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Constraints on the mechanism of short-term adaptation in area MT

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Constraints on the mechanism of
short-term adaptation in area MT

by

Nicholas Priebe

DISSERTATION

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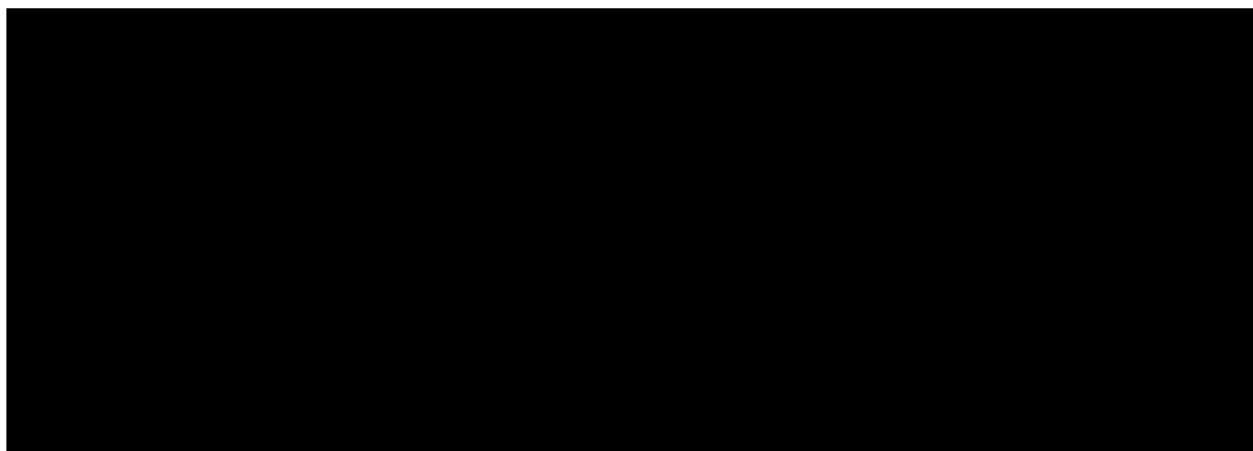
in

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in the

GRADUATE DIVISION

of the

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Date   University Librarian

Degree Conferred: ....

Dedicated to my mother,

Ann Priebe

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Constraints on the mechanism of

short-term adaptation in area MT

Nicholas Priebe

Neurons in a motion-sensitive area of extrastriate cortex, MT, have two phases of response to a step of target speed: a transient and a sustained phase. The transition from transient to sustained firing is a form of adaptation. In the present experiments, we constrain the possible biological sources of the dynamics in the MT neuron's response.

The adaptation of an MT neuron's response to constant motion could be ascribed to three classes of mechanisms. First, the change in the responsiveness of MT neurons may be due to interactions within the network of neurons in area MT. Second, the change in the responsiveness of MT neurons to a constant motion stimulus could be due to mechanisms local to the recorded neuron. Excitatory pyramidal neurons often show an activity-dependent reduction in gain when stimulated with steps of stimulus current. Finally, the reduction of responses may be due a reduction in the inputs from V1 neurons to area MT.

Using a paradigm in which we assess the effects of an adapting stimulus on the subsequent response to a test stimulus we were able to measure the direction, speed and spatial selectivity of the adaptation mechanism. The tuning of the adaptation mechanism is consistent with a mechanism for adaptation that is not based upon the neuron's activity or on a reduction in the inputs from V1, but based on the interactions of neurons within area MT.

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General Introduction

Our perception of the world is not simply based upon sensory information currently available from our environment but also on the context in which we receive information. In particular, our perception of visual motion relies both on the temporal and spatial setting in which that motion appears (Welch et al., 1997) and may be changed by both long- and short-term exposure to motion. For example, long-term exposure to motion in one direction induces a perception of motion for stationary stimuli (Wohlgemuth, 1911; Schrater and Simoncelli, 1998).

Changes in the perception of motion are based on altered responses of neurons in the visual system. Macaque visual area MT contains neurons that respond selectively to the direction, speed and spatial position of motion (Dubner and Zeki, 1971; Maunsell and Van Essen, 1983). At the onset of motion, many MT neurons respond with a transient high firing rate that settles to a lower firing rate after 30-50 ms and continues at this level for the duration of the stimulus motion. While MT neurons initially respond briskly, their responses adapt to a lower firing rate.

We use the term adaptation to describe the responses of MT neurons to steps of visual motion because the sensitivity of neurons to a stimulus is altered by the history and context of the stimulus presentation. In the same manner, psychophysicists use the term adaptation to indicate a change in the sensitivity or discriminability of observers making perceptual judgments.

These studies focus on the mechanisms of adaptation in motion-sensitive neurons of primate area MT. Previous work has demonstrated that the prior history of motion presentation can dramatically affect the response properties of MT cells

(Lisberger and Movshon, 1999). In this thesis, we make constraints on which candidate mechanism underlies the adaptation by measuring the direction, speed and spatial contexts of motion that induce adaptation in an MT neuron. In these studies we use a "conditioning-test" stimulus protocol to measure the tuning of adaptation observed in area MT. This is an adaptation protocol in which the response to a test stimulus is measured in isolation as well as in the context of a preceding conditioning stimulus.

The adaptation of an MT neuron's response to motion could be ascribed to three classes of mechanisms. First, the change in the responsiveness of MT neurons may be due to interactions within the network of neurons in area MT. Such interactions could be based upon either an increase of inhibition onto the recorded neuron or a loss of excitation onto the neuron. These interactions may be *independent* (Wörgötter and Koch, 1991; Heeger et al., 1996; Simoncelli and Heeger, 1998) or *dependent* on the neurons' preferences for direction, speed and spatial location of motion (Nelson et al., 1994; Ferster et al., 1996; Chung and Ferster, 1998; Troyer et al., 1998).

Second, the change in the responsiveness of MT neurons to a constant motion stimulus could be due to mechanisms local to the recorded neuron. Excitatory pyramidal neurons often show an activity-dependent reduction in gain when stimulated with steps of stimulus current (McCormick et al., 1985). In this case, spiking in the recorded neuron opens a hyperpolarizing channel, thus reducing its ability to fire at high rates.

Finally, the reduction of responses may be due to a reduction of the firing in the input from V1 neurons to area MT. MT neurons receive input directly from V1 (Movshon and Newsome, 1996) and respond transiently to flashed bars (Kulikowski et al., 1979; Tolhurst et al., 1980; Nelson, 1991). A reduction in the amount of input that MT neurons receive could come about either due to a reduction in the responses of V1 neurons or a reduction in the efficacy of the synapses that V1 neurons make onto MT neurons (Abbott et al., 1997).

In the first chapter, the effects of conditioning motions of varying direction or speed on the response of a neuron to test motion in the neuron's preferred direction and speed are measured. We demonstrate that while the direction tuning of adaptation is similar to the direction tuning of the neuron, the speed tuning of adaptation does not necessarily match the speed tuning of the neuron. The second chapter investigates the effect of conditioning motion that is spatially segregated from the test motion. We demonstrate in this study that adaptation transfers over spatial distances larger than the size of the receptive fields of input neurons in V1, establishing that the adaptation observed in area MT is derived from a stage after V1. Not only do we show that adaptation transfers over spatial distances larger than a V1 receptive field, we establish that the spatial extent for adaptation is not on the scale of the receptive fields of downstream motion processing areas such as area MST. In the final chapter we investigate the relationship between the activity of the neuron and the amount of adaptation induced by that activity. We do not find a significant link between the activity of the neuron and a subsequent suppression of responses.

Therefore, we conclude that the adaptation to motion observed in area MT is derived from interactions between neurons within area MT. These interactions are not random, but are tuned in terms of space, direction and speed in the same manner that the neurons' responses are tuned for space, direction and speed.

References

Abbott LF, Varela JA, Sen K, Nelson SB (1997) Synaptic depression and cortical gain control. Science 275:220-224.

Chung S, Ferster D (1998) Strength and orientation tuning of the thalamic input to simple cells revealed by electrically evoked cortical suppression. Neuron 20:1177-1189.

Dubner R, Zeki SM (1971) Response properties and receptive fields of cells in an anatomically defined region of the superior temporal sulcus in the monkey. Brain Research 35:528-532.

Ferster D, Chung S, Wheat H (1996) Orientation selectivity of thalamic input to simple cells of cat visual cortex. Nature 380:249-252.

Heeger DJ, Simoncelli EP, Movshon JA (1996) Computational models of cortical visual processing. Proceedings of the National Academy of Sciences of the United States of America 93:623-627.

Kulikowski JJ, Bishop PO, Kato H (1979) Sustained and transient responses by cat striate cells to stationary flashing light and dark bars. Brain Research 170:362-367.

Lisberger S, Movshon J (1999) Visual motion analysis for pursuit eye movements in area MT of macaque monkeys. Journal of Neuroscience 19:2224-2246.

Maunsell JHR, Van Essen DC (1983) Functional properties of neurons in middle temporal visual area of the macaque monkey. I. selectivity for stimulus direction, speed, and orientation. Journal of Neurophysiology 49:1127-1147.

McCormick DA, Connors BW, Lighthall JW, Prince DA (1985) Comparative electrophysiology of pyramidal and sparsely spiny stellate neurons of the neocortex. Journal of Neurophysiology 54:782-806.

Movshon JA, Newsome WT (1996) Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. Journal of Neuroscience 16:7733-7741.

Nelson S, Toth L, Sheth B, Sur M (1994) Orientation selectivity of cortical neurons during intracellular blockade of inhibition. Science 265:774-777.

Nelson SB (1991) Temporal interactions in the cat visual system. I. Orientation-selective suppression in the visual cortex. Journal of Neuroscience 11:344-356.

Schrater P, Simoncelli E (1998) Local velocity representation: evidence from motion adaptation. Vision Research 38:3899-3912.

Simoncelli EP, Heeger DJ (1998) A model of neuronal responses in visual area MT. Vision Research 38:743-761.

Tolhurst DJ, Walker NS, Thompson ID, Dean AF (1980) Non-linearities of temporal summation in neurones in area 17 of the cat. Experimental Brain Research 38:431-435.

Troyer TW, Krukowski AE, Priebe NJ, Miller KD (1998) Contrast-invariant

orientation tuning in cat visual cortex: Thalamocortical input tuning and

correlation-based intracortical connectivity. Journal of Neuroscience 18:5908-

5927.

Welch L, Macleod DI, Mckee SP (1997) Motion interference: perturbing perceived

direction. Vision Research 37:2725-2736.

Wohlgemuth A (1911) On the aftereffect of seen movement. Journal of Psychology

1:1-117.

Wörgötter F, Koch C (1991) A detailed model of the primary visual pathway in the

cat: comparison of afferent excitatory and intracortical inhibitory connection

schemes for orientation selectivity. Journal of Neuroscience 11:1959-1979.

Chapter 1

The direction and speed selectivity of short-term adaptation in macaque area MT

Abstract

Neurons in a motion sensitive area of extrastriate cortex, MT, have two phases of response to a step of target speed: a transient and a sustained phase. The transition from transient to sustained firing is a form of adaptation. We compared the tuning of the adaptation process with that of the cells' overall response by using a set of condition/test experiments with 64 ms pulses of motion. A test pulse of motion of preferred speed and direction was preceded by a conditioning pulse whose speed and direction varied. The time course of the effect of the conditioning stimulus was also measured by changing the temporal interval between conditioning and test pulse. For separation intervals less than 128 ms, the response to the test motion was suppressed by conditioning motion in the same direction and enhanced by conditioning motion in the opposite direction. The degree of suppression produced by prior motion in the preferred direction depended upon the speed of the conditioning pulse. Although some cells were suppressed by conditioning motion at the cells' preferred speed, others were suppressed by conditioning motions slower or faster than their preferred speed. Two observations indicate that the adaptation mechanism responsible for the transition from transient to sustained firing occurs in area MT and not upstream of area MT. First, the speed tuning of the adaptation mechanism did not always match the speed tuning of the neuron. That is, the adaptation mechanism did not depend on the activation of the neuron by preceding stimuli. Second, the tuning of the directionally-specific modulation was broader than the direction tuning of cells. We suggest that adaptation in MT cells is a property of the neural circuit and is not due exclusively to cell or synapse specific mechanisms.

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Introduction

Our perception of the world is not simply based upon sensory information currently available from our environment but also on the context in which we receive information. For example, our perception of motion is governed by both the temporal and spatial setting in which that motion appears (Wohlgemuth, 1911; Welch et al., 1997). The state of our motion "sensors" can be changed by both long- and short-term exposure to motion and these modifications reduce our ability to report accurate information about motion. For example, long-term exposure to motion in one direction induces a perception of motion in stationary stimuli (Wohlgemuth, 1911; Schrater and Simoncelli, 1998), while shorter presentations of motion (<200 ms) alter the discrimination of direction of motion for a brief time (Nakayama, 1985). Contextual information not only affects our perception of visual motion, but stimulus context is known to alter our perception of the orientation of bars (Gibson and Radner, 1937), the pitch of a sound (Stevens and Davis, 1938) and the position of an object on the arm (Kilgard and Merzenich, 1995).

What underlies the effect of context and recent sensory history on perception? The responses of neurons in sensory pathways also depend on the context of stimulus presentation. In the visual pathway, retinal ganglion cells (Victor, 1987; Kaplan et al., 1993), lateral geniculate cells (Saul and Humphrey, 1990) and cells in primary visual cortex (V1) (Kulikowski et al., 1979; Tolhurst et al., 1980; Nelson, 1991a; Muller et al., 1999) all respond dynamically to changes in luminance. Many neurons respond vigorously at the onset of the change in luminance, but respond less to its

continued presence. The overall gain of cortical responses is subject to modification

by altering the average contrast of gratings over long presentations (Ohzawa et al.,

1985; Carandini and Ferster, 1997). Neurons in the auditory and somatosensory

cortices also respond vigorously at the onset of a stimulus, but their responses settle

to a lower sustained rate of firing for the duration of the stimulus presentation

(Recanzone et al., 1992; Brosch and Schreiner, 1997). We use the term adaptation for

this alteration in the response properties of neurons because the magnitude of

neurons' responses to stimuli is altered by the history and context of the stimulus

presentation.

Macaque visual area MT contains neurons that respond selectively to the

direction, speed and spatial position of motion (Dubner and Zeki, 1971; Maunsell and

Van Essen, 1983). At the onset of motion, many MT neurons respond with a

transient high firing rate that settles to a lower firing rate after 30-50 ms and

continues at this level for the duration of the stimulus motion. The neuron's response

to motion therefore depends on its prior sensory history. While MT neurons are

initially able to respond briskly, they adapt to a lower firing rate. The transient

responses are interesting from a functional standpoint as well because they could

possibly be used to determine the acceleration of a moving visual stimulus (Lisberger

and Movshon, 1999).

In the present experiments, we aim to constrain the possible biological sources

of the dynamics in the MT neuron's response to presentations of constant motion.

The adaptation of an MT neuron's response to motion could be ascribed to three

classes of mechanisms. First, the change in the responsiveness of MT neurons may

be due to interactions within the network of neurons in area MT. Such interactions could be based upon either an increase of inhibition onto the recorded neuron or a loss of excitation onto the neuron. These interactions may be *independent* (Wörgötter and Koch, 1991; Heeger et al., 1996; Simoncelli and Heeger, 1998) or *dependent* on the neurons' preferences for direction, speed and spatial location of motion (Nelson et al., 1994; Ferster et al., 1996; Chung and Ferster, 1998; Troyer et al., 1998).

Second, the change in the responsiveness of MT neurons to a constant motion stimulus could be due to mechanisms local to the recorded neuron. Excitatory pyramidal neurons often show an activity-dependent reduction in gain when stimulated with steps of stimulus current (McCormick et al., 1985). In this case, spiking in the recorded neuron opens a hyperpolarizing channel, thus reducing its ability to fire at high rates. This mechanism is akin to feedback inhibition, but relies only on the neuron's own activity.

Finally, the reduction of responses may be due a reduction in the inputs from V1 neurons to area MT. MT neurons receive input directly from V1 (Movshon and Newsome, 1996) and do respond transiently to flashed bars (Kulikowski et al., 1979; Tolhurst et al., 1980; Nelson, 1991a). A reduction of the amount of input that MT neurons receive could come about either due to a reduction in the responses of V1 neurons or a reduction in the efficacy of the synapses that V1 neurons make onto MT neurons (Abbott et al., 1997).

The present paper focuses on the mechanism of adaptation in MT neurons, whereas previous work has shown that the prior history of motion presentation can

dramatically affect the response properties of MT neurons (Lisberger and Movshon, 1999). By measuring the tuning of the adaptation, that is, the direction, speed and spatial contexts of motion that induce adaptation, we can make constraints on candidate mechanisms. In this and the following two papers we use a "condition-test" stimulus protocol to measure the tuning of adaptation observed in area MT. In this protocol, the response to a test stimulus is measured in isolation as well as in the context of a preceding conditioning stimulus. In the current paper, we measure the effect of conditioning motions with varying direction or speed on the response of a neuron to test motion in its preferred direction and speed. We demonstrate in this paper that while the direction selectivity of adaptation is similar to the direction tuning of the neuron itself, the speed tuning of adaptation does not necessarily match the speed tuning of the neuron. Therefore we conclude that these data are consistent with a mechanism for adaptation that is not based upon the neuron's activity, but based on the interactions of neurons within area MT.

Materials and Methods

Physiological preparation

Single-unit microelectrode recordings were made in area MT of anesthetized, paralyzed macaque monkeys (*Macaca fascicularis*). After the induction of anesthesia with ketamine (5-15 mg/kg) and midazolam (0.7 mg/kg), cannulae were inserted into the saphenous vein and the trachea. The animal's head was then fixed in a stereotaxic frame and the surgery was continued under an anesthetic combination of isoflurane (2%) and oxygen. A small craniotomy was performed directly above the superior temporal sulcus (STS) and the underlying dura was reflected. The animal was maintained under anesthesia using an intravenous opiate, sufentanil citrate (8-16 micrograms/kg/hr), for the duration of the experiment. To minimize drift in eye position, paralysis was maintained with an infusion of vecuronium bromide (Norcuron, 0.1 mg/kg/hr) for the duration of the experiment and the animal was artificially ventilated with medical grade air. Body temperature was kept at 37°C with a thermostatically controlled heating pad. The electrocardiogram, electroencephalogram, autonomic signs and rectal temperature were continuously monitored to ensure the anesthetic and physiological state of the animal. The pupils were dilated using topical atropine and the corneas were protected with +2D gas-permeable hard contact lenses. Supplementary lenses were selected by direct ophthalmoscopy to make the lens conjugate with the display. The locations of the foveae were recorded using a reversible ophthalmoscope.

Tungsten-in-glass electrodes (Merrill and Ainsworth, 1972) were introduced

by a hydraulic microdrive into the anterior bank of the superior temporal sulcus (STS)

and were driven down through the cortex and across the lumen of the STS into area

MT. Location of unit recordings in MT was confirmed by histological examination

of the brain after the experiment, using methods described in Lisberger and Movshon

(1999). After the electrode was in place, agarose was placed over the craniotomy to

protect the surface of the cortex and reduce pulsations. Single units were isolated

using a dual window discriminator (Bak Electronics, DDIS-1) and action potentials

were amplified conventionally and displayed on an oscilloscope. Both a filtered

version of the neural signals and a tone indicating the acceptance of a waveform as an

action potential were played over a stereo audio monitor and the time of each

accepted waveform was recorded for subsequent analysis. The recording sessions

lasted between 84 and 120 hours. The units included in this study are from 29

electrode penetrations at different sites in 11 monkeys.

All methods for anesthetized monkeys had received prior approval by, and

were in compliance with, the regulations of the *Institutional Animal Care and Use*

Committee at UCSF.

Stimulus Presentation

After isolating a single unit in area MT, its receptive field was mapped on a

tangent screen by hand. We recorded the spatial position of each single unit's

receptive field and, for the majority of neurons, recorded the size of the minimum

response field. All of the neurons reported in this paper had receptive field centers within 10° of the fovea.

After the receptive field location was determined, a mirror was positioned such that a random dot texture on a display oscilloscope fell within the receptive field of the isolated neuron. Visual stimuli were then presented on an analog oscilloscope (Hewlett-Packard models 1304A and 1321B, P4 phosphor), using signals provided by digital-to-analog converter outputs from a PC-based digital signal processing board (Spectrum Signal Processing). This method affords extremely high spatial and temporal resolution, allowing a frame refresh rate of 500 or 250 Hz and a spatial resolution of 64K by 64K pixels. The apparent motion created by our display is effectively smooth at these sampling rates (Mikami et al., 1986; Churchland and Lisberger, 2000). The display was positioned 65 cm from the animal and subtended 20° horizontally by 20° vertically. Experiments were performed in a dimly lit room. Due to the dark screen of the display, background luminance was beneath the threshold of the photometer, less than one mcd/m^2.

Experiments consisted of a sequence of brief trials with an inter-trial interval of about 700 ms. All trials began with the appearance of a stationary, uniform random dot texture (0.75 dots/deg^2). Because many neurons in MT respond better if the moving texture is surrounded by a field of stationary dots, we used two overlapping textures of the same dot density. A surround texture remained stationary for the duration of the trial, while a texture in the center of the screen moved. For all trials, the textures appeared and were stationary for 256 ms. After that period, the center texture began to move. After the motion completed, the dots remained visible

for an additional 256 ms. Motion in the center texture was used to characterize the preferred direction by moving the texture in eight directions for either 512 or 256 ms. After the preferred direction was identified, the preferred speed of the neuron was measured by moving the center texture in the preferred direction at speeds of 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, and 128°/s. Because neurons in area MT are known to modulate their firing based on the size of the moving texture (Allman et al., 1985a; Allman et al., 1985b), we next measured the size tuning of the single unit by adjusting the size of the center and surround textures such that moving texture subtended 2.5°, 5°, 10°, 15° and 20°. Once the preferred direction, speed and size of each single unit were characterized, the direction and speed selectivity for the short-term adaptation was measured using a condition/test technique (Lisberger and Movshon, 1999). For these experiments, a 64 ms pulse of motion in the preferred direction and speed of the neuron (referred to as "test motion") was preceded by 64 ms of motion that varied in either the direction or speed (referred to as "conditioning motion"). For the condition/test experiments in which the direction of the conditioning motion was changed, the conditioning motion moved at the preferred speed of the neuron. For the condition/test experiments in which the speed of the conditioning motion was changed, the conditioning motion moved in the preferred direction of the neuron. For both the conditioning direction and conditioning speed experiments, the direction and speed tuning of the neuron was measured for the 64 ms stimulus duration, instead of the longer presentations used in the initial characterization of the direction, speed and size tuning of the single unit

For each trial block, trials were sequenced by shuffling the list of possible

trials and presenting each trial at random until all the trials in the list had been

presented. The texture for each trial was generated using a different seed to generate

pseudorandom sequence of initial dot positions. For all of the data shown in this

paper, the minimum number of repeats recorded for the direction, speed and size

tuning of the neuron was 8 (varied from 8-264), and for all additional experiments the

minimum number of repeats was 12.

Data Acquisition and Analysis

Experiments were controlled by a computer program running on a UNIX

workstation. The workstation sent commands to a Pentium PC that both controlled

the stimuli and acquired data. A hardware discriminator was used to convert the

extracellular action potentials to TTL pulses and the time of each pulse was recorded

by the computer to the nearest 10 µs. After each trial, data were sent via the local

area network to the UNIX workstation and saved for later analysis, along with a

record of the commands given to generate the stimulus.

For the single unit data, we aligned the responses to multiple repetitions of the

same stimulus at the onset of target motion and computed the average firing rate as a

function of time. The direction tuning of the single units was measured by first

measuring the peak 32 ms of response to each direction of texture motion. The

average firing during this analysis epoch (usually the first 32 ms after the latency to

respond) for 4 different neurons is shown in Figure 7, and the standard error was

computed by measuring the firing rate during the analysis on a trial-by-trial basis in

the standard fashion. Gaussians were fitted to the direction tuning data using a least squares minimization algorithm in the Statistics Toolkit of Matlab version 5.3 (Mathworks Inc.). The equation was:

$$R(\Theta) = d + a * e^{-\left(\frac{(\Theta - b)^2}{2*c^2}\right)},$$

(1)

where θ indicates the direction of the texture, a is the amplitude of the response, b is the preferred direction, c is the width of tuning and d' is the background firing rate. Confidence intervals for the fit values were then computed by first computing the Jacobian, a matrix which defines how changes in the parameter estimates affect the predictions of the model (Sokal and Rohlf, 1995). After the Jacobian was computed, 95% confidence intervals were also computed. Gaussian functions were also used to fit the direction tuning of adaptation for the condition/test experiments. The response to test motion was measured by first subtracting off the response to the conditioning motion alone, and then measuring the response to the test motion in the same manner as described for the direction tuning.

A similar procedure was used to measure both the speed tuning of the neurons to single 64 ms pulses of motion as well as the modulation of the test response by conditioning motion speed. Instead of using a Gaussian function to fit this data, the following function was employed:

$$G(s) = R_{max} \left(e^{-\left[\frac{\log\left(\frac{s}{\mu_s}\right)}{\sigma_s + \varsigma \log\left(\frac{s}{\mu_s}\right)} \right]^2} - e^{-\left(\frac{1}{\varsigma}\right)^2} \right) + R_{back}$$

(2)

where R_{max} is the maximal firing rate, μ_s is the optimal speed, s is the speed of the stimulus, σ_s is the tuning width, ζ is the skew of the neuron, and R_{back} is the background firing rate of the neuron. To evaluate the significance of the fits made to the modulation of the test response based on the conditioning speed, a nested hypothesis technique was used. We fit both the responses to single pulses of motion and the modulation of the test response with the constraint that the μ_s, σ_s and ζ were the same in both conditions. We then compared the χ^2 of such a fit with the χ^2 of fits in which μ_s was vary between the two conditions. We then evaluated whether allowing μ_s to vary provided fits that were significantly better than when μ_s was fixed. The method was used to determine the significance of the change in preferred speed between the responses to single pulses and the modulation of the test response; all fits shown in the figures were not made under any constraints. The quality of the fits was excellent for both the direction and speed tuning of the neurons.

Results

The response to steps of motion of many neurons in area MT contains a short period of high firing followed by a period of lower sustained firing. An example of a typical response profile is shown in Figure 1. This neuron fired at a high rate for a brief period of time after the motion of the texture was initiated, but after ~50 ms settled to a lower sustained firing rate. The shift from the transient period of high firing to the sustained period of firing is a form of short-term adaptation. Not only is the firing of the neuron reduced with the continued presence of the stimulus, but the recovery from the adaptation takes about ~120 ms. The goal of this research is to make constraints on the mechanism that produces this adaptation.

