system's ability to correctly report, with millisecond-precision, the onset time of the stimulus. In both conditions the animals maintained fixation on the central point and the gabor stimulus was left on inside of the buffer patch for 200ms.

After the gabor was turned off, small red spots were presented in the two buffer patches. When the central fixation point was turned off, subjects reported the location where the gabor stimulus had appeared by making an eye movement to one of the two spots within 300ms of target extinction (this short choice period was used to prevent any extraneous saccade planning during the 200ms gabor duration, which was a concern in one animal). Correct responses were immediately followed by a juice reward. The intertrial interval was 2-4 seconds. The range of 2-4 seconds was set such that correct choices led to a 2s interval, and certain errors produced during the task would increase

the interval to 4s as a form of "timeout" for the animal. Many other interval times were used during training, but a vast majority of the experiments were used with the 2-4s intervals.

One potential concern about this experimental paradigm is the fact that using a saccade signal to turn on a stimulus during the task will surely affect the variability of stimulus onset time and duration (due to variability in saccade duration). Because of this, the SACCADE condition stimulus was actually left on 3 more CRT refresh frames than in the FIX-FLASH condition. Thus, the actual stimulus duration on the CRT screen in the SACCADE condition was ~224ms, and the time that the V1 RF was covering this stimulus was always between 208-224ms. Because stimulus duration needed to be coded before trials began, there was no way to avoid this issue unless saccade durations could be adjusted to fit perfectly with our stimulus duration and monitor refresh rate. Note that this longer stimulus duration in the SACCADE condition is not a limitation of the experiment, as the hypothesis states that we expect lower responses and weaker perceptual sensitivity in this condition – I've stacked the cards against the hypothesis, and as we'll see in the results this did not matter. Also note that the neural data was always sampled from the first 200ms of stimulus duration (ignoring any extra CRT frames), making it unlikely that the extra frames in the SACCADE condition affected our neural data plots.

Methods

Experimental Subjects and Preparation

Three male rhesus macaques (*Macaca mulatta*; Monkey F weighing 10.4kg, Monkey S weighing 9.9kg, Monkey Z weighing 14.5kg) were used in these experiments. All animal procedures conformed to National Institutes of Health guidelines and were approved by the Brown University Institutional Animal Care and Use Committee. Each animal was implanted with a custom titanium headpost and a 96-channel "Utah" array (Blackrock Microsystems) of 1mm electrodes was placed in right hemisphere V1. Electrode recordings were made while animals sat in a primate chair (Crist Instrument Co.) and performed the behavioral tasks described above. Eye position was recorded at 1 kHz using an EyeLink 1000 infrared eye tracker (SR Research). These recordings were used to verify eye position during the experiments and they were saved with a Cerebus recording system (Blackrock Microsystems) for offline analysis.

Physiological Recordings

A Cerebus system recorded neuronal spiking activity and raw neural activity at 30kHz. A preliminary isolation of single unit activity was made online and later confirmed with Offline Sorter (Plexon). In some instances, as mentioned below, results are reported for multiunit activity. Receptive field locations were mapped with a hand mapping procedure using the Monkeylogic control system (Asaad et al., 2013). Though this

control system now has an RF-mapping procedure, the versions used during experiments presented here did not use that mapping function because it had not yet been created. Rather, RF locations were mapped by presenting a small moving bar stimulus on a homogenous grey background while the animal fixated a central fixation spot. A joystick was used to move the stimulating bar and find the RF location while the experimenter tracked output from the Cerebus system by watching spiking activity on an individual array channel as well as listening to this activity over an audio amplifier.

After RF location and size were mapped, two short experiments were run to determine the unit's preferred orientation and spatial frequency, in that order. To find orientation preference, gabor stimuli of 4cpd were presented at 80% contrast at 12 different orientations in 30degree increments while the spiking rate was observed between conditions. Once preferred orientation was determined, the sine-wave frequency of the gabor was varied between 1, 2, 4, 6, and 8cpd to determine the unit's spatial frequency preference at the preferred orientation. For some units that showed responses to multiple orientations, the orientation tuning was mapped again after determining preferred spatial frequency.

There were a total of five electrode arrays used in these experiments in 3 different animals. The arrays typically covered about 4-8 square degrees of visual field located approximately 3 degrees eccentric from the fovea. A vast majority of the receptive fields were ~1 degree in size, sometimes larger. Thus, the grey buffer patches during the experiment were only a few degrees from the central fixation point. It was due to the small eccentricities of these patches that very low contrasts were used during our experiments in this 2AFC task.

Visual Stimuli

In these experiments, the visual stimulus was a gabor patch on a full-screen natural-image background or a uniform gray background. All stimuli were presented in a dimly lit room on a CRT monitor with a P22phosphor. The refresh rate was 120Hz (Illyama Viewmaster) and the resolution was 1280x1024 pixels. The visual display was 63cm from the subject and subtended 33 degrees wide x 26 degrees high. The two-dimensional gabor stimuli had spatial frequencies of 1-8cpd and peak Michelson contrast of 84%, though this highest contrast value was only used during training. Michelson contrast was defined as

$$\text{Michelson contrast} = \frac{I_{\max} - I_{\min}}{I_{\max} + I_{\min}}$$

where I is the luminance of the sine wave grating.

The natural scene used as a background was taken from the van Hateren database of greyscale images (van Hateren & van der Scaaf, 1998). The mean luminance of the natural scene was 55cd/m2; when a uniform grey background was used, it had the same luminance. Homogenous grey buffer patches also had this luminance.

Prior to an experiment, stimuli were generated in MATLAB (Mathworks, Natick, MA) and stored as jpeg images. The functions used to create the sine-wave dampened by a Gaussian were identical to those used by PsychToolBox (Brainard, 1997; Pelli, 1997;

Kleiner, 2007) in their driftGrating.m demonstration file; however, this file itself was only used for its mathematical description of a gabor stimulus using MATLAB functions.

Stimuli were presented using the Monkeylogic control system, which is essentially a MATLAB toolbox that runs under Microsoft Windows in conjunction with other display software to provide nearly real-time command of experiments. A photodiode system connected to the Cerebus hardware was used to confirm the timing and duration of visual stimuli and other task components relative to eye movements.

Contrast Sensitivity Experiment

The main goal of the study was to measure the perceptual contrast sensitivity function and the neural contrast response functions. These measurements were compared in the FIX-FLASH and SACCADE conditions to quantify any influence of the saccade that immediately preceded the test stimulus (i.e., the influence of natural vision). Contrast sensitivity and contrast response were measured with the method of constant stimuli. Within each of the two general conditions (FIX-FLASH and SACCADE), there were 10 or 12 sub conditions where gabor contrast was varied within a small range. In half of those conditions the stimulus was presented in the upper visual field and in half of the trials the stimulus was presented inside of the RF. Thus, using the method of constant stimuli, there were 5 or 6 unique contrasts used, which produced 20-24 total conditions per recording session.

The contrast range chosen each day depended on the eccentricity of the RF under study as well as the spatial frequency of that stimulus (which was also chosen based on

neuronal preference, as was mentioned above). This range was set such that at the lowest contrasts tested, the animal was at or near chance performance during the 2AFC task. The highest contrast tested was set such that the animal was at or near perfect on the task (near 100% correct, though this perfect value was rarely reached by the animals). At the start of training experiments, choosing contrast values involved a lot of guess-and-check and careful monitoring of the animal's behavioral performance. However, a major benefit of the electrode arrays was that the neuronal RFs shifted only slightly between electrodes and between different recording days. Thus, over time it became fairly easy to choose an appropriate range of contrasts that spanned the animal's psychometric dynamic range at a given eccentricity. The contrast range, depending on eccentricity, spatial frequency, and animal was often 5-20% on a given day of recording. If a good psychometric fit (Data Analysis section below) could not be made on the data, then that day's behavioral data could not be used. This rarely happened, as the animal's performance was constantly observed by the experimenter. We defined contrast threshold to be the contrast at which the animal performed at 80% correct in the SACCADE and FIX-FLASH conditions. The inverses of these 80% threshold values are what we defined as contrast sensitivity.

To summarize the contrast sensitivity experiment: CS was measured by the method of constant stimuli, presenting gabor patches of 5 or 6 different contrasts in order to find the contrast needed for the subject to detect the stimulus in 80% of trials. The orientation and SF of the stimulus for a given day of recording was set to be the preferred values for that day's RF. During each recording session, this yields 2 CS values, one for the SACCADE condition and one for the FIX-FLASH condition. For the CS experiment,

it is these two sensitivity values that we use as our measure of perceptual performance for the animals. In addition, responses from the V1 unit, both raw 30kHz activity and spiking activity, during a session were recorded for every trial in every condition.

Spatial Frequency Experiment

To test a mechanism hypothesis that arose after conducting the contrast experiments, we made recordings in Monkey S that focused on spatial frequency instead of contrast. In each of these 16 recording sessions, the contrast was set to be fairly high, 30-48% contrast, and was not varied. Rather, the spatial frequencies were varied between levels of 1, 2, 4, 6, and 8cpd. The goal of this was to uncover how neural responses might vary between SACCADE and FIX-FLASH conditions after being presented with different spatial frequencies.

Diminished Adaptation Experiment

In an additional test of a mechanism hypothesis, we altered the visual stimulus present in the RF on the first fixation (before the saccade to the gabor). This experiment was performed in 20 recording sessions with Monkey F. The only difference from the main contrast sensitivity experiment was that, on the first fixation, uniform grey patches were placed over the natural scene at the location of the RF and at an equal eccentricity superior to the fixation point (i.e. the two locations, relative to fixation, at which the

gabor stimuli would appear on the second fixation). The intent was to eliminate adaptation to the natural scene at the test locations on this penultimate fixation.

Data Analysis Overview

The general analyses are briefly described here. However, in the following Results sections, additional and more specific information will be given when necessary.

Custom MATLAB analysis scripts were used to analyze both the physiological and psychophysical data. For each day's recording session, two psychometric curves were created, one for the FIX-FLASH condition and one for the SACCADE condition. Each curve was then fit with a logistic function using the Palamedes toolbox in MATLAB (Prins & Kingdom, 2009). Contrast threshold was defined as the contrast at which the subject correctly reported the gabor location in 80% of the trials. Contrast sensitivity is reported here as the inverse of the contrast threshold determined by our psychometric fits.

Single unit and multiunit responses were classified and discriminated using Offline Sorter before being exported into MATLAB. For population analyses, neural responses on different days were normalized within-session before being averaged. Thus, most neural plots will show normalized responses instead of raw spike rates, and the shaded regions always depict standard error of the mean normalized response. Normalization was performed by dividing PSTHs by the peak response. This peak response was often in the FIX-FLASH condition, but not always, which is why averaged plots do not reach the value of 1. Smoothing was performed by convolving with a Gaussian function. 100ms of activity outside of the data plotted was also smoothed to

prevent any edge effects of the convolution. This technique was used on all of the neural data presented here.

Results

The overview of experimental results, the complete experimental story for the contrast sensitivity experiment, spatial frequency experiments, and diminished adaptation experiments, will be shown here. However, many details of single unit responses and supplemental psychophysics findings will be added in sections afterwards.

Contrast Sensitivity Experiment

The main goal of the Contrast Sensitivity Experiment was motivated by the results of Ruiz & Paradiso (2012) and MacEvoy et al., (2008). Those papers reported that stimuli entering the RF of a V1 unit by saccade across a complex scene background produce a different response compared to when the stimulus is flashed in the RF after a forced fixation period. This finding has important implications for our understanding and assessment of vision in more natural situations. Extrapolating the results from the Ruiz and Paradiso study we formed two hypotheses: 1) neural contrast responses will be reduced in a saccade paradigm compared to a fixation paradigm (FIX-FLASH); and 2) perceptual contrast sensitivity will be reduced in the saccade paradigm (SACCADE).

We first used the task to determine whether V1 responses are different between the FIX-FLASH and SACCADE conditions. Figure 7 shows a single unit example of response in Monkey F between these two conditions.

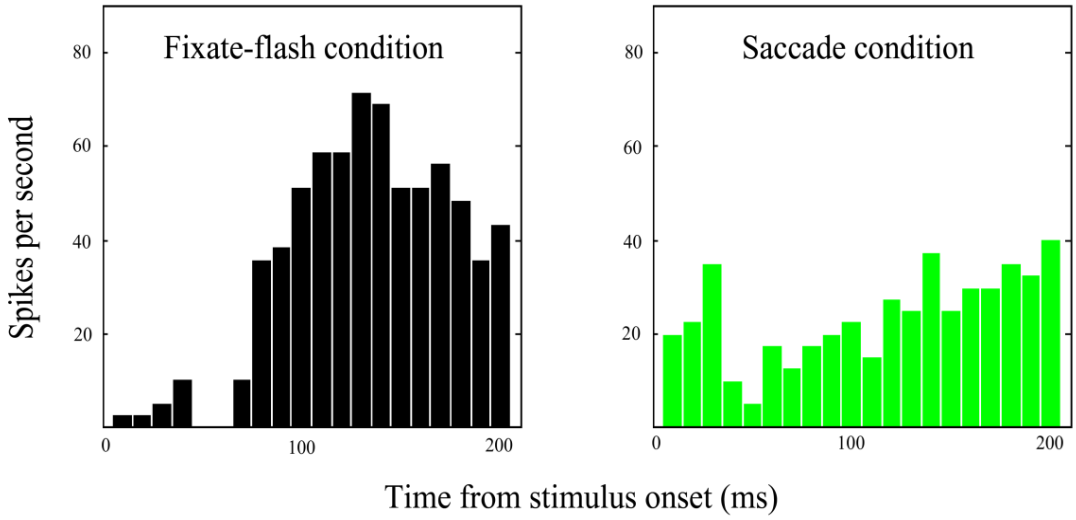

Figure 7 shows a PSTH of average spike rate as a function of time from stimulus onset in the RF in the FIX-FLASH condition (left) and more natural SACCADE condition (right). Bin sizes are 10ms. The gabor stimulus in these experiments was set to have spatial frequency and orientation equal to the unit's preference (2cpd, and vertical), and the contrast level shown here is 11%. Note that the FIX-FLASH condition produced a much stronger spike rate than the SACCADE condition.

A large majority of units in the three animals gave a stronger response in the FIX-FLASH condition compared to the SACCADE condition (though some units also displayed a rebound effect from the saccade, which will be discussed in a later section). Recall that for a given recording session, multiple contrast levels were used. The data from Figure 7 comes from the highest Michelson contrast tested in the range, 11%. Below is a figure showing the normalized average response across all units tested in the Contrast Sensitivity Experiment, N=64.

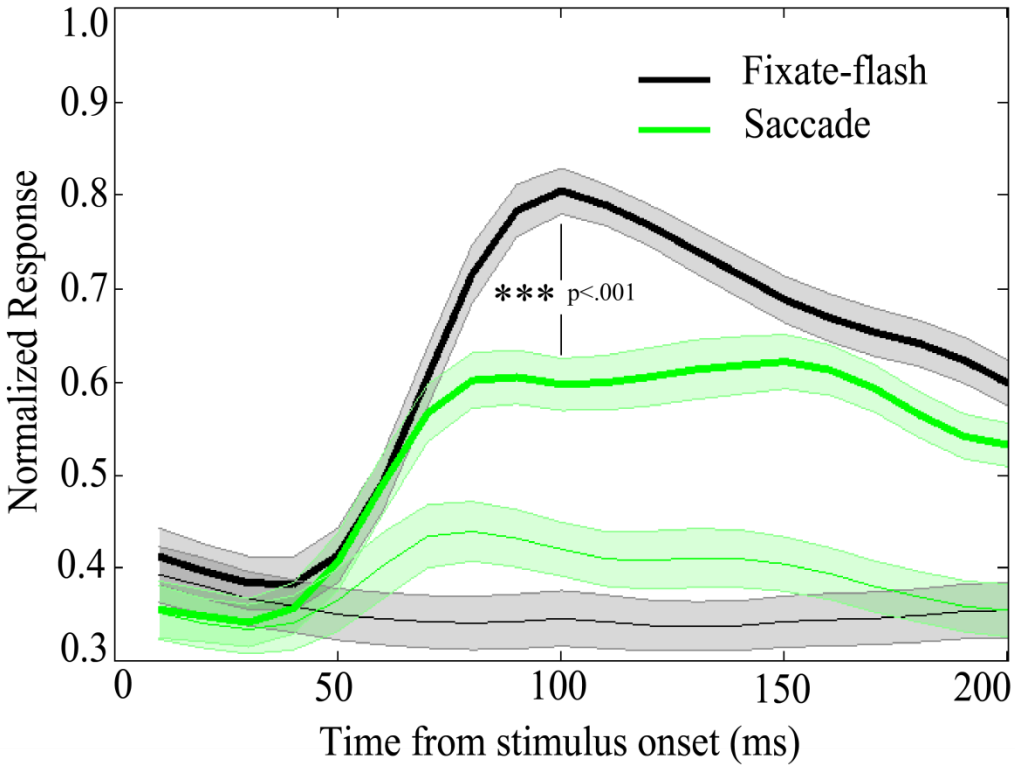

Figure 8 shows the average normalized response between the FIX-FLASH (black) and SACCADE (green) conditions in 64 V1 units. The thick lines represent response when the stimulus was presented in the lower left visual quadrant inside the RF. Thin lines show response when there was no stimulus, only grey buffer patch, inside the RF. Shaded regions are the SE of the mean normalized response across units. The peak response in the FIX-FLASH condition was significantly larger than the SACCADE condition (P<.001, t-test). Normalization was performed on individual units' data sets by dividing the smoothed average response by the peak response across conditions. This plot shows the average of those smoothed normalized figures. The highest value does not reach 1 because not all units gave the highest response in the same condition.

For each unit in this plot, the highest contrast tested was the value used in the figure. Because 5-6 contrast values were used in each recording session, the lowest values often produced no response across conditions. Note that, sometimes even the highest contrast tested did not elicit a strong response from all neurons. Thus, even though there is variation in the contrasts used to produce responses in this plot, the

population response is still significantly higher in the FIX-FLASH condition. Also note that, despite not being plotted here, a figure of this form could be made 5-times over at each contrast tested during different recordings. The largest contrast value used simply displays the effect most clearly, and is most comparable to the 48% contrast used in the Ruiz & Paradiso (2012) study.

The response latency is similar in the FIX-FLASH and SACCADE conditions, but the peak response is significantly greater in the former. The responses in the two conditions begin to converge after about 150ms. These results show that for the same stimulus contrast there is a lower peak response and lower sustained response out to 150ms in the SACCADE condition.

Figure 8 also shows average V1 responses when the gabor was presented in the upper visual field (i.e. well outside the classical receptive field). As expected, the response to a gabor flashed outside the RF is flat. However, there is a weak response in the SACCADE condition even when the gabor appears at a location distant from the RF. This observation was also reported in Ruiz and Paradiso 2012; it appeared to be a result of the background image crossing and stimulating the RF during the saccade, and will be discussed more in a later section.

The results shown in Figure 8 confirm the Ruiz & Paradiso 2012 results that the response to a gabor stimulus is lower in the SACCADE condition than in the FIX-FLASH condition, at least at a highest contrast and at the single spatial frequency tested for each cell. In other words, adding naturalness to the experimental paradigm created a weaker response compared to the reduced fixate-and-flash-a-stimulus paradigm frequently used in vision studies. We next set out to test the psychophysics hypotheses

underlying this study, i.e. that contrast sensitivity differs in the SACCADE and FIX-FLASH conditions and this difference covaries with V1 neuronal contrast response functions.

Perceptual Contrast Sensitivity and the Effect of Spatial Frequency

Contrast sensitivity was defined as the inverse of contrast threshold where subjects were performing at 80% correct in the task. Figure 9 (psychophysics) shows the contrast sensitivity function of one animal, Monkey F, between the two conditions.