We used a paired stimulus protocol called condition/test, in which a neuron is presented with two components of motion. We measured the effect an initial presentation of motion (the conditioning motion) had on the neuron's response to a second presentation of motion (the test motion). In these experiments, the test motion was always delivered in the direction and speed that drove the largest response of the neuron, while the direction or speed of the preceding conditioning motion was systematically varied. The adapted test response was measured by subtracting the response to the conditioning motion alone from the response to the conditioning and test motion. A corresponding tuning curve (subsequently referred to as the adaptation tuning curve) is calculated from the test responses given the conditioning motion. The subtraction procedure is shown in Figure 2, in which the conditioning and test
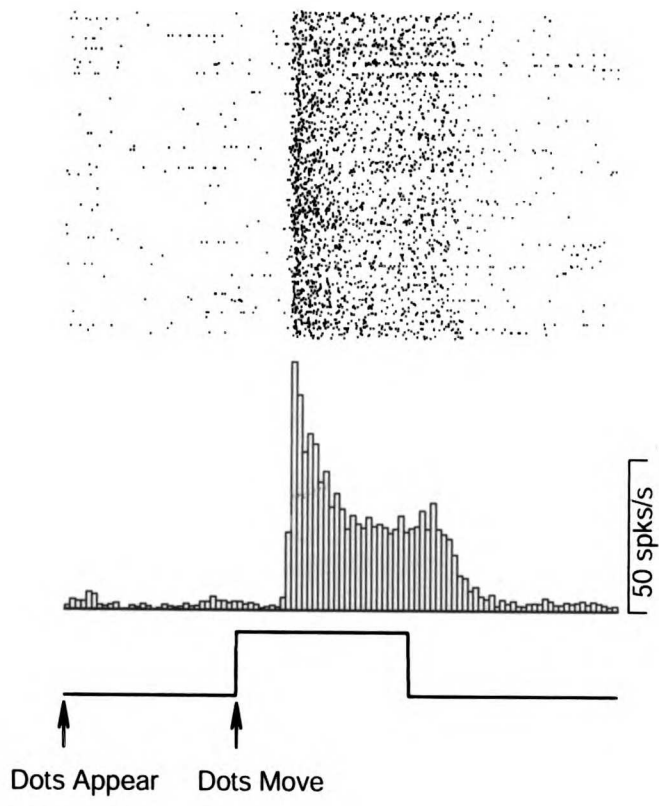
Dots Appear   Dots Move

50 spks/s

Figure 1
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Figure 1. The response of an MT neuron to a step of stimulus velocity. In the top

panel, the response of an example MT neuron is shown to multiple repetitions

of the same stimulus. In the middle panel the response of the neuron is shown

as a histogram with a bin size of 8 ms. A random dot texture was turned on at

the beginning of each trial and was stationary for 256 ms. The texture then

moved in the neuron's preferred direction and speed for 256 ms. After the

phase of texture movement, the texture was stationary for the rest of the trial.

The time course of stimulus motion is indicated by the step at the bottom of

the figure.

motion are both in the same direction and speed, but separated in time. The middle

histogram shows the response of the neuron to the conditioning motion alone. The

response to the conditioning motion alone was subtracted from the response to both

the conditioning and test stimuli to extract the response to the test stimulus alone,

shown in the bottom histogram. We used 64 ms each of conditioning and test motion

because the duration of the transient is less than 64 ms and we could thus be sure that

the conditioning motion would be long enough to modulate the response to the test

motion. For the experiments reported here, there was no interval between the

conditioning and test motion unless explicitly stated.

Because the response to a single, long presentation of motion causes a

sustained reduction in the firing of many MT neurons, as shown in Figure 1,

conditioning motion in the preferred direction and speed reduces the neuron's

response to test motion. However, the dependency of this adaptation mechanism on

the conditioning motion's direction and speed is not known. The tuning of adaptation

could come in three forms, as illustrated schematically in Figure 3. The dashed line

indicates the tuning of the firing of a neuron for a tuning parameter such as direction

or speed. The tuning to such single presentations of motion will henceforth be

referred to as the response tuning of the neuron. The solid line indicates the response

of the neuron to motion in its preferred direction and speed given that the test motion

was preceded by the conditioning motion indicated on the abscissa. In Figure 3A, the

neuron's response tuning is similar to the adaptation tuning. That is, the response to

test motion is most reduced when the response to the conditioning motion is the

largest. As the response to the conditioning motion decreases the adaptation induced

Condition/Test Response (A)
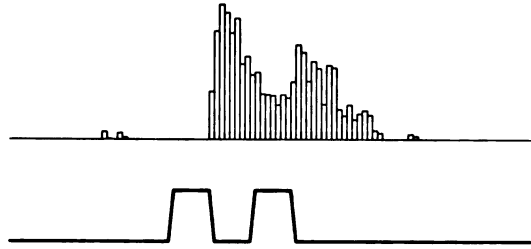
Condition Response (B)
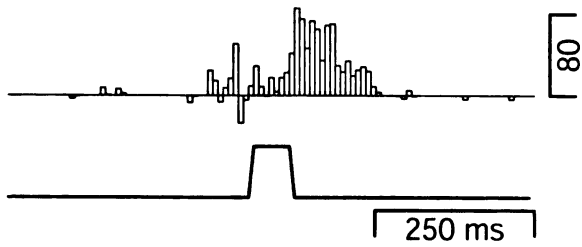
Test Response (A-B)

80

250 ms
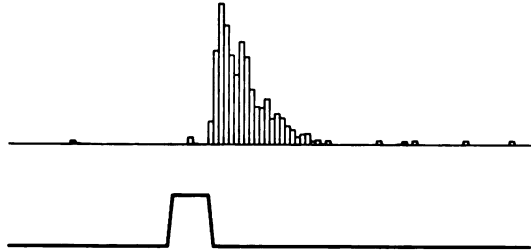
Figure 2

Figure 2. The protocol of the condition/test experiments. The top panel indicates the

response of a neuron in the form of a histogram to two components of motion,

the conditioning and test motion. These two components of motion are

indicated by the short pulses in the trace immediately below the histogram.

The middle panel shows the response of the neuron to conditioning motion

alone. In the bottom panel the difference in the condition/test response and

the condition response is shown. The bin size for all of the histograms in the

figure is 8 ms.

by conditioning motion also decreases. The peak of the adaptation tuning is therefore

defined as the direction or speed that most inhibits the neuron's response to test

motion. As the modulation of the test response by conditioning motion decreases, the

adaptation induced by conditioning motion is described as decreasing. In Figure 3B,

the response to test motion is also decreased by conditioning motion, but in an

untuned manner such that any conditioning motion regardless of direction or speed

causes the neuron to have a reduced response to test motion. Finally, as shown in

Figure 3C, the tuning of the adaptation mechanism may be different than the tuning

of the neuron, such that conditioning motion modulates the neuron's test response in a

tuned fashion, but independent of the response tuning of the neuron.

Each of these different possibilities for the tuning of adaptation puts

constraints on the site of adaptation. If the tuning for adaptation is the same as the

tuning of the neuron as in Figure 3A, the adaptation mechanism may be the result of

interactions at the level of MT between neurons with similar tuning properties, or the

result of an activity-dependent process within the neuron, or the result of a change in

the amplitude of the input to MT. If there is no specific tuning to the adaptation

mechanism, as in Figure 3B, the site of adaptation must involve a network-based

mechanism utilizing interactions between neurons independent of their preferences

for the direction or speed of motion. In this case, an adaptation mechanism based on

the activity of the neuron is implausible since the neuron's response is reduced

whether it was activated by the conditioning stimulus or not. Finally, as illustrated in

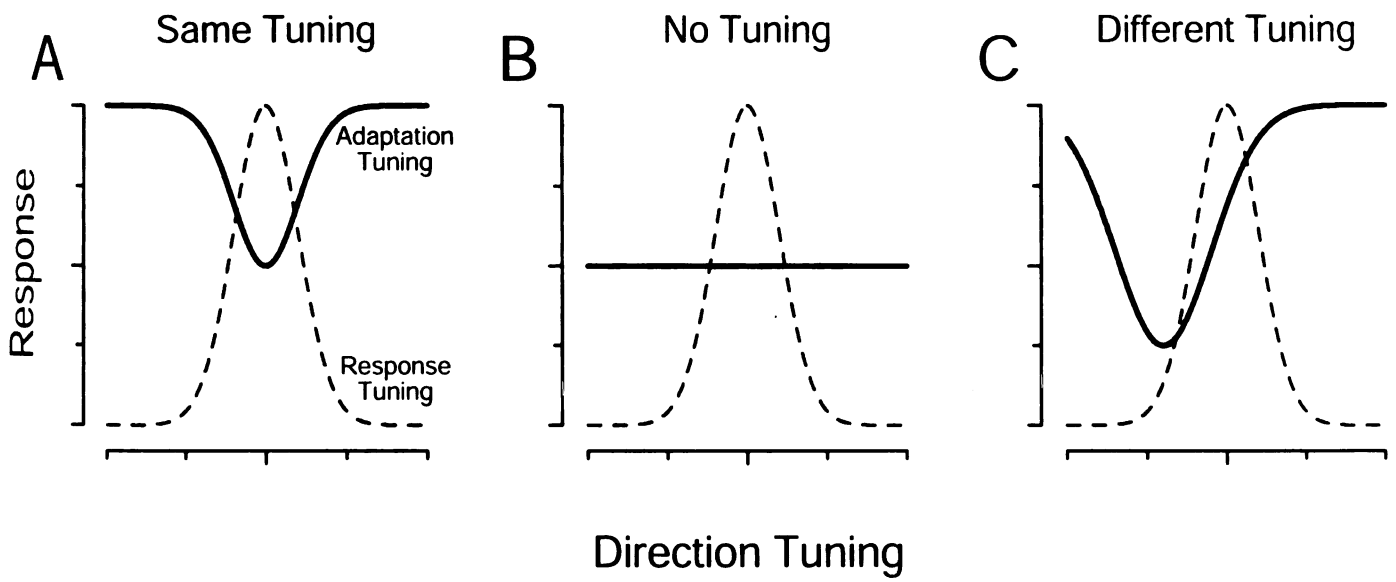Figure 3C, if the tuning of adaptation is different from the neuron's response tuning, a

Figure 3

Figure 3. A schematic representation of the classes of adaptation tuning. *A,B,C*: The

response of a neuron as the direction of a single stimulus is changed is shown

by the dashed line. The response to motion in the preferred, or test direction,

given that the test motion was preceded by conditioning motion indicated by

the abscissa is shown by the thick line. *A*: The adaptation tuning of the neuron

has the same tuning as the response tuning of the neuron, since the adaptation

tuning is defined as the conditioning direction that causes the greatest

suppression of responses. As the difference in the direction of the

conditioning motion and test motion increases, the effect of conditioning

motion on the test response decreases. *B*: The adaptation of the neuron's

response to test motion does not depend on the direction of the conditioning

motion. *C*: The adaptation of the neuron's response to test motion depends on

the direction of the conditioning motion as in panel *A*, but the preferred

direction of adaptation is different than the preferred direction of the neuron's

response to single stimulus presentations.

cellular activity-dependent mechanism for adaptation is also implausible because the

adaptation tuning is distinct from the activity of the neuron. The adaptation

mechanism is tuned in this case so that it must not be the result of interactions

between neurons independent of their preferences for tuning.

In the first section of this paper, we examine the direction selectivity of the

adaptation mechanism, and in the second portion of the paper, we examine the speed

selectivity of the adaptation mechanism.

The Direction Selectivity of Adaptation

The direction selectivity of adaptation was measured in 96 neurons in

macaque area MT by varying the direction of the conditioning motion, while the test

motion was in the neuron's preferred direction. An example of a typical response

profile of a single unit recorded is shown in Figure 4A. The direction to which the

neuron responded best is shown as the rightward direction, a convention used

throughout this paper. If a neuron's preferred direction was not rightward, we have

simply rotated its tuning for presentation purposes. Each histogram shows the

response of the neuron to conditioning motion in one of eight directions followed by

the response of the neuron to motion in the test direction. The direction of

conditioning motion is shown by the direction of the thick arrow, as well as the

placement of the histogram in the panel. This neuron responded well to both 0° and

45° conditioning motion (indicated by the thick lines overlying the response

histograms), but the amplitude of its response to test motion of 0° depended on the

direction of the conditioning motion. This is clearly visible after the response to the
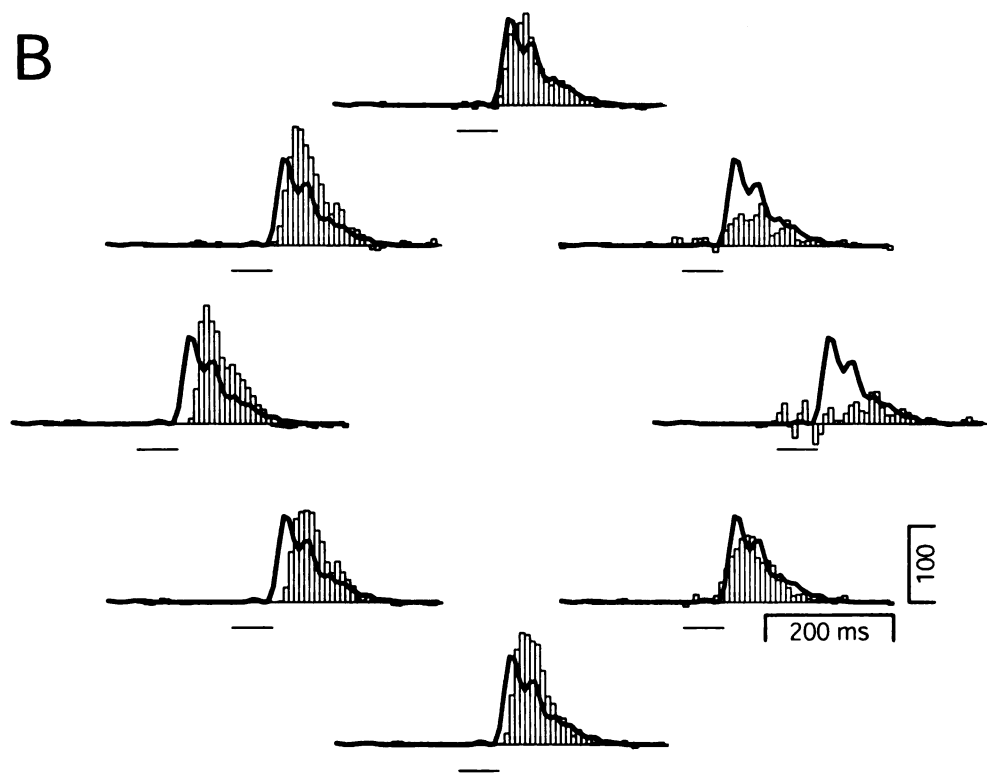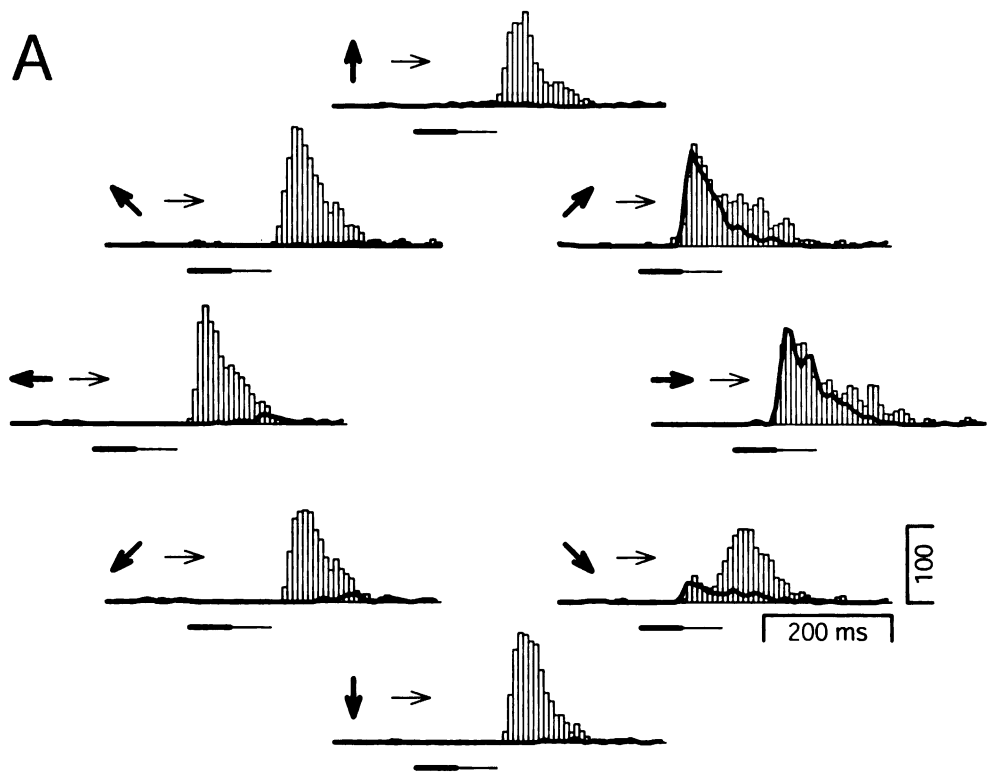
Figure 4

Figure 4.   The responses of a neuron to the condition/test experiment as direction

varied. *A*: The response of a neuron to conditioning and test motion is shown

in each histogram of this panel. The test motion was in the rightward

direction as indicated by the thin arrow. The direction of the conditioning

motion was varied systematically and is indicated by the placement of the

histogram in the figure and the direction of the thick arrow. The times of the

conditioning and test motion onset is shown by the thick and thin lines

underneath each histogram, respectively. The random dot texture turned on at

the start of each trial, not only when there was conditioning and test motion.

The response of the neuron to conditioning motion alone is indicated by the

thick trace overlying each histogram. *B*: As in *A*, the placement of each

histogram indicates the direction of the conditioning motion. The histograms

show the result of subtracting the response of the neuron to conditioning

motion from the responses to both conditioning and test motion. The thick

trace on each histogram shows the response of the neuron to test motion alone.

conditioning motion alone has been subtracted off, shown in Figure 4B. Overlying

each histogram is the response of the neuron to test motion in the preferred direction

alone, aligned at the onset of test motion. When conditioning motion was in the test

direction, the test response of the neuron was diminished substantially, while when

the conditioning motion was opposite the preferred direction of the neuron, the

response was greater than if no motion had been presented before the test motion. As

the direction of the conditioning motion approached the test direction, the responses

to the test motion alone were reduced in comparison to the response to the test motion

alone. As the direction of the conditioning stimulus approached the direction

opposite the test direction, the responses were actually greater than the response to

test motion alone. The direction of the conditioning motion not only affected the

amount of response, but also changed the latency of response. Conditioning motion

in the opposite direction of test motion caused an increase in the latency of response

while paradoxically increasing the response amplitude.

To quantify the direction tuning of adaptation, we used two different

approaches. First, we measured the amplitude of the response to the test motion

based upon the direction of conditioning motion. To separate the effect of

conditioning direction on latency from the amplitude of response, we measured the

peak 32 ms of response during a 100 ms window after the previously determined

response latency of each neuron. To compare neurons with different firing rates, we

normalized the amplitude of the response to the test motion after conditioning motion

by the response to test motion alone. We then made histograms of the normalized

response amplitude for all of the neurons in our sample population as a function of

the direction of conditioning motion (Figure 5). At one extreme, the rightmost

histogram summarizes the effect of conditioning motion in the preferred direction on

the response to test motion in the preferred direction. Almost all the neurons showed

some suppression for this conditioning and the mean test response amplitude was

43% of control. At the other extreme, the leftmost histogram summarizes the effect

of conditioning motion in the anti-preferred direction on the response to test motion

in the preferred direction. On average, there was little change in normalized

response, but many neurons showed large amounts of suppression or enhancement of

response to the test stimulus. As the direction of the test pulse moves around the

circle of histograms either way from the leftmost to the rightmost histogram, the

amount of suppression and the distribution of the population effect changes gradually.

To determine whether the effects in individual neurons were statistically

significant, we made polar plots of the response amplitude as a function of direction

(filled symbols, center of Figure 5) and of the amplitude of the response to the test

pulse as a function of the direction of the conditioning pulse (open symbols, center of

Figure 5). The response and the adaptation were direction selective across our sample

population, and the tuning of the response was stronger than that of the adaptation.

For every neuron in our sample, we did an ANOVA to determine whether the

responses to the test motion were significantly modulated by the conditioning motion

($P < 0.05$). As shown in Figure 5, where neurons with significant modulation are

shown as filled bars, 65% of the neurons we recorded had statistically significant

direction tuning to their adaptation. Because statistical significance depended on a

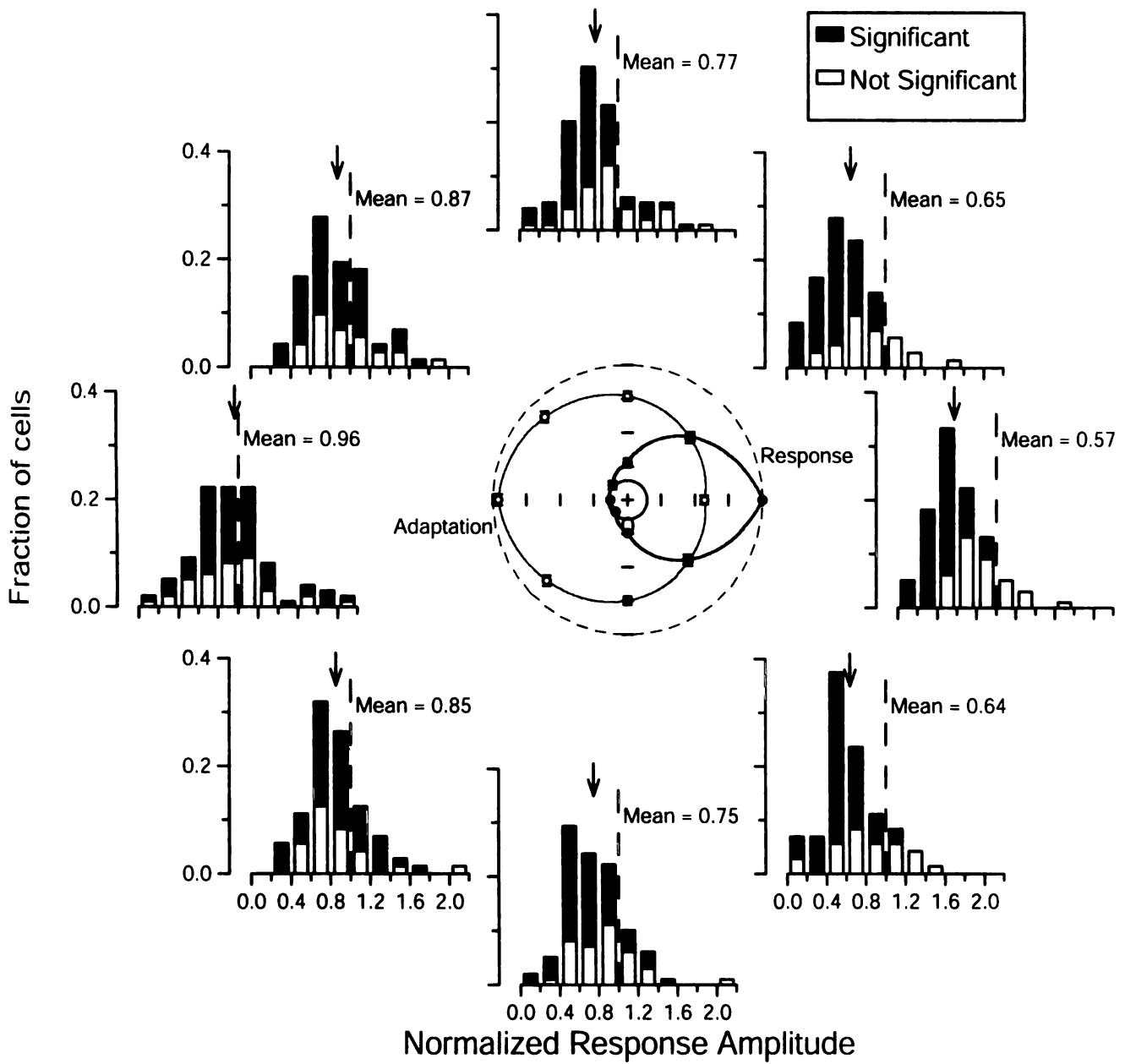consistent effect of direction of conditioning pulse on the response to the test motion,

Figure 5

Figure 5. Population responses to the direction condition/test experiment. Each

histogram of the figure represents the normalized test response amplitude of

all the neurons in our sample population. The conditioning direction of each

histogram is indicated by the placement of the histogram in the figure. For

each neuron, the test direction was rotated so that it was in the rightward

direction. The direction of the conditioning motion is shown by the placement

of each histogram, relative to the test direction (rightward). The stacked

histograms show data for neurons that were found to have both significant and

not significant directionally specific adaptation, as assayed by an ANOVA

(P<0.05). These two groups are indicated by the shading of the bar. The

mean amplitude of response for each conditioning direction is indicated by the

text and arrow in each histogram.

many neurons had small amounts of suppression for some directions of test motion and still had significant effects. Note that the normalized response amplitudes were distributed evenly around one for all directions for neurons that did not have significant direction tuning to their adaptation, an observation that is to be expected if this kind of statistical test is valid.

This occurred even for directions that did not even elicit responses from the majority of neurons. For example, the average bandwidth (width at half height) of the response direction tuning of the neurons in our sample population was 110°, indicating that the conditioning motion alone 135° from the preferred direction of motion did not increase the neurons' firing. However, the test response after conditioning motion in these oblique directions was reduced. The response direction tuning averaged over all of the neurons in the sample population is shown in the center panel of Figure 5 by the filled circles while the adaptation direction tuning curve for all neurons in the sample population is shown by the open circles.

Although on average the oblique and null directions (135° and 180° away from the test direction) did not elicit a response from the population, the width of direction tuning of individual neurons was variable and the suppression observed may be caused by only those neurons that did have a greater than baseline response to those oblique directions. One measure of the directionality of neurons is the direction index (DI), defined by

$$DI = 1 - \frac{R_N - R_{Back}}{R_P - R_{Back}} \tag{3}$$

where R_P is the response to motion in the preferred direction, R_N is the response to motion in the null direction and R_{Back} is the baseline response of the neuron. If the directionality of the neuron affected the response to the test motion, there should be a relationship between the DI and the amount of suppression induced by conditioning motion. We measured this relationship using principal components analysis (Sokal and Rohlf, 1995). However, we found no statistically significant relationship between the neurons' DI and the modulation of the test response by any direction of conditioning motion (data not shown). Thus the modulation of the neuron by the conditioning motion in the oblique and null directions did not determine the strength of suppression observed in the test response.

The second approach we used to quantify the response tuning and adaptation tuning was to fit the responses with Gaussians (Figure 6). The top panel shows the response direction tuning of the neuron from Figure 4 with the Gaussian that best fit the data (0° indicates the direction used for test motion). The lower panel shows the tuning of the adaptation direction. Note that the adaptation tuning is inverted because the graph shows the amplitude of the response to the test motion after conditioning in different directions, and the adaptation causes suppression when conditioning and test motions are both in the neuron's preferred direction. The dashed lines indicate the upper and lower bounds of the error on the estimate of the response to motion in the test direction alone. The preferred direction of adaptation was similar to that for response tuning. The width of the adaptation tuning is broader than the width of the response tuning, and this neuron showed both a suppression of response when there was conditioning motion in the test direction, and an enhancement

Response Direction Tuning
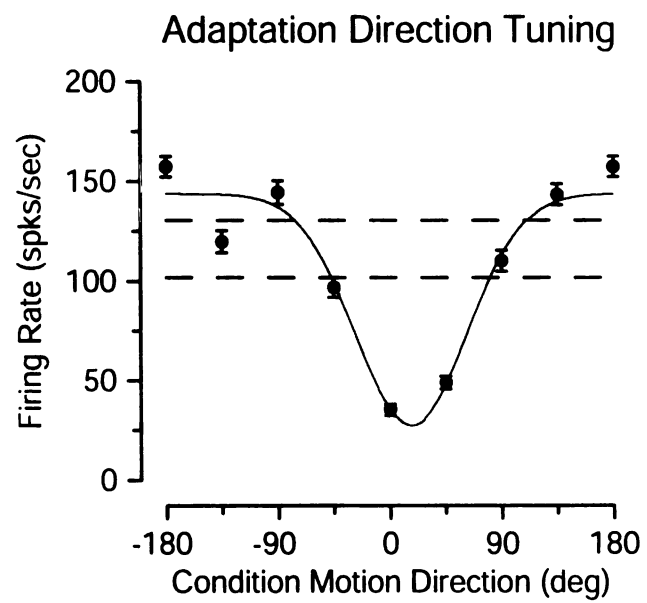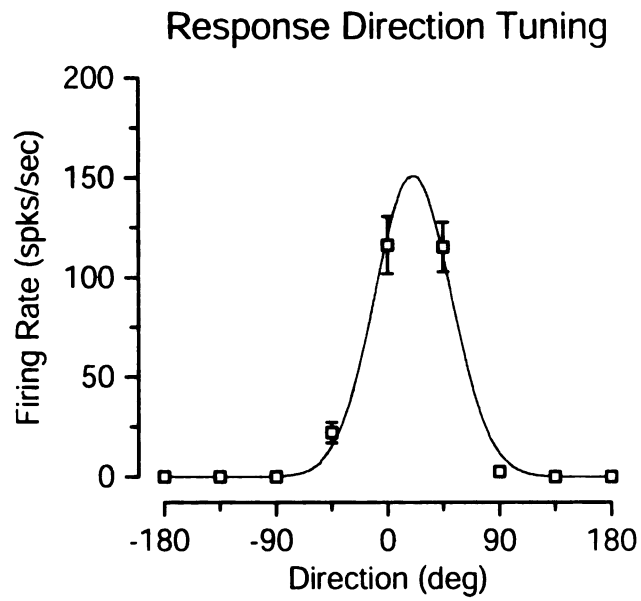

Adaptation Direction Tuning

Figure 6

Figure 6. The effects of conditioning direction on the test responses for an example

neuron. In the top panel, the response of a neuron to single 64 ms

presentations of motion is shown. A Gaussian fit of the response direction

tuning curve is shown by the solid line. The bottom panel indicates the

response of the same neuron to test motion at 0°, given the conditioning

directions indicated. The dashed line indicates the upper and lower bounds on

the standard error of the response to test motion alone. A Gaussian fit to the

adaptation direction tuning curve is shown by the solid line. Error bars

indicate the standard error of the mean firing rate for both panels.

of response when the conditioning motion was in the neuron's anti-preferred direction.

The effect of conditioning motion on the neurons' response to test motion had effects that were either both enhancing and suppressive, as shown in the previous example, or only suppressive. These two classes of effects are shown for four example neurons in Figure 7. Two neurons that showed both enhancement and suppression of test response given different conditioning motion are shown in the top panels (Figure 7A,B).

The open squares indicate the tuning of the neuron to single presentations of motion in different directions while the filled circles indicate the response to the test motion (always shown as 0°) given conditioning motion. The lines correspond to Gaussian fits to both the adaptation tuning and the response tuning. The responses of these neurons demonstrate two properties: first, the highest amount of suppression occurred when conditioning motion was in the same direction as the test direction, and second, the responses to test motion were greater when preceded by conditioning motion 180° away from the test direction. The neurons in Figure 7 C, D always had a suppressed response to test motion if it was preceded by conditioning motion. However, as for the neurons in Figure 7 A, B the test responses were most suppressed by conditioning motion in the same direction as the test direction and least suppressed by conditioning motion opposite the test direction.

Using the fits to the test responses, we made histograms of the preferred direction of adaptation, relative to the test direction, shown in Figure 8A. The preferred direction of adaptation for the majority of neurons (70/96) was within 45
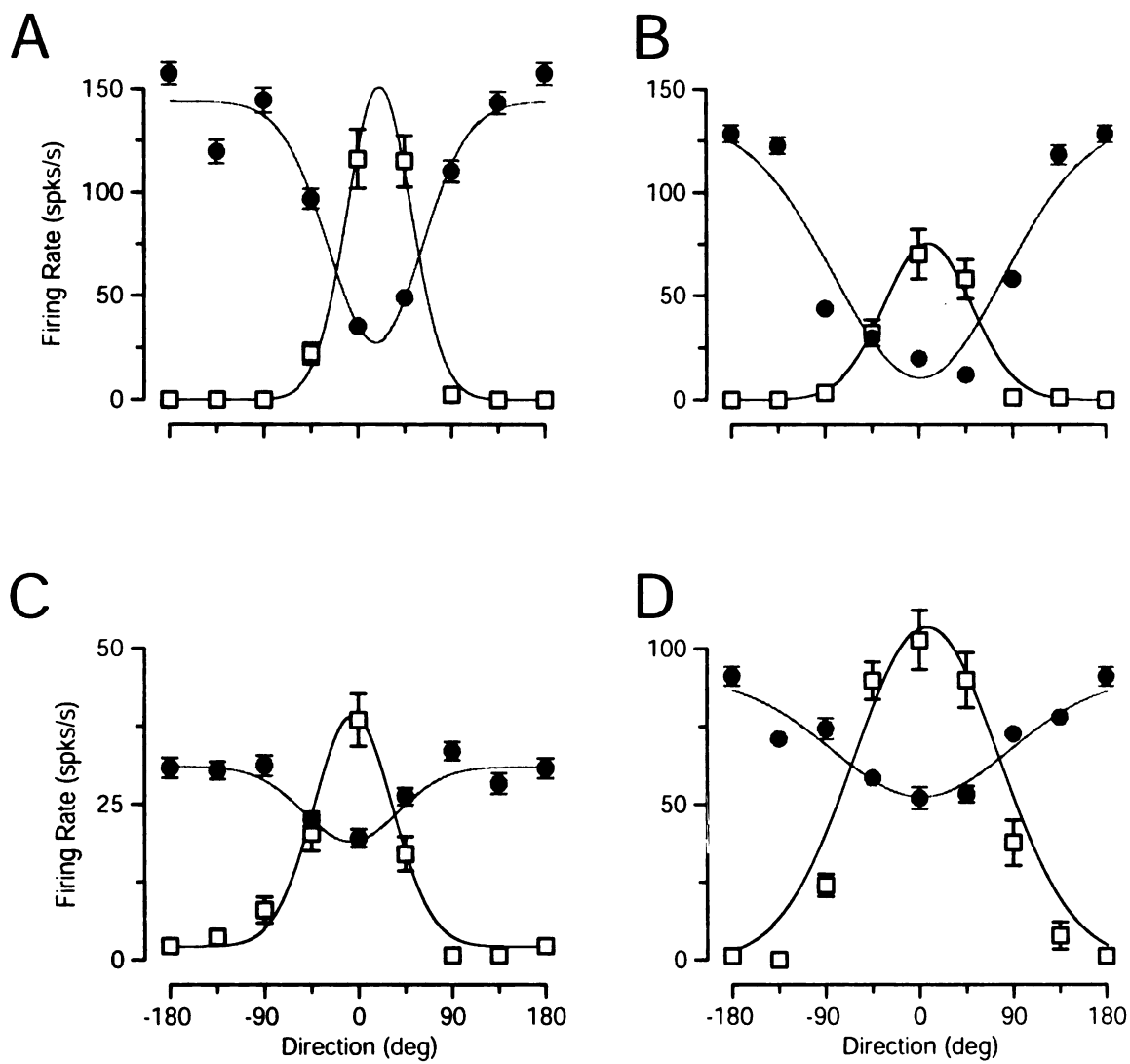
40

Figure 7

Figure 7. The effects of conditioning direction on the test responses of four example

neurons. *A,B,C,D*: The response of the neurons to single presentations of

motion in the direction indicated by the abscissa is shown by the dark, open

squares and the Gaussian fits are indicated by the dark solid lines. The

response to test motion of 0° after the conditioning motion indicated by the

abscissa is shown by the gray, filled circles. Fits to the adaptation responses

are shown by the gray lines in each panel. Bars for each data point indicate

the standard error of the mean.

degrees of the direction of the test stimulus. We next compared the preferred

direction of the adaptation mechanism to the preferred direction of the neurons,

extracted from the Gaussian fits. The preferred direction of the neuron as determined

by the Gausian fits was often different from the test direction actually used in the

experiments, because the criterion to pick the test direction was simply the direction

that elicited the best response, and no fits were done while the experiment was being

performed. The difference between the preferred direction of adaptation and response

could therefore be due to errors in picking the test direction actually used in the

experiment. As can be seen in Figure 8B, there is no significant relationship between

the preferred direction of the neurons' response to single presentations of motion and

the preferred direction of adaptation (principal components analysis, (Sokal and

Rohlf, 1995), P=0.57). The filled circles symbols indicate neurons for which the

95% confidence interval of the fit value a in equation 1 did not overlap with 0. The

open circles did not yield fit values that were deemed statistically significant from

zero by this criterion. Because there is no significant relationship between the

preferred response direction of the neuron and the preferred direction of adaptation,

we conclude that errors in the online approximation of the preferred direction of the

neuron for use as a test stimulus are not responsible for the differences between the

preferred direction of the neuron and the preferred direction of the adaptation

mechanism.

From these fits of the direction tuning of adaptation we also extracted the

amplitude and width of Gaussians that best fit the data. As shown in the previous

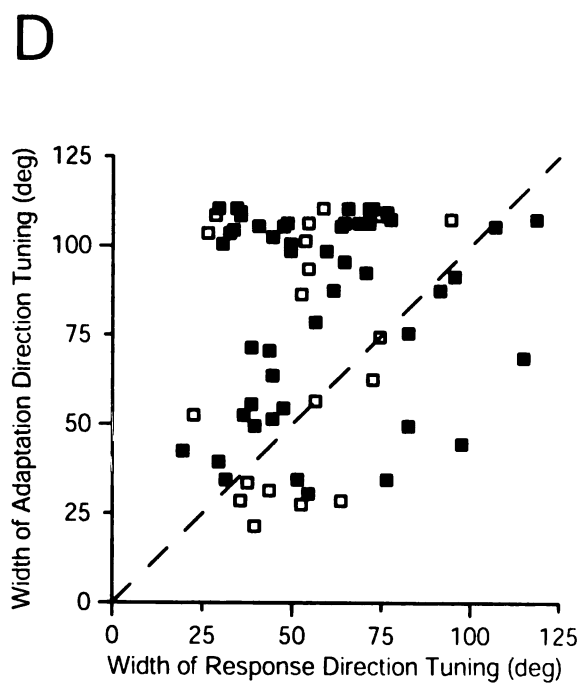figure, the preferred direction of adaptation was usually in the direction of the test

A
Direction Tuning of Adaptation
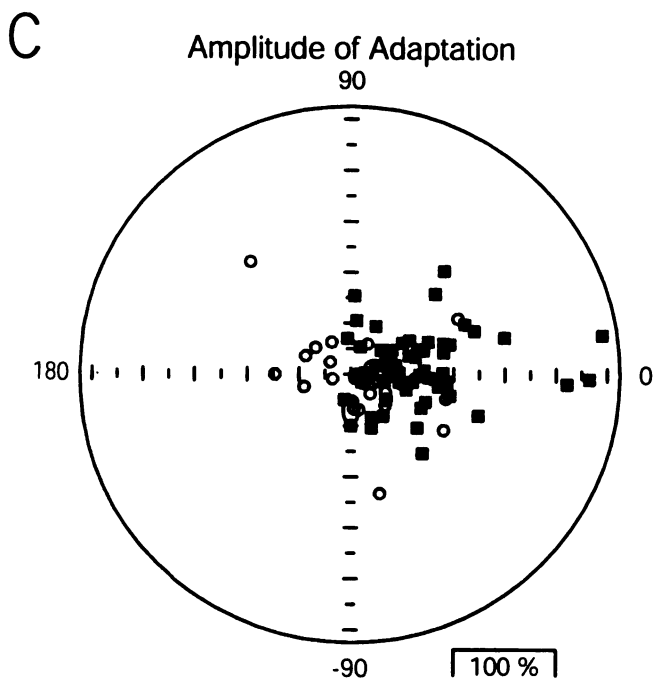

B

C
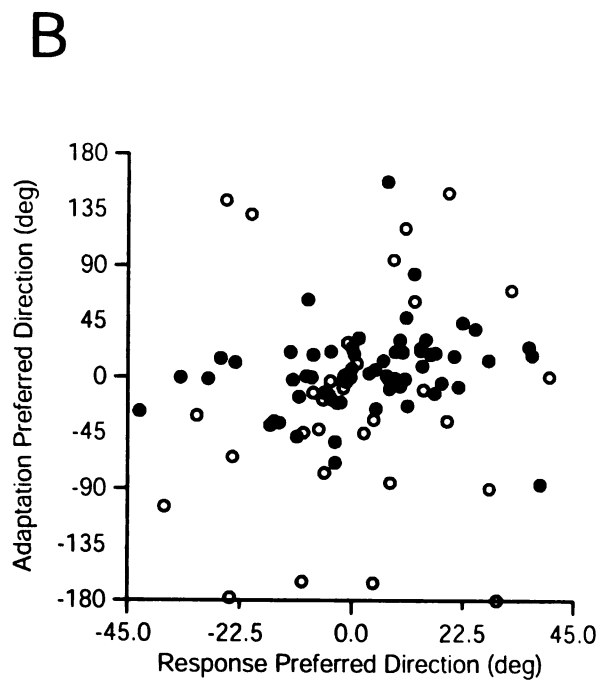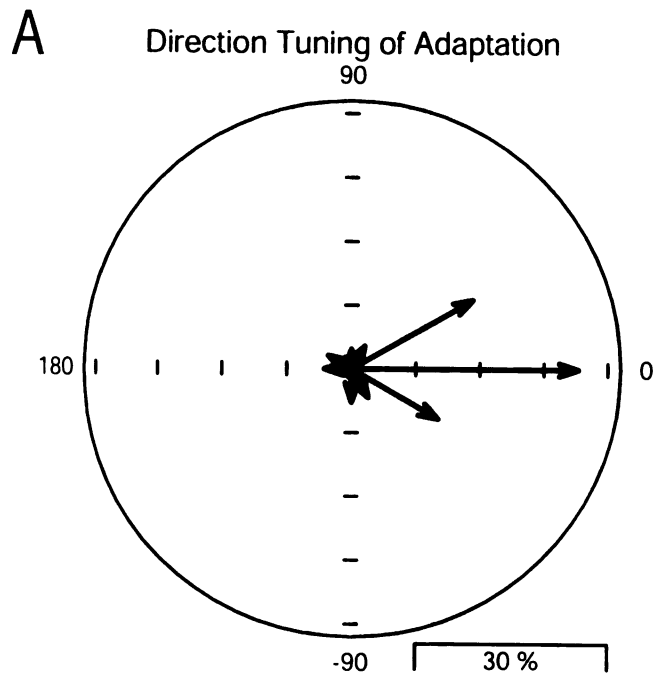## Amplitude of Adaptation

D

Figure 8

Figure 8. The response and direction tuning of adaptation across the population of

neurons. *A*: A histogram of the preferred direction of the adaptation

mechanism is shown in polar coordinates. The direction of the test motion

was rotated to be 0° for all neurons. The length of each arrow indicates the

percentage of neurons and the angle of each arrow indicates the preferred

direction of the adaptation mechanism, as extracted from the Gaussian fits.

B,C,D: Filled symbols indicate neurons with statistically significant fit

adaptation amplitudes (P<0.05). The open symbols did not have significant

adaptation amplitudes. B: The preferred response direction of each neuron,

extracted from the Gaussian fits of the response curves, relative to the test

direction at 0°, is shown plotted relative to the adaptation preferred direction.

C: Each neuron is plotted on polar axes where the distance from the center

indicates the amplitude of adaptation, normalized by the response to the test

motion alone, and the angle indicates the preferred direction of adaptation. *D*:

The half-width of the response and adaptation tuning curves is shown for each

neuron in the population. These values were taken by measuring the half-

width at half-height of the fit Gaussians for the response and adaptation

curves.

motion. However, there are cases in which the tuning for adaptation and response do not appear aligned. As shown in Figure 8C, when the amplitude of the Gaussian that best fit the data and the direction selectivity of adaptation are shown together, it is apparent that the strength of adaptation for these neurons is lower, and many times did not reach statistical significance by the same criterion used above. Although the preferred directions of adaptation and response were similar when adaptation was strong, as shown in the example in Figure 6, the width of adaptation tuning appears broader than the width of the response direction tuning. We systematically measured the width of tuning of the adaptation mechanism and compared it to the width of tuning to single presentations of motion and found that for 81% (78/96) of the recorded neurons, adaptation tuning widths were broader than the response direction tuning of the neurons (Figure 8D).

Finally, to estimate the effect of the direction of conditioning motion on our sample population, the conditioning direction that yielded the maximal test response from our population of neurons and the conditioning direction that yielded the minimal test response relative to the test direction were extracted from the Gaussian fits. The direction that yielded the best response for each neuron is shown by the angle in Figure 9A, where the response amplitude (normalized to the test response) is indicated by the distance from the center to each symbol. Many neurons show some enhancement of response to the test motion in the presence of conditioning motion, but many also show a suppression of response to the test motion to all directions of conditioning motion. Note that these two response characteristics do not arise from a bimodal distribution, but a single distribution. Across the population of neurons,

Condition Direction Yielding Maximal Test Response

90

All Suppressed

1.0

90

0

-90
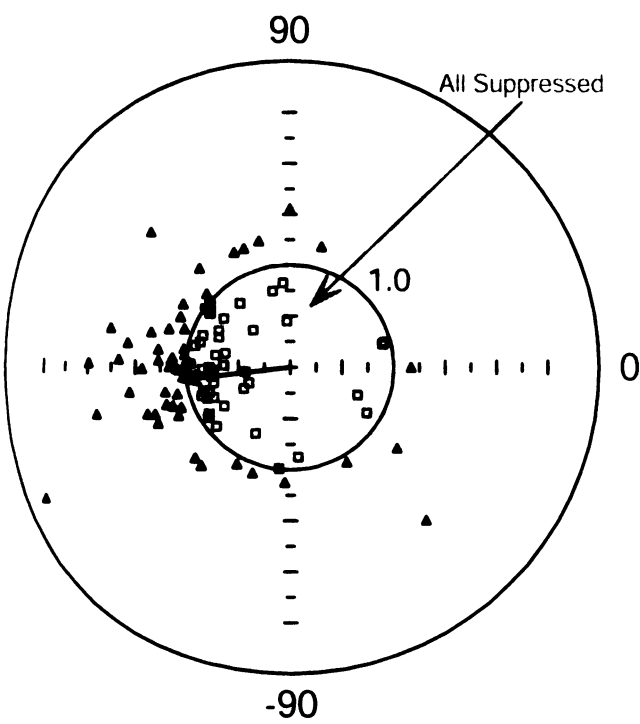
Condition Direction Yielding Minimal Test Response

90

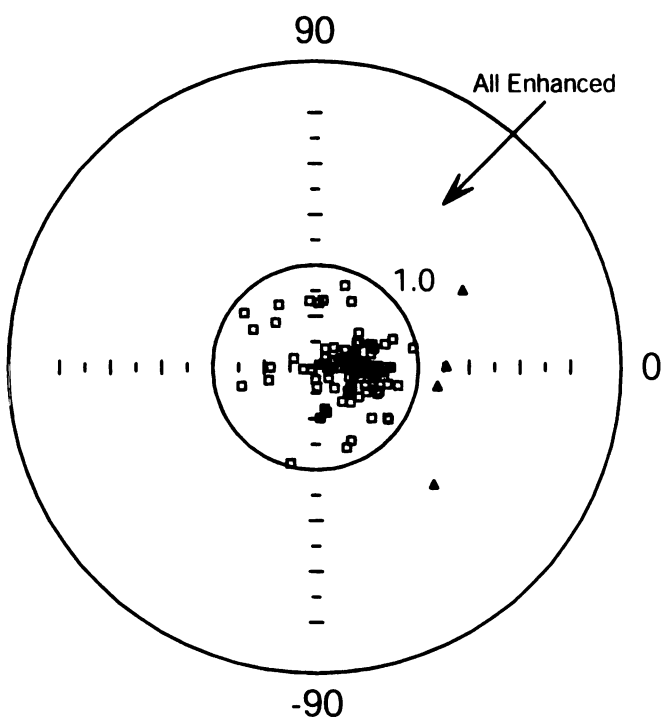All Enhanced

1.0

180

0

-90

Figure 9

Figure 9. The directions yielding maximal and minimal responses across the

population of neurons. Each panel indicates the normalized response of

individual neurons by the distance of the symbol from the center of the circle,

while the direction of the response is indicated by the angle of the each

symbol. The arrows in each panel indicate the average direction and

amplitude of response across the population. The inner circle represents a

normalized amplitude of 1. Triangles indicate suppressed responses while

squares indicate enhanced responses. All the values were extracted from the

Gaussian fits to the response and adaptation direction tunings. In the left

panel the conditioning direction that yielded the highest test response is

indicated by the angle and the response amplitude is indicated by the distance

from the center of the circle. The right panel shows the directions that

elicited the smallest test response and that test response is shown by the

distance of the symbols from the center of the circle.

the enhancement and suppression cancel, as shown when the average conditioning direction and test amplitude of the population is computed. This vector is pointed in the null direction, and has length of 1.03. This indicates that the neurons always suppressed by conditioning motion are balanced in our population by those neurons that exhibit enhancement in the presence of conditioning motion.

The directions that elicited the greatest amount of suppression and the amplitude of that response to test motion for each neuron is shown in Figure 9B. The great majority of neurons showed suppression when the conditioning motion was in the test direction. When the adaptation was tuned to directions other than the test direction, it induced less suppression of response than when the adaptation was in the test direction. Once again, the average amplitude and direction of the strongest component of adaptation is indicated by the arrow. This population response vector indicates that neurons were most suppressed by motion in the preferred direction and the amplitude of the response of all of the neurons in our population was reduced to 54% of the normal.

To measure the recovery of the neurons from adaptation, data was also collected when there was a period of time between the conditioning and test motion. This period, the inter-stimulus interval (ISI), was varied from 0 to 256 ms for each neuron. The recovery of MT neurons from adaptation has been previously described (Lisberger and Movshon, 1999), and we sought only to confirm that the direction specific effects of adaptation had the same time course as the previously described effects. An example of the recovery of the MT neuron shown in Figure 7 is shown in Figure 10. As the ISI is increased, the effect of the direction of the conditioning
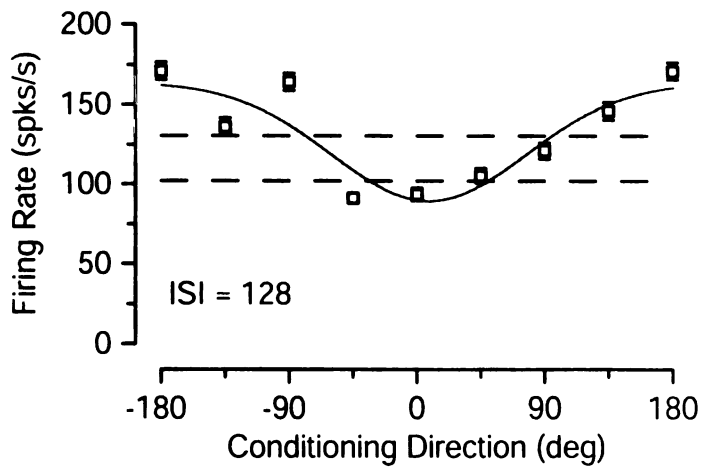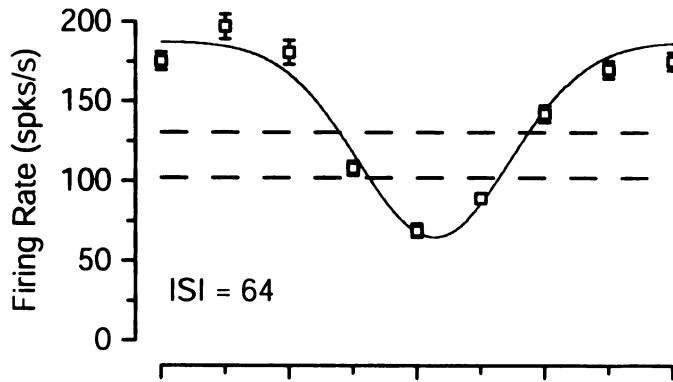
Direction Tuning
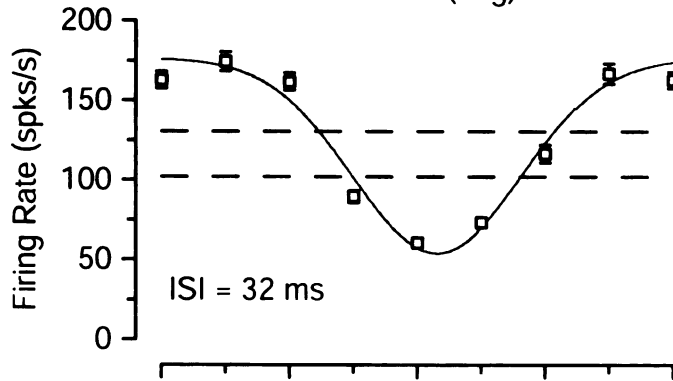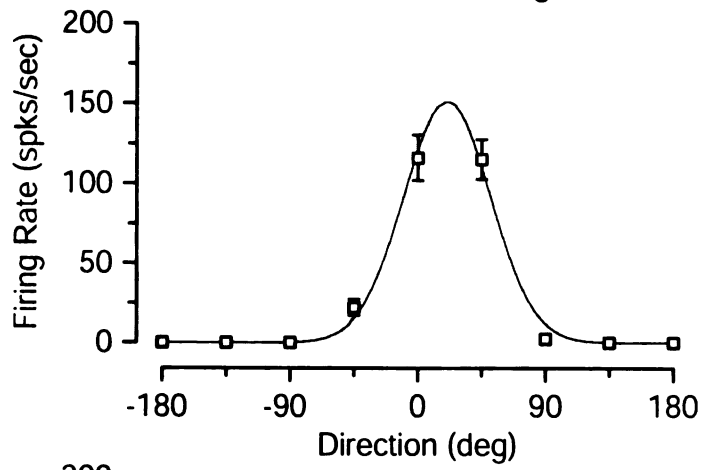
Figure 10

Figure 10. The time course of the recovery from adaptation. The top panel indicates

the direction tuning of the neuron. The bottom panels indicate the response to

the test motion at 0° given each preceding conditioning direction. The

interval between the conditioning and test motion is indicated in each panel by

the ISI. Gaussian fits to the response and adaptation direction tuning are

shown by the solid lines in each panel.

motion on the test response is reduced such that with an ISI of 128 ms, there was little

modulation of the response due to the conditioning motion. At an ISI of 256 ms, the

response of the neuron was not statistically different from the response of the neuron

with no preceding conditioning motion. This time course of recovery from adaptation

is very similar to the time course of ~120 ms that was reported by Lisberger and

Movshon (1999).