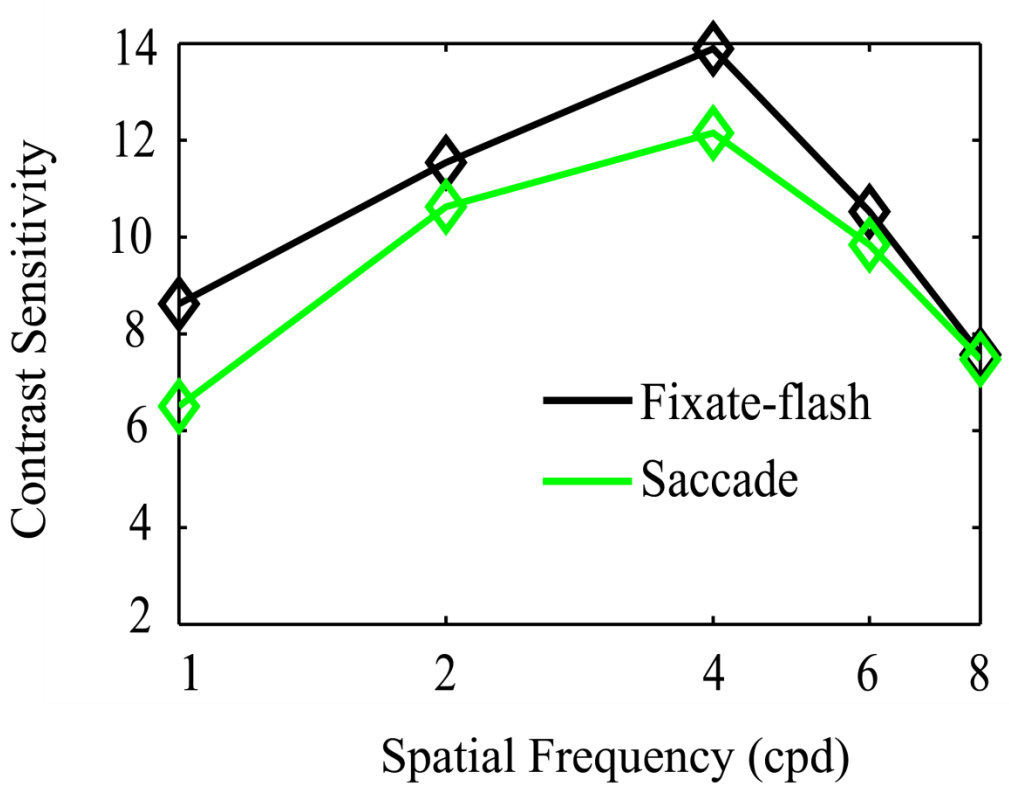

Figure 9 displays the contrast sensitivity functions for Monkey F during the task. Contrast sensitivity is plotted as a function of spatial frequency (log axis). Sensitivity is reported as the inverse of contrast

threshold, where the animal was performing at 80% correct. To create this plot, five different days' behavioral data was taken. On individual days the spatial frequency of the gabor was set to be either 1, 2, 4, 6, or 8cpd. For this plot, all gabor stimuli were always presented in the same retinotopic location (1deg gabor size set 3.6deg eccentric from fovea). Further, all stimuli had the same orientation and size. This was done in order to reduce any variation in contrast sensitivity that might have occurred due to eccentricity or stimulus parameters.

The contrast sensitivity function shows that the animal's perceptual performance on the 2AFC task is better when a stimulus is flashed on after a forced fixation period compared to when an eye movement brings visual fields to a stimulus. This difference in sensitivity is only seen at the lower spatial frequencies tested: 1, 2, and 4cpd gabor stimuli. At higher spatial frequencies the effect is not observable. This fact was also observed in the preliminary human psychophysics data shown earlier in Figure 5.

Figure 10 was created to demonstrate this effect on a finer scale by highlighting individual psychometric curves created from the animal data. The figure shows the contrast threshold values for the two conditions at either 1cpd or 8cpd for Monkey F. At low spatial frequencies the psychometric curves are noticeably different between the FIX-FLASH and SACCADE conditions, but are nearly identical for the highest spatial frequency tested, 8cpd.

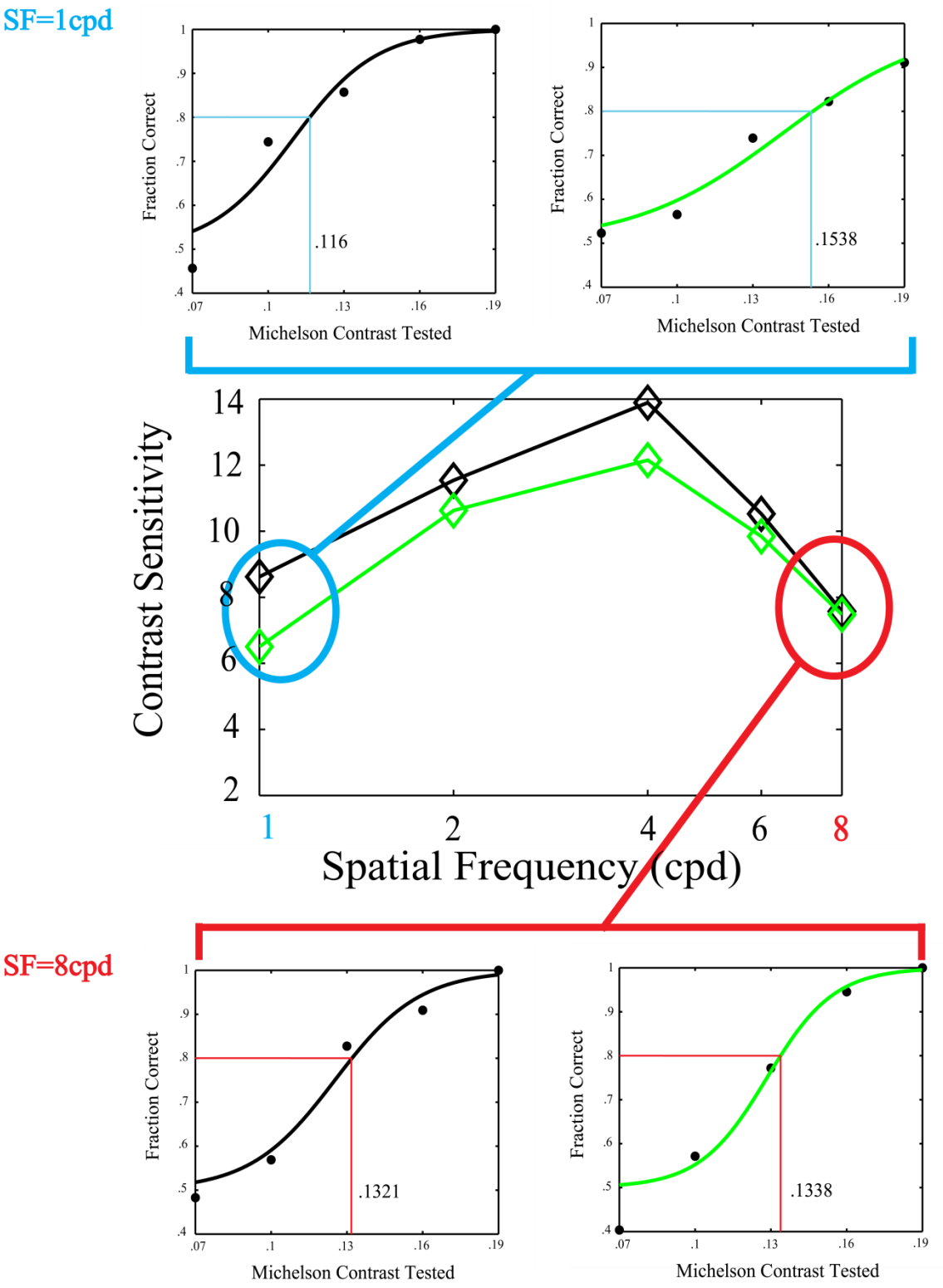

Figure 10 shows, in detail, the effect of spatial frequency on contrast sensitivity between the FIX-FLASH and SACCADE conditions. In all figures, black lines represent the FIX-FLASH condition while green lines represent the SACCADE condition. The top two figures show psychometric curves for Monkey F

being tested with a 1cpd gabor stimulus between the two conditions (grouped in blue). The center panel shows the CSF for the animal. The bottom panels show the psychometric functions between the two conditions for 8cpd stimuli (grouped in red). The small lines inside of the psychometric plots are simply to show where the 80% correct point is, and demonstrate how that value leads to the contrast threshold measurement. The inverse of those values is what is plotted in the contrast sensitivity functions.

Contrast sensitivity functions of two animals are displayed below. The first panel shows the same CSF that was already plotted for Monkey F, while the second panel shows the CSF for Monkey S. Though the sensitivity values are different between animals (Monkey F generally performed better), the low-SF specific effect is apparent in both plots.

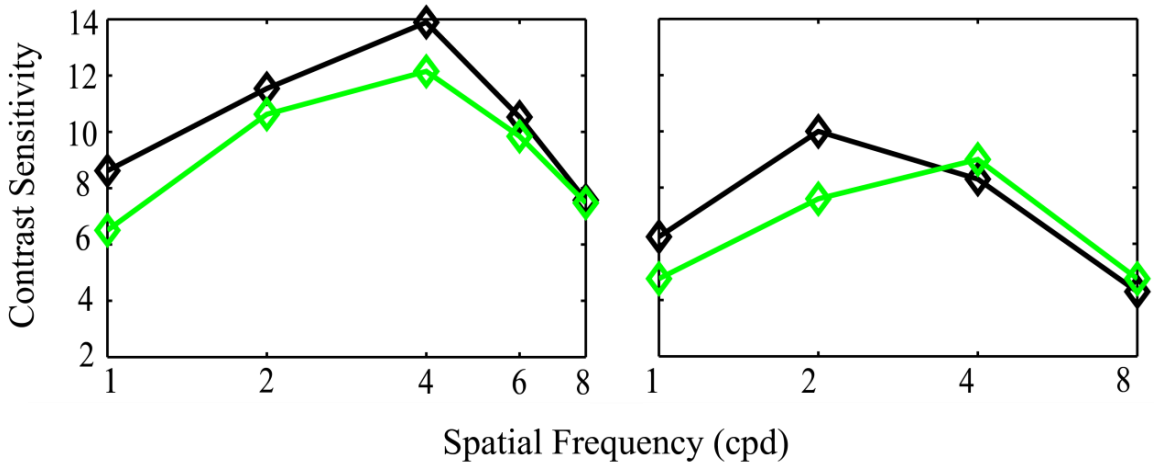

Figure 11 shows contrast sensitivity functions of Monkey F (left) and Monkey S (right) together: sensitivity is plotted as a function of log spatial frequency tested. Black lines represent the FIX-FLASH condition while green lines represent the SACCADE condition. Though the sensitivity values are different between animals, the general effect is still very clear at lower spatial frequencies. The stimulus size, orientation, and eccentricity were identical for these two animals across trials.

In terms of absolute contrast sensitivity, the monkey perceptual results are different from the human psychophysics data shown earlier in Figure 5. This is almost

certainly due to differences in the experimental paradigm. The human study was performed with a 1.5-cycle gabor stimulus presented at a different eccentricity and size than the monkey task and with slightly different timing parameters. Most importantly, the monkey task involved a spatial 2AFC task, while the human data was collected in a paradigm that only used one spatial location for the stimulus. However, as a final check, the monkey experiment was also performed on the experimenter, JN (myself), using the same stimulus parameters as were used during the monkey task. This human CSF is shown below.

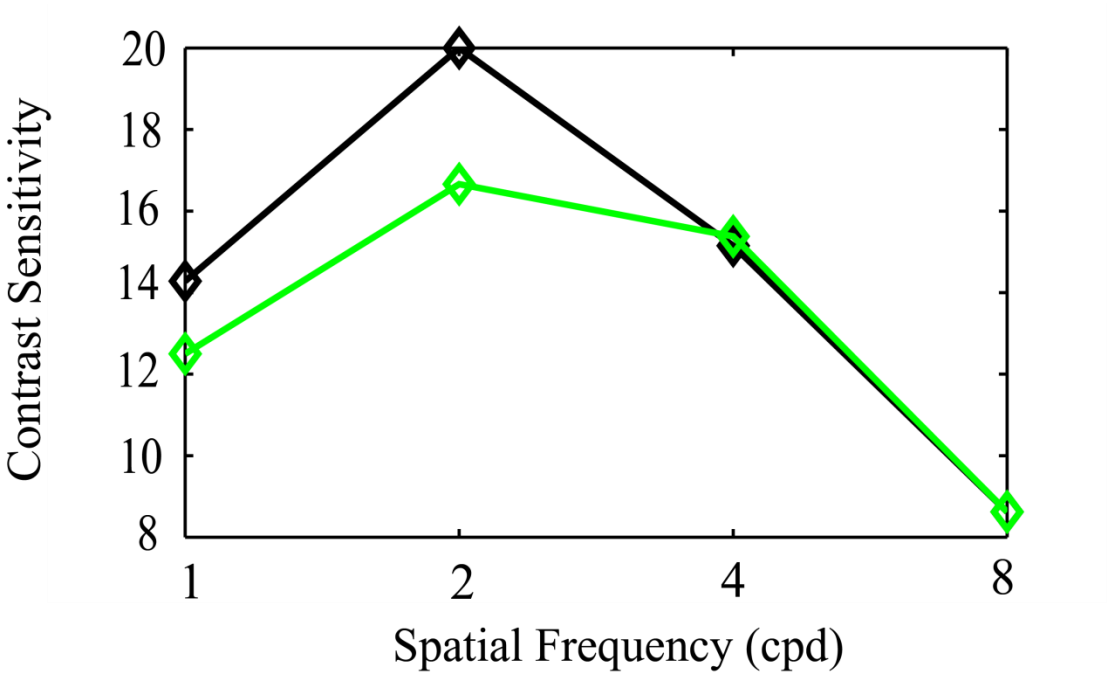

Figure 12 plots contrast sensitivity functions for a human observer, the author/experimenter between the FIX-FLASH condition (black) and SACCADE conditions (green) across four spatial frequencies tested. All parameters during this were the exact same as what was used during the monkey CSF experiments. Note, however, that the sensitivity values begin at 8 in this figure instead of 2.

Summary

Neural responses in V1 are clearly different between our FIX-FLASH condition and more natural SACCADE condition. Similarly, though the sensitivity values are different between the three subjects, the overall effect is very clear and in-line with what was seen in the previous human psychophysics data from Figure 5: at lower spatial frequencies, the perceptual detection of a gabor stimulus immediately following a saccade on a natural scene is impeded. When that same stimulus is flashed on after a forced fixation interval it is more detectable. This effect disappears for stimuli of higher spatial frequency. This leads us to an obvious question: What are the effects of spatial frequency on the neural responses?

Spatial Frequency Experiment

The previous section showed two important results: 1) V1 responses are reduced in more naturalistic experimental conditions, and 2) perceptual sensitivity is also reduced. The perceptual sensitivity reduction was specific to lower spatial frequency stimuli tested. It was most noticeable for stimuli between 1-4cpd. The following experiment was performed with the purpose of examining whether there is any similar difference in neuronal responses to stimuli of differing spatial frequency.

Paradigm and Methods

The experimental paradigm used here is the exact same as what was shown previously in Figure 6. The important difference in the experiment is that the stimulus shown during a recording session is not set to the V1 neuron's preferred spatial frequency. In the previous experiments the gabor stimulus had parameters set to elicit the strongest possible firing rate (which was likely important since many stimuli were very low contrast). However, for the sake of understanding how SF might affect the neural response between conditions, in this task I vary the SF while keeping the Michelson contrast stable across trials. Thus, the data here are not capable of showing a perceptual contrast sensitivity function, but rather simply show the different types of responses from these V1 neurons when presented with different spatial frequency stimuli.

The contrasts used ranged between about 10-48% contrast. The top value of 48% was chosen because that was the contrast of bar stimuli used in the Ruiz & Paradiso

(2012) study. The lower bound of 10% was chosen because the behavioral component of this study was not useful; using very low contrasts would serve no purpose. The average contrast used across the 16 recordings was 27.4%.

Note that, by using fairly high contrasts, the behavioral task was not difficult in this experiment. Only one monkey was used here, and he performed very well across spatial frequencies tested. When the animals were implanted with arrays it was important to keep them working on the primary contrast sensitivity experiments; thus, this small data set is most useful only for its relationship to the above contrast sensitivity data, but the behavioral results of this task will not be shown.

Results

With a set contrast, V1 neuronal responses were measured in 16 recording sessions in one animal. The averaged normalized responses from these 16 units is shown in Figure 13.

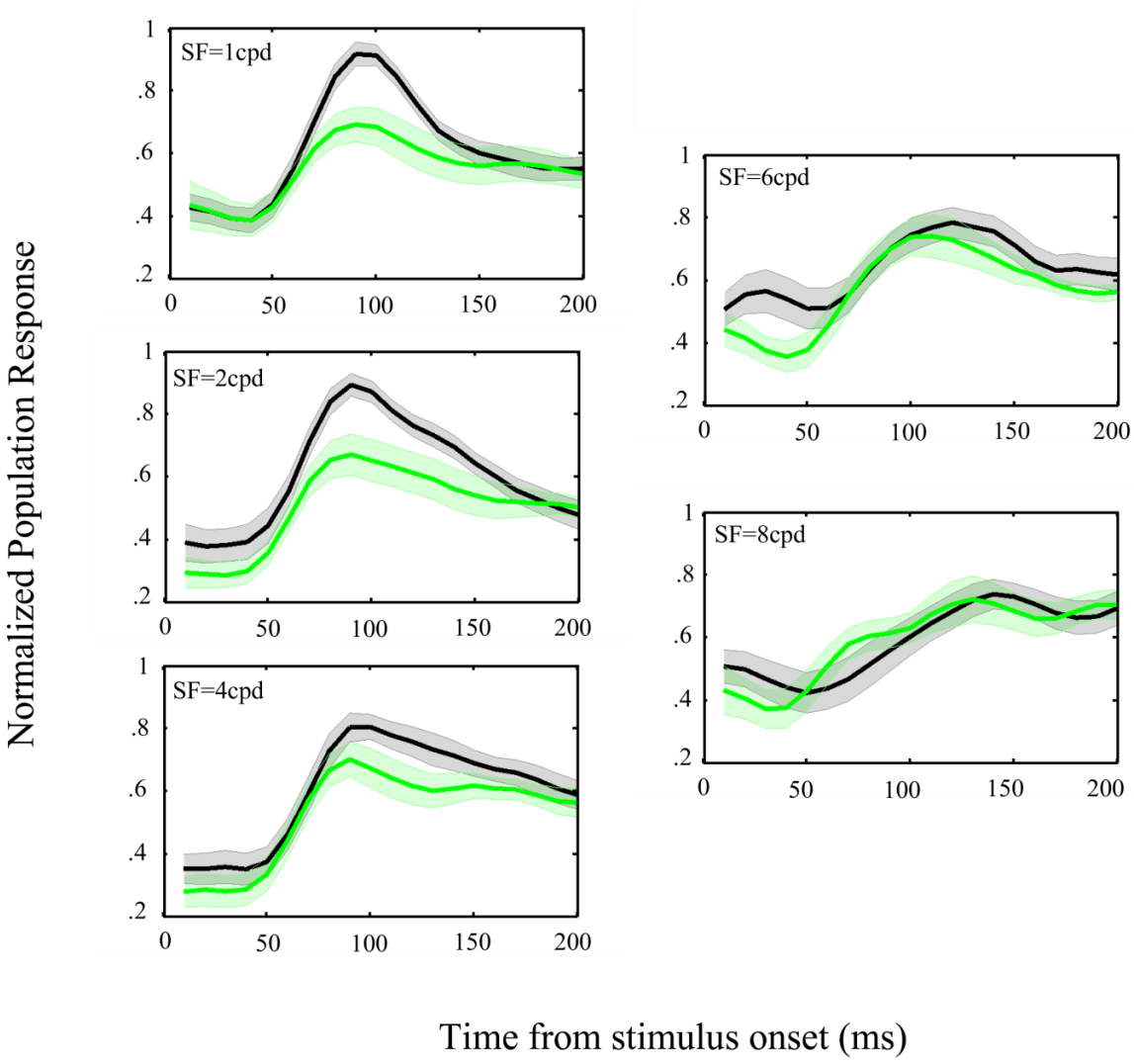

Figure 13 displays five plots of average normalized responses for a population of 16 V1 units from Monkey S. Again, black lines represent the FIX-FLASH condition and green represents the SACCADE condition. Shaded area is SE of the mean normalized response. The panels are labelled by the spatial frequency being tested in each of the 5 conditions. Contrast of the gabor was identical between conditions within a given recording session, but could vary across days. All other stimulus parameters, except spatial frequency, were set to the preferred values for an individual RF. Data from the conditions in which the stimulus was presented in the upper visual field, outside of the RFs, are not shown here.

The figures highlight the difference in response between FIX-FLASH and SACCADE conditions caused by the spatial frequency of stimuli. At low spatial

frequencies, 1, 2, and 4cpd, the response is stronger in the FIX-FLASH condition than in the SACCADE condition. However, at 6 and 8cpd, the units' responses are fairly similar between the two conditions. Note that there is still a stimulus-induced response at these higher SFs, but the response profiles between conditions are much more similar than at lower SFs.