Not only was the amplitude of the response affected by the direction of the

conditioning motion, but the latency of response was also affected. Conditioning

motion in the direction opposite the test direction caused an increase in the latency of

response for many MT neurons. The shift in response latency depended on the

direction of the conditioning motion, shown for an example neuron in Figure 11. The

neuron's response to both the conditioning and test motion is shown in the left

column, each row indicating a different direction of conditioning motion. The latency

of the neuron's response to the test motion is shown in the fifth row, where the

conditioning and test motion are in the same direction. After subtracting the

responses of the neuron to the conditioning motion alone, shown in the right column,

the directional effect on latency was extracted. The dashed line in this column

indicates the prediction of the latency of response, given the latency when there is no

conditioning motion. There was no change in the latency of response when the

conditioning and test motion were in the same direction. However, when the motion

was more than 90° from the test motion, clear effects on the latency to test response

are seen. For this neuron, the latency of response was estimated for each direction of

conditioning motion, and the shift in the latency of response from the expected
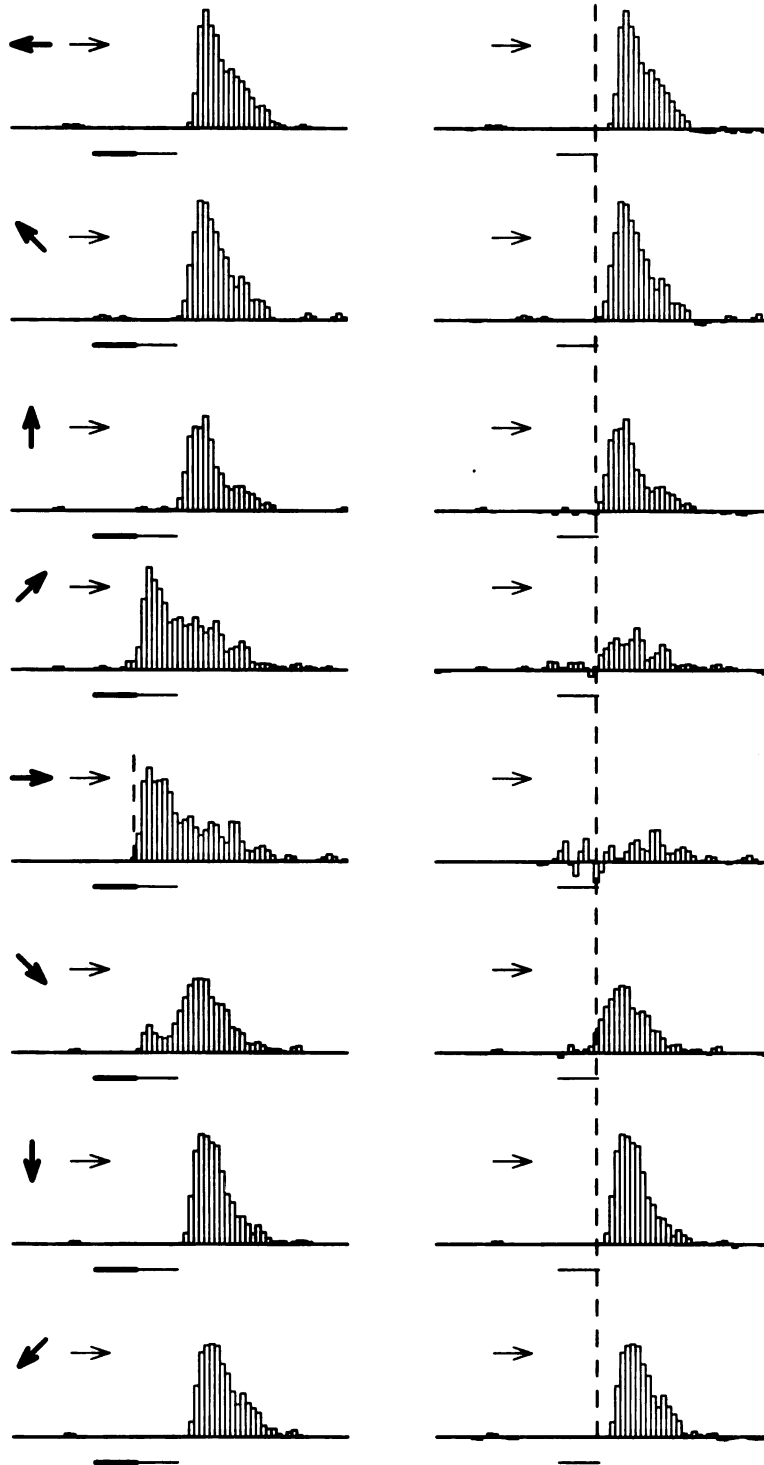
Condition/Test Response   Test Response

Figure 11

Figure 11. The direction of conditioning motion affects the response latency to test

motion. The condition and test responses of an example neuron are shown by

the histograms in the left column. The direction of the conditioning motion is

indicated by the direction of the thick arrow, while the direction of the test

motion is indicated by the thin arrow. The timing of the conditioning and test

motion is indicated by the thick and thin lines underneath each histogram.

The latency of the response to test motion is shown in the fifth panel by the

vertical dashed line. In the right column, the result of the subtraction of the

conditioning motion alone is shown. The vertical dashed line indicates the

predicted latency of response to the test motion.
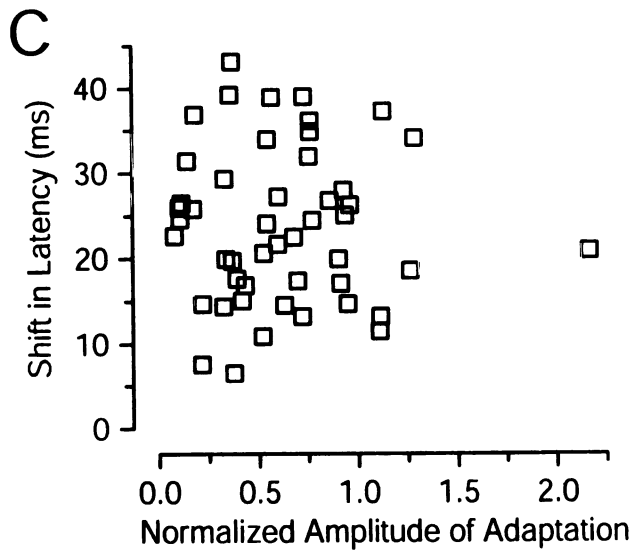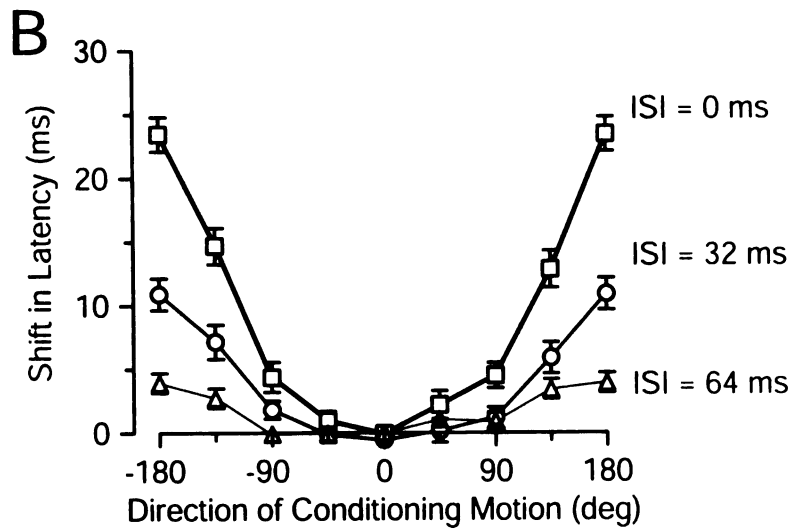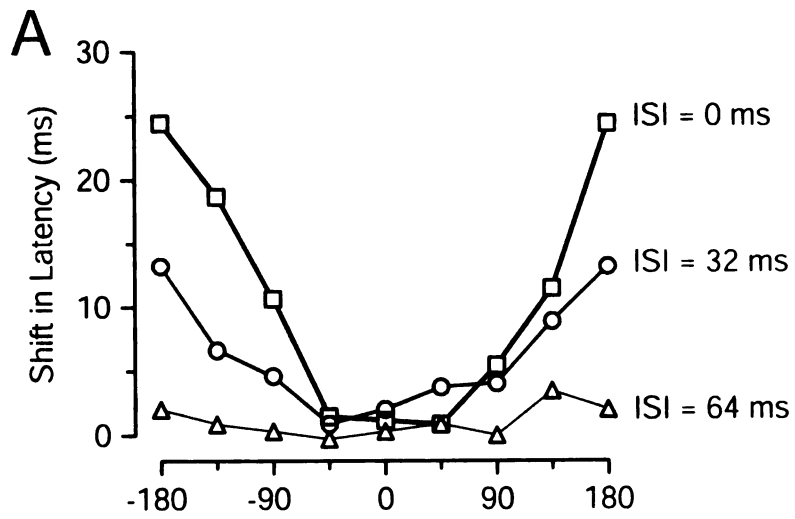
Figure 12

Figure 12. The time course of latency shifts. *A,B*: For each conditioning direction, the increases in the latency of response relative to the response latency to the test alone is shown. Squares indicate the latency shift for an ISI of 0 ms, the circles indicate the shift for and ISI of 32 and the triangles indicate the shift for 64 ms. *A*: The response latency for the example neuron in Figure 11 is shown. *B*: The average shift in response latency across 49 neurons in our population is shown. *C*: The normalized amplitude of adaptation (the fit Gaussian amplitude normalized for the response to test motion alone) for each neuron did not predict the shift in the latency of response to conditioning motion opposite the test motion.

latency is shown in Figure 12A (thick lines). For an ISI of 0 ms (as shown in Figure 11), the change in latency was maximal when the conditioning motion was in the direction opposite the test direction. As the ISI increased to 64 ms, the effect of conditioning motion also decreased such that there was not an apparent effect of conditioning motion on the latency of response. Although the effects of the conditioning motion on latency were very small at 64 ms, there was still a large effect of the direction of conditioning motion on the amplitude of the neuron's response to test motion (Figure 11).

The effect of the direction of conditioning motion on the latency of response was found for many of the neurons in our sample population. For 49 neurons we were able to measure the latency of response. The effect of the direction of conditioning motion on the latency to respond was variable, but motion in the direction opposite the test motion always induced an increase in the latency of response. The average shift in latency is shown in Figure 12B. As with the example neuron shown in Figure 12A, the shift in latency was small with an ISI of 64 ms or more. The shifts in latency are not linked to the amount of suppression or enhancement induced by the conditioning motion. In particular, the amplitude of adaptation (a in equation 1) had no relationship to the shift in latency caused by conditioning motion in the direction opposite the test motion across the neurons in our population (Figure 12C).

The speed tuning of adaptation

The speed selectivity of the adaptation mechanism was measured in 88 neurons in area MT. The speed selectivity for adaptation was assessed with the same protocol used to assess the direction tuning of adaptation, except that the direction of conditioning and test motion was fixed, while the speed of the conditioning motion was changed. We measured the speed tuning of the neuron in response to single presentations of motion, as well as the responses to both conditioning and test motion. An example of the responses to the conditioning and test motion is shown in the upper row of Figure 13. This neuron was tuned to 4°/s and was presented with conditioning motion ranging from 0.5°/s to 64°/s, sampled on a logarithmic scale. The response to conditioning motion of different speeds is shown in the middle row. To extract the test response from the upper row, the response to the conditioning motion alone was subtracted from the response to both the conditioning and test motion, and the resulting histograms are shown in the bottom row of Figure 13. Here we see a profile of response to test motion similar to that found for the direction tuning of adaptation: the greater the response of the neuron to conditioning motion, the more suppressed the response to test motion.

This response profile, however, does not represent the speed tuning of adaptation for many other neurons. For example, the response of another MT neuron, recorded just following the single unit presented in Figure 13, is shown in Figure 14. In this example, conditioning motion that was slower than the test motion reduced the response to the test, while conditioning motion faster than the test response actually

ondition and Test Responses

:reasing Conditioning Speed ⟶

ondition Responses

ist Responses

120 spk/s

120 spk/s

200

Figure 13

Figure 13. Examples of the speed tuning of adaptation. In the first row, the

responses of a neuron to both conditioning and test motion are shown. Each

column contains the response of the neuron to different speeds of conditioning

motion. The time of the conditioning and test motion is indicated by the thick

and thin bars, respectively. The response of the neuron to conditioning

motion alone is shown in the middle row, while the bottom row contains the

result of the subtraction of the second row from the first row to yield the

response to the test motion given each conditioning speed. The vertical arrow

above the top histograms indicates when conditioning and test motion were at

the same speed.

increased the response of the neuron to test motion. Surprisingly, when conditioning

and test motion were at the same speed, little adaptation was found. Unlike the first

example in Figure 13, the speed tuning of the adaptation mechanism was different

than the neuron's response speed tuning.

In our population of neurons we found that the speed tuning of adaptation

could be either the same or different than the response speed tuning. In Figure 15,

each panel shows the speed tuning of a neuron as well as the speed tuning of the

adaptation mechanism, as assessed by the effect of the conditioning motion speed on

the test response. In the top row, the two neurons' adaptation and response speed

tunings have very similar preferred speeds. The squares indicate the responses of the

neurons to single presentations of motion and a fit to these responses using equation 2

is shown by the thin line. The triangles indicate the test response after conditioning

motion and the thick line indicates the fit to these data using equation 2. In the

middle row, we show two examples in which the speed tuning of adaptation was

lower than the response speed tuning. These neurons' test responses are most

suppressed by conditioning motion that does not elicit large responses. The bottom

row shows the responses of two neurons in which the response speed tuning of the

neuron also does not match the adaptation speed tuning. However, the greatest

suppression was induced by conditioning motion at speeds greater than the test speed.

The ratio of the fit of the preferred speed of adaptation (μ_s in equation 2) and

the preferred response speed is shown in Figure 16. As is apparent from the

histogram, the distribution of adaptation preferred speeds was broad and peaked at

** condition and Test Responses**

Increasing Conditioning Speed →
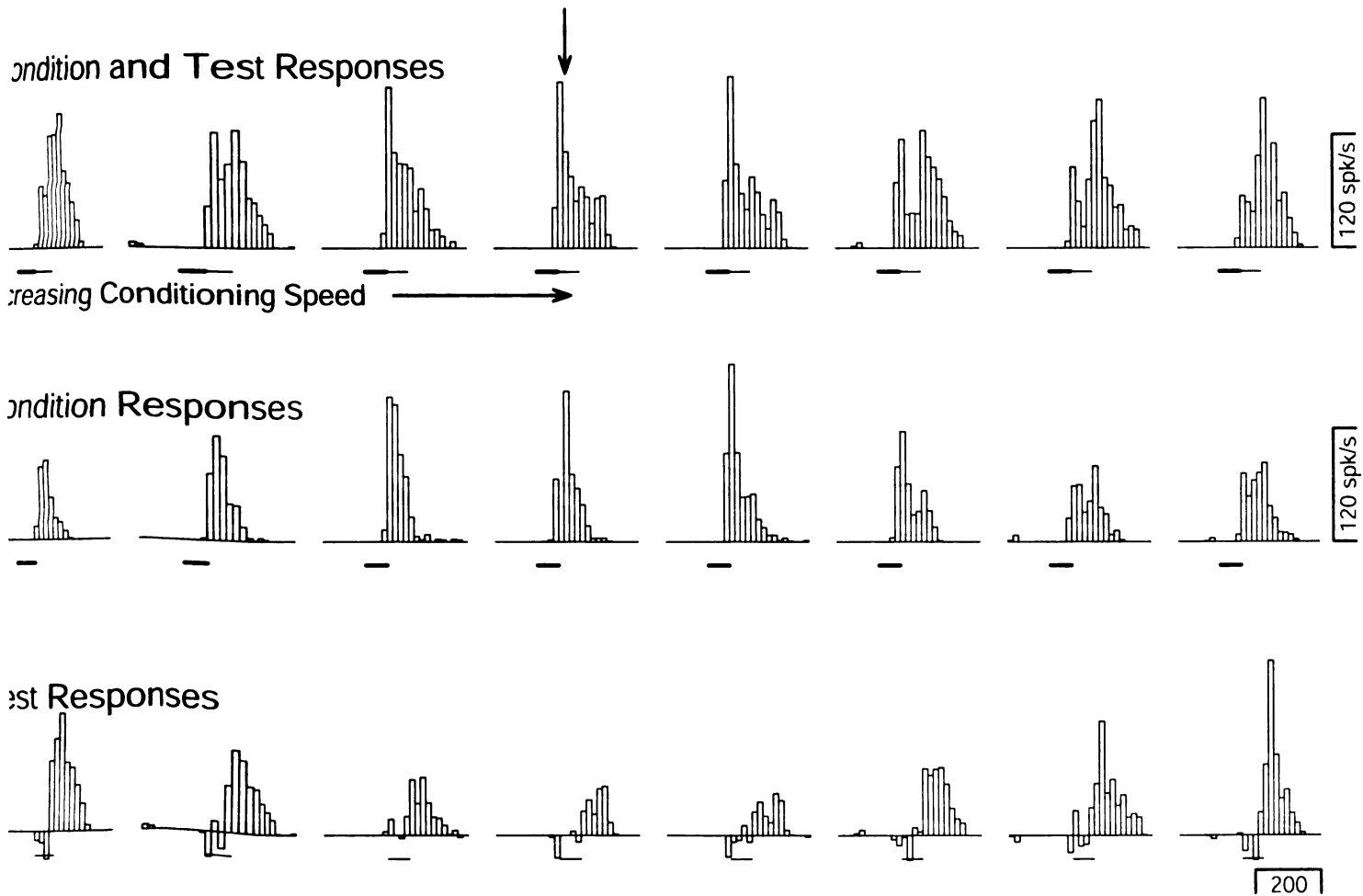
condition Responses
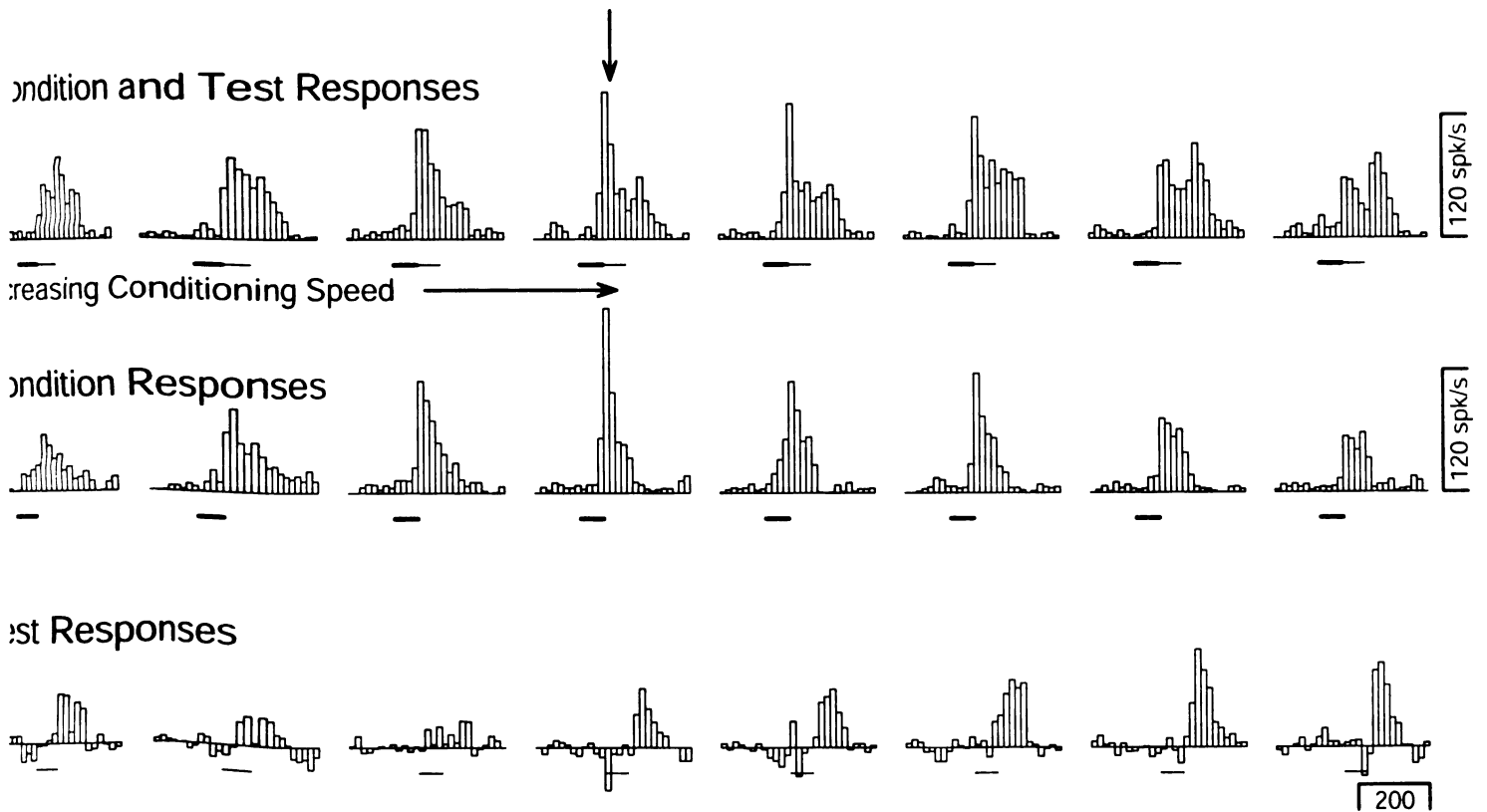
Test Responses

Figure 14

Figure 14. Examples of the speed tuning of adaptation. In the first row, the

responses of a neuron to both conditioning and test motion are shown. Each

column contains the response of the neuron to different speeds of conditioning

motion. The time of the conditioning and test motion is indicated by the thick

and thin bars, respectively. The response of the neuron to conditioning

motion alone is shown in the middle row, while the bottom row contains the

result of the subtraction of the second row from the first row to yield the

response to the test motion given each conditioning speed. The vertical arrow

above the top histograms indicates when conditioning and test motion were at

the same speed.

Figure 15

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Figure 15. The analysis of six example neurons for the speed conditioning/test

experiment. *A,B,C,D,E,F*: The filled squares in each panel indicate the

response of the neuron to single presentations of motion for each speed. The

gray triangles indicate the response of the neurons to the test motion given

conditioning motion of the speeds indicated. Fits to these data points are

shown by the dark and gray lines. Bars for each data point indicate the

standard error of the mean.

speeds slightly above the test speed. There are two reasons why the preferred speed of adaptation might be faster than the test speed. First, it has been shown that the initial transient firing of these neurons is tuned to speeds faster than the later sustained component of firing (Lisberger and Movshon, 1999). The test speed used in these experiments was derived from the sustained response and not the transient response, and this may account for some shift of the adaptation speed to a higher speed. Second, the speed tuning of neurons in area MT depends critically on the duration of the stimulus presentation. When the duration of a stimulus is reduced, the speeds that elicit responses are faster than when the stimulus duration is long (Priebe and Lisberger, unpublished observations). The test speeds used in these experiments were selected from the responses of the neurons to longer (512 ms) presentations of stimulus motion. However, the effect of stimulus duration on the speed tuning of neurons is generally observed for only very short stimulus durations (<48 ms). Neither of these caveats explains why the speed tuning for adaptation might be lower than the response speed tuning.

Because the test speed used in these experiments might not have been the exact preferred speed of the neuron, we measured the relationship between the preferred speed of both the adaptation tuning and the response tuning of the neuron, shown in Figure 17. Across the same population there is certainly a positive relationship between the preferred speeds of adaptation and response (PCA, slope = 1.13, P <0.05), but as the distribution illustrates, there are many neurons whose
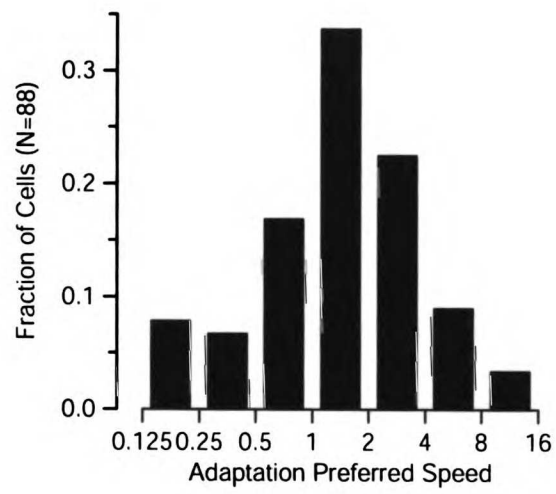
Figure 16

Figure 16. The preferred speed of the adaptation mechanism. The histogram shows

the frequency of the fit of the preferred speed of adaptation. The test speed

for each neuron is normalized to 1 on this histogram.

adaptation speed tuning is different than the neurons' preferences of speed from a single presentation of motion. Although the adaptation mechanism did not depend on activation by the conditioning motion for many of the neurons from which we recorded, we found that for 49% (43/88) of the neurons, the preferred speed of the adaptation mechanism was within one log unit of the preferred speed of the neuron to single presentations of motion.

The difference between the adaptation speed tuning and the response tuning could be the result of poor fits of the adaptation tuning curve. The filled and open squares in Figure 17 indicate neurons in which the fit preferred speed for adaptation was statistically different using a nested hypothesis technique (see Methods). A slight majority of the neurons (47/88) had a preferred speed of adaptation that was considered statistically different than the preferred speed of the response to single presentations of motion.