This finding correlates well with what was observed in the contrast sensitivity experiment presented above. In that experiment, the contrast sensitivity values were shown to be different between FIX-FLASH and SACCADE conditions at lower spatial frequencies but not different at higher spatial frequencies. Specifically, the FIX-FLASH condition yielded better perceptual ability in the contrast sensitivity tests, and it also yields better neuronal responses in V1.

Summary

The overall neurophysiology effect (Figure 8) is clear: flashing a stimulus after a forced fixation period yields a stronger response compared to when that stimulus is brought to an RF by a saccade over a natural scene background. This neural effect is only seen at lower spatial frequencies (at or below 4cpd; Figure 13). Furthermore, there is a strong correlation between the neural data and the perceptual performance of the animals (Figure 11) and even of a human observer (Figure 12). Perceptual contrast sensitivity is reduced in the more natural SACCADE condition at lower spatial frequencies, just as the V1 neuronal responses are also reduced.

Diminished Adaptation Experiment

The above findings suggest that there is something unique about natural vision that is neglected in most studies of the visual system. When a stimulus is presented on an image background immediately following a saccadic eye movement (the way vision works in the real world) then neuronal responses to that stimulus and the perceptibility of that stimulus are reduced. The data shown above demonstrates this. However, what is the mechanism for this effect?

There are a few potential sources of the reduced visual function following an eye movement on a natural scene background. First, the saccadic eye movement itself could be causing the reduction. As seen in Figure 1 of the introduction, even a saccade on a homogenous grey background can affect neural activity. A second possibility is that the natural image could be causing the reduced visual function. A third potential mechanism for the effect shown above is that there could be some interaction between the saccade and the natural scene background.

One piece of evidence that can't be ignored from the above experiments is that the effect is specific to low spatial frequency stimuli. A fact that has been well established in studies of natural scene statistics is that they tend to be dominated by low spatial frequency content (Field, 1987). This led us to focus on examining the effects of the natural scene background first.

Test Number 1: Grey Background

To immediately rule out any effect of the eye movement on the perceptual effect observed, the contrast sensitivity experiment was re-run on a single animal (Monkey S) after removing the natural scene background. This slight adjustment to the paradigm is shown in Figure 14.

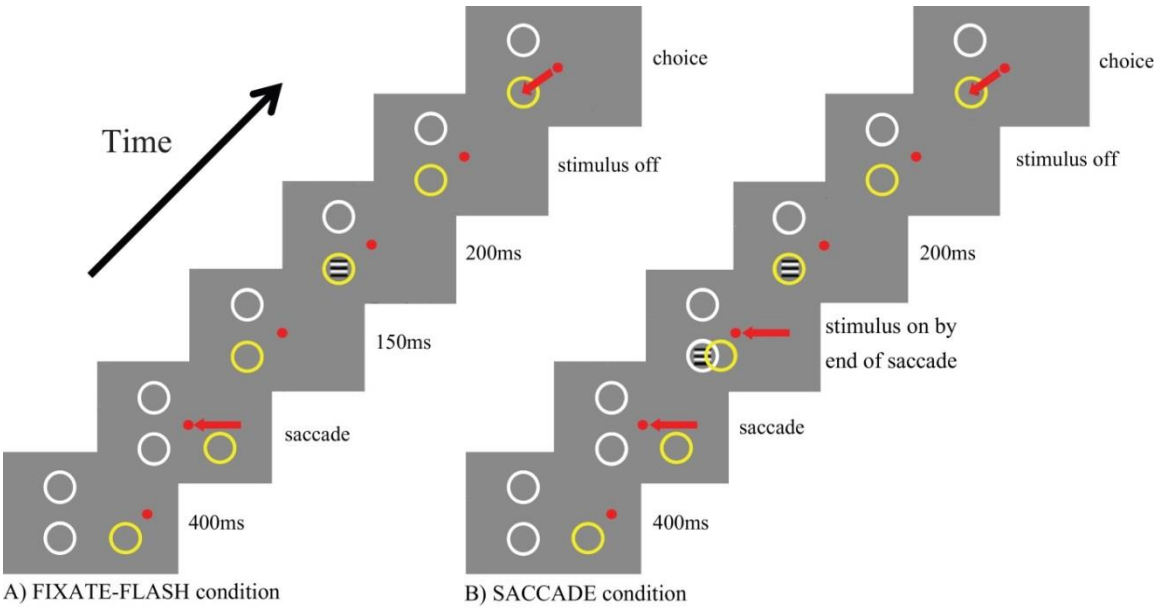

Figure 14 shows the first paradigm used to examine effects of the natural scene on contrast sensitivity in our FIX-FLASH (A) and SACCADE (B) conditions. The edges of individual frames are not shown, but the paradigm is exactly the same as what was shown in Figure 6 except that the natural image background has been removed. As in Figure 6, the yellow and white circles were not actually present during the experiment. They're presented here simply to show hypothetical locations of a V1 RF (yellow) and the two potential stimulus locations (white). Also note, again, that the target stimulus was a gabor, not a simple grating as shown here for demonstrative reasons.

This paradigm keeps the contrast sensitivity experiment the exact same except for the natural image background being removed. Thus, if any effect is still seen then it is likely caused by the eye movement.

Another important note about this paradigm is that the grey buffer patches are no longer present. The entire screen is a homogenous grey except for the fixation points and gabor stimulus. In the earlier paradigm, with a natural image background, the grey buffer patches allowed the subject to know exactly where a stimulus might be appearing. Without these patches, it could be argued that there is an inability to allocate attention spatially between the two possible stimulus locations. Therefore, by removing the image background the task is actually more difficult than what one would have previously thought.

Results of Test Number 1 (Grey Background)

This grey background paradigm was run on Monkey S after training and recording sessions had been performed in the main contrast sensitivity experiment with a natural image background. The CSFs for that animal between the FIX-FLASH and SACCADE condition are shown below in Figure 15.

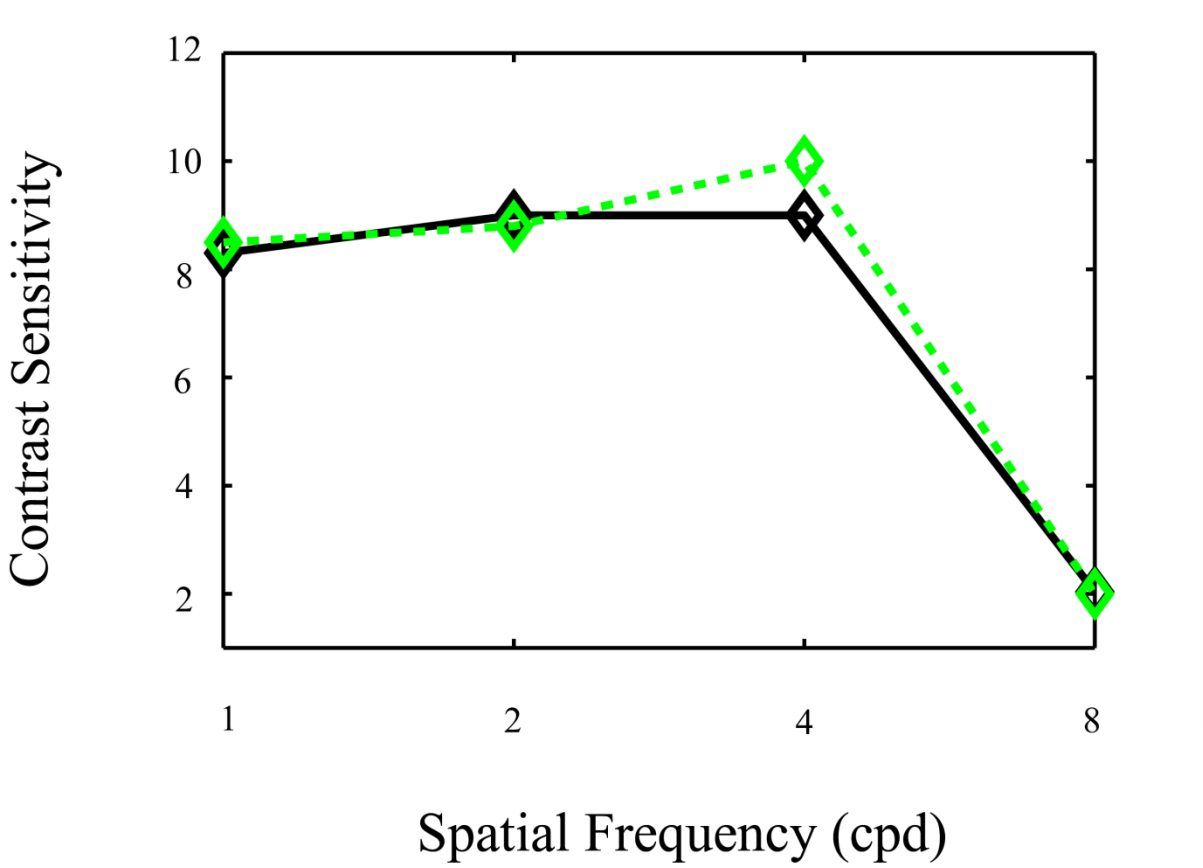

Figure 15 shows the contrast sensitivity functions of Monkey S between the FIX-FLASH (black) and SACCADE (green) conditions during the grey background test. The gabor stimuli for this test were all of the same size, orientation, and eccentricity. These values were also the same as those used in the previous contrast sensitivity experiment with a natural scene background.

Figure 15 shows that the eye movement by itself is likely not responsible for the reduction in sensitivity seen in the SACCADE condition during the contrast sensitivity experiment (see Figure 11, right panel). By simply removing the natural image background, but leaving the saccadic eye movement, the CS values for this animal are nearly identical between conditions.

As mentioned above, there is no grey buffer patch to guide spatial attention. Rather, over trials, the animal had no special cues about where exactly the stimulus

would appear. Without these cues, the task is likely more difficult. Despite this increase in difficulty with a homogenous background the contrast sensitivity values still increase compared to the earlier task with a natural image background. In fact, the only spatial frequency that shows a decrease in sensitivity is 8cpd, and that was the highest SF tested.

The findings from the grey background experiment led to an amended hypothesis: the natural vision effect seen in the neural data (Figure 8) and perceptual data (Figures 11-12) is primarily due to the natural scene background, not the saccadic eye movement.

Amended Hypothesis About the Mechanism of the Effect

All previous data has suggested that the effect of adding "naturalness" to a research paradigm likely comes from a combination of eye movements and complex image backgrounds. However, the grey background test above suggests that this is not true. By removing the background image, we completely lost the effect seen previously. Thus, there must be something related to the natural scene that drives most, if not all, of the effects observed.

One possible explanation comes from the fact that natural scenes are dominated by low spatial frequency content (Field, 1987). This can be easily observed in most viewing conditions: if one were to look at single pixel on a screen or single point in the world, the luminance of nearby pixels or points is very likely to be the same. There is not much change in luminance of the natural world until an edge is encountered. The results presented so far have all been specific to low spatial frequencies, which led to the new hypothesis that low spatial frequency content of the natural scene is what drives the effect.

The merit of this hypothesis can be seen when considering the experimental paradigm: at the start of all trials, the subject fixates on a point on the image background for 400ms prior to initiating the first saccade (Figure 6). In the SACCADE condition, the RF travels directly from image background to an already-present stimulus. In the FIX-FLASH condition, the RF travels to a grey buffer patch where it sits for 150ms before a stimulus appears. It is possible that, during the initial 400ms fixation, adaptation to the scene background might be occurring in the RF. In the SACCADE condition, this adaptation may affect responses to stimuli at the next fixation site. In the FIX-FLASH condition, this adaptation has a 150ms washout period. This could mean that adaptation effects might occur in the SACCADE condition, but not the FIX-FLASH condition.

In order to determine whether adaptation might be occurring during this short fixation period and selectively reducing perceptual ability and neural responses at subsequent fixation sites, a second paradigm was created.

Test Number 2: Diminished Adaptation

In the previous experiment, the natural scene was completely removed. To examine whether the effects of the natural scene were specific to the RF locations, and to examine whether adaptation to the natural image background may be driving the effect seen earlier, a new paradigm was created. In this new paradigm (Figure 16), the natural image background was kept on the screen during the task, but additional grey buffer patches were included at the first fixation site.

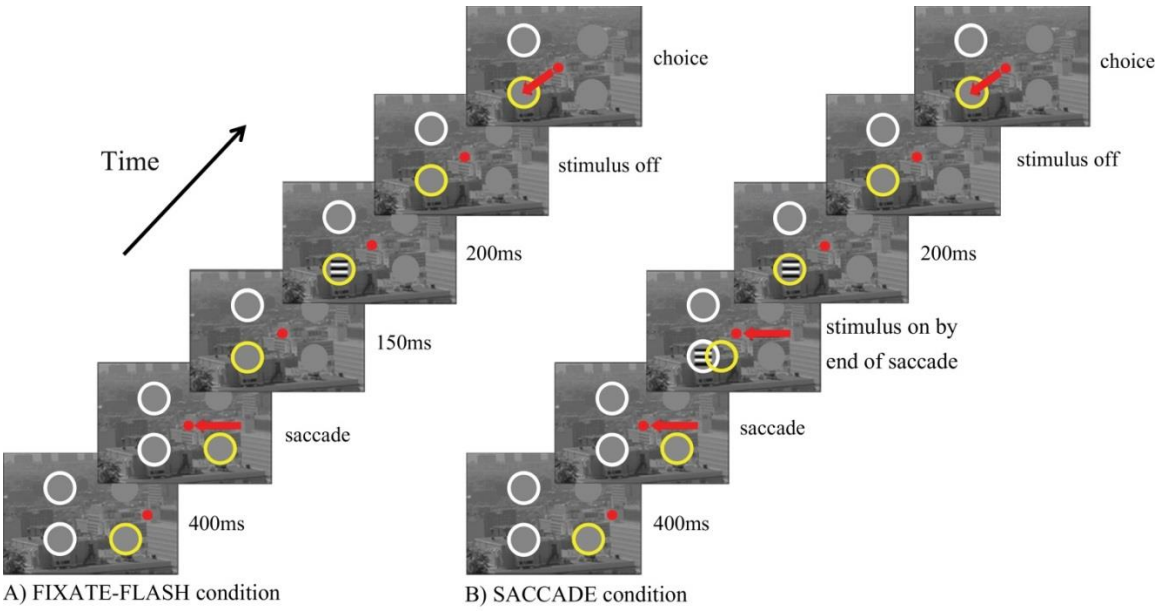

Figure 16 shows the Diminished Adaptation paradigm for the FIX-FLASH condition (A) and SACCADE condition (B). Like in the previous paradigm figures, the white and yellow circles were not present during the task – they're included here simply for highlighting the stimulus probe and hypothetical RF locations. The only difference between this paradigm and the original contrast sensitivity task is the presence of grey buffer patches in the RF positions at the first fixation site. This diminished any chance for adaptation to occur during the 400ms fixation at the start of the trials.

With this paradigm, the eye movement and natural scene are still present; however, any opportunity for adaptation to occur at the RF site (yellow) is diminished. The natural scene does not contact the RF for the first 400ms of the trial. If the above hypothesis is correct, that adaptation to low spatial frequency content of the part of the image within the receptive field is driving the difference in neural responses and contrast sensitivity between the FIX-FLASH and SACCADE conditions, then we expect a reduction in this difference with this paradigm.

Results of Test Number 2 (Diminished Adaptation)

Monkey S had already shown a loss of the perceptual effect with a homogenous grey background, so the paradigm from Figure 16 was presented to Monkey F. First, the behavioral component of the experiment was examined. Below are the contrast sensitivity functions between the two conditions using this Diminshed Adaptation paradigm (Figure 17).

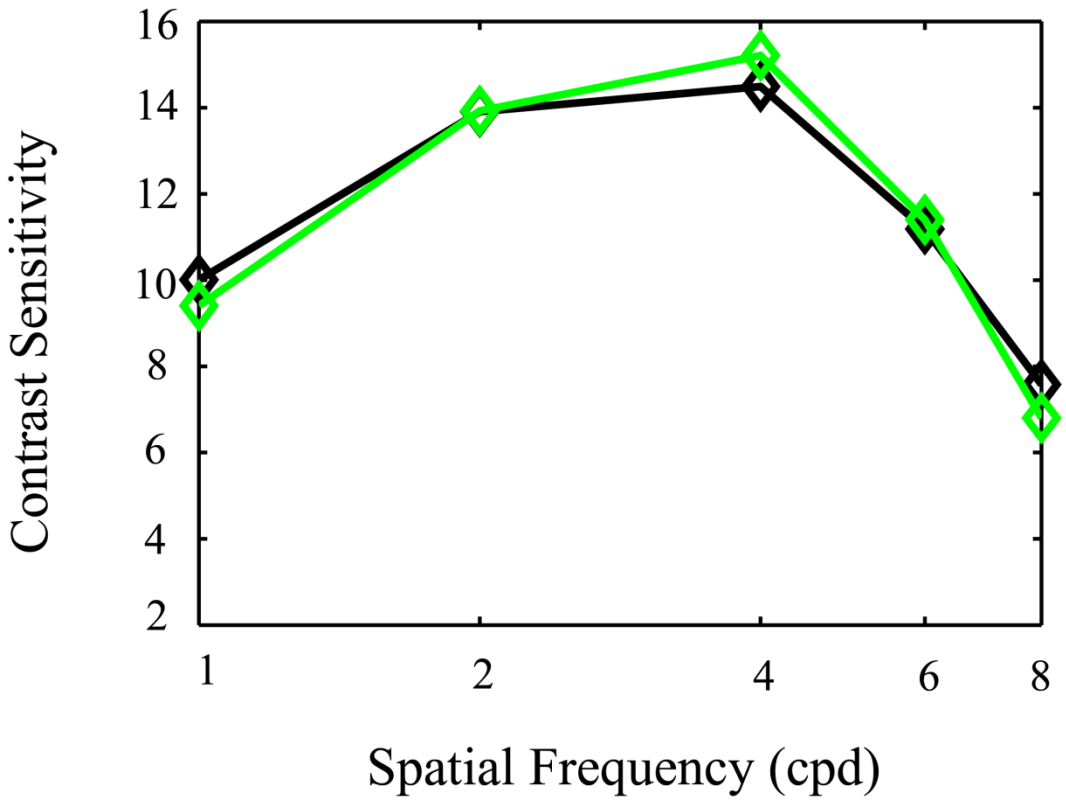

Figure 17 displays the contrast sensitivity functions between the FIX-FLASH (black) and SACCADE (green) conditions from Monkey F during the Diminished Adaptation paradigm. For this figure, the orientation, size, and eccentricity of the gabor stimulus was held constant across these behavioral recording sessions.

By including a grey buffer patch over the image background at the first fixation site, the perceptual effect nearly disappears. This supports the amended hypothesis and suggests that the original, natural, contrast sensitivity paradigm was displaying effects caused by adaptation occurring during the first 400ms fixation in the trials. When that fixation period requires the RF to sit over a homogenous grey patch (Figure 16), then the contrast sensitivity values between the FIX-FLASH and SACCADE condition are very similar.

To further determine whether the mechanism causing the original effect is indeed adaptation, the next step obvious step is to understand if neuronal responses are shaped differently in the Diminished Adaptation condition. In Monkey F, a set of 20 recording sessions was performed on V1 units using this paradigm. The general recording procedure used was the exact same as what was outlined during the Contrast Sensitivity Experiment. Figure 18 shows the average normalized V1 neural population response of 20 V1 units.

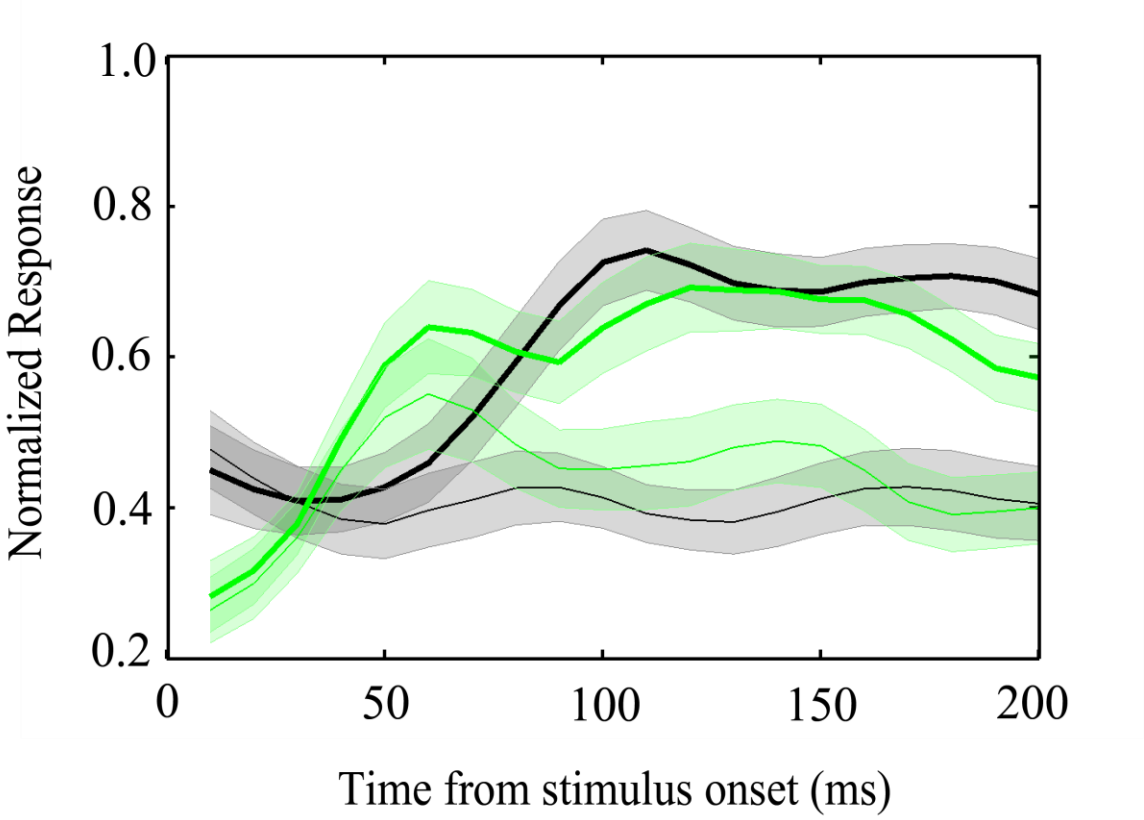

Figure 18 plots the average normalized neuronal response from a population of 20 V1 units being recorded during the Diminished Adaptation task. Black lines represent the FIX-FLASH condition while green lines represent the SACCADE condition. Thick lines represent average normalized activity when the gabor stimulus appears in the RF, and thin lines represent the conditions when the RF does not get stimulated by the gabor. Shaded area is SEM of the normalized response; the peak response at time 110ms in the FIX-FLASH condition is not significantly higher than in the SACCADE condition (p=.3054, t-test). The orientation, eccentricity, size, and spatial frequency of the gabor stimuli across these 20 sessions was set to be the preferred values for an individual V1 unit RF being recorded.

The neural activity between the FIX-FLASH and SACCADE conditions is similar during the Diminished Adaptation experiment. This finding is directly in line with what was observed with the contrast sensitivity data in Figure 17. Combined, these findings suggest that the stronger response observed in the FIX-FLASH condition during the original Contrast Sensitivity task was a result of adaptation occurring in the SACCADE

condition. This adaptation appears to occur within the 400ms initial fixation period and carry over across the saccade to the central fixation point.

Figure 18 shows that the responses are fairly similar between the SACCADE and FIX-FLASH conditions, but the FIX-FLASH condition still gives a stronger peak response than the SACCADE condition (though not significantly stronger). Figure 19 shows the original data (64 units used) plot next to the new data set from Figure 18 (20 units), but with the thin lines removed so that only the stimulus-induced responses are shown.

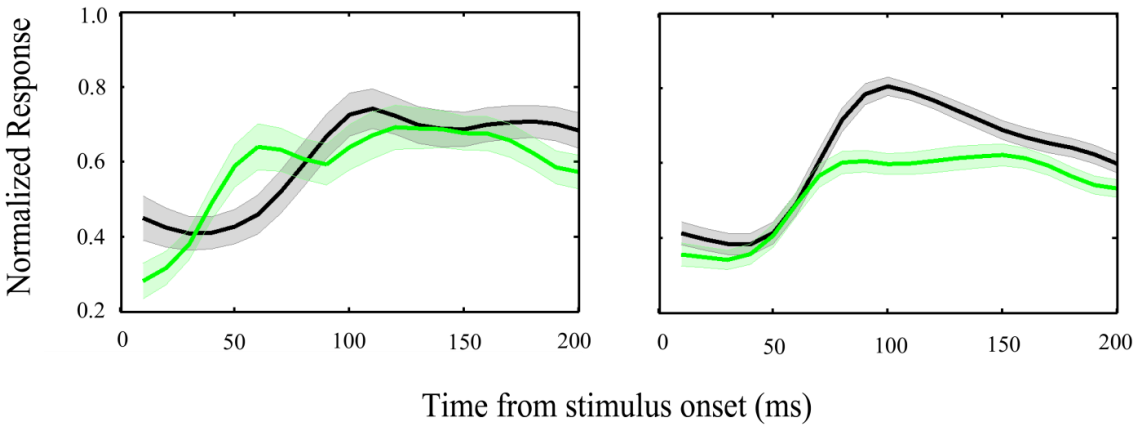

Figure 19 shows the population responses from the Diminished Adaptation experiment (left panel; N=20 units) next to the population response from the original experiment with a full natural image background (right panel; N=64 units). Black lines represent the FIX-FLASH condition and green represents the SACCADE condition. Shaded area is SEM of the normalized response. The conditions in which no gabor stimulus was presented to the RF are not shown here for clarity. The left panel figure is composed of data from units only in Monkey F, while the right figure shows average normalized activity across all three animals. However, because the data is normalized within-session, the differences between conditions are comparable between days.

The FIX-FLASH condition is much more clearly dominant in the original Contrast Sensitivity Experiment compared to the Diminished Adaptation Experiment.

However, another interesting thing to note is that the response in the SACCADE condition of the Diminished Adaptation Experiment (left panel of Figure 19) shows a much earlier peak than it did in the original experiment (right panel). This makes sense when thinking of what has changed for the contents of the V1 RF: in the Diminished Adaptation Condition, the RF sits on a grey buffer patch for 400ms before crossing over the natural scene. Thus, this early response is likely caused by stimulation from the natural image during the saccade. In the original experiment this stimulation likely showed less of an effect because the neuronal RF was starting out on the natural image background. More information about these early responses will be discussed later.

Experimental Summary

The strong difference in V1 activity between conditions is apparent in the right panel of Figure 19, and nearly gone in the left figure. The effect that is so clear in the right panel disappears by simply adding grey buffer patches near the initial fixation site in the experimental paradigm. This strongly suggests that rapid adaptation occurs after a 400ms fixation on a natural scene background and this adaptation is capable of carrying across an eye movement and affecting neural activity and perception at subsequent fixation sites. Further, this adaptation effect was specific to low spatial frequencies, which was likely a result of low spatial frequency content in the natural scene (information about the natural scene's Fourier spectrum is discussed later).

A major benefit of using non-human primates is that perception can be measured at the same time that neural activity is recorded. All of the neuronal figures presented above were created from data collected while the animals were performing the contrast

sensitivity tests. Contrast sensitivity functions displayed the same effects as the neural activity, even in a spatial-frequency-specific fashion. Thus, this experiment gives insight into the full picture of visual function in more naturalistic paradigms.

In the real world, most mammals move their eyes frequently across visually complex scenes full of low spatial frequency content. The data presented here suggests that this natural method of saccading over images creates different neural representations and perceptual abilities than what is observed in most lab experiments of vision. The effects above occur during a 400ms fixation, which is within the range of normal fixation times during normal vision (Kayser et al., 2006), and carries across a 7-degree eye movement.

The previous sections have presented a series of neural and psychophysical experiments, along with a brief summary of the results. Further discussion will be made in its own section later. First, however, more specific results from the neuronal and contrast sensitivity experiments will be presented.

More Specific Neural Results

Figure 8 showed the population response of 64 V1 units recorded during experiments. The effect is obvious: responses to stimuli are stronger when those stimuli are flashed on after a forced fixation period compared to when the stimulus is brought to the RF by a saccade. This was true in 43 of the 64 units (67.2%) included in that population figure. An example of the data from a single unit showing this effect in Monkey Z is shown below in Figure 20.

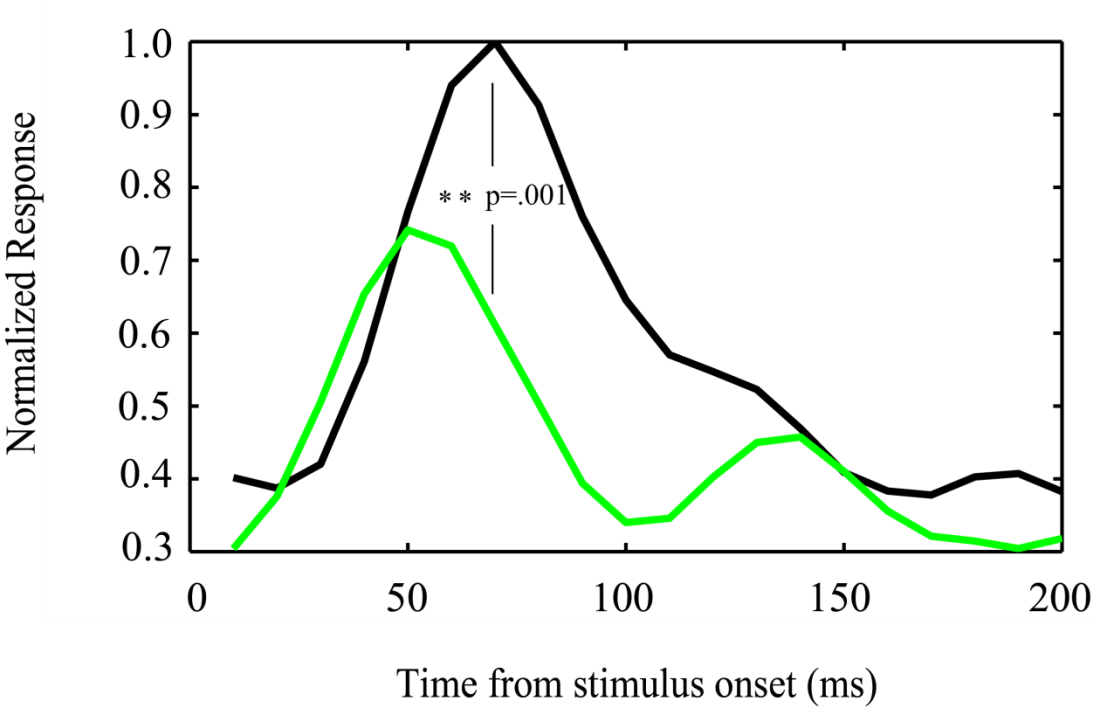

Figure 20 shows the average normalized response from one single unit used in the population plot from Figure 8. The activity in the FIX-FLASH condition is black, SACCADE is green. The peak response reaches 1.0 in this figure because that was the normalizing value. The gabor stimulus parameters were optimal for this unit, and the contrast used here was 30%.

A majority of units performed in this fashion, giving stronger firing rates to stimuli in the FIX-FLASH condition. However, there was a subset of units that gave stronger responses at the end of the eye movement in the SACCADE condition. An example of such a unit from Monkey S is shown below in Figure 21.

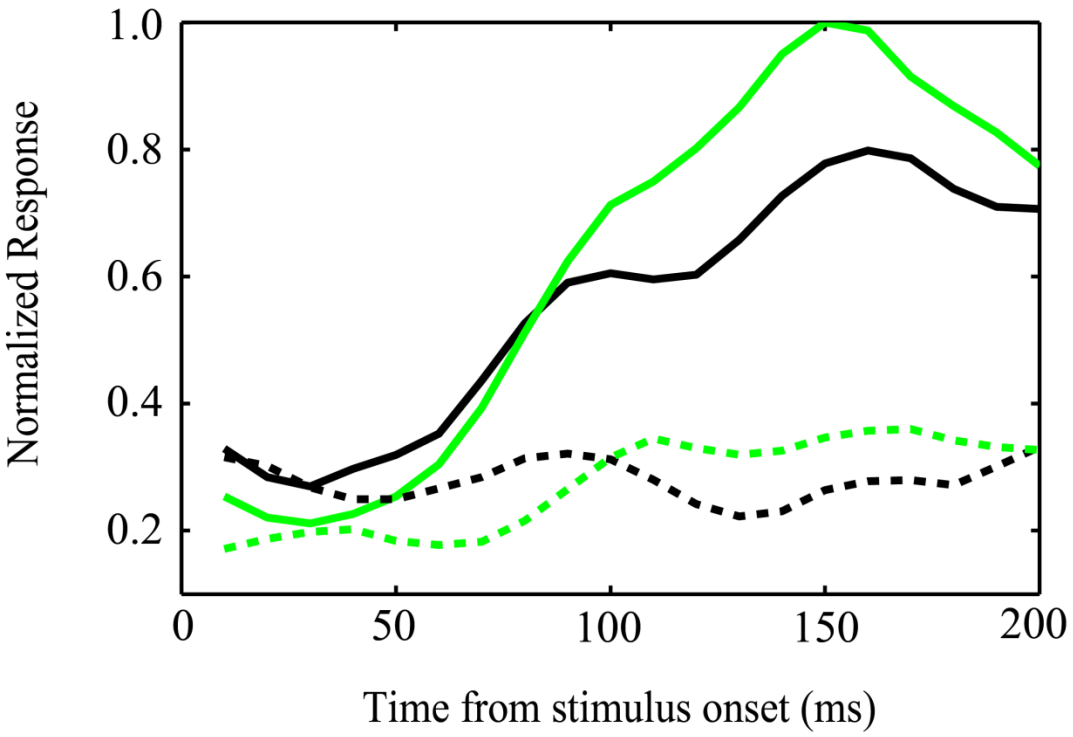

Figure 21 shows the average normalized response from one single unit in Monkey S. Black lines represent the FIX-FLASH condition while green represents the SACCADE condition. Dotted lines show the response of the neuron when there was no stimulus in the RF; this is shown here to demonstrate that the high response in the SACCADE condition is not simply due to any post-saccadic enhancement. The contrast used in this condition was 15%, and all other gabor parameters were optimal for the unit (the preferred SF for this cell was 4cpd). The difference at the peak response time (~t=150ms) was not significant (p=.242, t-test).

Note that the unit in Figure 21 still displays a very clear response to the stimulus in the FIX-FLASH condition, but does not follow the general pattern of other neurons in that the response is stronger during the more natural SACCADE condition. Units like this one were rare, but can still be explained with the general model presented above: the proposed mechanism behind the stronger responses in the FIX-FLASH condition is that adaptation occurs at the start of trials and carries over to affect neuronal responses at the second fixation site. Because adaptation is pattern-specific, the pattern presented to the RF at the first fixation site will determine the amount of adaptation that will occur. One possible explanation for why this unit is responding better in the SACCADE condition is that the RF may have been stimulated by a non-optimal pattern at the first fixation site. If that is true, then the firing rate before the saccade may have been greatly reduced compared to its response over a homogenous grey patch, which could have led to a stronger response to an optimal stimulus at the end of the eye movement. This possibility will be examined further in the Discussion section.

Varying-Contrast Responses

The main neural population figure that has been shown in this document is for the highest contrast level tested across various days of recordings (Figure 8). However, as mentioned previously, a different population response figure could be made at each of these contrast levels. Examples of population responses (with fewer than 64 units) at two intermediate contrast levels tested are shown below.

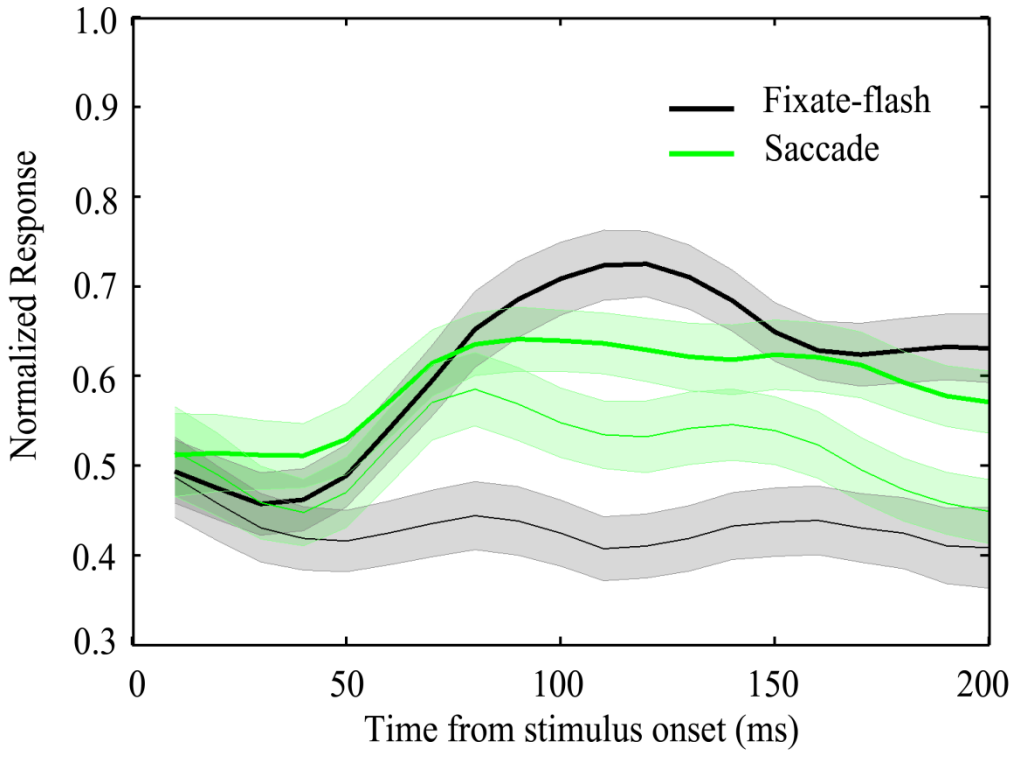

Figure 22 shows a population response of V1 neurons, analogous to the population figure shown in Figure 8, to an intermediate contrast level tested. Note that the previously-observed effect is still present: the Fixate-Flash condition still gives a higher response than the Saccade condition. Also note that the average normalized response does not reach the higher point seen in Figure 8 because there were fewer units that showed their highest response to the flashed stimulus. See text for more discussion of this as well as saccade-related activity.

Figure 22 shows the population response to a lower contrast gabor stimulus than was used in Figure 8. The FIX-FLASH condition still yields a higher response than the SACCADE condition, but the effect is not as strong as what was seen previously to the highest contrast stimuli tested. In Figure 23 I show an even lower contrast level tested.

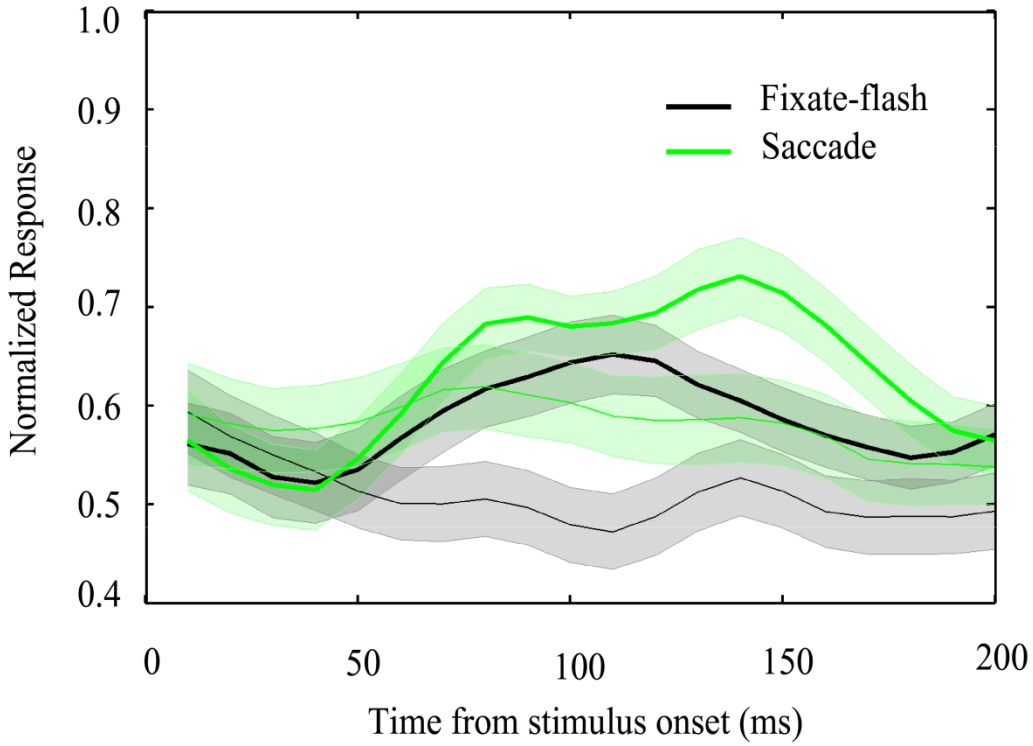

Figure 23 plots a population response of V1 neurons to a lower contrast level than Figure 22. Note that the strongest response is no longer shown in the Fixate-flash condition. However, the difference in thick and thin black lines, compared to the thick and thin green lines, indicates that the stimulus-induced response was still stronger in the Fixate-flash condition.