The adaptation mechanism might also be less powerful when the adaptation tuning is very different than the response tuning. The amplitude of the adaptation (as measured by the modulation of firing due to the speed of the conditioning motion, R_{back} in equation 2) was also not affected by whether the adaptation had the same tuning as the neuron or not, shown in Figure 18. The amplitude of the adaptation process is therefore independent of the relationship of adaptation preferred speed to the response preferred speed. From this data the preferred speed for adaptation did exceed the preferred speed of the response to single presentations of motion (for 51 of the 88 neurons in the population this trend existed), in agreement with previous work

showing that the transient firing of many MT neurons is tuned to higher speeds than

the sustained firing (Lisberger and Movshon, 1999).
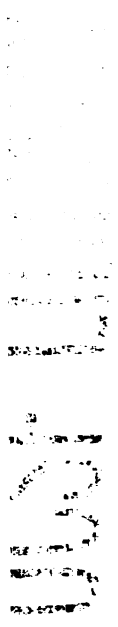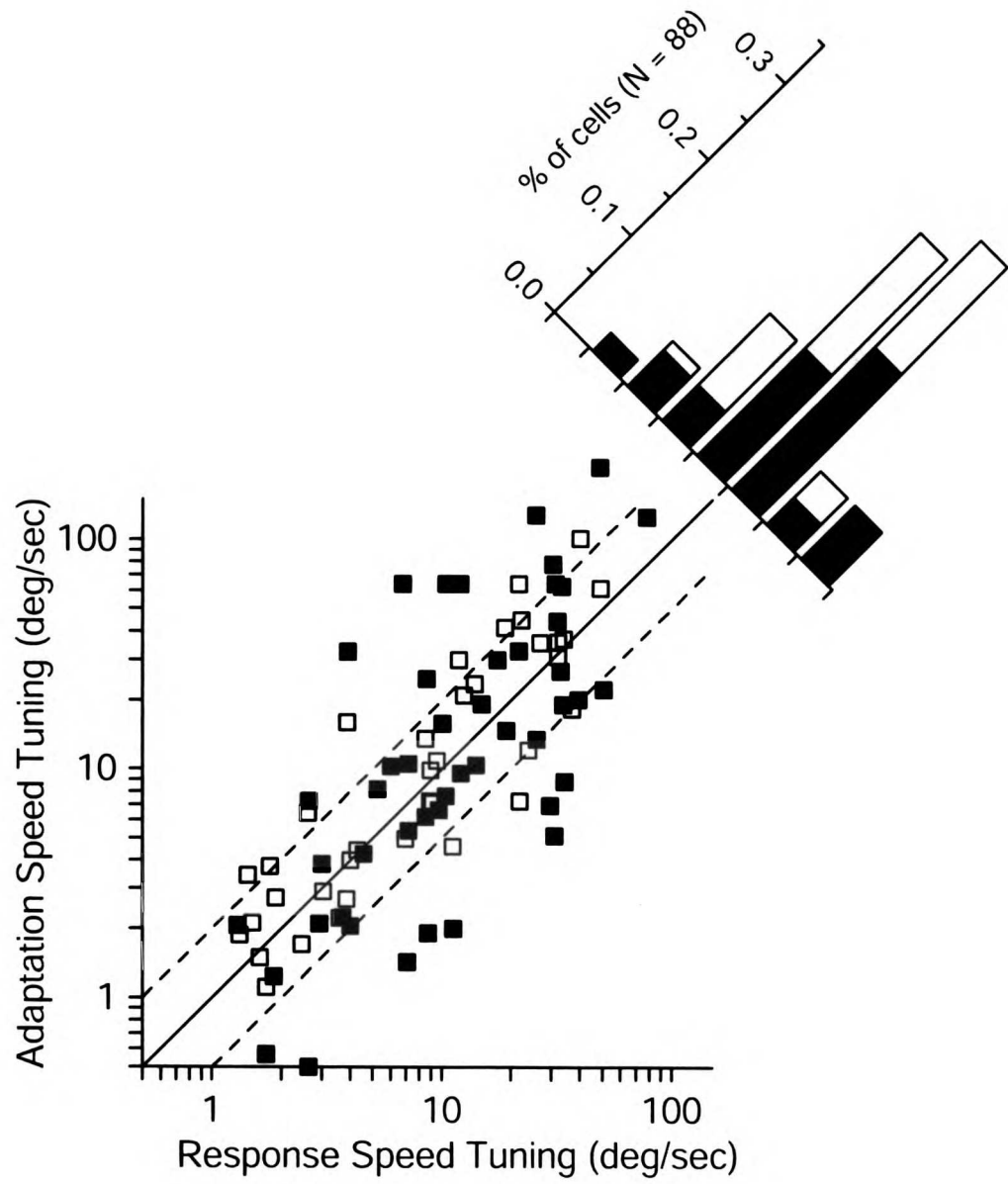
Figure 17

Figure 17. The response preferred speed and adaptation preferred speed. Each

square indicates the actual preferred speed of the neuron to single

presentations of motion and the preferred speed of adaptation. The filled

squares indicate fits for which the preferred speed of the adaptation tuning

was deemed significantly different from the preferred speed of the response

tuning. The solid line indicates a slope of 1, while a slope of 2 and 0.5 is

indicated by the two dashed lines.
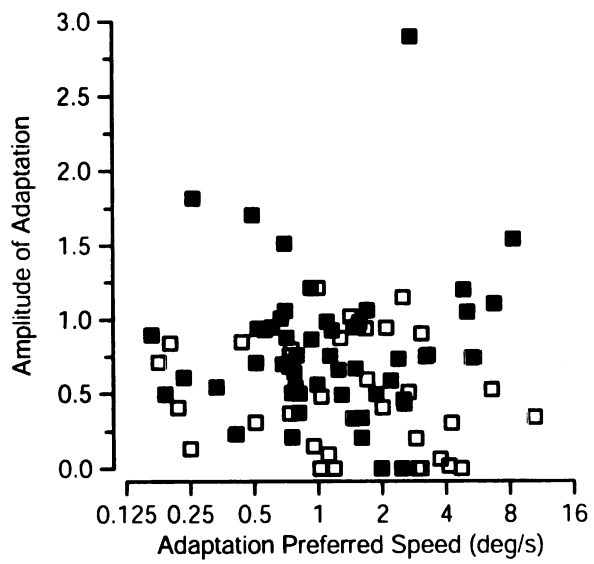
Figure 18

Figure 18. The preferred speed and amplitude of adaptation. The amplitude of

adaptation, defined as the fit value of R_{max} in equation 2 normalized by the

response of the neuron to the test motion alone, is shown relative to the

adaptation preferred speed. Filled squares indicate fits for which the

amplitude of the adaptation tuning had a preferred speed significantly

different from the preferred speed of the response tuning. Hollow symbols

were not deemed statistically significant by this criterion.

Discussion

We have studied the direction and speed tuning of short-term adaptation in neurons in area MT by systematically varying the direction and speed of the first component of stimulus motion and measuring its effect on the response to a second component of stimulus motion. The measured selectivity of adaptation for direction and speed allows us to put constraints on the possible mechanisms that underlie adaptation in area MT.

Constraints resulting from the direction tuning of adaptation

For the majority of neurons in our population, adaptation was greatest in the direction that also elicited a response and it was weakest in the opposite direction. This indicates that adaptation is not the result of an untuned mechanism based upon interactions regardless of the neurons' tunings for direction (Heeger et al., 1996; Carandini et al., 1997; Simoncelli and Heeger, 1998). However, the direction selectivity of adaptation is consistent with other mechanisms for adaptation. In particular, network interactions based on the tuning of neurons, cellular activity-dependent adaptation processes, synaptic depression and V1 neuron input dynamics are all mechanisms that could lead to the directionally selective responses observed here.

However, two findings lead us to question a cellular, activity-based mechanism for adaptation such as spike rate adaptation (McCormick et al., 1985; Connors and Gutnick, 1990). First, the adaptation direction tuning is broader than the

response direction tuning. In many cases, the neuron did not respond to the conditioning motion, yet the response to the test motion was decreased after that conditioning motion. For an activity-dependent mechanism to account for this result, it would have to utilize the subthreshold activity of the neuron, and not the suprathreshold activity that we actually measure. Second, we found that the adaptation mechanism not only reduced the responses of many neurons, but could also increase the responses of the neurons to test motion. When the background firing rate of neurons is low as is the case for many MT neurons (see Figure 4), a cellular activity-based mechanism would not be able to account for an enhancement in the response in the presence of conditioning motion.

In a manner similar to activity-based adaptation, synaptic depression would predict that the greater that neurons respond to the conditioning motion, and are thus driven by their inputs, the more the efficacy of individual synapses providing input would be reduced. The preferred direction for adaptation would therefore always be in the conditioning direction that elicited the largest response: the same direction used as the test stimulus. However, conditioning motion in the direction opposite the test motion also reduced the response of many neurons to the test stimulus. In order for synaptic depression to mediate adaptation, the conditioning motion opposite the test motion would have to activate synapses to reduce their efficacy. It is possible that some neurons in area MT receive input from neurons that are tuned for orientation instead of direction, although studies characterizing V1 neurons that project to MT indicate that these neurons are already directional and respond very weakly to motion in the null direction (Movshon and Newsome, 1996).

Although we have demonstrated that the effect of conditioning motion was largest when the conditioning and test directions were the same, there were some changes in the responses of neurons to motion in the opposite directions. In particular, the response to the test motion was delayed by ~20 ms when the conditioning motion moved in the opposite direction. This delay is explored in detail in the third paper in this series, but it deserves mention here because our analysis of the response to the test motion separated the effects of conditioning motion on the time course of response from the amplitude of response. The peak 32 ms of firing over the response period was measured for each direction of conditioning motion so that only the effect of conditioning motion on the response amplitude was measured. If this delay is ignored, and the same analysis period is used for all directions of conditioning motion, the direction selectivity of adaptation does not change; conditioning motion in the test direction still suppresses the test response to the largest degree. However, fewer neurons show an enhancement of response after conditioning motion in the direction opposite the test direction when using the same analysis period. The effects of conditioning motion on the latency of response appear to be separate from the changes in response amplitude. Although the shifts in latency were strongest in the direction opposite the test direction, the shifts were not linked to changes in response amplitude across neurons. In addition, the effects on latency had a much shorter time course than the effects on response amplitude. We therefore believe that these effects are derived from the integration of motion signals, and not the induction of short-term adaptation.

Constraints resulting from the speed tuning of adaptation

The analysis of the speed tuning of adaptation yielded results similar to the direction tuning of adaptation. Adaptation was also tuned for speed, indicating that adaptation does not arise from untuned interactions. Further, we saw that the preferred speed of adaptation could be the same *or* different from the preferred speed of neuron to single presentations of motion. Such a distinction between the tuning curves for adaptation and response indicates that a mechanism based on the activity of a neuron is not the primary component of the adaptation we observe in area MT. An activity-based mechanism would elicit the most suppression for the conditioning motions that most excited the neuron and the tuning curves of adaptation and response would thus be linked. Instead, this adaptation tuning is consistent with a network-based model in which the tuning of neurons interacting may be same or different. Additionally, this tuning could be derived from the response properties of neurons in V1, where neurons may also be modulated by changes in the speed of motion. If V1 neurons are not modulated by the speed of conditioning motion in the same manner as observed in area MT, synaptic depression alone could not account for observed difference in the tuning of adaptation and response. The synapses strongly activated by the conditioning motion, and generating a large response in the neuron, would be depressed during the test motion. But the conditioning speeds that generated the greatest response were often not the conditioning speeds that modulated the test response. These response properties are consistent with the view that many neurons in MT not only respond to the direction and speed of motion, but also to acceleration (Lisberger and Movshon, 1999). Given these constraints from the

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direction and speed tuning of adaptation, the most likely candidate mechanisms for

adaptation observed in area MT are V1 neuron dynamics or tuned network

interactions.

Links to previous studies

Other groups have examined the source of short-term adaptation in V1

(Kulikowski et al., 1979; Nelson, 1991a, b, c). These neurons respond with a

transient period of high firing when presented with a flashed bar (Kulikowski et al.,

1979). Using a similar condition/test paradigm, Nelson showed that a conditioning

bar flashed in the same orientation as a test bar suppressed the responses of neurons,

while conditioning bars flashed in the orthogonal orientation had little effect on the

test bar response. Nelson also injected a $GABA_A$ blocker into V1 to test if the

adaptation was extinguished in the absence of inhibitory circuitry; he found that some

adaptation remained. Nelson concluded that adaptation was presynaptic in origin

because inhibition through $GABA_B$ channels would be too slow to account for the

fast adaptation of responses and the input neurons from the LGN did not have the

same paired stimulus suppression. That study suggests that inhibition does not play a

central role in short-term adaptation of V1 neurons and instead supports a synapse-

specific mechanism for adaptation. Our results in the present discourage, but do not

rule out, a synapse specific mechanism (but see Priebe, chapter 2). However,

accounting for the speed selectivity of adaptation through such a synapse-specific

mechanism would require that the activity of a subset of synapses, tuned, for

example, to fast motion, could decrease the efficacy of a different subset of synapses,

tuned for slow motion. Such an interaction between synapses (linked to the tuning of the synapses) has not been previously described in V1 or MT.

Britten and Heuer (1999) used a paired-stimulus paradigm to measure the interaction between two simultaneously moving stimuli placed within a single MT neuron's receptive field (Britten and Heuer, 1999). MT neurons' responses to both stimuli were not well predicted by a summation but instead by the average of the response to each stimulus alone, independent of stimulus location. If the same underlying mechanism were responsible for the short-term adaptation reported here, we would expect that the test response after conditioning motion in the null direction would lead to a reduction of response while conditioning motion in the preferred direction would lead to no change in the response to the test motion; however, this is in complete opposition to our measurements. An important difference in our paradigm and that of Britten and Heuer is that their stimuli were displaced spatially but synchronous while our stimuli were spatially overlapping but asynchronous. Spatial and temporal interactions may not be subserved by the same adaptation mechanisms. We did find an interaction between the null conditioning motion and test response in the form of a delay in response and this delay may be a residual of a fast-acting inhibitory process that elicits the averaging Britten and Heuer observed.

Function of adaptation

Psychophysics has long used adaptation as a method to discern which components of sensory processing are linked. By adapting to a single stimulus and measuring the effects of the adaptation on the processing of other stimuli, the overlap

between functional information processing channels can be estimated. Recently there has been a greater appreciation for the function of adaptation in information processing. Muller and colleagues (1999) have shown that rapid adaptation by V1 neurons to the orientation of a bar can actually decrease the correlation between neurons tuned to different orientations but responding to the same stimulus. Such a reduction in correlation between neurons also allows neurons to reduce the redundancy in their firing and pass more information per spike (Muller et al., 1999).

Adaptation also allows sensory systems to respond more to changes in the environment rather than to the absolute amplitudes of sensory input like luminance for V1 neurons or motion for MT neurons. Some behaviors actually require information about the change in a stimulus over time. Ocular smooth pursuit attempts to match the velocity of the eye with the velocity of targets in world. Modeling studies of smooth pursuit eye movements indicate that target velocity and acceleration are critical inputs to yield appropriate pursuit behavior. Sensing the velocity and acceleration of target motion requires not only that information about the movement of a target, but how the movement of the target changes in time. The response properties recorded in this study appear to provide the necessary signals for the proper function of the behavior: neurons in MT are not only sensitive to the velocity of motion, but are modulated by changes in the velocity of motion.

References

Abbott LF, Varela JA, Sen K, Nelson SB (1997) Synaptic depression and cortical gain control. Science 275:220-224.

Allman J, Meizin F, McGuinness E (1985a) Stimulus specific responses from beyond the classical receptive field: neurophysiological mechanisms for local-global comparisons in visual neurons. Annual Review of Neuroscience 8:407-430.

Allman J, Miezin F, McGuinness E (1985b) Direction- and velocity-specific responses from beyond the classical receptive field in the middle temporal visual area (MT). Perception 14:105-126.

Britten KH, Heuer HW (1999) Spatial summation in the receptive fields of MT neurons. Journal of Neuroscience 19:5074-5084.

Brosch M, Schreiner CE (1997) Time course of forward masking tuning curves in cat primary auditory cortex. Journal of Neurophysiology 77:923-943.

Carandini M, Ferster D (1997) A tonic hyperpolarization underlying contrast adaptation in cat visual cortex. Science 276:949-952.

Carandini M, Heeger DJ, Movshon JA (1997) Linearity and normalization in simple cells of the macaque primary visual cortex. Journal of Neuroscience 17:8621-8644.

Chung S, Ferster D (1998) Strength and orientation tuning of the thalamic input to simple cells revealed by electrically evoked cortical suppression. Neuron 20:1177-1189.

Churchland MM, Lisberger SG (2000) Apparent motion produces multiple deficits in visually guided smooth pursuit eye movements of monkeys. Journal of Neurophysiology 84:216-235.

Connors BW, Gutnick MJ (1990) Intrinsic firing patterns of diverse neocortical neurons. Trends in Neurosciences 13:99-104.

Dubner R, Zeki SM (1971) Response properties and receptive fields of cells in an anatomically defined region of the superior temporal sulcus in the monkey. Brain Research 35:528-532.

Ferster D, Chung S, Wheat H (1996) Orientation selectivity of thalamic input to simple cells of cat visual cortex. Nature 380:249-252.

Gibson J, Radner M (1937) Adaptation, after-effect and contrast in the perception of tilted lines: I. quantitative studies. Journal of Experimental Psychology 20:453-467.

Heeger DJ, Simoncelli EP, Movshon JA (1996) Computational models of cortical visual processing. Proceedings of the National Academy of Sciences of the United States of America 93:623-627.

Kaplan E, Mukherjee P, Shapley R (1993) Information filtering in the lateral geniculate nucleus. Contrast Sensitivity 5:183-199.

Kilgard MP, Merzenich MM (1995) Anticipated stimuli across skin. Nature 373:663-663.

Kulikowski JJ, Bishop PO, Kato H (1979) Sustained and transient responses by cat striate cells to stationary flashing light and dark bars. Brain Research 170:362-367.

Lisberger S, Movshon J (1999) Visual motion analysis for pursuit eye movements in area MT of macaque monkeys. Journal of Neuroscience 19:2224-2246.

Maunsell JHR, Van Essen DC (1983) Functional properties of neurons in middle temporal visual area of the macaque monkey. I. selectivity for stimulus direction, speed, and orientation. Journal of Neurophysiology 49:1127-1147.

McCormick DA, Connors BW, Lighthall JW, Prince DA (1985) Comparative electrophysiology of pyramidal and sparsely spiny stellate neurons of the neocortex. Journal of Neurophysiology 54:782-806.

Merrill EG, Ainsworth A (1972) Glass-coated platinum-plated tungsten microelectrode. Med Biol Eng 10:495-504.

Mikami A, Newsome W, Wurtz R (1986) Motion selectivity in macaque visual cortex. II. Spatiotemporal range of directional interactions in MT and V1. Journal of Neurophysiology 55:1328-1339.

Movshon JA, Newsome WT (1996) Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. Journal of Neuroscience 16:7733-7741.

Muller JR, Metha AB, Krauskopf J, Lennie P (1999) Rapid adaptation in visual cortex to the structure of images. Science 285:1405-1408.

Nakayama K (1985) Biological image motion processing: a review. Vision Research 25:526-660.

Nelson S, Toth L, Sheth B, Sur M (1994) Orientation selectivity of cortical neurons during intracellular blockade of inhibition. Science 265:774-777.

Nelson SB (1991a) Temporal interactions in the cat visual system. I. Orientation-selective suppression in the visual cortex. Journal of Neuroscience 11:344-356.

Nelson SB (1991b) Temporal interactions in the cat visual system. II. Suppressive and facilitatory effects in the lateral geniculate nucleus. Journal of Neuroscience 11:357-368.

Nelson SB (1991c) Temporal interactions in the cat visual system. III. Pharmacological studies of cortical suppression suggest a presynaptic mechanism. Journal of Neuroscience 11:369-380.

Ohzawa I, Sclar G, Freeman RD (1985) Contrast gain control in the cat's visual system. Journal of Neurophysiology 54:651-667.

Recanzone GH, Merzenich MM, Schreiner CE (1992) Changes in the distributed temporal response properties of SI cortical neurons reflect improvements in performance on a temporally based tactile discrimination task. Journal of Neurophysiology 67:1071-1091.

Saul A, Humphrey A (1990) Spatial and temporal response properties of lagged and nonlagged cells in cat lateral geniculate nucleus. Journal of Neurophysiology 64:206-224.

Schrater P, Simoncelli E (1998) Local velocity representation: evidence from motion adaptation. Vision Research 38:3899-3912.

Simoncelli EP, Heeger DJ (1998) A model of neuronal responses in visual area MT. Vision Research 38:743-761.

Sokal RR, Rohlf FJ (1995) Biometry : the principles and practice of statistics in biological research, 3rd Edition. New York: W.H. Freeman.

Stevens SS, Davis H (1938) Hearing. Its Psychology and Physiology. New York: Wiley.

Tolhurst DJ, Walker NS, Thompson ID, Dean AF (1980) Non-linearities of temporal summation in neurones in area 17 of the cat. Experimental Brain Research 38:431-435.

Troyer TW, Krukowski AE, Priebe NJ, Miller KD (1998) Contrast-invariant orientation tuning in cat visual cortex: Thalamocortical input tuning and correlation-based intracortical connectivity. Journal of Neuroscience 18:5908-5927.

Victor JD (1987) The dynamics of the cat retinal X cell centre. Journal of Physiology 386:219-246.

Welch L, Macleod DI, Mckee SP (1997) Motion interference: perturbing perceived direction. Vision Research 37:2725-2736.

Wohlgemuth A (1911) On the aftereffect of seen movement. Journal of Psychology 1:1-117.

Wörgötter F, Koch C (1991) A detailed model of the primary visual pathway in the cat: comparison of afferent excitatory and intracortical inhibitory connection schemes for orientation selectivity. Journal of Neuroscience 11:1959-1979.

Chapter 2

The spatial selectivity of short-term adaptation
in macaque area MT

Abstract

Neurons in area MT, a motion sensitive area of extrastriate cortex, respond to target motion in two phases: an initial transient phase lasting ~30-50 ms followed by a sustained phase of reduced firing. The biological basis for this transition in firing, or adaptation, has not been determined. Three classes of adaptation mechanisms are: input- or synapse-specific mechanisms such as short-term synaptic depression, cellular mechanisms such as spike rate adaptation, and network mechanisms such as feedback inhibition. We measured the contribution of input-specific mechanisms to the transient firing of these neurons using a condition/test paradigm. Conditioning and test stimuli were placed within MT receptive fields but were spatially segregated so that the two stimuli would activate different populations of V1 neurons. Motion of either of the two stimuli produced responses in the isolated MT cell. The amplitude of transient firing of MT cells was measured in response to test motion preceded by conditioning motion. All neurons showed some reduction of transient firing to test motion following conditioning motion, demonstrating a spatial transfer of gain control. The transient firing to the test target was reduced on average by 73% by conditioning motion. The time course for the spatial transfer of adaptation by conditioning target motion was measured by changing the temporal interval between conditioning and test target movement. Consistent with our previous measurements of the temporal recovery from adaptation, temporal separation intervals of 120 ms showed significant transfer of adaptation. These results indicate that the shift from transient to sustained firing observed in MT cells is not solely due to an input-specific mechanism.

Introduction

The responses of sensory neurons to a stimulus depend upon the context of the stimulus presentation. In particular, responses of neurons in visual area MT undergo adaptation that depends upon the recent history of visual motion. For example, a brief presentation of visual motion causes dramatic changes in the response of an MT neuron to successive presentations of motion (Lisberger and Movshon, 1999). This paper investigates whether the spatial extent of the adaptation observed in MT is more consistent with a substrate within MT or before MT.

The responses of neurons along the visual pathway also exhibit adaptation similar to that observed in area MT. Retinal ganglion neurons, thalamic neurons and primary visual cortical neurons all respond with an initial transient high firing rate to the presentation of a stimulus inside their receptive field, but then the response quickly settles to a lower sustained rate of firing for the duration of the visual stimulus. For example, in primary visual cortex (V1), the neurons adapt to the presence of oriented bars; repeated presentations of the bar yield less response. This adaptation depends strongly on the orientation of the bar (Nelson, 1991). Presentation of a bar oriented differently from the neurons' preferred orientation does not elicit adaptation. We have previously shown that the adaptation induced in the responses of MT neurons also depends strongly on the neurons' preference for direction (Priebe, Chapter 1).

Because adaptation is known to occur at stages prior to area MT, it is possible that the adaptation observed in area MT is the result of an adaptation of the inputs to area MT. Neurons in V1 project directly to area MT and provide the majority of its

input. The response properties of the V1 neurons that project to MT and the neurons in MT are similar: both sets of neurons are directionally selective (Movshon and Newsome, 1996). However, the spatial extent of the receptive fields of V1 neurons is much smaller than the spatial extent of MT neurons' receptive fields at the same eccentricity. According to Hubel and Wiesel (1974), V1 neurons representing the central ten degrees of visual space have receptive fields that extend less than a degree (Hubel and Wiesel, 1974). The size of MT neuron receptive fields grows with the eccentricity of the neuron's receptive field, so that at an eccentricity of 10°, receptive fields extend about 10° (Maunsell and Van Essen, 1983; Britten and Heuer, 1999).

We used the difference between the sizes of the receptive fields in MT and V1 to investigate whether the adaptation observed in MT could be based upon a change in the strength of the input from V1. There are two different input-based mechanisms that could account for the adaptation observed in MT neurons. The neurons in V1 could be undergoing adaptation to the motion stimulus, or the synapses of projecting V1 neurons to MT could be undergoing short-term synaptic depression (Abbott et al., 1997). Both adaptation mechanisms rely on the input to area MT undergoing the same adaptation as is observed in MT neurons. Because of the differences between the receptive field sizes of neurons in V1 and MT, if the mechanism for adaptation in MT is either of these input-based mechanisms, then the spatial extent of adaptation should be on the same scale as the receptive field size of neurons in V1. We can thus measure the spatial extent of adaptation to determine whether an input-specific mechanism could account for the adaptation we observe in MT. The approach taken in this paper is to induce adaptation in one portion of an MT neuron's receptive field

and then to measure whether that adaptation is still evident when a different portion of the receptive field is stimulated with motion. The spatial transfer of adaptation occurs when the adaptation induced in one portion of the MT neuron's receptive field affects the response to motion in another portion of the receptive field. Because the receptive fields in area MT are large, it is possible to place two non-overlapping stimuli inside a single receptive field and generate robust responses from motion in either stimulus location.

We first demonstrate that the adaptation is transferred over spatial extents larger than the receptive field of a V1 neuron. Therefore, the short-term adaptation in MT cannot be based on an input-specific mechanism. We then measure the effect of the distance between the conditioning and test motion on the transfer of adaptation. Finally, we were concerned that motion in our stimuli might modulate the responses of V1 neurons outside the classically defined receptive field. To control for the effects of motion beyond the classically defined receptive field, we measured the responses of directionally selective neurons in V1 to the same stimulus configuration used for recordings in area MT. In these V1 neuron recordings, we found no significant modulation of response to stimulus motion inside the receptive field of neurons by preceding motion outside the receptive field. By recording in V1, we were able to directly measure any adaptation that occurs in these neurons. We found that the neurons in V1 did not adapt to our stimulus as the neurons in area MT adapted to stimulus motion. Because V1 neurons did not adapt to our stimulus motion the basis for the adaptation observed in area MT cannot be adaptation occurring in V1.

Materials and Methods

Physiological preparation

Extracellular single-unit microelectrode recordings were made in areas MT

and primary visual cortex of anesthetized, paralyzed macaque monkeys (*Macaca*

fascicularis, mulatto) and in a single awake, behaving monkey. Details of the

anesthesia, surgical preparation and recording from the anesthetized monkeys have

been explained elsewhere (Priebe, Chapter 1) and were identical, except that

recordings were also made in primary visual cortex. For recording in V1, a small

craniotomy was performed directly over the central representation of visual space and

small perforations were made in the underlying dura to allow the insertion of

microelectrodes. The locations of unit recordings in MT were confirmed by

histological examination of the brain after the experiment, using methods described in

Lisberger and Movshon (1999).

Experiments were also run on a male rhesus monkey (*Macaca mulatta*) that

had been trained to fixate spot targets. The experimental and training protocol has

been described before (e.g. Lisberger and Westbrook, 1985). Eye movements were

measured with the scleral search coil method (Judge et al., 1980), using eye coils that

had been implanted with sterile procedure while the animal was anesthetized with

isofluorane. In a separate surgery, stainless steel plates were secured to the skull and

attached with dental acrylic to a cylindrical receptacle that could be used for head

restraint. In addition, a craniotomy was performed over the superior temporal sulcus

and a cylinder was attached to the surface of the skull (Crist, California).

Microelectrodes were introduced through this cylinder into the cortex and lowered into area MT. During experiments, the head was immobilized by attaching a post to both the receptacle and the ceiling of a specially-designed primate chair. Animals were rewarded with juice for accurately fixating a target at the center of the display. Experiments were run daily, typically lasting two hours.

All methods for recordings in awake and anesthetized monkeys had received prior approval by, and were in compliance with, the regulations of the *Institutional Animal Care and Use Committee* at UCSF.

Stimulus Presentation

After isolating a single unit in area MT of anesthetized monkeys, its receptive field was mapped on a tangent screen by hand. All of the neurons reported in this paper had receptive field centers within 10° of the fovea. In the experiments on anesthetized animals, a mirror was then positioned such that a random dot texture on a display oscilloscope fell within the receptive field of the isolated neuron and the direction, speed and spatial tuning of the neuron were measured as described previously (Priebe and Lisberger A). We used an online analysis program to determine the spatial extent of the receptive field. If the receptive field of the neuron was not within the confines of our display, we adjusted the mirror that positioned the visual stimulus so that it would be presented at the center of the unit's receptive field. If the position of the mirror was changed, we once again measured the spatial extent of the receptive field.