Figures 22 and 23 show that the main effect observed in Figure 8 is dependent on contrast. This is not surprising because the neurons recorded in these experiments were chosen for their stimulus-induced responses. In fact, neurons that did not respond to the gabor stimuli were not used in these studies. Another way of describing this finding is to say that, in order to observe a stimulus-induced effect, I needed to supply the neurons' RFs with a stimulus strong enough to drive their activity. The main finding that responses are stronger in the FIX-FLASH condition is still true, but these figures show that this effect is dependent on sufficient amounts of stimulus contrast.

These population figures also highlight another important finding: there is a clear response from many V1 neurons even when there is no stimulus present in the RF. The thin green lines of Figure 22 and Figure 23 (and even Figure 8) show that, regardless of stimulus location, there is an increase in firing rate at the end of the saccade. This finding was not true for every neuron recorded; in fact, the data could be stratified into various forms of saccade-related responses seen from different neurons. A few of the more common saccade-related responses will be discussed below.

Saccade Responses

One fact, mentioned earlier in the Introduction and then largely ignored until the above figure, is that V1 neural responses are affected by eye movements (Figure 1). This is true for LFPs (Feldman and Cohen, 1968), and single-unit spiking responses (Gee et al., 2010; Reppas et al., 2002). Some units recorded in the Contrast Sensitivity experiment also showed this, and can be classified into two separate groups: 1) units that respond during a saccade over a natural image, and 2) units that respond at the end of a saccade. Units that respond during a saccade are identifiable by showing a strong response at the very start of the stimulus period in the SACCADE condition, which is at the very end of the eye movement. Figure 24 shows one such unit recorded in Monkey S.

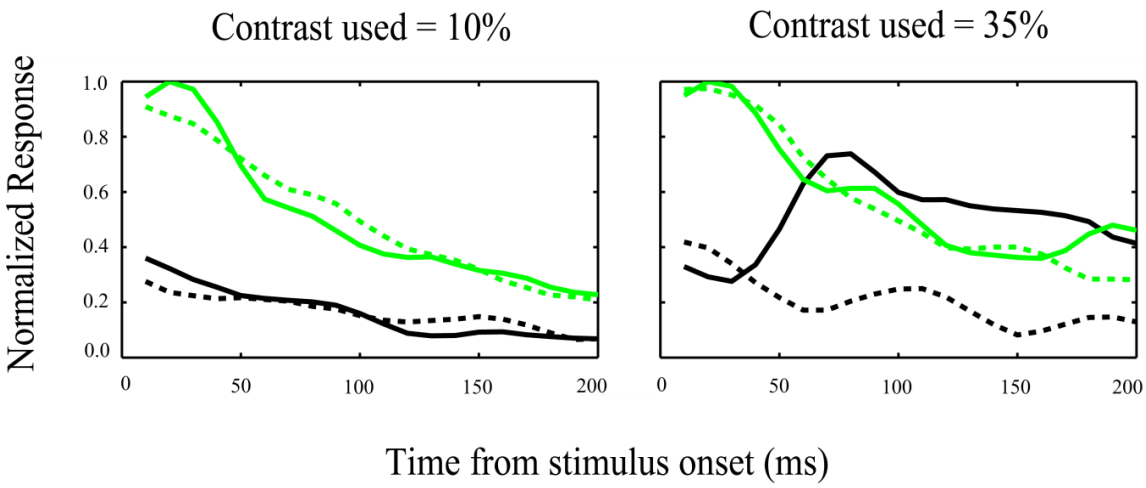

Figure 24 shows the average response of a V1 unit in Monkey S at two contrast levels tested, 10% (left panel), and 35% (right panel) between the FIX-FLASH (black) and SACCADE conditions (green). Dotted lines show conditions in which there was no stimulus in the RF. Gabor parameters were optimal for the unit.

Figure 24 shows a unit that was responding during the saccade. The green lines, representing the SACCADE condition, begin at very high values and only decrease over the course of the stimulus interval. Notice that there is no stimulus-induced response in these SACCADE conditions. This raises the question of whether some units may not be visually responsive to the stimulus during the task; however, there is a strong stimulus-induced response in the FIX-FLASH condition when the stimulus contrast is 35% (right panel). Therefore, we know this unit is responsive to visual stimuli and is also displaying a high firing rate during the saccade. Only 9/64 neurons showed this effect (~14%), which is likely why they do not greatly skew the population response profile (Figure 8). Ruiz and Paradiso (2012) and MacEvoy et al., (2008) also reported the existence of neurons that respond to scene stimuli present during eye movements. In those studies, the reported number of cells responding during saccades was about 10%.

Another form of saccadic response is not during the saccade itself, but rather immediately following the end of the eye movement. Multiple studies have noted cells in visual cortex that show this "post-saccadic enhancement" (Kohn, 2007). However, those response enhancements are typically in response to a stimulus inside of the RF. In the data above there are many units that show a response after the saccade regardless of whether a stimulus is present in the RF or whether the RF lands on the grey buffer patch. These post-saccadic responses can be seen in the 64-unit population figure (Figure 8), which is highlighted below in Figure 25 (and can be easily observed in Figures 22 and 23).

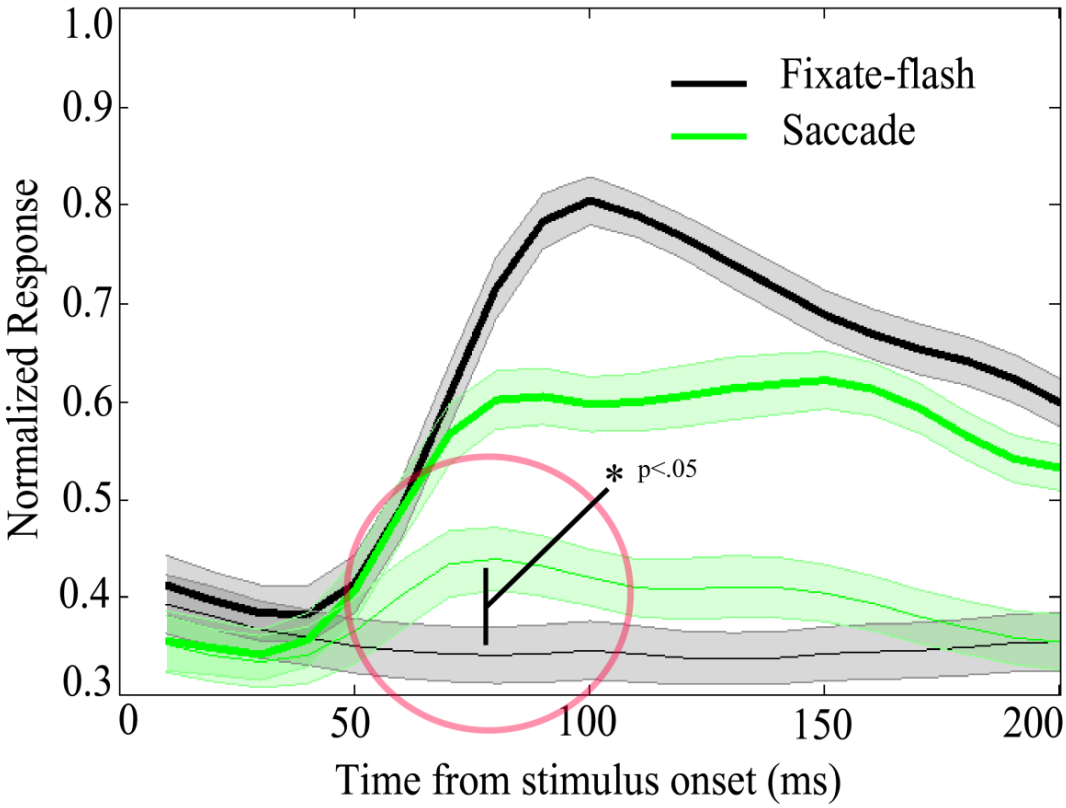

Figure 25 is the population figure shown in Figure 8, with a red circle to highlight the post-saccadic response seen in many of the neurons recorded during the SACCADE conditions (which, even when averaged over days that included units not showing the effect, is significant at p=.02, t-test). The thick lines represent conditions in which the stimulus was present in the RF, and thin lines represent the conditions in the 2AFC task in which the stimulus was not presented to the RF. The circle here highlights the finding that many units show a response at the end of the eye movement even when there is no stimulus in the RF.

This average normalized plot (Figure 25) does not accurately represent this post-saccadic response. Most units did not show this response; however, the ones that did respond at the end of a saccade tended to respond very strongly. Below is a set of plots showing three units from Monkey F that display this post-saccadic rebound.

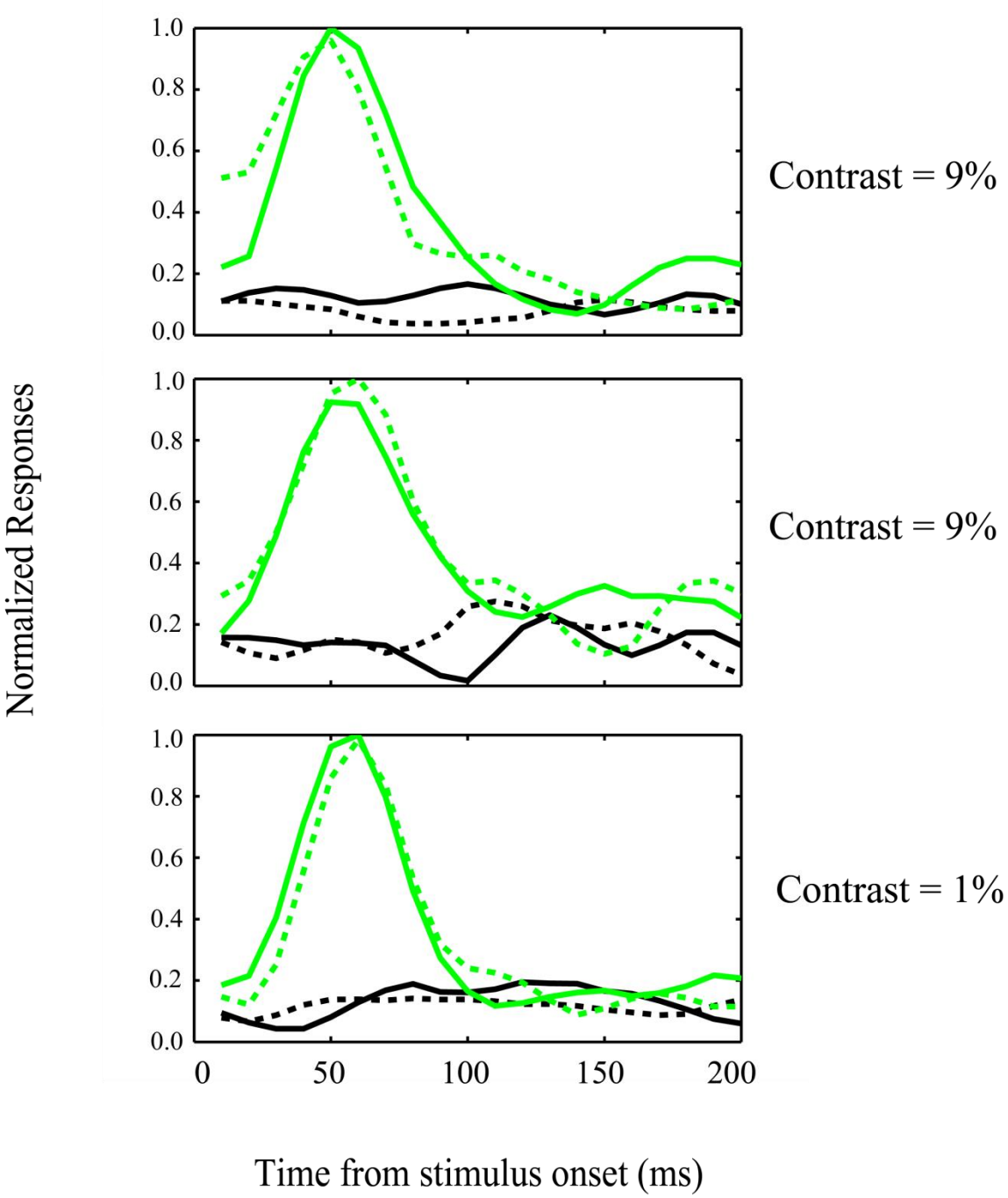

Figure 26 displays three separate single-unit response profiles that have been normalized within-condition in Monkey F, recorded from three different neurons. Solid lines show conditions in which the gabor stimulus was presented inside the RF, dotted lines are average response when there was no stimulus inside the RF, and green lines denote SACCADE condition responses while black lines represent FIX-FLASH responses. These are three exemplar units showing an immediate post-saccadic "rebound" response in the SACCADE condition: the data from dotted lines shows that there was a strong increase in firing rate at the end of the eye movement even when the stimulus was not presented in the RF. Note that, despite the similarity in responses, these three units were recorded on separate electrodes on separate days of the task.

Low contrast levels were chosen to plot here to help clarify that this rebound response has nothing to do with the stimulus (a 1% contrast gabor never gave a noticeable response in any units studied).

A large fraction of units showed this effect (23/64, 35.9%). During recordings these cells were loosely classified as "rebound" responses, but it could be argued that they are comparable to post-saccadic enhancement responses similar to those observed in other studies (Kohn, 2007; Kagan et al., 2008). The important difference, however, is that the data sets above show that these post-saccadic enhancement responses do not require a stimulus to be elicited. The SACCADE condition forces the RF to move across the natural scene background, a process that takes about 30ms, before placing that RF on a homogenous grey patch. This is very different from other studies in which the saccade brings an RF to a stimulus that is already present after the eye movement (comparable to the data plotted in solid lines in Figure 26).

A final interesting saccade-related phenomenon seen in the data here is a complete inhibition of firing rate during the saccade, followed by a slowly developing response after the eye movement in the SACCADE condition. These V1 units did not show an immediate "rebound" response at the end of the eye movement, but rather showed a slowly-developing response over the course of the stimulus duration. Figure 27 shows one such neuron in Monkey F.

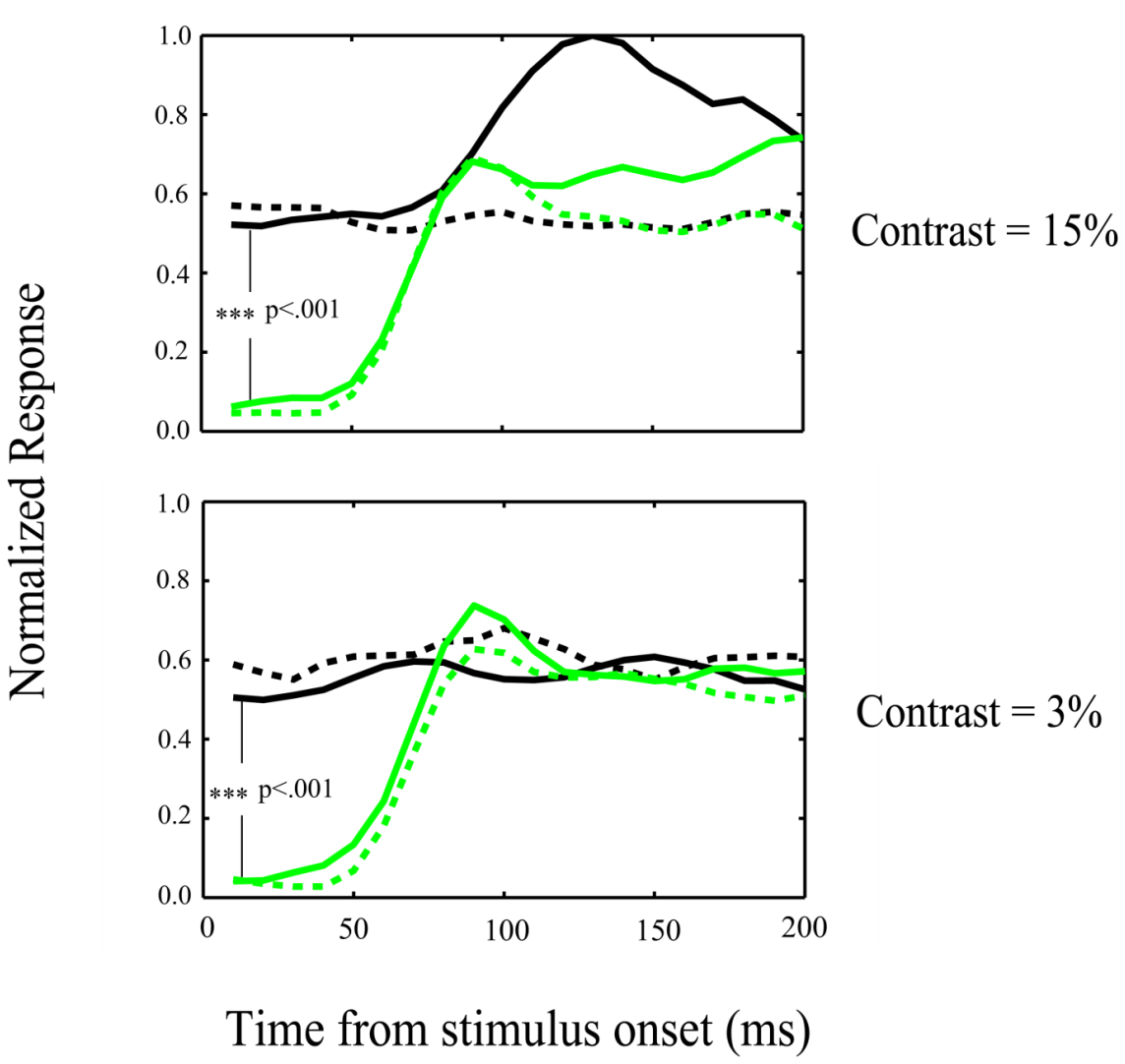

Figure 27 displays a V1 unit's response between two conditions during the Contrast Sensitivity Experiment. Solid lines represent activity when the stimulus was present in the RF. Black lines represent the FIX-FLASH condition, and green lines represent the SACCADE condition. These two plots show activity from the same unit between two contrast levels used during the task, the highest and lowest presented during this session. These conditions were both normalized to the peak response in the 15% contrast condition. The initial response in the SACCADE condition (at both contrast levels) was significantly below the initial response in the FIX-FLASH condition (P<.001, t-test).

This unit showed strong inhibition during the saccade, followed by an increase in response after the eye movement ended regardless of stimulus location. This particular

unit appears to require 100ms after a saccade before returning to a baseline firing rate, which likely affected its firing rate to the stimulus in the SACCADE condition. About 18 of the 64 units showed responses similar to this (28.1%; though not all of these units showed the effect this clearly), and thus contributed to creating sustained SACCADE responses seen in the 64-unit population figure (Figures 8 and 25).

Summary of Saccade-Related Responses

A few forms of saccade-related response profiles were shown above. Some units showed high firing rates during the eye movement in the SACCADE condition (Figure 24), some showed a rebound in response (or post-saccadic enhancement) at the end of the eye movement (Figure 26), and some showed strong inhibition during the eye movement (Figure 27). All of these saccade-related responses contribute to the overall shape of the population plots.

In short, these different firing rate profiles demonstrate that there exist many unique effects of natural vision. Each V1 unit is unique in how it responds during eye movements over natural images. However, the main finding is clear: when a stimulus is flashed on after a 150ms fixation period on homogenous grey patch then the V1 response is almost always much stronger compared to occasions when the eye movement brings RFs to a stimulus on an image background.

Dip in FIX-FLASH responses

Another interesting finding from the data was that many units showed an immediate drop in response rate early on during the FIX-FLASH conditions. This can be seen in the population figure (Figure 8), and will be re-highlighted below.

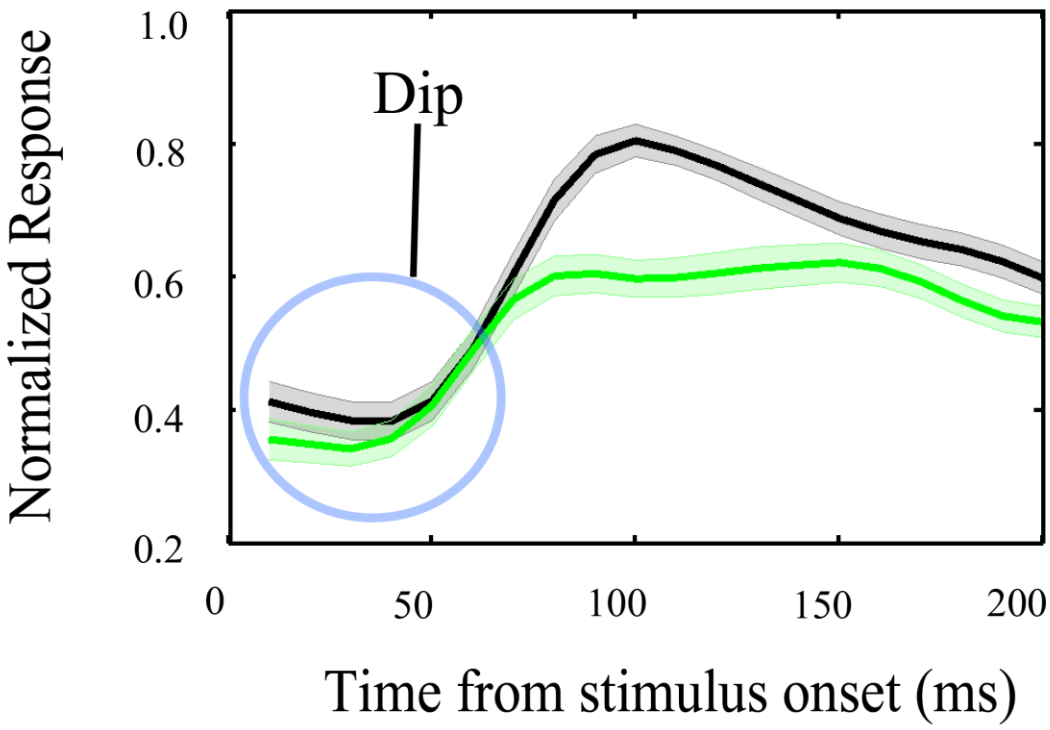

Figure 28 shows the stimulus-induced activity profiles from Figure 8. The circle was added to highlight the location of a drop in firing rate early on in the trials. The conditions in which no stimulus was present in the RF are not included here for clarity. However, refer to Figure 8 to see that there is no dip in response during those conditions.

This inhibition dip occurred early on, and is not quite significant in the population data. However, it was apparent in many single unit responses as well. Below is an example unit showing a strong inhibition of firing rate right after stimulus onset in the FIX-FLASH condition.

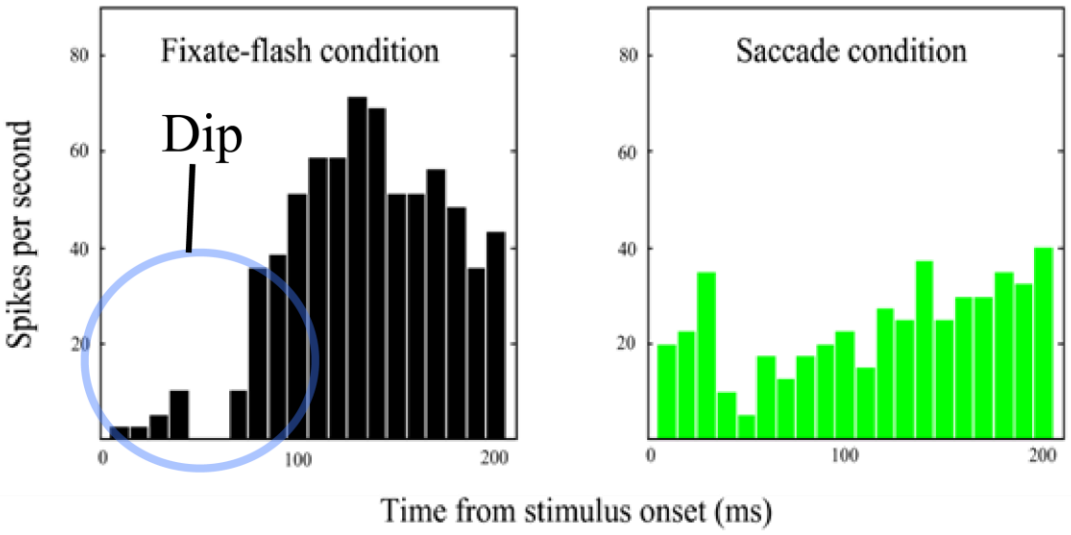

Figure 29 shows the PSTH for a single channel during the task. Again, the inhibition in the FIX-FLASH condition is circled. There is some drop in response during the SACCADE condition as well, but there also appears to be some post-saccadic enhanced response or "rebound" at the end of the eye movement.

Some units showed the effect strongly, and some did not show this effect much at all; however, this inhibition is noticeable in the population figure and deserves some explanation. In 2013, a study was published by Lee et al., showing a very similar phenomenon. In their experiments they required monkeys to fixate while a gabor stimulus was flashed on a grey background, sometimes inside of V1 RFs that were being recorded from. Importantly, the behavioral task of the animal was to make a saccade to the gabor once it was detected. Thus, the general components of their study are exactly the same as ours: a monkey fixates in one location, and occasionally a stimulus is flashed inside of a V1 RF, and then the animal must initiate a saccade to that stimulus's location. A figure from their experiment is shown below.

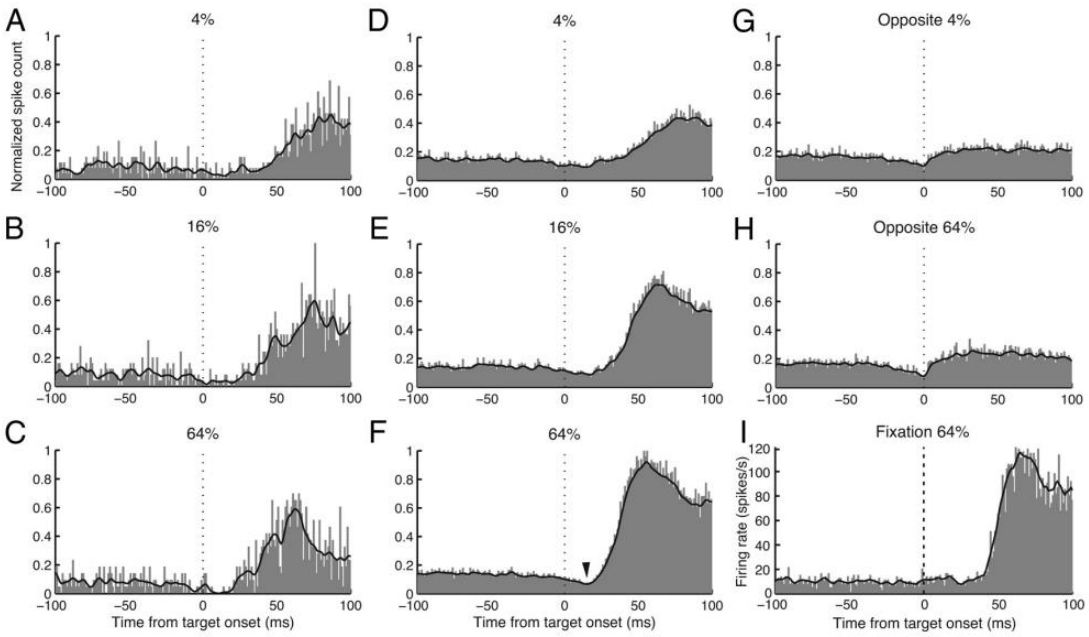

Figure 30 is an image taken from Lee et al., (2013), their figure number 1. Plotted here are responses of a single V1 unit (A, B, C), and a population response from 101 units (D, E, F). Panels G and H show responses when the stimulus was outside of the V1 RF. Panel I shows the response when no saccade was made to the stimulus. The percentage labels refer to the contrast of the gabor.

Figure 30 displays the overall finding from their study: when a saccade is made to a gabor stimulus, the response of V1 units to that gabor stimulus show a very early, small (but significant) drop in firing rate. The arrow in panel F highlights this effect – at about 20ms after stimulus onset in the RF there is a drop in response below the baseline firing rate of the population.

Also note that the effect is even slightly observable in panel E, when the gabor target was only set to 16% contrast. 16% contrast is very near where many of our experiments were performed. Thus, it is likely that our early inhibition in the FIX-FLASH condition is caused by the same mechanism as the Lee et al., (2013) study.

In their article, the authors claim that this suppression (which they call pre-response suppression or PRS), could be useful to the visual system by enhancing the

signal-to-noise ratio. By decreasing their response rate, these V1 units may provide down-stream visual areas with information about the stimulus appearing, and the suppressed response would also result in less noise being sent to these downstream areas. It's currently unclear whether this PRS might have implications for our study. However, note that the main finding from our experiments is that responses are enhanced in the FIX-FLASH condition, which means that if PRS is the cause of the inhibition dip then it is still not strong enough to overcome the overall finding. Any potential implications likely depend on how strong this effect is during the SACCADE condition, assuming it is present there as well.

More Specific Behavioral Results

The perceptual effect observed in the Contrast Sensitivity Experiment was that CS values are reduced immediately following an eye movement over a natural scene background. The contrast sensitivity curves that showed this were in Figures 11 and 12. In those plots, individual SFs were tested in their own sessions as contrast was varied. To ensure that the values were as comparable as possible between days, the eccentricity of the stimuli was not changed. In other words, for those data sets, the exact same stimulus location was used to measure all of the psychometric functions.

When comparing contrast sensitivity between different days' recordings during the task, however, the stimulus parameters varied depending on the V1 unit's preference. This could make contrast sensitivity measurements between different sessions incomparable. In hopes of finding a method of using all of the behavioral data recorded during the task in a fair manner, a simple solution was created: rather than comparing absolute CS values between sessions, one could compare the difference in CS between the FIX-FLASH and SACCADE conditions. There is no reason to believe that the effect studied is specific to stimuli at certain spatial frequencies. Thus, examining the difference in sensitivity between conditions should yield values that can be compared between many days of behavioral data recording. Figure 31 shows bar plots of these differences between the original Contrast Sensitivity Experiment and the Diminished Adaptation Condition.

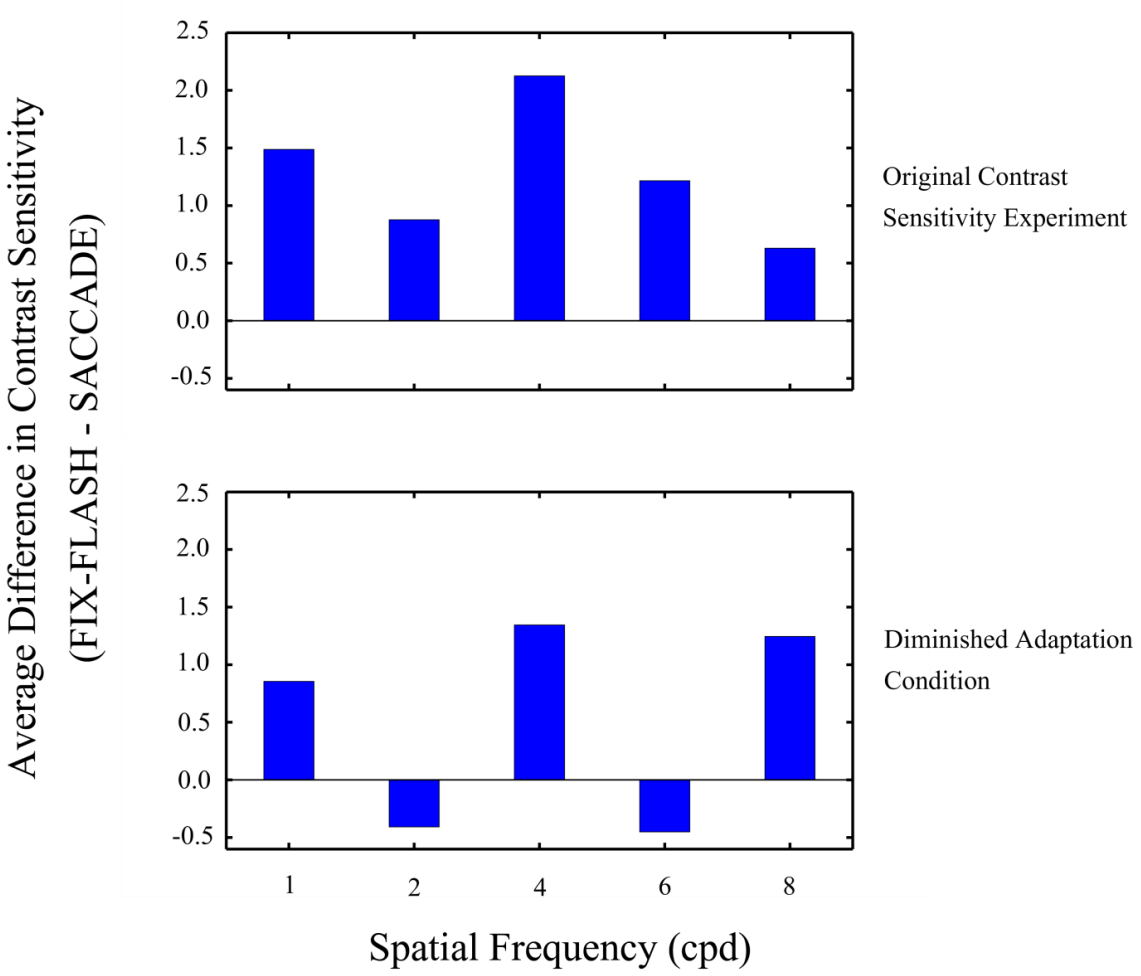

Figure 31 displays bar plots of differences in the FIX-FLASH and SACCADE condition (FIX-FLASH_CS – SACCADE_CS) at the five spatial frequencies tested in Monkey F. The upper panel shows average differences in CS from the original Contrast Sensitivity Experiment, while the lower panel shows average CS differences in the Diminished Adaptation Condition. Positive values mean that the CS values were, on average, better in the FIX-FLASH condition; negative values mean that the CS values were better in the SACCADE condition. Values close to zero mean that there was no clear difference in the average CS between the FIX-FLASH and SACCADE conditions. The upper panel was created from 51 behavioral sessions, and the lower panel was created from 24 sessions.

By subtracting the CS values in the SACCADE condition from the CS values in the FIX-FLASH condition, within session, the resulting value represents the difference in sensitivity between the two conditions. To compare across days when the stimulus

location was varying in eccentricity, taking the average of this difference is a more fair way than to simply create a CS function. The data in Figure 31 reinforce two important findings: 1) Contrast sensitivity is better in the FIX-FLASH condition than the SACCADE condition when there is a natural scene background. 2) This difference in sensitivity is not as strong, and not even present at all SFs, when a grey buffer patch is placed in the RF at the first fixation location (Diminished Adaptation Condition).

Another way to plot this data is to simply average the CS values between sessions. Though this is less careful in terms of controlling for stimulus differences between sessions, it yields a simple line plot that displays the general trends. Figure 32 shows one such plot from Monkey F (same data as what was used to calculate differences in Figure 31).

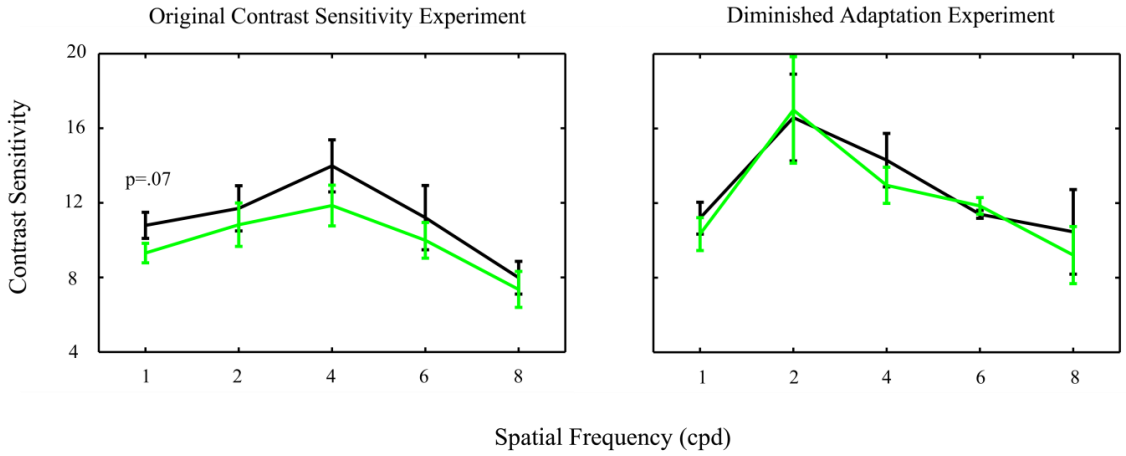

Figure 32 displays the average contrast sensitivity values across all the behavioral sessions from Figure 28 in Monkey F. Black lines represent the CS values in the FIX-FLASH condition while green lines represent CS in the SACCADE condition. Error bars are SE of the mean CS value at a specific spatial frequency. The largest difference, at SF=1cpd in the Contrast Sensitivity Experiment, is not significant from a t-test (p=.0726), though the general trend is clear that CS shows more difference between conditions in the original Contrast Sensitivity Experiment compared with the Diminished Adaptation Experiment.

Note that there is considerable variation in CS values day-to-day, which is partly what makes Figure 32 so important: despite stimuli changing between sessions, the overall trend of better CS in FIX-FLASH conditions is still apparent. Also important to recall is that these plots are not CSFs, they are line plots presenting the simple average of CS values over many days of behavioral recording. One benefit to examining this plot is that we can easily observe an important trend between the two experiments here. In the Diminished Adaptation Experiment, when a grey buffer patch was placed in the RF at the first fixation location, the CS values at every individual SF become higher compared to the original contrast sensitivity experiment. Though this finding does not account for differences in eccentricity (which certainly affects sensitivity), it does support our claim that the adaptation effect occurring in the first 400ms fixation is strong enough to affect CS in both conditions after a saccade.

The largest difference in CS, at 1cpd in the Contrast Sensitivity Experiment, was not significant below p=.05; however, this average CS plot is not the gold standard of contrast sensitivity measurement. When CS is measured in a research subject, it is always shown in a single contrast sensitivity function, like those displayed in Figure 11. In those figures, each individual CS value comes from a psychometric fit after many hundreds of trials at a specific SF. It is rare for a CS measure to be taken many times over at specific SFs like is shown here. Thus, the fact that no significant differences are seen in Figure 32 does not undermine the main finding that CS is better in the FIX-FLASH condition compared to the SACCADE condition in the Contrast Sensitivity Experiment.

Fourier Spectrum of the Natural Image

So far, the fact that the increase in CS during the FIX-FLASH condition occurs most strongly at low SFs has been explained by claiming that the natural scene used in these experiments is dominated by low spatial frequencies. Thus, in the FIX-FLASH condition, when the RF sits over a grey patch for 150ms, any adaptation effects that may have occurred in the RF at the first fixation site will have had time to wash away. This claim depends on the natural image actually showing a 1/f-like distribution of power as spatial frequency increases. Below is an image of the natural scene used in the experiments and its 2D power spectrum.

Natural Image Used

2D Fourier
Power Spectrum

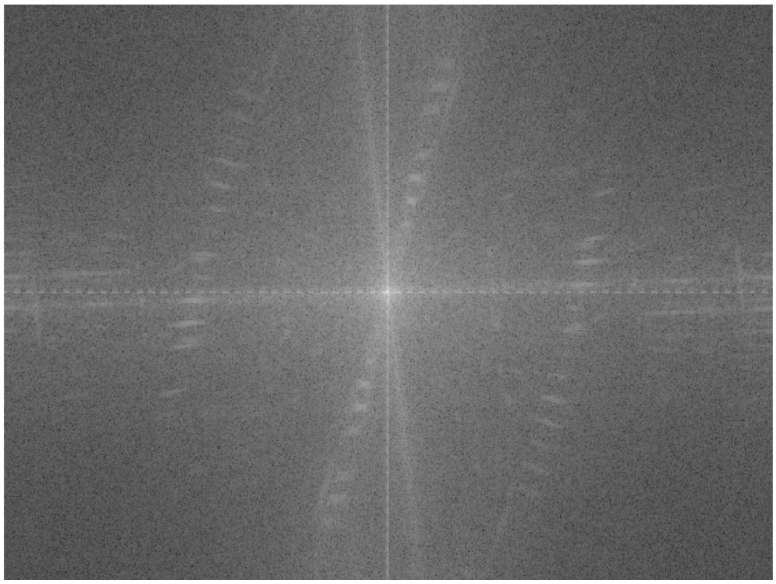

Figure 33. The upper image is the natural scene picture used as the background during all experiments (grey buffer patches not present). The lower image is the 2D power spectrum of the natural scene. This lower panel shows power at spatial frequencies represented as low (origin) to highest (edges), and also contains information about orientations (represented in 360 degrees around the image) where this power is strongest.