After the spatial extent of the receptive field was determined, we chose two locations to place two textures of dots within the receptive field of the MT neuron. These two textures were separated by at least 2° for most of our units (43/67), but we did record from some neurons with textures only separated by 1.2°. After the position of the two moving textures was determined, we measured the responses of the neurons to motion in one texture followed by motion in the other texture. The motion in the textures was always asynchronous and the interval between motion in the two textures was varied (0, 32, 64, 96, 128 and 256 ms).

The presentation of the stimulus to the awake animal was similar. After isolating a single unit in area MT, its receptive field was initially mapped by measuring the response to small (4° by 4°) moving textures on the oscilloscope while the monkey fixated a spot in the center of the display. The preferred direction and speed of the neuron was measured in the same manner as in the anesthetized recordings. However, the moving textures in these experiments were not surrounded by a field of stationary dots. The locations for textures were chosen to ensure that the textures were spatially separated from each other by at least 1.5° and the motion in either texture generated a response. As in the anesthetized recordings, we measured the response of the neurons to motion in one texture followed by motion in the other texture. The motion of the textures was always asynchronous, but there was no interval between the first component of motion (referred to as "conditioning motion") and the second component of motion (referred to as the "test motion").

For the recordings in primary visual cortex of anesthetized monkeys, the same protocol was employed for extracting the preferred direction, speed and spatial

location of individual single units. After the center of the receptive field was directed towards the center of the display, a texture of moving dots (4° by 4°) was used to stimulate the neuron (referred to as the "test motion"). This motion was preceded by motion in one of eight textures surrounding the texture at the center of the display. The dot density of the display for all anesthetized recordings was 0.75 dots/deg^2. For the awake recordings, the dot density was 0.5 dots/deg^2.

Data Acquisition and Analysis

Experiments were controlled by a computer program running on a UNIX workstation (Priebe and Lisberger A). In both anesthetized and awake recordings, trials were sequenced by shuffling the list of possible trials and presenting each trial at random until all the trials in the list had been presented. The texture for each trial was generated using a different seed to generate pseudorandom sequence of initial dot positions, except where explicitly noted. For all of the data shown in this study, the minimum number of repeats recorded for the spatial interaction experiment was 34 (varied from 34-285).

The direction, speed and spatial selectivity of each neuron in areas MT and V1 was determined by the single unit's mean firing rate during the stimulus presentation. To measure the directional selectivity of neurons in V1, we used a directional index (DI), defined by:

$$DI = 1 - \frac{R_N - R_{Back}}{R_P - R_{Back}} \tag{1}$$

where R_p is the response elicited by motion in the preferred direction of the neuron and R_n is the response elicited by the direction 180° away from the preferred

direction. R_{back} is the response of the neuron to a stationary texture. In this study, we included neurons with a criterion of a DI of greater than 0.5 (29). Since many neurons in V1 are not directionally selective, the responses of only those that were directionally selective are included in this analysis.

Results

As illustrated previously (Priebe, chapter 1, Lisberger and Movshon, 1999),

many neurons in area MT undergo adaptation in response to moving stimuli. While

these neurons are initially highly responsive to visual motion in their receptive field,

their response quickly decreases and remains steady at a sustained firing rate for the

duration of the motion stimulus. Two mechanisms that could account for the

adaptation are the short-term depression of the efficacy of synapses that provide input

from primary visual cortex (V1) to area MT or adaptation occurring at the level of V1

and simply replayed in area MT.

To investigate whether either of these input-based mechanisms underlies the

adaptation observed in area MT, we recorded the responses of neurons in areas MT

and V1 in response to motion stimuli in more than one spatial location. The spatial

extent of the receptive fields of MT neurons is relatively large in comparison to the

size of receptive fields of V1 neurons at corresponding eccentricities. MT neurons

appear to pool the responses of neurons in V1 that have different spatial receptive

locations, thus giving the MT neurons larger receptive fields. This hypothesis is

illustrated in Figure 1: a single MT neuron integrates the responses of V1 neurons

with different spatial receptive fields. Our experiments took advantage of this

difference in receptive field size; it is possible to stimulate a single MT neuron with

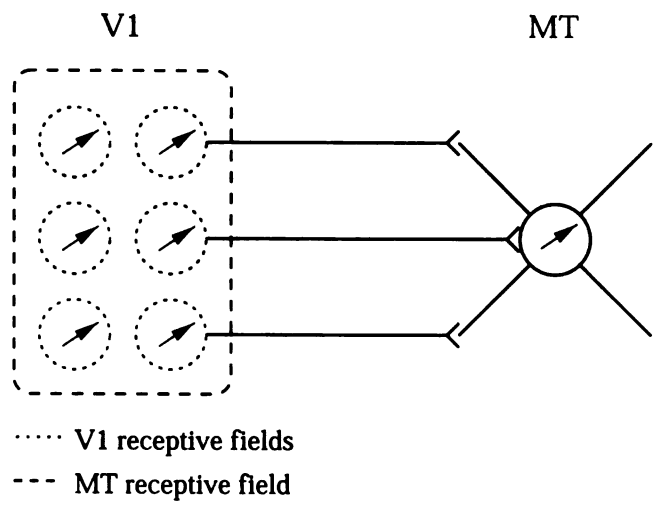non-overlapping motions that excite different sets of neurons in V1. Our protocol

V1   MT

····· V1 receptive fields
--- MT receptive field

Figure 1

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Figure 1. A schematic representation of the convergence of input from V1 neurons to

a single MT neuron. This schematic shows the size of V1 receptive fields

relative to the size of an MT receptive field. The V1 receptive fields are

indicated by the fine dashed lines, while the MT receptive field is indicated by

the large dashed lines. MT neurons receive input from directionally-selective

V1 neurons, as indicated by the arrows drawn in the centers of both the V1

and MT neurons.

induced adaptation in an MT neuron by displaying motion in one portion of its receptive field and then measured the transfer of that adaptation to the response to motion in a different portion of the receptive field. If adaptation in MT is based upon a reduction in the efficacy of synapses from V1 to MT or an adaptation of the responses of neurons in V1, the spatial selectivity for adaptation should be on the scale of the receptive fields sizes in V1 and will not transfer from one portion of an MT receptive field to another. On the other hand, if adaptation is derived from mechanisms within area MT, the spatial selectivity for adaptation should be on the scale of the receptive field sizes of MT neurons and will transfer. We first demonstrate that the spatial selectivity for adaptation in area MT is transferred between spatial locations larger than a receptive field in V1. We then recorded in V1 in order to confirm that no effects outside the receptive fields of V1 neurons affect their response to motion inside their receptive fields

The spatial transfer of adaptation

We tested whether adaptation in area MT could transfer between spatial locations larger than the size of a V1 receptive field. This was done by inducing adaptation in one portion of an MT neuron's receptive field and measuring the transfer of adaptation to the response to motion in a distinct location within the receptive field. The receptive fields of 67 neurons in area MT were initially mapped by placing small (4° by 4°) textures in different locations on our display and measuring the response in all locations. All of the neurons in our sample population had receptive fields within 10° of the fovea. An example of a receptive field of a
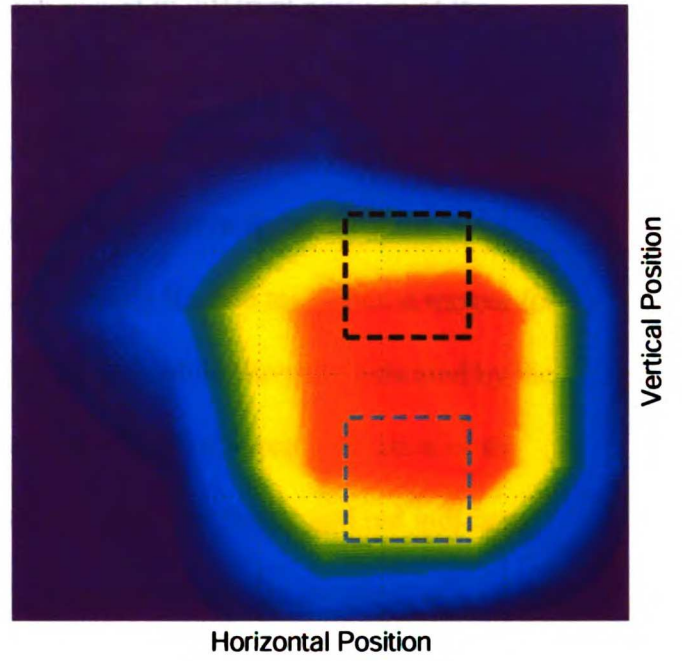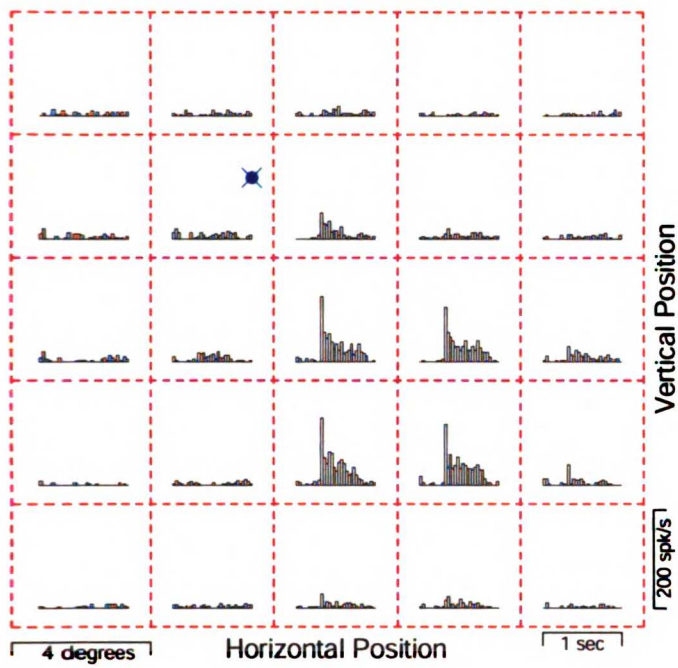
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Figure 2

Figure 2. The spatial extent of an MT neuron's receptive field. The left panel shows

the response of a MT neuron to motion placed in different portions of the

visual field. The position of motion is indicated by the placement of each

histogram in the red grid. The response of the cell to each position of texture

movement is indicated by the histogram. The texture appeared at the

beginning of each trial and remained stationary for 256 ms. Then it moved for

512 ms and was stationary again. The location of the fovea is indicated by the

blue circle and cross. In the right panel, a pseudocolor representation of the

receptive field is shown in which blue indicates low firing, and red indicates

high firing. The gray and black dashed boxes indicate the locations of

conditioning and test motion. Fine dashed lines indicate position in 4 degree

steps.

single unit in MT is shown in Figure 2. In this example, moving textures appeared in each of the 25 different locations on the display. The response to motion in each of those locations is shown by the histogram at each location of the left panel and by color in the right panel. After the spatial extent of the neuron's receptive field was determined, two locations were chosen that were separated by at least 1.2° and that could individually excite the neuron. For the neuron in Figure 2, the locations of the two textures are indicated by the dashed lines. These two locations do not overlap and the distance between them is more than 2°.

Adaptation was first induced by stimulating the neuron in one location, called the conditioning motion, then measuring the change in the response of the neuron to motion in another location, called the test motion. To extract the effect of conditioning motion on the response to the test motion, the response to the conditioning motion alone was also measured so that it could be subtracted from the response of the two motion components together. The neuron with the receptive field illustrated in Figure 2 responded with a high transient firing rate to conditioning motion in either location, and then settled to a lower sustained firing rate (Fig. 3A,B). The response of the neuron to a stimulus consisting of the conditioning motion followed by the test motion is shown in the Figures 3C and D. At the time when the test motion alone would have evoked a large transient of firing rate in the absence of prior conditioning motion, the transient response to the test motion was small (Fig. 3D) or absent (Fig. 3C). Subtraction of the response to the conditioning motion alone from the response to the condition-test pair revealed the response to the test motion when preceded by conditioning motion, confirming that the transient response to test
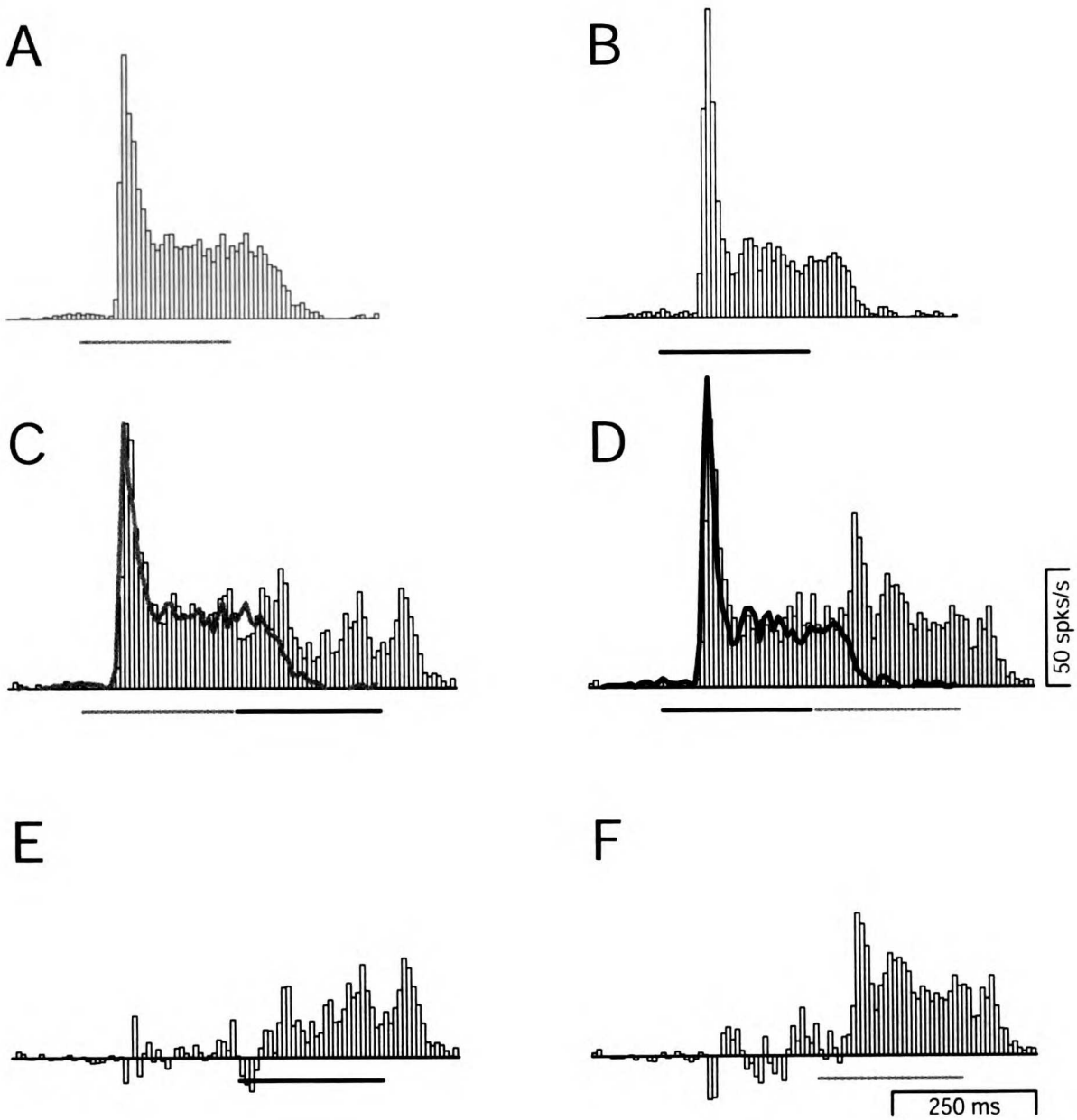
Figure 3

Figure 3. The transfer of adaptation across space. *A,B*: The responses of the neuron

shown in Figure 2 are shown to motion in the area defined by the gray box (*A*)

or the black box (*B*) alone. *C,D*: The response of the neuron is shown to

motion in the gray box followed by the black box (*C*) or motion in the black

box followed by motion in the gray box (*D*). *E,F*: The result of the

subtraction of the response to the conditioning motion alone.

motion was severely attenuated by the presence of prior test motion at another site in the receptive field.

As was the case for the neuron in Figure 3, the adaptation induced in one spatial location significantly reduced the amplitude of the transient response to motion in another location for most of the neurons in our sample population. A measure of the transient amplitude of a neuron is the peak firing rate relative to the sustained firing rate, or transient-to-sustained ratio. We initially measured the effect of the conditioning motion on the test response by comparing the transient-to-sustained ratio of each neuron in the absence and presence of conditioning motion. The transient response of the cell to the test motion was determined by measuring peak 32 ms of response that occurs within 150 ms after test motion began. The sustained response of the cell is defined as the average response of the cell during the period 150 to 250 ms after the motion in the test location began. A comparison of the transient-to-sustained ratios with and without conditioning motion for all the neurons in our sample population is shown in Figure 4A. The majority of the neurons lie below the line of slope one, indicating that the adaptation from the conditioning motion at one site caused a decrease in the transient-to-sustained ratio for a test motion at another site. The decrease was statistically significant in 52 of the 67 MT neurons tested in this experiment (filled symbols, p<0.05, paired t-test).

The degree of the transfer of adaptation from motion in one spatial location to another was quantified by measuring the decrease in the amplitude of the transient, relative to the sustained firing rate. A transient index (TI) was defined as:

$$TI = \frac{R_{testlcondition} - R_{sustained}}{R_{transient} - R_{sustained}} \tag{2}$$
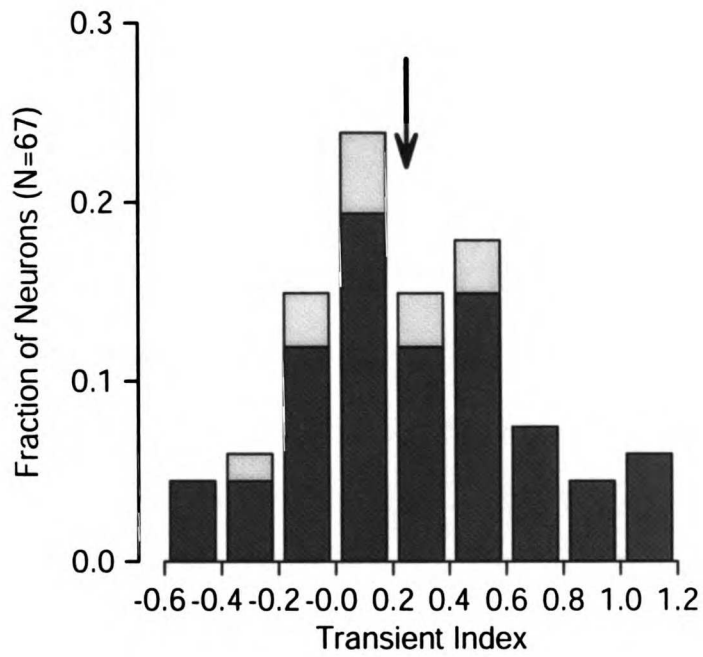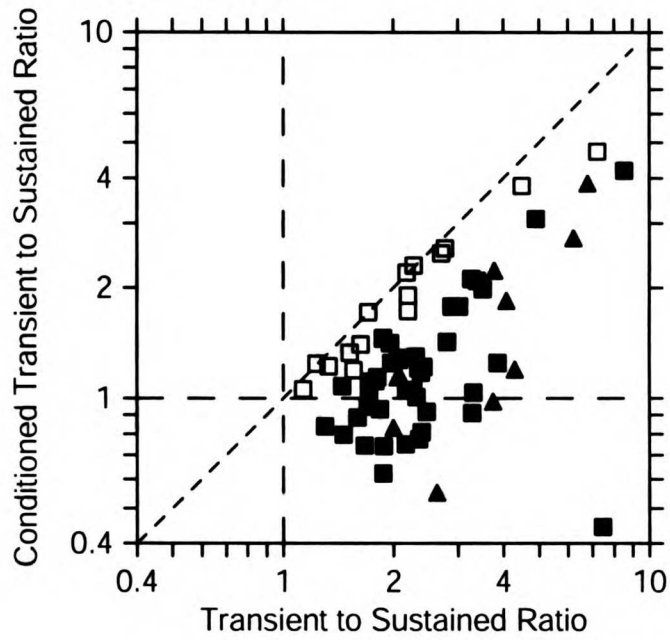
Figure 4

Figure 4. The spatial transfer of adaptation across the population of neurons. In the

top panel, the transient-to-sustained ratio measured in the absence of

conditioning motion is plotted relative to the transient-to-sustained ratio after

conditioning motion in another portion of the receptive field. The filled

symbols indicate neurons that had significant changes in transient firing due to

the conditioning motion (P<0.05, t-test). The neurons shown as open symbols

did not show a statistically significant effect. Neurons represented by squares

were recorded from the anesthetized animal, while triangles indicate neurons

recorded in the awake animal. The bottom panel shows the transient index

(TI, see Results) for all of the neurons in our population. Neurons recorded

from the anesthetized animal are shown by the dark bars, neurons recorded

from the awake animal are shown as light bars.

where $R_{transient}$ and $R_{sustained}$ are the transient and sustained responses of the neuron to the test motion when the test motion is presented alone, while $R_{test|condition}$ is the transient response to the test motion after presenting conditioning motion in another portion of visual space. A TI of zero indicates that the response to the test did not contain a transient response. A TI of one indicates that the transient response was not affected by the conditioning motion. For the neuron in Figure 3, the TI was -0.24 when test motion was in the location indicated by the dark bar, indicating a suppression of response below the sustained response, and 0.32 when the test motion was in the location indicated by the gray bar. Across our sample population, the mean TI was 0.23, demonstrating that on average the adaptation induced by conditioning motion in one portion of the receptive field reduced the amplitude of the transient to the subsequent test motion by 77%.

The response of some of the neurons to the test stimulus was reduced to levels below the sustained response by the conditioning motion. This may be an effect of the subtraction of the response to the conditioning motion alone from the response of both the conditioning and test motion. By making this subtraction we are making an assumption of linearity in the responses of the neurons. Estimating the transient response to the test motion without making this subtraction is problematic because the beginning of the response to the test motion is ambiguous. In computing the TI without making a subtraction we assumed that the test transient response should be measured at the same latency used to compute the transient when only the test motion was presented. The reduction in the transient responses of the neurons to the test motion is large enough that even without a subtraction, the mean TI was 0.47. This

TI is a conservative estimate of the effect of conditioning motion on test response because it does not isolate the response of the neuron to test motion alone. However, it is still evident that conditioning motion induced adaptation that was transferred to other portions of the receptive field.

The spatial selectivity of adaptation

The previous experiment demonstrates that adaptation can transfer over distances larger than a V1 receptive field; we also wanted to measure the spatial extent over which the transfer of adaptation could occur. A signal for adaptation may also come from a different area of visual cortex, such as MST. If adaptation in MT were caused by the activity of MST neurons, then the spatial selectivity of the adaptation would be larger than the size of receptive fields found in area MT. We measured the change in the transient response of neurons to test motion near the center of their receptive field by conditioning motion placed at different spatial distances from the test motion location. The conditioning motion was placed in 8 or 24 different locations surrounding the test motion at different distances. An example of the responses of a neuron to test motion, given different locations of the conditioning motion, is shown in Figure 5. In the rightmost panel, the conditioning motion (location indicated by the thick box) does not excite the neuron, and the transient response to the test motion (location indicated by the thin box) is unchanged by the conditioning motion. However, when the conditioning motion is placed inside the receptive field of the MT neuron, where the conditioning motion elicits responses, the amplitude of the transient to the test motion is reduced (middle three panels of
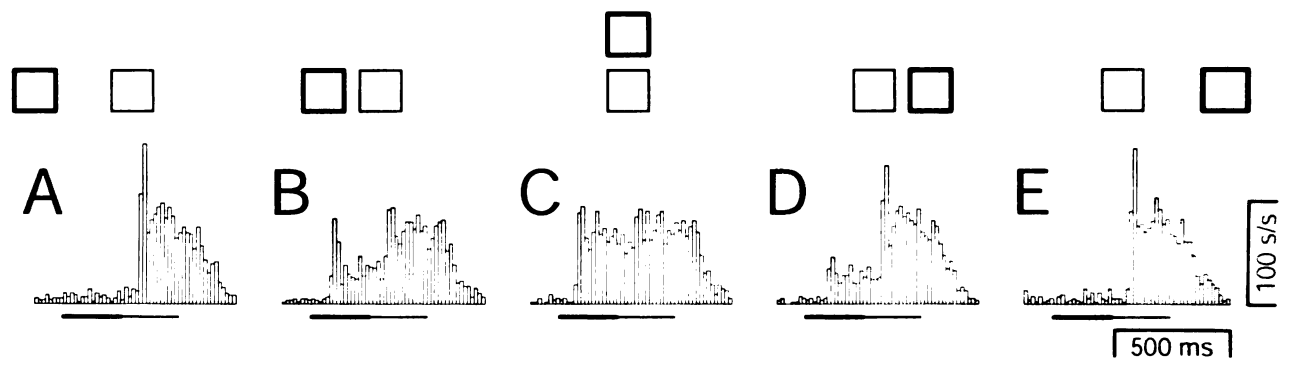
Figure 5

Figure 5. The relationship between distance and transfer of adaptation. *A,B,C,D,E*: The responses of an example neuron are shown to conditioning motion in different portions of the neuron's receptive field and test motion near the center of its receptive field. The location of the test motion is indicated by the thin box, while the location of the conditioning motion is indicated by the thick box. Each dot texture extended 4° by 4°. The distance between the centers of each texture were 11.3° (*A,E*) or 5.2° (*B,C,D*).

Figure 5). The leftmost panel shows the response when the conditioning motion is outside the receptive field of the neuron, where the neuron's response to the test motion is once again large.