This figure demonstrates that the natural scene used in the experiments here does follow the general 1/f-like falloff of power with spatial frequency, though the specific values aren't calculated here. To better demonstrate that this is true, a 3D plot of the Fourier spectrum is shown in Figure 34.

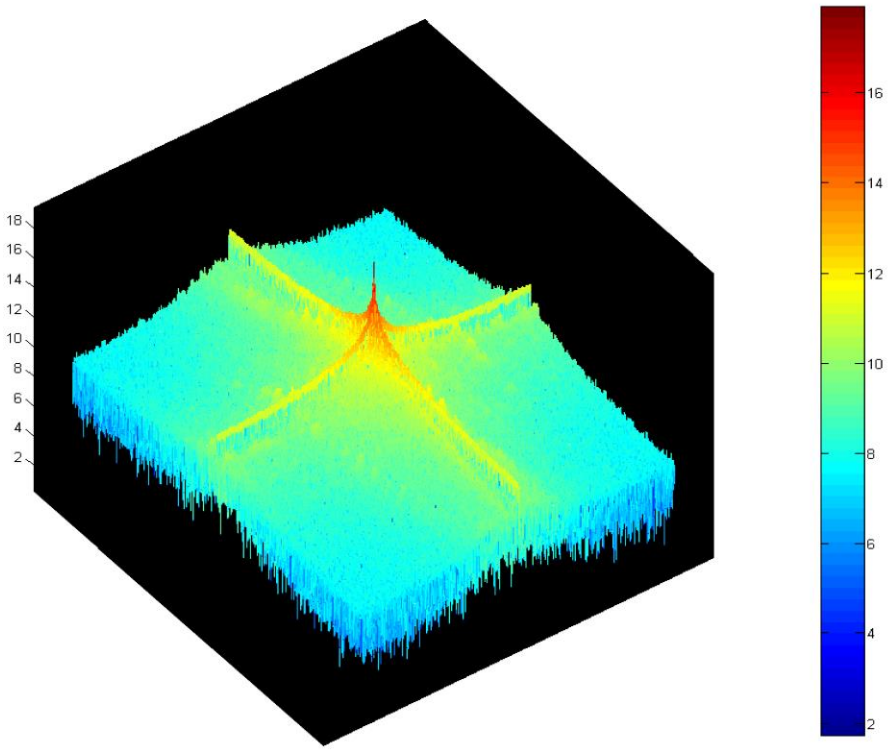

Figure 34 displays a 3D-meshed version of the power spectrum plotted in Figure 31. The brighter colors represent higher power, and here show a fast fall-off of power as spatial frequency (represented as eccentricity from the center of the figure) increases.

The exact spatial frequencies that were tested in the CS tasks (1, 2, 4, 6, and 8cpd) aren't shown here. These plots are simply presented to demonstrate that there is a fast falloff of power with increasing spatial frequency, which is close to the rapid falloff seen in most natural images (Field, 1987).

Because most of the RFs studied in these experiments were around 1 degree in size, the overall distribution of power at different spatial frequencies does not actually tell us if the hypothesis about adaptation to low SF content is correct. To truly test that, every individual piece of image content seen by different RFs at the first fixation site would need to be analyzed. Furthermore, orientation of any edges seen by the RF at the first fixation site would need to be taken into consideration. For example, if a V1 unit preferred vertical orientation, and received a horizontal edge in the image structure at the first fixation site, and then was probed with a vertical gabor stimulus, its response may be stronger than if it had adapted to a grey buffer patch at the first fixation site: the unit in Figure 21, showing a strong SACCADE condition response, maybe have experienced this.

In summary, the image used in the experiments does have most power concentrated at lower spatial frequencies, lending credence to the claim that adaptation may be occurring specifically at lower SFs. Currently, nothing more can be said with certainty about the exact effect of the image at the first fixation site on neural responses unless further analysis is performed on the particular image pieces displayed in RFs during the first fixation period of the experiments. However, below, we present psychophysics data to support this belief.

A Human Test of Adaptation Occurring within 400ms

Our main claim from the monkey psychophysics data is that adaptation occurs within the first fixation period of the tasks, in 400ms, and carries across an eye movement to affect perception at the next fixation location. In the previous section it was explained that the exact image content shown at the first fixation site could lead to the differences in CS and neuronal responses seen between FIX-FLASH and SACCADE conditions. One quick test that was performed on the author (JN) was to force adaptation to very specific spatial frequencies using the Contrast Sensitivity Experiment paradigm (Figure 6). However, instead of only showing natural image content at the first fixation site, a sine-wave grating square was presented instead. A single panel from this experimental paradigm is shown below.

Figure 33. A schematic single starting frame is shown from an adaptation test performed on human subject JN. Instead of image content or a grey grating patch shown at the first fixation site (red dot), a sine-wave grating was presented. This grating was set to have the same Root Mean Square (RMS) contrast as the piece of natural image that it covered, which was about 33% RMS here. RMS contrast was used instead of Michelson because it is a more valid measure of contrast in images. RMS contrast is simply the average difference in pixel luminance from the overall average luminance in the image piece.

Figure 35 shows one frame of the adjusted experimental paradigm. All other components of the experiment were the same as what was displayed in Figure 6. There were two versions of this experiment: either the initial adapting gratings were set to be 1cpd or 8cpd. The two resulting CSFs are shown below.

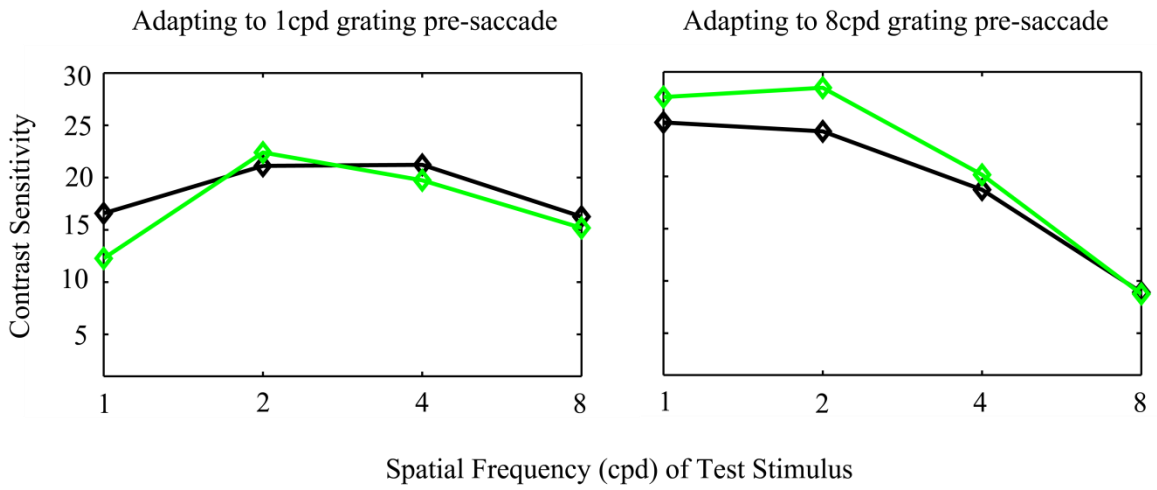

Figure 36 shows contrast sensitivity functions between the FIX-FLASH conditions (black) and SACCADE conditions (green) after adapting to a 1cpd grating stimulus (left panel) or 8cpd grating stimulus (right panel). This CS data is from one human subject (the author) with about 700 trials per SF, still using the contrast threshold at 80% correct as in the earlier CS figures.

The above CSFs show that adaptation does occur within the first 400ms fixation period. In the left panel, when a 1cpd grating is shown during the first fixation period,

the CS differences in FIX-FLASH and SACCADE conditions remain as before (compare to Figure 12) at 1cpd. This particular condition mimics what the natural image contributes: power in low spatial frequencies. Conversely, when the adapting grating is an 8cpd stimulus (right panel), the differences at low SFs in the FIX-FLASH and SACCADE conditions disappears, and even reverses. This fits with the hypothesis that adaptation occurs in the first fixation period and carries across the saccade, affecting sensitivity at the new location. By adapting to higher SFs (8cpd), and then testing with a 1cpd gabor, the SACCADE condition produces better perceptual sensitivity. Also notice that contrast sensitivity clearly increases to both 1cpd and 2cpd gabors when a high frequency grating is shown, further suggesting that adaptation is occurring.

What is potentially confounding in this figure is that, by adapting to high SFs (right panel), the difference in sensitivity values does not reverse for high SFs tested (8cpd). The sensitivity values at 8cpd are higher in the left panel than in the right panel, suggesting some adaptation effect occurs, but the difference between FIX-FLASH and SACCADE conditions is not apparent. If there is adaptation to high SFs (right panel), then we might expect to see the CS values at 8cpd get better in the FIX-FLASH condition (following the logic behind the differences seen at 1cpd after adapting to a 1cpd grating). One possible explanation is that 8cpd could be beyond the range for this fast-acting adaptation effect we're observing. Other studies have reported a lack of sensitivity facilitation from adaptation at high spatial frequencies. For example, a study by De Valois (1976) found little CS threshold elevation at 8cpd after adaptation (her Figure 8), and that study used an adaptation period of 1 minute, much longer than the 400ms period occurring in the tests presented here.

However, despite this, there is still a drop in sensitivity at 8cpd after adapting to an 8cpd grating (compare 8cpd data points in the two panels of Figure 34) – in other words, there does appear to be spatial frequency-specific adaptation occurring even for 8cpd stimuli. Thus, it is not entirely clear why the difference in CS values is not more apparent for 8cpd stimuli presented after adapting to a 1cpd grating.

Discussion

The experiments above show that adding "naturalness" appears to have the power to reduce neuronal responses in macaque V1 and reduce perceptual sensitivity in both macaque and human visual systems. The definition of "naturalness" used here is conditions involving eye movements over a complex natural scene. Furthermore, the cause of this reduction in visual function appears to be rapidly-forming adaptation that occurs during individual fixations and carries across eye movements. This effect has not been studied before and the finding is relevant for typical studies of the visual system, as well as how contrast sensitivity is often measured.

During normal vision, non-human primates make about 2-3saccades per second when viewing natural scenes, with fixation durations close to 400ms (Kayser et al., 2006). This time scale is comparable to the experimental conditions used above, which suggests that adaptation is likely affecting our moment-to-moment perceptual abilities in natural vision, as well as visual cortical responses. If most visual studies are performed in the absence of saccades and natural image backgrounds then findings such as this one are likely to go unnoted.

As was mentioned in the introduction, previous studies have shown conflicting results on this topic. MacEvoy et al., (2008) reported a significantly stronger response from V1 units during natural vision conditions compared with flashed stimuli. Ruiz & Paradiso (2012) reported a significantly weaker response in more natural conditions. The findings outlined here show that both results were accurate: the increase or decrease in responsiveness in more natural conditions depends on rapidly occurring adaptation

effects before the saccade begins. The exact stimulus timing and receptive field locations between the two studies were different. Thus, it is conceivable that the neurons recorded in the 2008 study were being stimulated at the first fixation site by non-preferred spatial frequencies (and perhaps non-optimal orientation of image segments or edges in the scene). In this case, then after the saccade, the neurons would be more responsive to a preferred stimulus at the end of the eye movement. This response would be similar to, or even better than, the response to a flashed stimulus after a forced fixation interval. Meanwhile, in the 2012 study, neurons may have been stimulated by image content that was more similar to the neurons' preferences (for orientation and spatial frequency), which would reduce their response to a preferred stimulus immediately following the saccade. That is the effect that I've shown here, but we believe that the reduction or enhancement of responses following saccades depends primarily on the stimuli in the RFs immediately before the saccade was initiated. Thus, it would not be entirely correct to claim that "natural vision <u>always reduces</u> V1 responses". Rather, rapid adaptation during natural vision changes V1 responses to stimuli after eye movements.

Saccadic effects on vision

Saccadic suppression experiments report very similar findings to our own: perceptual contrast sensitivity is known to fall immediately around the time of an eye movement, and low spatial frequency stimuli are particularly affected by these eye movements while higher spatial frequencies appear relatively immune to any suppression (Burr et al., 1994; Hass & Horwitz, 2011). Below is a commonly-cited figure from Burr et al. (1994)

demonstrating that low spatial frequencies are affected by eye movements, which gives s similar trend to the contras sensitivity functions shown in our results above.

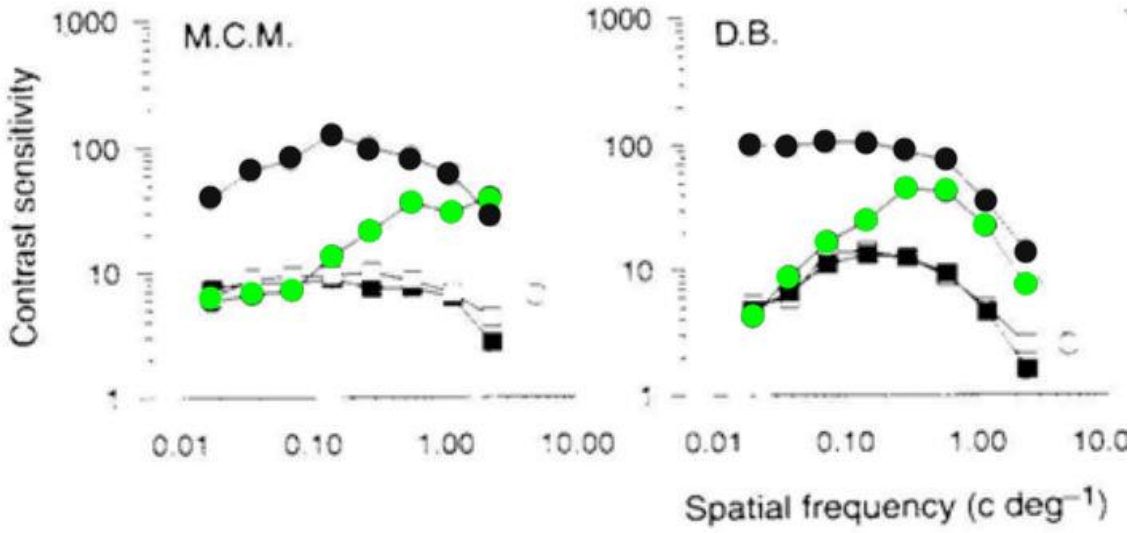

Figure 37 shows CSFs from Burr, Morrone, and Ross (1994), taken from Figure 1 of their study. Contrast sensitivity is plotted as a function of spatial frequency for two human observers (left and right panels). Green circles denote CS during saccades, and black circles denote CS without saccades – the colors were added to make the plot congruent with the CSFs plotted in figures 11 and 12. In this 1994 study, the experimenters discovered that saccadic suppression only occurs to stimuli of lower spatial frequencies. Square data points represent CS in response to color stimuli, which is not pertinent for us.

Figure 37 shows that contrast sensitivity is selectively affected by saccades at lower spatial frequencies. This finding is similar to our effect, which was also specific to low spatial frequencies. However, saccadic suppression cannot explain our results. The time course of saccadic suppression effects is about 75ms before eye movement onset to 50ms after eye movement end (Diamond et al., 2000), which is much shorter than the duration of our 200ms stimuli. We would expect any saccadic suppression mechanisms to stop functioning by the time our stimuli are turned off. Furthermore, we find that any decreases in contrast sensitivity or neural responses are recovered when we apply a grey

patch at the first fixation in our task during the diminished adaptation condition. In this condition an eye movement is still present, but we did not observe any decrements in CS or neural sensitivity. Lastly, the spatial frequencies of stimuli that are most affected by saccadic suppression are about 1cyc/deg or less (Burr et al., 1994; Ross et al., 2001). Our stimuli ranged from 1-8cyc/deg, and the effects we observed occurred at 1-4cyc/deg. Therefore, our results were not created by saccadic suppression.

Spatial frequency-specific effects

Our experiment shows that contrast sensitivity and V1 responses are lower in more natural conditions for certain spatial frequencies, but not others. As stated above, our results are not explained by saccadic suppression, though saccadic suppression is known to selectively affect low SF stimuli. The low-SF effect that we report here is likely due to our natural scene image. Natural scenes are known to be dominated by low spatial frequency content (Tolhurst et al., 1991; van der Schaaf & van Hateren, 1996), and contrast adaptation in the context of natural scenes has been shown to selectively affect low spatial frequencies after long adaptation periods: in one study (Webster & Miyahara, 1997), experimenters showed that after an initial 5 minute adaptation period of randomly displayed natural scenes there was a decrease in contrast sensitivity in observers that was specific to low spatial frequencies. We believe that our findings result from similar mechanisms, but occur on a much shorter time scale (~400ms) that is on par with natural vision conditions.

Adaptation and fixations

Adaptation to grating patterns is known to affect both contrast sensitivity and visual cortical activity (Blakemore & Campbell, 1969), and occurs on multiple timescales (Webster, 2011; Wark et al., 2009; Baccus & Meister, 2002). We have shown here that quickly-forming adaptation, occurring within the time period of a normal fixation (~400ms), will carry across 7-degree saccadic eye movements and lower CS and V1 cortical responses. Previous studies have shown similar adaptation effects that occur after lengthy viewing of natural images (Webster & Miyahara, 1997) or brief viewing of high contrast gratings (Dragoi et al., 2002); however, none have shown this natural scene effect to occur in the time frame of a normal fixation period and carry across saccades.

In real-world scene viewing, studies report that fixation durations vary from below 50ms to over 1000ms, and average about 330ms in humans (Henderson & Hollingworth, 1999), and average about 380ms in non-human primates (Kayser et al., 2006). The 400ms initial fixation period in our experiments is in the range of normal fixation durations. We have demonstrated that, in this fixation period (plus the saccade latency), the content of the visual scene can induce adaptation. It is also worth noting that our lab previously published a report with qualitatively similar results (reduced neural responses in natural conditions) in which animals began trial with a 300ms fixation period (Ruiz & Paradiso, 2012). Assuming the similar finding results from a similar mechanism to the one reported here, this means that V1 neural adaptation can occur and affect neural responses to stimuli after subsequent eye movements in as short as 300ms.

The potential influence of microsaccades

Microsaccades, or fixational saccades, are small involuntary ballistic eye movements that occur during fixations and have traditionally been defined as having a size less than 12 arcminutes, or about one fifth of a degree, but more recently any eye movement under a full degree in size have been labelled microsaccades (Collewijn & Kowler, 2008;). Some researchers report a decrease in visual function associated with microsaccades (Leopold & Logothetis, 1998; Herrington et al., 2009). In one recent perceptual/physiology experiment, these small eye movements were associated with a decrease in perceptual performance as well as a decrease in V1 spiking activity (Hass & Horwitz, 2011). However, other researchers have reported increased sensitivity around the time of microsaccades (Deubel &Elsner, 1986; Martinez-Conde et al., 2000). Thus, it is unknown how exactly microsaccades might affect our results.

In our experiment we require the animals to maintain fixation within a .8 degree window, which is certainly large enough to allow microsaccades; however, the grey buffer patches used are set to be larger than the gabor stimuli such that any eye movement within the fixation window would not allow the receptive field to touch the edge of our patches. In other words, small eye movements during the task would not result in our neurons leaving the stimulus buffer patches. It is still possible that microsaccades may occur over the stimulus itself, but the typical frequency of microsaccades in nonhuman primates is only a few per second (Martinez-Conde et al., 2004, Table 4). Because the stimulus duration is only 200ms, it is unlikely that fixational

saccades can explain the findings of stronger response in the FIX-FLASH condition. Furthermore, we lose the stronger responses in the FIX-FLASH condition with our Diminished Adaptation Experiment. We have no reason to believe that the frequency of microsaccades would change during this control, so they are unlikely be the source of the main findings.

Addendum Experiment: Offset Response Experiment

Background

One ongoing project in our lab is aimed at understanding how much information about eye movements is available in visual cortex. While eye movements clearly affect neural activity in V1 (Green, 1957), more recently some experimenters have been attempting to isolate the usefulness of such effects; i.e., does the visual system actually use saccade-related activity to aid in vision? Is there enough information in V1 about eye movements to determine the direction and size of an upcoming saccade? These types of questions are being pursued in multiple labs (Morris et al., 2013; Morris et al., 2012; Ito et al., 2013;), including our own.