To analyze the effect of the location of conditioning motion on the transient response to the test motion, as shown in Figure 5, we measured the TI for each location of conditioning motion. For this neuron, we used 24 different conditioning motion locations, all surrounding the center of the receptive field at various eccentricities. The relationship between the response to the conditioning motion and the transient response for the neuron in Figure 5 is shown in Figure 6A. Each point in the panel represents a different conditioning motion location. As the conditioning motion elicited greater responses in the neuron, the transient response to the test motion decreased. To quantify this relationship, we computed the correlation coefficient between the response to the conditioning motion and the TI. For this neuron, the correlation coefficient was -0.82, indicating a strong negative relationship between the response of the neuron to the conditioning motion and the TI. This strong negative correlation between the response to the conditioning motion and the TI was found in all of the neurons recorded and is shown in Figure 6C. The first principal component was also computed from these data points, providing an estimate of the relationship between the amount of response and the transient response to the test stimulus (Sokal and Rohlf, 1995). Using the slope and y-intercept of the first principal component, we computed the response amplitude at which the transient index returns to one. As seen in Figure 6A, the transient response of neurons to test motion was often reduced when no response occurred to the conditioning motion.
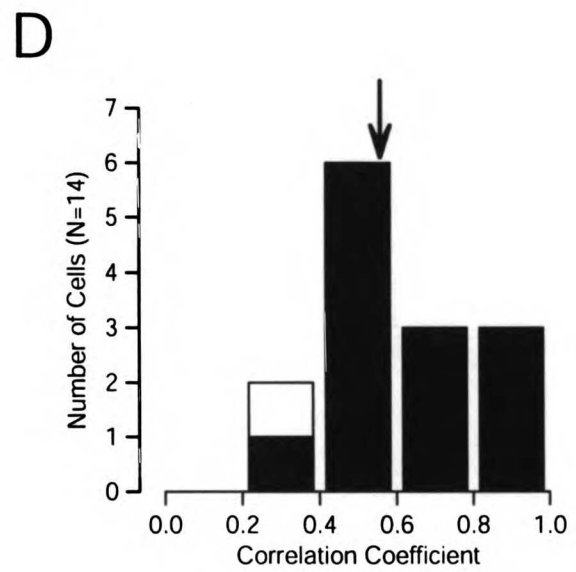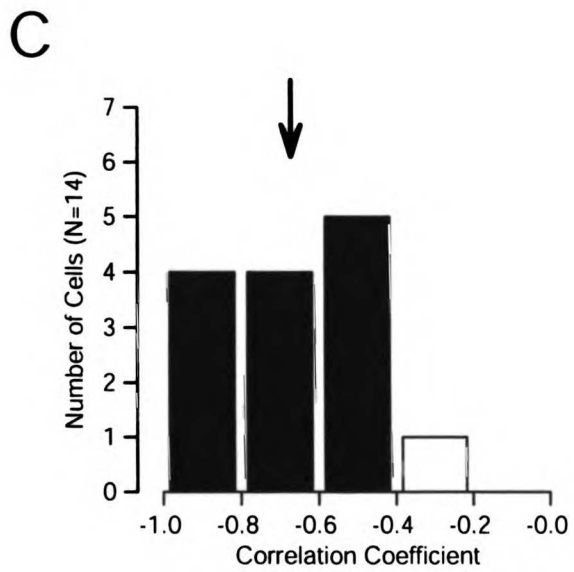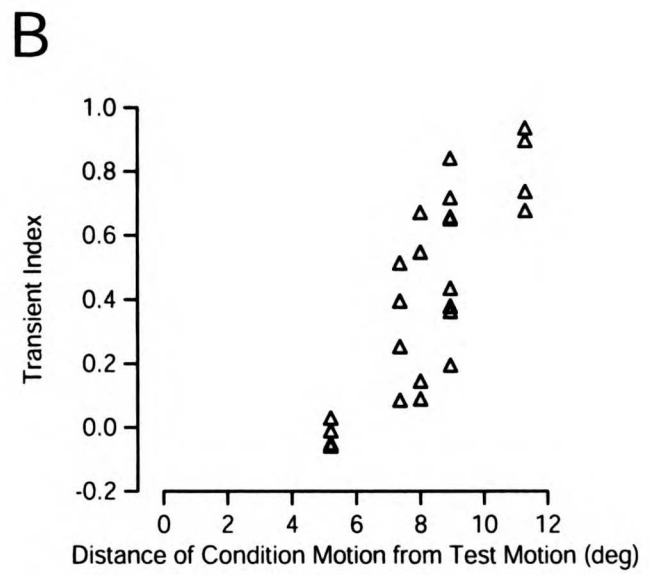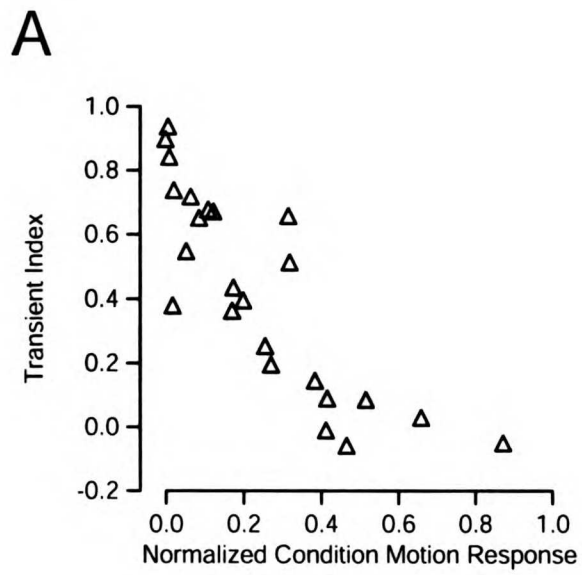
Figure 6

Figure 6. The dependence of the transient index on conditioning response and

distance. *A,B*: For the example neuron in Figure 5, the transient index (TI) is

shown for each location of conditioning motion. The TI is shown relative to

the conditioning responses (*A*) or the distances between the center of test and

conditioning motion locations (*B*). *C,D*: Histograms of the correlation

coefficients for all of the neurons tested between the transient index and the

conditioning motion response (*C*) or the transient index and the distance

between the conditioning and test motion (*D*). The arrows indicate the mean

correlations of the population.

The response rate at which the transient index should return to one should be negative. Across the population of neurons, the mean conditioning response amplitude at which the neurons should return to a baseline transient index was −1.09. The negative value does not indicate that the neuron should be suppressed by conditioning motion to yield normal transient responses, but indicates the degree to which the conditioning motion must be outside the receptive field of the neurons.

Because the amplitude of response to the conditioning motion decreased as the conditioning motion left the receptive field of the neuron, a correlation linking the distance separating the conditioning and test motion and the TI should also exist. This is shown in Figure 6B for the same neuron shown in Figure 6A. As the conditioning motion is placed at increasingly distant locations, its effect on the transient response to the test motion diminished. For this neuron, the correlation coefficient was 0.76, and was consistent with the correlation found in the other neurons in the sample population. A histogram of the correlation coefficients found for the other recorded neurons in shown in Figure 6D. The amount of the transfer of adaptation depends on the spatial location of the conditioning motion, such that conditioning motion closer to the test motion elicits greater transfer of adaptation. The mean correlation between the distance and the transient index was 0.56, not as strong as the correlation found between conditioning motion response and the transient index (-0.67).

The time course of recovery from adaptation

Although adaptation is induced rapidly in area MT, within 30-50 ms, the recovery from adaptation usually takes 120-250 ms (Priebe et al., 1998; Lisberger and Movshon, 1999). The recovery from adaptation has been measured when the conditioning and test motion were in the same spatial location, unlike the paradigm used to measure adaptation in this paper. We therefore wanted to determine if the adaptation induced by conditioning motion in a different location than the test motion is same phenomenon that was studied when the conditioning and test motion were in the same location (Lisberger and Movshon, 1999). If the underlying mechanism is the same, the recovery from adaptation should have the same time course as has been reported when the two components of motion were in the same location. Recovery from adaptation is measured by varying the inter-stimulus interval (ISI) between the conditioning and test motion presentations and measuring the amplitude of the transient response to the motion in the test location.

We found that the recovery from adaptation had a similar time course when the conditioning and test motion were not in the same location. An example of the recovery of the transient response is shown in Figure 7. As we have shown earlier, when there is no interval between the conditioning and test motion, the transient response to the test motion is strongly attenuated (Fig. 7A). As the time interval between the conditioning and motion stimuli is increased from 16 ms (Fig. 7B) to 256 ms (Fig. 7F), the transient response of the neuron to the test motion also increases. For this neuron, the transient response fully recovered from adaptation when the ISI was 256 ms. This time course of recovery is consistent with the recovery from

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ISI = 0 ms

ISI = 16 ms

ISI = 32 ms

ISI = 64 ms

ISI = 128 ms

ISI = 256 ms
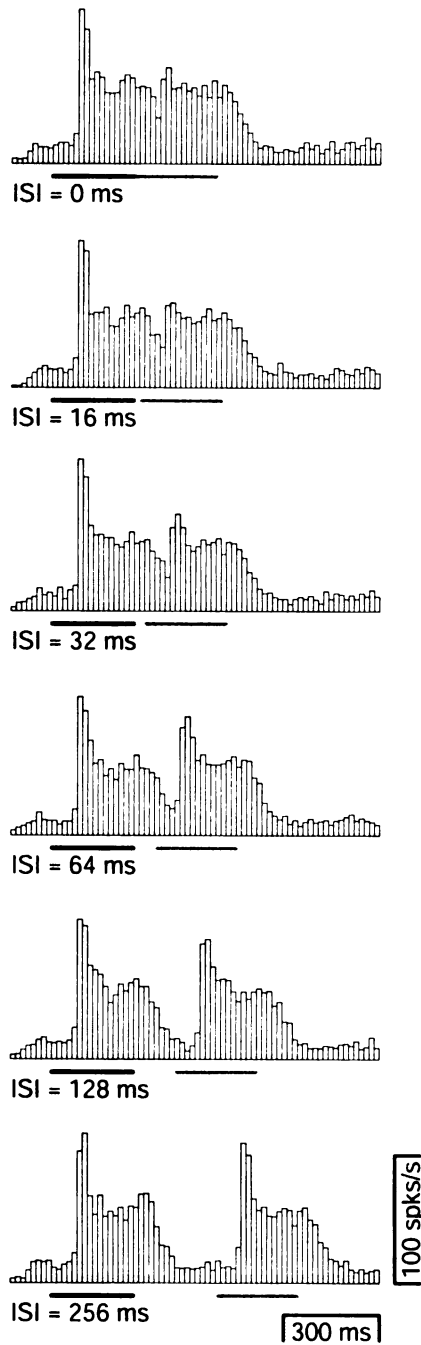
100 spks/s

300 ms

Figure 7

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Figure 7. The time course of recovery from adaptation. The recovery from

adaptation is shown by increasing the ISI. Each panel shows the response of

an MT neuron to motion in the conditioning and test locations. The time and

duration of the motion in each location is indicated by the black bar

(conditioning location) and the gray bar (test location).

adaptation observed when the conditioning and test motion are placed in the same location.

The recovery from adaptation was measured in 36 neurons. The amount of adaptation due to the conditioning motion was assessed by measuring the TI for each neuron at each ISI. The recovery shown in the neuron in Figure 7 was also seen across the population of neurons recorded in MT. A histogram of the transient indices for the neurons in our sample population is shown in Figure 8 for each ISI. The first panel shows the distribution of transient indices at an ISI of 0 ms. This is similar to the histogram shown in Figure 4, but includes only a subset of the neurons included in Figure 4. As shown by the example neuron in Figure 7, as the ISI increases, the size of the neurons' transient responses also increases, yielding larger TI values, until at 256 ms, the mean TI is 0.94, indicating an almost complete recovery of the neurons' transient responses.

The spatial transfer of adaptation in V1

Adaptation to motion stimuli in area MT transferred between locations farther away than the receptive field size of a V1 neuron at the same eccentricity. These results appear to rule out an adaptation mechanism based in V1 or at the synapse between V1 and MT. However, the calculation of receptive field size for macaque V1 by Hubel and Wiesel at these eccentricities only included the minimal response field (Hubel and Wiesel, 1974) or smaller. The minimal response field, or classical receptive field, of a neuron is the spatial area in which a stimulus actually elicits a response. However, many researchers have found that stimuli outside the classically
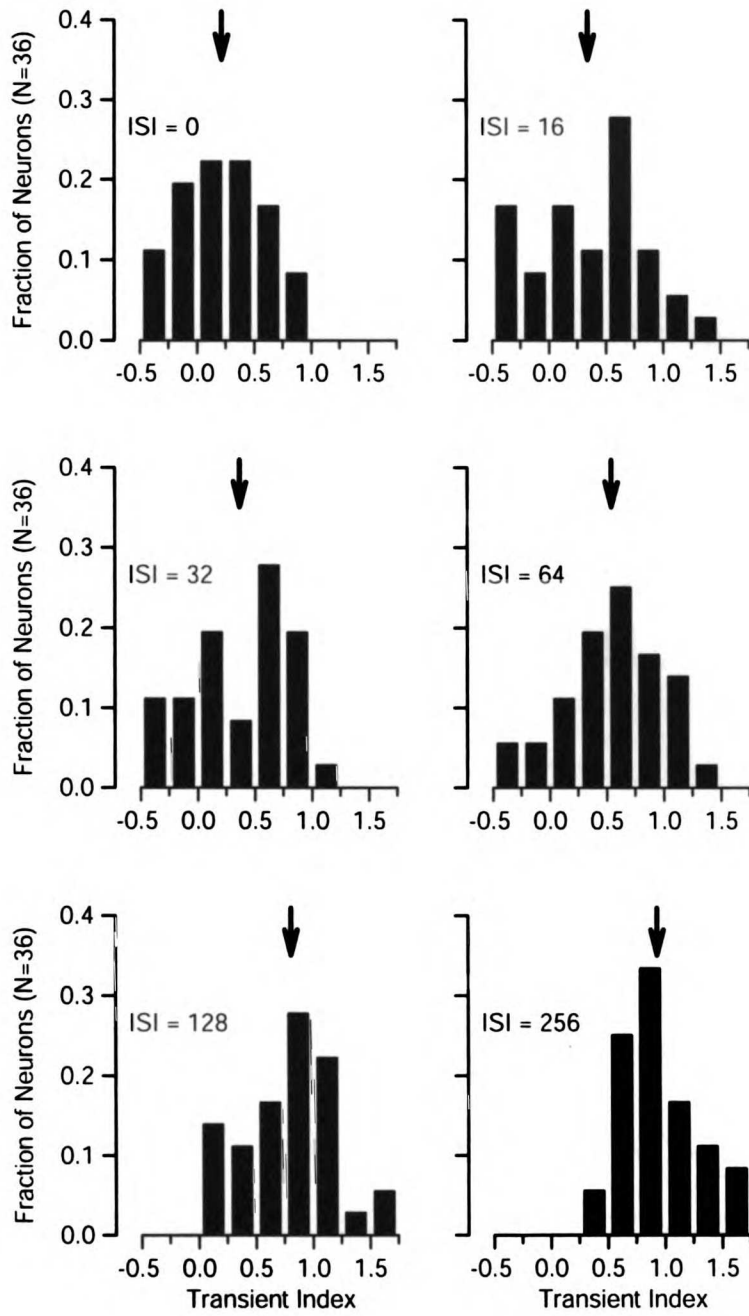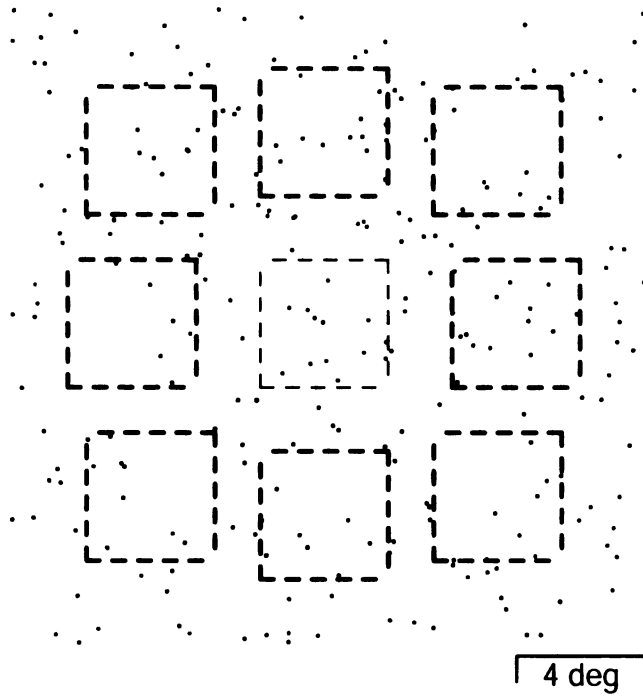
Figure 8

Figure 8. The time course of recovery for the population of neurons. Histograms of

the transient indices of each neuron are shown for different ISIs. The ISI is indicated

in each panel, and the arrow above each panel shows the mean TI for that interval.

defined receptive field can alter the response of V1 neurons to stimuli inside the receptive field (Hubel and Wiesel, 1965; Knierim and van Essen, 1992; Zipser et al., 1996; Cavanaugh et al., 1998; Walker et al., 1999). Although the adaptation in area MT extends beyond the classically defined receptive fields of V1 neurons, the response of those V1 neurons to the test motion inside their receptive field may be altered by the conditioning motion outside their receptive fields.

To rule out the effects of conditioning motion outside the classically defined receptive field on the responses to test motion in the receptive field, we recorded from 159 single units in macaque V1 using the same paradigm used to measure the transfer of adaptation in area MT. In addition, we wanted to know if V1 neurons respond to motion with the same transient and sustained phases of firing found in area MT. Although these neurons respond transiently to flashed bars, the transient response of V1 neurons to motion stimuli has not been previously described.

Because directionally selective neurons in V1 provide the input to area MT, we restricted our analysis to the 29 neurons that were considered directionally-selective by having a criterion directional index of 0.5 (see Methods). As previously reported, the majority of the directionally selective neurons were found directly above layer 4 and in layer 6 of cortex. The center of the receptive fields of the neurons recorded from in V1 varied from 3° to 5° eccentric from the fovea, with receptive field sizes of less than degree. We used a similar stimulus configuration to that used in the MT recordings. Responses of V1 neurons were initially measured to a test stimulus alone placed directly in the receptive field of the neuron. The response of

A

B
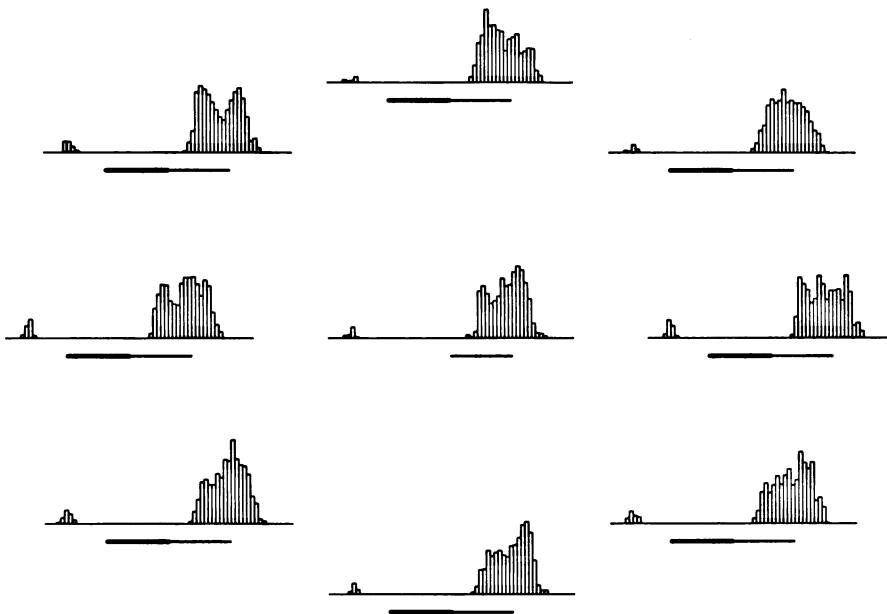
Figure 9

Figure 9. The spatial transfer of adaptation in primary visual cortex. *A*: The stimulus used to assay the transfer of adaptation is shown. The locations of the conditioning motion are shown by the boxes with thick lines. The thin lines indicate the area where the test motion was located. The dots shown are of the same density used in these experiments. No dashed lines were actually on the display, these are used only to demarcate the zones where motion occurred.

B: The response of an example neuron is shown. The location of the histograms indicates the spatial location of the conditioning motion, except for the central histogram, which was not preceded by conditioning motion. The time of the conditioning motion is indicated by the thick bars underneath each histogram while the thin bars indicate the time of test motion.

the neuron to the test motion was then measured after conditioning motion in one of eight locations surrounding the location of the test motion. The locations of the conditioning motion used were the same used in the MT recording: a distance of 1.2° was maintained between the locations of the conditioning and test motion. A diagram of this stimulus paradigm is shown in Figure 9A. The dashed box at the center of the panel indicates the location of the test motion. The eight boxes surrounding the test location indicate the locations of the conditioning motion.

The response of a V1 neuron to the test motion alone is shown in the center panel of Figure 9B. The panels surrounding the center panel indicate the response of the neuron to the conditioning motion followed by the test motion. This neuron never responded to the conditioning motion alone, since the conditioning motion was outside its receptive field, but did respond well to the test motion. Although the neuron was driven by motion in the test location, unlike many neurons in MT, it did not respond to the motion with a short transient high firing rate followed by a sustained period of reduced firing. In addition, inspection of the responses of the neuron to the test motion, given the preceding conditioning motion, does not reveal a significant effect of conditioning motion on the response to the test motion.

To quantify the effect of conditioning motion on the response of V1 neurons to the test motion, the peak response of the neurons to the test motion alone was compared to the peak firing of the neurons when conditioning motion preceded the test motion. The panels in Figure 10 display this comparison for two neurons. In these polar plots, the angle indicates the location of the conditioning motion, relative to the location of the test motion, while the distance from the center indicates the peak

A 30 spks/s

B 100 spks/s

Figure 10

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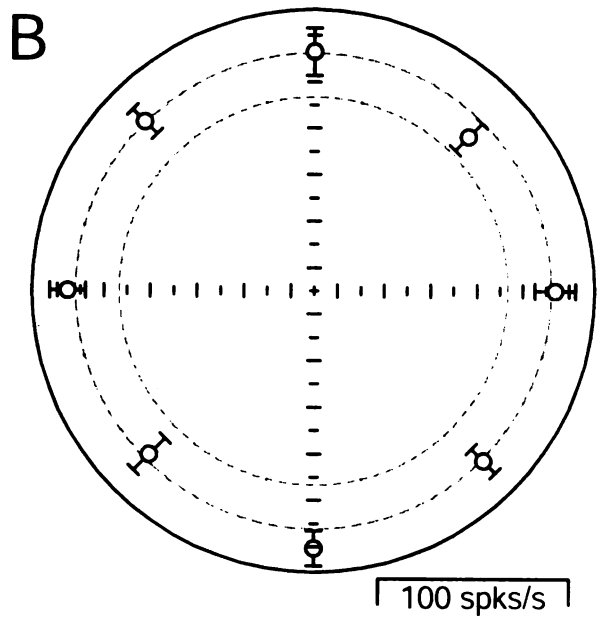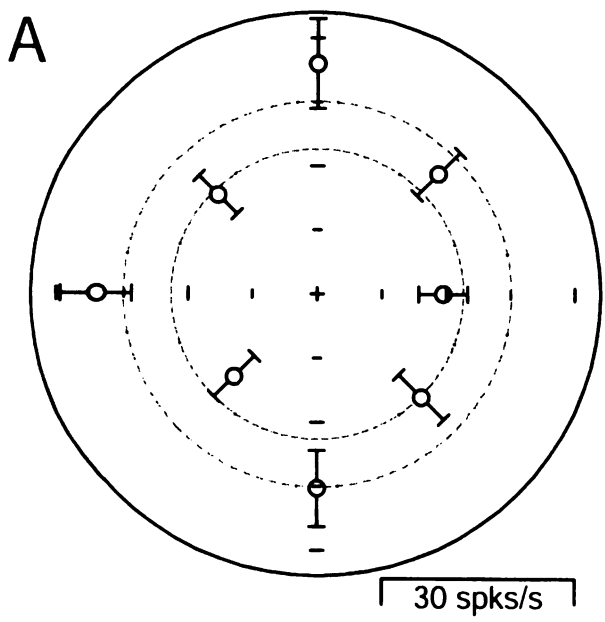
Figure 10. Analysis of spatial condition/test experiment for two neurons. *A,B*: The response of each neuron to test motion is shown by the distance of each symbol from the center of the circle. The location of the conditioning motion is indicated by the angle of each symbol on the polar axes. The dashed lines indicate the error bounds on the estimate of the response to test motion alone. The bars on each symbol indicate the standard error of the mean. Each tick represents 10 spks/s.

firing rate of neuron to the test motion. The dashed circles indicate the upper and lower bounds on the estimate of the response of the neuron to motion in the test location alone. The effects of conditioning motion on the test response were small. A few neurons (7/29) did show statistically significant effects of conditioning motion on responses to test motion (paired t-test, $P< 0.05$). The neuron shown in Figure 10B is an example where motion in one of the conditioning locations did induce a statistically significant difference in the response of the cell to motion in the test location. However, because there were eight different comparisons made for each neuron in our population, the probability that random fluctuations will appear statistically significant is greater. A stricter criterion of statistical significance must therefore be used to determine significance. Given that eight different comparisons are being made, we used a criterion of $P<0.00625$ to determine significance (Scheffee's Correction). None of the neurons in our population had statistically significant changes in response to the test motion using this stricter criterion. We therefore conclude that the conditioning motion did not affect the responses of V1 neurons to the test motion

Finally, we compared the transient-to-sustained ratio of neurons in V1 and area MT for steps of target speed at each neuron's preferred speed. As shown in the example neuron in Figure 9B, the directionally-selective V1 neurons in our sample population did not exhibit the same transient and sustained periods of firing to motion. However, some neurons in area MT also do not have transient responses to motion. This comparison of the transient firing of neurons in V1 and MT is shown Figure 11. As has been previously noticed (J. A. Movshon, *personal*

communication), directionally-selective neurons in V1 did not have the same degree of transient response to motion that many neurons in area MT exhibit. The average transient-to-sustained ratio of the directionally-selective neurons in our sample population was 1.07, as compared to a mean of 1.63 for MT neurons using the identical stimuli. This value is not high, considering we measured the *peak* 32 ms period in the initial 100 ms of firing to be the transient firing rate, while the sustained firing rate is derived from the average firing rate over the sustained period of response.
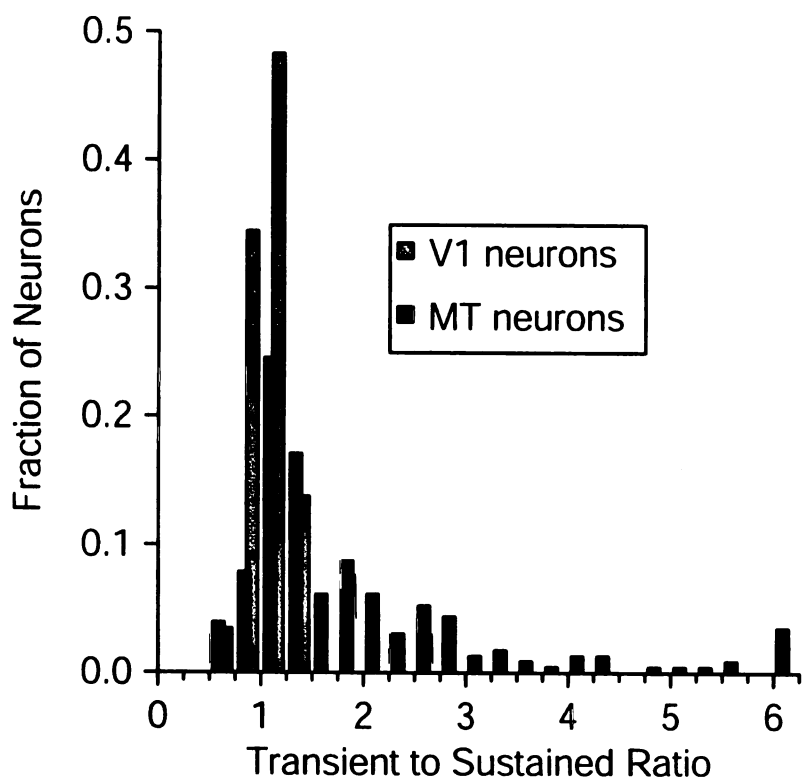
Figure 11

Figure 11. The transient-to-sustained ratio of V1 and MT neurons. The frequency of

transient-to-sustained ratios in a population of MT neurons (N=213) and the

directionally-selective V1 neurons (N=29) is shown by the dark bars and gray

bars, respectively.

Discussion

In this paper we explored the spatial selectivity of short-term adaptation observed in the neuronal responses in area MT. We found that adaptation induced by motion in one portion of an MT neuron's receptive field transfers to other portions of the MT neuron's receptive field, even over distances larger than a V1 receptive field. To account for adaptation in area MT with an input-based mechanism, the spatial selectivity for adaptation should be on the same scale as the receptive field size of the neurons providing input to area MT. Given that we do observe such a transfer of adaptation over distances larger than a V1 receptive field, we conclude that input-based mechanisms cannot account for adaptation in area MT.