In most of these studies, the goal is to take neural signals in the brain around saccade times and try to predict eye movements in other contexts (and possibly extract metric information about the saccade). The hypothesis in those experiments is simply that "eye movement information is available in visual cortex". These types of studies are often performed with uniform stimulation; either with flickering stimuli or homogenous grey backgrounds. However, as I've described in detail in the main thesis experiments, in normal viewing conditions saccades are typically made across visually complex scenes. Therefore, it is possible that studies of saccade information are ignoring any saccade-related activity that might be stimulus-induced during normal vision.

Specifically, there's a possibility that a lot of information about eye movement start or end times might arise from neural activity related to stimuli after a previous eye movement. To test this possibility I take advantage of a unique form of response in V1 neurons: the response to a stimulus offset.

Offset responses, sometimes called "off responses" and "after-discharges", are response transients that occur when a stimulus disappears from a receptive field. They are known to occur in visual cortical neurons (Richmond et al., 1999; Xiao-Jian et al., 2012; Lian et al., 2008), and it has been reported that these responses might actually play a role in stimulus visibility (Macknik & Livingstone, 1998). If these offset responses occur to stimuli turned off inside of a V1 receptive field, then might they also occur with an eye movement bringing an RF away from the stimulus? In other words, are offset responses a part of natural vision? This is the question tested here: Can offset responses be induced by a saccadic eye movement? If so, then these responses do not only matter for processing visual information, but may also provide the visual system with a signal that an eye movement has just begun.

Paradigm

One monkey (Monkey F from earlier studies) was trained to fixate a point on a homogenous grey screen (luminance ~55cd/m^2). After a 200ms hold period, a stimulus was flashed on inside of the RF for 400ms. After 400ms the stimulus either flashed off (FlashOff condition), or the monkey received a saccade target presented 7-degrees to the right of the central fixation point. In this EyeOff condition, the monkey was required to

move his eyes to the saccade target within 150ms, and hold fixation there for at least another 100ms. The paradigm is shown below in Figure A-1.

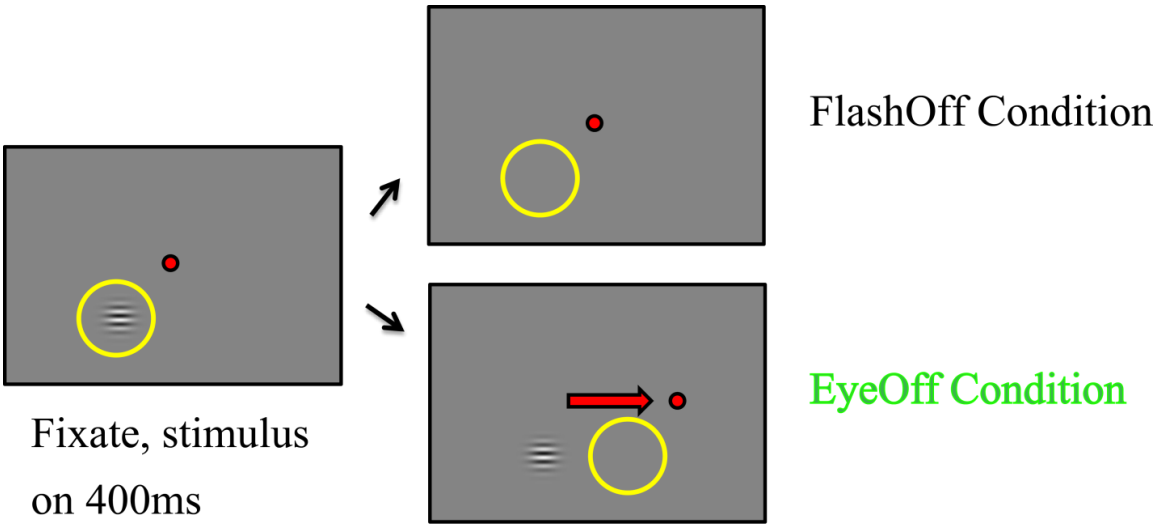

Figure A-1 shows the paradigm for the Offset Response Experiment. Trials began after the animal fixated a central red spot. After 200ms, the stimulus was flashed inside of the RF for 400ms (left panel). At this point, either the stimulus flashed off (FlashOff condition, top right panel) and the animal was rewarded, or a saccade target was presented 7-degrees to the right of the central fixation spot (EyeOff condition, lower right panel). In the EyeOff condition, if the monkey moved his eyes to the saccade target within 150ms, and held it for another 100ms, then he was rewarded. Thus, the only difference in conditions is whether the stimulus flashes off after 400ms or whether an eye movement causes the RF to leave the stimulus after 400ms.

Note that, with this paradigm, the exact amount of time that the stimulus spends in the RF may vary. In the EyeOff condition, the saccade target is presented after 400ms of gabor stimulation in the RF; however, because the stimulus is not turned off at that time, the entire stimulus period is actually 400ms + the saccade latency. Furthermore, though the Monkey F's saccades typically occurred within 120ms, each trial's saccade latency could be slightly different.

Methods

Single units were isolated using the criteria for the above studies of contrast sensitivity. In fact, this experiment was only run after a successful session of contrast sensitivity testing in Monkey F. The stimulus presented was a gabor of 80% contrast with preferred size and spatial frequency. In the first half of recordings (~15 sessions), the orientation of the gabor was always set to be horizontal. The rationale for forcing the horizontal orientation was that it would reduce the amount of change in luminance at the start of the saccade in the EyeOff condition. In the second half of recordings the stimulus orientation was always set to be the preferred orientation for the unit being studied.

One important thing to note is that, in the figures here, I do not align the data "fairly" between conditions. To truly measure the offset responses in the FlashOff and EyeOff trials, the plots should be aligned by stimulus offset time (in the FlashOff Condition) and by stimulus offset in the RF during the EyeOff condition. In order to do that, each individual trial's eye position in the EyeOff condition needs to be measured to find the exact time when the RF left the stimulus. That data is stored but has not been examined yet. However, as can be seen in the Results Section, even without this proper alignment there still exists a clear offset response in the EyeOff conditions.

Results

Of the 30 units recorded on this task, 17 (56.7%) showed a second response peak to the stimulus offset in the FlashOff Condition. These responses have not been sorted by significance from baseline response, but all conditions had between 50-80 trials. Figure

A-2 shows an example of a unit with a strong offset response in the FlashOff Condition, but with no clear offset response in the EyeOff condition.

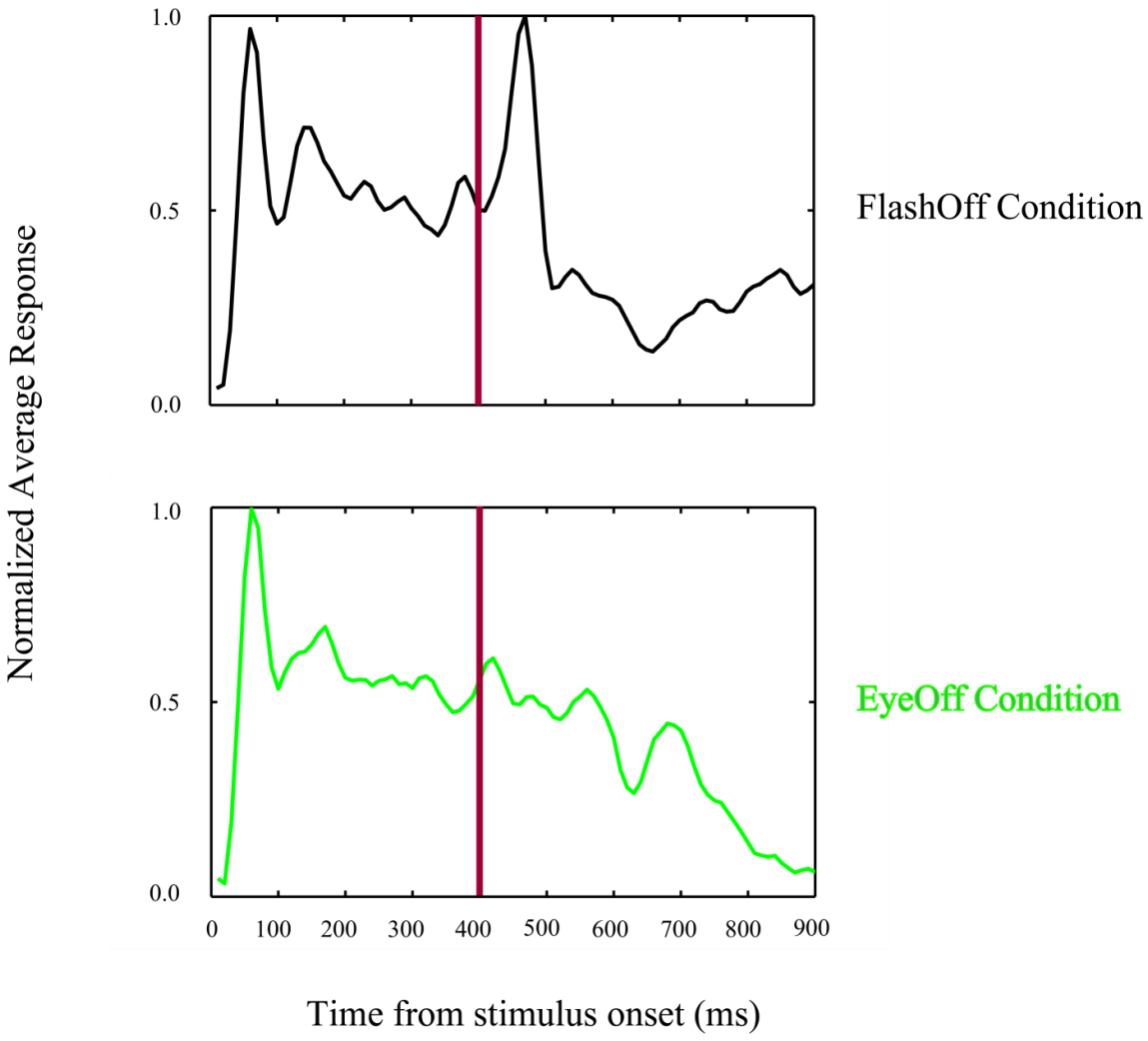

Figure A-2 shows the average normalized response of one unit between the FlashOff Condition (top panel) and EyeOff Condition (bottom panel) as a function of time from stimulus onset in the RF. The red line at 400ms denotes the time when the stimulus was turned off in the FlashOff Condition, or when the saccade target appeared in the EyeOff Condition.

The unit in Figure A-2 shows a clear offset reponse in the FlashOff condition, but no clear offset response caused by an eye movement. However, some neurons (9/30) showed at least a partial offset response in the EyeOff condition. Figure A-3 shows one such unit.

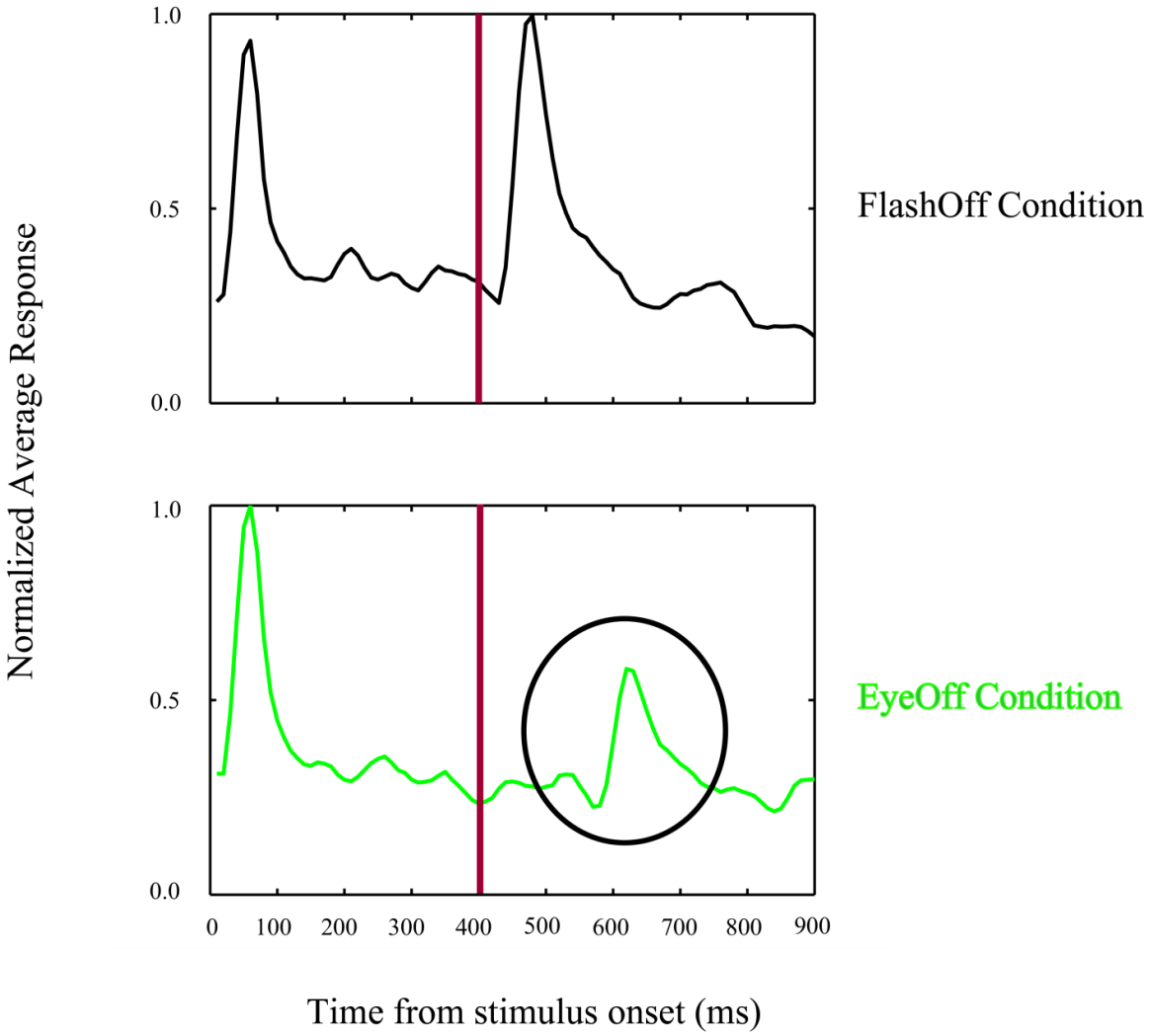

Figure A-3 shows one unit displaying an offset response caused by the eye movement. The average normalized response in the FlashOff condition is shown in the upper panel, and the response of the EyeOff condition is shown in the lower panel. The red line indicates the time at which the stimulus disappeared in the FlashOff condition, and the time that the peripheral saccade target appeared in the EyeOff condition. The black circle in the lower panel is present to highlight the offset response seen in the EyeOff condition.

The offset response in the FlashOff condition is very large, about the same size as the onset response. This unit also showed an offset response in the EyeOff Condition highlighted in the circled section of A-3's lower panel, though this circled response is not nearly as strong as in the FlashOff condition.

Some units showed offset responses in the FlashOff condition, some did not, and some showed offset responses in both conditions. An averaged population figures (N=30 units) is shown below in Figure A-4.

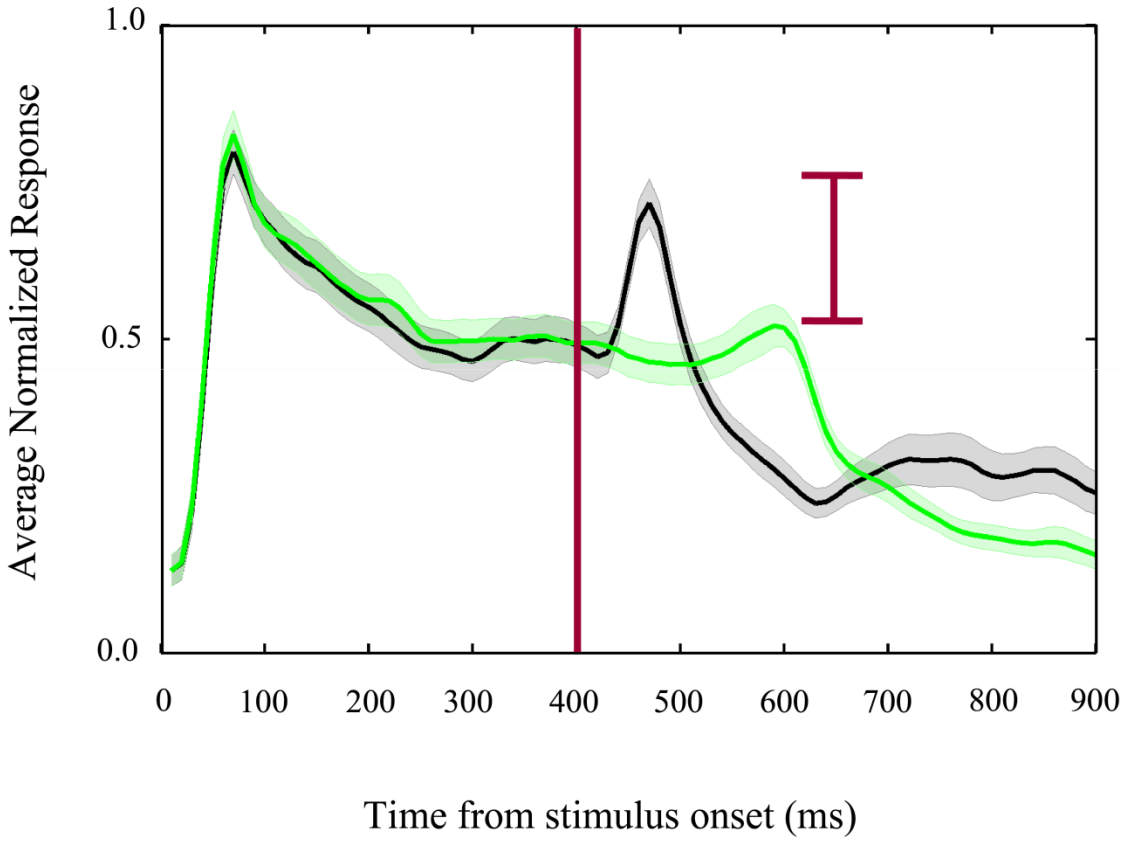

Figure A-4 shows the average normalized population response from 30 V1 units recorded in Monkey F. Black shows responses in the FlashOff Condition and green shows responses in the EyeOff Condition. Shaded area is SE of the mean normalized response across units. The red line at 400ms represents the time when the stimulus was flashed off in the FlashOff Condition, or the time that the saccade target appeared in

the EyeOff Condition. The red I-bar is present to highlight the difference in sizes between the offset responses in the two conditions.

Figure A-4 demonstrates that, while not all units showed an offset response caused by an eye movement, there is still a noticeable peak caused by the saccade away from the gabor stimulus. Also interesting is the size difference between the peaks by the I-bar shown in the figure; this difference could have relevance for saccadic suppression, which will be discussed below.

Discussion and Conclusion

The data shows that eye movements can indeed induce offset responses in V1 neurons. Not all neurons display this type of response, and none of the units studied showed EyeOff responses similar in size to the ones seen when the stimulus was flashed off. This type of response has been linked with visual perception (Macknik & Livingstone, 1998), but has never been examined in the context of eye movements. The importance of this finding is that, if the visual system is looking for signals about eye movements, an offset transient occurring at the start of an eye movement may be one type of natural signal that the visual system receives about a saccade. This information could be used in conjunction with other signals about saccades originating from eye movement centers of the brain (such as FEF and SC) to aid in visual continuity. However, all that has been tested here is that these offset responses can be caused in V1 by saccades. Further experiments would be needed before one could make any claim about the usefulness of these signals in perception and in providing saccade information.

Another potentially important piece of information from this experiment is that the offset response in the EyeOff condition is clear but is not as large as the offset response in the FlashOff condition (see red I-bar in Figure A-4). Assuming the saccade causes an offset on a similar timescale to the FlashOff Condition, this response could be expected to be equal in size between conditions. One possible reason that the off response is weaker with a saccade is that saccadic suppression may be affecting this activity: a saccade-related signal could be changing the overall responsiveness to a stimulus leaving the RF. Thus, these offset responses or "after discharges" could have implications for the testing of saccadic suppression effects in V1.

One ideal future experiment would be to measure this response in a new condition where the stimulus slides from the receptive field at the speed of a saccade. Thus, the retinal image motion of the saccade would be present, but there would be no saccade-related signal issued to V1. This would allow for a dissociation of how much these offset responses depend on an eye movement signal vs visual input.

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