Although we have shown that the spatial selectivity for adaptation is larger than the size of a V1 receptive field, it could be that motion outside a classically-defined V1 receptive field could affect the response to subsequent motion inside the receptive field. To control for this effect, we recorded the responses of neurons in V1 to the same adaptation paradigm used for the MT recordings. We did not find a significant effect of motion outside the V1 neurons' receptive fields on the responses to subsequent motion inside the receptive fields. That is, the transfer of adaptation did not occur at the level of V1. In addition, few V1 neurons showed the transient responses to motion inside their receptive field commonly found among neurons in area MT. This finding corroborates our conclusion that input-based mechanisms do not account for adaptation in area MT.

Although the adaptation induced by motion in one portion of an MT neuron's receptive field transfers to other portions of the receptive field, the amount of adaptation that transfers depends on the location of the adapting stimulus. The farther away the adapting stimulus is from the center of the receptive field of the neuron, the less the transfer of adaptation. This spatial selectivity of adaptation was on the same scale as the spatial receptive fields of MT neurons from which we recorded. As has been shown for both direction and speed, adaptation in area MT is tuned spatially (Priebe and Lisberger A). The recovery from adaptation was measured to establish that adaptation induced by conditioning motion in a different location that the test motion has the same time course as the adaptation found when the conditioning and test stimuli are in the same location.

Because we found that adaptation transferred over spatial distances larger than a V1 receptive field, input-based mechanisms are not the likely source of adaptation in area MT. In addition, the adaptation transferred over distances slightly larger than the receptive fields of neurons in area MT which indicates that areas downstream of area MT, such as MST, are also unlikely candidates for the generation of the adaptation signal. MST neurons have receptive fields that are much larger (usually about 10 times) than those within MT and the spatial selectivity for adaptation would need to be on scale of those receptive fields, and not the smaller spatial selectivity found in our sample of neurons. Therefore, our results strongly indicate that the adaptation mechanism is occurring within area MT.

However, motion information also enters area MT from other visual areas, primarily from the directionally-selective neurons in area V2 (DeYoe and Van Essen,

1985). Directionally-selective V2 neurons, located in the thick cytochrome oxisdase stripes (Hubel and Livingstone, 1987), have receptive fields that are larger than the receptive fields found in V1, but much smaller than the fields in area MT (Gattass et al., 1981). The transfer of adaptation observed in area MT may be due to adaptation occurring at the level of V2, instead of MT. The receptive fields of V2 are 50-100 % larger than the receptive fields found in V1 at the same eccentricity. At an eccentricity of 10°, V2 receptive fields extend an average 3.5° (Gattass et al., 1981), although the actual size of the subset of V2 neurons that project to area MT is known to be smaller than the receptive fields sizes of the neurons in pale and thin stripes (Roe and Ts'o, 1995). Although we cannot completely rule out a role for area V2 in adaptation, the majority of the neurons reported here (57/67) showed a spatial transfer of adaptation using a separation of the conditioning and test motion of more than 2°. It is therefore unlikely that V2 is providing the primary source of adaptation observed in area MT.

The data presented here raise two important questions. First, if adaptation occurs within area MT, why did many neurons give a transient response to the test motion given the conditioning motion? Although the transient response to the test motion was reduced, as is evident in the mean TI of 0.23, neurons did have a transient response to the test motion. The residual transient firing indicates that the mechanism for adaptation in area MT is based upon interaction of neurons with overlapping receptive fields. The effect of the conditioning motion may be to turn on the adaptation in a subset of the network of MT neurons, but because the adaptation process is spatially dependent, those neurons in the network, tuned to different spatial

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locations, will not be shifted into the adapted state by the conditioning motion. The responses of these unadapted neurons could be providing the basis for the residual transient observed in our data.

Second, if V1 neurons respond transiently to flashed bars (Kulikowski et al., 1979; Nelson, 1991), why didn't we observe transient responses to our motion stimulus? A simple explanation for the lack of transient response in V1 neurons is that while MT neurons responded to the motion of the texture, V1 neurons responded to individual dots in the texture passing through their receptive fields. The dot density of our textures was 0.75 dot/deg^2, while the size of a receptive field of V1 neurons at the eccentricities examined is about one half of a degree. Therefore a moving dot was not always in the receptive field of the neuron and the time at which the V1 neurons began to respond was different for each trial, since the initial position of dots in our stimulus was randomized. The V1 neurons may not have responded with transients to the motion because their latency to respond was different for each presentation of the stimulus. Although we cannot rule out that V1 neurons may adapt to motion in a similar manner as MT neurons do, they did not adapt to the same motion stimulus that induces adaptation in MT neurons. It is therefore unlikely that adaptation in V1 causes the adaptation observed in area MT.

Although it appears that the amount of adaptation depends on the response of the MT neuron to the conditioning motion, we have shown in another study (Priebe and Lisberger C) that adaptation does not depend directly on the spiking of the neuron, and is therefore disassociated from the activity of the neuron. Thus, it is likely that the mechanism for adaptation must be based upon interactions between the

MT neurons, and not on an activity-dependent mechanism for adaptation such as spike frequency adaptation (McCormick et al., 1985; Connors and Gutnick, 1990).

Other researchers have measured the effect of multiple components of motion inside the receptive fields of MT (Ferrera and Lisberger, 1997; Britten and Heuer, 1999; Majaj et al., 2000). However, these studies measured the interaction between two spatially distinct motion stimuli moving simultaneously, unlike our stimulus in which the two motion components always moved asynchronously. The studies of Britten and Heuer (1999), Ferrera and Lisberger (1997), and Majaj et al. (2000) indicate that the responses of MT neurons to each motion component alone do not sum when the motion components are displayed simultaneously, but instead averages. Because the two motion components can be separated spatially, these studies implicate area MT, and not V1, in the averaging process, consistent with our finding that adaptation is occurring at the level of area MT. However, Britten and Heuer (1999) report that the averaging process can occur over spatial distances larger than the interaction shown in our data. They found motion components as distant as 2 to 3 receptive field radii could interact to yield an averaging of the responses to both locations. Our work demonstrates that the transfer of adaptation is well linked to the receptive field of the neuron, but the transfer of adaptation is also over distances larger than the receptive field of the neuron. It may be that the interaction observed by Britten and Heuer is based upon different mechanisms than the adaptation explored in our research, but the spatial distances over which both effects are present are consistent.

Along with the data presented in the companion paper (Priebe and Lisberger A), we have provided constraints on the underlying mechanism for the short-term adaptation of responses in area MT. We have shown that the mechanism for adaptation is tuned for direction, speed and spatial location and is derived from the responses of neurons within area MT. The adaptation could be derived either from a loss of excitatory drive onto an MT neuron or from a gain of inhibitory input onto the neuron. With extracellular techniques we cannot distinguish between these two mechanisms. Correlation-based connectivity suggests that excitation occurs between neurons with similar tuning, while inhibition occurs between neurons that have opposite tuning (Maunsell and Van Essen, 1983; Heeger et al., 1999). Because the adaptation mechanism studied here has the same tuning as that of the neurons to single presentations of a stimulus, it seems more likely to be an effect of a loss of excitatory input from the network of neurons in MT than from inhibitory interactions between neurons of similar tunings.

References

Abbott LF, Varela JA, Sen K, Nelson SB (1997) Synaptic depression and cortical gain control. Science 275:220-224.

Britten KH, Heuer HW (1999) Spatial summation in the receptive fields of MT neurons. Journal of Neuroscience 19:5074-5084.

Cavanaugh JR, Bair W, Movshon JA (1998) Signals setting contrast gain arise from iso-oriented domains aligned with the receptive field axis of macaque striate cortex neurons. Society for Neuroscience Abstracts 24:1875.

Connors BW, Gutnick MJ (1990) Intrinsic firing patterns of diverse neocortical neurons. Trends in Neurosciences 13:99-104.

DeYoe EA, Van Essen DC (1985) Segregation of efferent connections and receptive field properties in visual area V2 of the macaque. Nature 317:58-61.

Ferrera VP, Lisberger SG (1997) Neuronal responses in visual areas MT and MST during smooth pursuit target selection. Journal of Neurophysiology 78:1433-1446.

Gattass R, Gross CG, Sandell JH (1981) Visual topography of V2 in the macaque. Journal of Comparative Neurology 201:519-539.

Heeger DJ, Boynton GM, Demb JB, Seidemann E, Newsome WT (1999) Motion opponency in visual cortex. Journal of Neuroscience 19:7162-7174.

Hubel DH, Wiesel TN (1965) Receptive fields and functional architecture in two non-striate visual areas (18 and 19) of cat. Journal of Neurophysiology 23:229-289.

Hubel DH, Wiesel TN (1974) Uniformity of monkey striate cortex: a parallel relationship between field size, scatter, and magnification factor. Journal of Comparative Neurology 158:295-305.

Hubel DH, Livingstone MS (1987) Segregation of form, color, and stereopsis in primate area 18. Journal of Neuroscience 7:3378-3415.

Judge S, Richmond B, Chu F (1980) Implantation of magnetic search coils for measurement of eye position: an improved method. Vision Research 20:535-538.

Knierim JJ, van Essen DC (1992) Neuronal responses to static texture patterns in area V1 of the alert macaque monkey. Journal of Neurophysiology 67:961-980.

Kulikowski JJ, Bishop PO, Kato H (1979) Sustained and transient responses by cat striate cells to stationary flashing light and dark bars. Brain Research 170:362-367.

Lisberger S, Movshon J (1999) Visual motion analysis for pursuit eye movements in area MT of macaque monkeys. Journal of Neuroscience 19:2224-2246.

Lisberger SG, Westbrook LE (1985) Properties of visual inputs that initiate horizontal smooth pursuit eye movements in monkeys. Journal of Neuroscience 5:1662-1673.

Majaj N, Smith MA, Movshon JA (2000) Contrast gain control in macaque area MT. Society for Neuroscience Abstracts 26:Abstract No -399 392.

Maunsell JHR, Van Essen DC (1983) Functional properties of neurons in middle temporal visual area of the macaque monkey. I. selectivity for stimulus direction, speed, and orientation. Journal of Neurophysiology 49:1127-1147.

McCormick DA, Connors BW, Lighthall JW, Prince DA (1985) Comparative electrophysiology of pyramidal and sparsely spiny stellate neurons of the neocortex. Journal of Neurophysiology 54:782-806.

Movshon JA, Newsome WT (1996) Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. Journal of Neuroscience 16:7733-7741.

Nelson SB (1991) Temporal interactions in the cat visual system. I. Orientation-selective suppression in the visual cortex. Journal of Neuroscience 11:344-356.

Priebe NJ, Bair W, Cavanaugh JR, Movshon JA, Lisberger SG (1998) Direction and speed selectivity of gain control in single neurons in macaque visual area MT. Society for Neuroscience Abstracts 24:648.

Roe AW, Ts'o DY (1995) Visual topography in primate V2: multiple representation across functional stripes. Journal of Neuroscience 15:3689-3715.

Sokal RR, Rohlf FJ (1995) Biometry: the principles and practice of statistics in biological research, 3rd Edition. New York: W.H. Freeman.

Walker GA, Ohzawa I, Freeman RD (1999) Asymmetric suppression outside the classical receptive field of the visual cortex. Journal of Neuroscience 19:10536-10553.

Zipser K, Lamme VA, Schiller PH (1996) Contextual modulation in primary visual cortex. Journal of Neuroscience 16:7376-7389.

Chapter 3

The role of spike-timing dependent mechanisms in short-term adaptation in macaque area MT

Abstract

The responses of many motion selective neurons in the macaque area MT to a moving texture are characterized by two phases of response: a short transient phase in which the response is high and a sustained phase in which the response settles to a lower rate that continues for the duration of the stimulus. The transition from transient to sustained firing is a form of adaptation since the neuron's sensitivity to motion is altered by the history of motion. Many mechanisms may account for this adaptation, including mechanisms intrinsic to the recorded neuron. In this paper we investigate the role of the neuron's own activity in causing the observed adaptation of responses. Spikes from excitatory cortical neurons often open hyperpolarizing currents that reduce neuronal excitability. We estimate the effect of such activity-dependent mechanisms using three techniques. We first estimated what the sustained firing rate would be if there were no interactions between individual spikes and compared this firing rate to the observed transient firing rate. On average, the adjusted sustained firing rate accounted for 18% of the shift from the transient to sustained rate of firing. Second, we extracted a recovery function from each neuron that related the change in probability of a spike induced by a spike in the past. We assessed the impact of the spike recovery function on the transient firing rate. On average, the recovery functions did not account for the adaptation observed in the firing of MT neurons. Finally we compared the response of neurons during a period immediately after the transient phase of firing when there had been spikes and when there had not been spikes. We did not find a statistically significant relationship

between the response in the transient period and the response after the transient

period. We therefore conclude that activity-dependent mechanisms within the

recorded MT neuron do not lead to its adaptation.

Introduction

One prominent characteristic of sensory neurons is that their response is not simply a function of the presence of a stimulus, but also the temporal context in which the stimulus is delivered. A sensory neuron usually responds with an initial high firing rate when its preferred stimulus is initially presented, but the response settles to a lower sustained firing rate over the continued duration of the stimulus presentation (Tolhurst et al., 1980; Nelson, 1991; Muller et al., 1999).

This initial transient response is particularly evident in the responses of neurons in macaque extrastriate visual area MT. MT neurons respond selectively to the direction, speed and spatial location of motion in the visual field. When motion in a neuron's preferred direction, speed and spatial location is presented, it responds initially with a short (~30-50 ms) period of high firing that then settles to a lower firing for the duration of stimulus motion. The neuron's ability to respond briskly to the presentation of motion in its receptive field recovers over a period of ~120 ms. We refer to the change in the sensitivity of the MT neurons to motion as short-term adaptation since the time courses of the induction and recovery are much shorter than other forms of adaptation, such as the motion aftereffect (Wohlgemuth, 1911).

What is the underlying mechanism for the change in MT neurons' sensitivity to visual motion? Perhaps the simplest explanation for this response property is that there is a change in the amount of input from primary visual cortex (V1) to area MT. Area MT receives direct input from directionally-selective neurons in V1, but recordings in these V1 neurons do not reveal a change in response amplitude over the

period of the presentation of a motion stimulus (Priebe and Lisberger B). In addition, the spatial receptive field for adaptation is slightly larger than the receptive fields of MT neurons (Priebe, chapter 2). From these experiments we concluded that adaptation occurs on spatial scales larger than the receptive field size of a neuron in V1, but smaller than the receptive field sizes of areas downstream of MT like area MST. Our data therefore indicate that the short-term adaptation observed in MT neurons is an effect of a mechanism at work within area MT and not external to it.

Data presented in previous papers imply that the adaptation observed in the response of MT neurons is based upon a "tuned" mechanism (Priebe and Lisberger A). In the domain of direction of motion, adaptation shows the same tuning as neural responsiveness. In the domain of speed of motion, however, the tuning of adaptation and response are not always the same: the speeds that evoke the greatest suppression of response to successive stimuli are not necessarily the preferred speeds of the neurons.

Two different mechanisms within area MT could account for the tuning of adaptation. First, there could be interactions between MT neurons that could produce a change in the neurons' abilities to respond to the presence of subsequent motion. These interactions could arise from either an increase in the amount of inhibition or a decrease in the amount of excitation onto a neuron from other MT neurons. For the interaction to account for the tuning of adaptation observed in MT neuron responses, the interactions between MT neurons would need to depend on the direction, speed and spatial selectivity of the neurons. Second, there may be a mechanism intrinsic to each neuron that controls the excitability of the neuron. Such mechanisms for

controlling the excitability of excitatory cortical neurons are known to exist. In particular, action potentials of many excitatory neurons induce a current that reduces the neuron's ability to continue spiking (McCormick et al., 1985). This spike-dependent current is called the after-hyperpolarization current (I_{AHP}) and is thought to depend on the influx of calcium during an action potential. When calcium enters, it activates potassium channels and hyperpolarizes the neuron (Yarom et al., 1985), making it less able to fire action potentials. This mechanism is also a tuned mechanism since it depends on the response of the neuron to motion.

A key distinction between these two mechanisms for adaptation is that the intrinsic mechanism depends only on the activity of a single neuron in response to the stimulus, while the mechanism based upon interactions between MT neurons depends on the excitation of other neurons in addition to the one being recorded. Therefore the amount of adaptation due to the intrinsic mechanism should be tightly linked to the excitation of a neuron on a trial-by-trial basis. This need not be the case for a mechanism that depends upon other neurons of area MT.

Not only should the excitation of the neuron be tightly linked to the amount of adaptation for an intrinsic mechanism of adaptation to be effective, but the timing of the neuron's action potentials should affect the neuron's ability to respond to future stimuli. Usually the response of a neuron is associated with a stimulus in the environment by correlating the average firing rate of the neuron with the stimulus. However, the use of firing rate as a metric for the response of the neuron may vastly under-represent the real relationship between stimulus and response. The assumption of firing rate as the metric for a neuron's response assumes that neurons generate

spikes that are independent of one another (Rieke, 1997). We know that this is not true, as after a neuron spikes, it goes through a refractory period (Teich et al., 1978; Berry and Meister, 1998). There are usually two phases to this period, a short absolute refractory period (~1 ms) during which time the neuron cannot generate a spike and a relative refractory period when the probability of spiking is reduced (Hodgkin and Huxley, 1952). Refractory periods can reduce the firing rate of neurons to prolonged stimulation (McCormick et al., 1985).

In this paper we show that there is not a strong correlation between the activity of MT neurons and the amount of adaptation induced. To compute the actual contribution of a spike-timing dependent mechanism on the dynamic response of MT neurons, we extracted a spike-dependent recovery function for each neuron. This function relates the effect of a single spike on the ability of the neuron to spike in the future. Once we computed the recovery function, we determined empirically the contribution of the recovery function to the transient and sustained firing found in our sample population of MT neurons by generating spikes from a simulation with the same spike-dependent recovery function. We find that the recovery function could contribute to a small fraction of the adaptation observed, but errs in predicting a much faster time course for the onset of adaptation. In addition, we demonstrate that the response of the neuron immediately after the transient phase of firing is not related to the actual response of the neuron during the transient phase. Because the adaptation does not depend on the activation of the neuron in terms of the generation of spikes, we conclude that adaptation does not arise from a mechanism intrinsic to the

individual MT neurons. Rather, the adaptation process must be due to an interaction

among neurons in area MT.

Materials and Methods

Physiological preparation

Extracellular single-unit microelectrode recordings were made in area MT of

anesthetized, paralyzed macaque monkeys (*Macaca fascicularis*). Details of the

anesthesia, surgical preparation and recording from the anesthetized monkeys have

been explained elsewhere (Priebe and Lisberger A). Briefly, after the induction of

anesthesia with ketamine (5-15 mg/kg) and midazolam (0.7 mg/kg), cannulae were

inserted into the saphenous vein and the trachea. The animal's head was then fixed in

a stereotaxic frame and the surgery was continued under an anesthetic combination of

isoflurane (2%) and oxygen. A small craniotomy was performed directly above the

superior temporal sulcus (STS) and the underlying dura was reflected. The animal

was maintained under anesthesia using an intravenous opiate, sufentanil citrate (8-16

micrograms/kg/hr), for the duration of the experiment. To maintain a steady

anesthetic state of the animal, the opiate was delivered at a continuous, steady rate by

an infusion pump. To minimize drift in eye position, paralysis was maintained with

an infusion of vecuronium bromide (Norcuron, 0.1 mg/kg/hr). The pupils were

dilated using topical atropine and the corneas were protected with +2D gas-permeable

hard contact lenses. Supplementary lenses were selected by direct ophthalmoscopy to

make the lens of the eye conjugate with the display.

Tungsten-in-glass electrodes (Merrill and Ainsworth, 1972) were introduced

by a hydraulic microdrive into the anterior bank of the superior temporal sulcus (STS)

and were driven down through the cortex and across the lumen of the STS into area

MT. The recording sessions lasted between 84 and 120 hours. The units included in this study are from 34 electrode penetrations at different sites in 9 monkeys.

All methods for recordings in anesthetized monkeys had received prior approval by, and were in compliance with, the regulations of the *Institutional Animal Care and Use Committee* at UCSF.

Stimulus Presentation

After isolating a single unit in area MT of anesthetized monkeys, its receptive field was mapped on a tangent screen by hand. All of the neurons reported in this paper had receptive field centers within 10° of the fovea. Visual stimuli were presented on an analog oscilloscope (Hewlett-Packard models 1304A and 1321B, P4 phosphor), using signals provided by digital-to-analog converter outputs from a PC-based digital signal processing board (Spectrum Signal Processing). This method affords extremely high spatial and temporal resolution, allowing a frame refresh rate of 500 or 250 Hz and a spatial resolution of 64K by 64K pixels. The apparent motion created by our display is effectively smooth at these sampling rates (Mikami et al., 1986; Churchland and Lisberger, 2000). The display was positioned 65 cm from the animal and subtended 20° horizontally by 20° vertically. Experiments were performed in a dimly lit room. Due to the dark screen of the display, background luminance was beneath the threshold of the photometer, less than one mcd/m^2.

All trials began with the appearance of a stationary, uniform random dot texture (0.75 dots/deg^2). Because many neurons in area MT respond better if the moving texture is surrounded by a field of stationary dots, we used two textures of the

same dot density. A surround texture remained stationary for the duration of the trial, while a texture in the center of the screen moved. For all trials, the textures appeared and were stationary for 256 ms. After that period, the center texture began to move. After the motion completed, the dots remained visible for an additional 256 ms. Motion in the center texture was used to characterize the preferred direction by moving the texture in eight directions for either 512 or 256 ms. After the preferred direction was identified, the preferred speed of the cell was measured by moving the center texture in the preferred direction at speeds of 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, and 128°/s. Because neurons in area MT are known to modulate their firing based on the size of the moving texture (Allman et al., 1985), we next measured the size tuning of the single unit by adjusting the size of the center and surround textures such that the moving texture subtended 2.5°, 5°, 10°, 15° and 20°.

For each trial block, trials were sequenced by shuffling the list of possible trials and presenting each trial at random until all the trials in the list had been presented. The texture for each trial was generated using a different seed to generate pseudorandom sequence of initial dot positions, except where explicitly noted.

Data Acquisition and Analysis

Experiments were controlled by a computer program running on a UNIX workstation (Priebe and Lisberger A). Trials were sequenced by shuffling the list of possible trials and presenting each trial at random until all the trials in the list had been presented. For the data shown in this paper, the response to many repeats of the same stimulus were recorded. Each repeat of the preferred stimulus was interleaved

with other trials with motion at different directions, speeds or spatial locations. For all of the data shown in this study, the minimum number of repeats recorded was 46, and the average number of repeats was 87. To record enough repeats for each neuron it was necessary to record from the same neuron for an extended period of time, from 15 minutes to 96 minutes.

The responses to multiple repetitions of the same stimulus were aligned by the onset of target motion. The average firing rate, r(t), was then computed by binning the spikes into 4 ms intervals and computing the average firing rate of the neuron during that time period. For display purposes in the figures, the firing rate of the neurons has been binned into 8 ms intervals.

In Figure 2, all of the neurons in our sample population for which we had enough data (N=66) are shown. However, in order to record enough repeats of a single stimulus condition, neurons were often recorded from for an extended length of time. Over the course of the recording, some neurons' overall excitability changed. Changes in the excitability of neurons were assessed by measuring the mean response of the neuron over the sustained period of firing for each trial and looking for statistically significant fluctuations in response amplitude (one way ANOVA P<0.05). Of the 66 original neurons in our sample population, 29 neurons showed significant changes in response amplitude and were therefore discarded from further analysis in this paper.

Results

Quantification of the transient-to-sustained transition in

MT neurons' responses to steps of target speed

In this paper, we report the responses of 66 neurons in area MT to brief (256 or 512 ms) periods of motion in the neurons' preferred directions and speeds. The response of many MT neurons is characterized by an initial period of high firing followed quickly by a sustained rate of response. An example of the response of an MT neuron to a step of motion is shown in Figure 1. After a latency of 70 ms after the motion of a random dot texture began, this neuron gave a brisk response, but this high firing rate quickly settled to a lower sustained firing rate. The responses of the neurons to many repeats of the same stimulus were recorded, interleaved with other stimuli that did not excite the neuron. We identify the relationship between the initial excitation of the neuron to the step of stimulus motion and the amount of the reduction of response that follows the initial period of high firing. The neurons included in this study were selected from a larger sample population because they had transient responses to steps of motion and because many repeats of the preferred stimulus had been recorded. The firing rate of the neuron during the second phase of the response, hereafter referred to as the sustained response, was steady for the duration of our stimulus, either 256 ms as in this example or 512 ms for other neurons in our sample population.

Tau   = 31.1 ms
Fmax = 80.7 spks/s
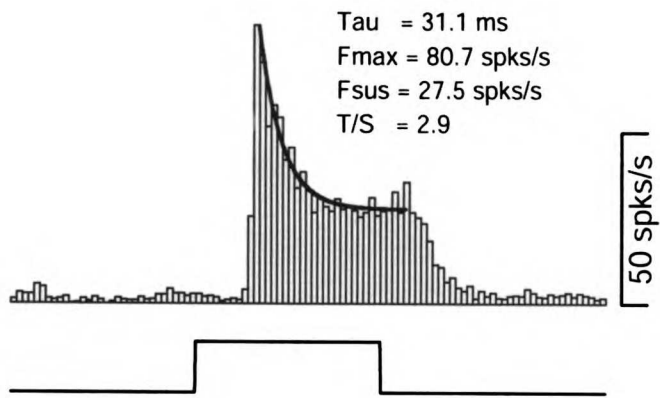Fsus = 27.5 spks/s
T/S   = 2.9

50 spks/s

Figure 1

Figure 1: The response of a neuron to a step of image velocity. The response of an MT neuron to multiple repetitions of the same stimulus is shown by the histogram with a bin size of 8 ms. The time course of stimulus movement is indicated by the trace at the bottom of the figure. At the beginning of each trial a random dot texture appeared and was stationary for 256 ms. The texture then began to move for 256 ms and then stopped and remained stationary for the duration of the trial. The thick line is an exponential fit (equation 1) of the firing rate of the neuron using the values shown.

Because a thorough analysis of the transition from the transient high firing rate to the lower sustained responses of MT neurons to motion has not been presented before, we begin by presenting some of the basic response attributes of the neurons in our sample population. Fits were made of the transition from transient firing to sustained firing of the neuron with single exponentials of the form:

$$R(t) = f_{sus} + (f_{max} - f_{sus}) * \exp(\frac{-t}{\tau}) \qquad (1)$$

where f_{sus} is the firing rate during the sustained portion of the response, f_{max} is the peak firing rate and τ is the time constant of the exponential. We also define the transient to sustained ratio as $T/S = f_{max}/f_{sus}$. Fits were made over the time from the peak of the neuron's response to 200 ms later.

An example of a fit using this function is shown in Figure 1 overlying the histogram of the response of the neuron. The time course of the shift from the transient to sustained phase of firing was diverse for the neurons in our sample population. As shown in Figure 2A, the fit value of τ varied between neurons from 8 ms to 80 ms. We did find a relationship between the fit values for both f_{sus} and f_{max} in our sample population of neurons, shown in Figure 2B. Finally, there was no significant correlation between the transient to sustained ratio of each neuron and the time constant of decay of firing to the sustained rate (Figure 2C).
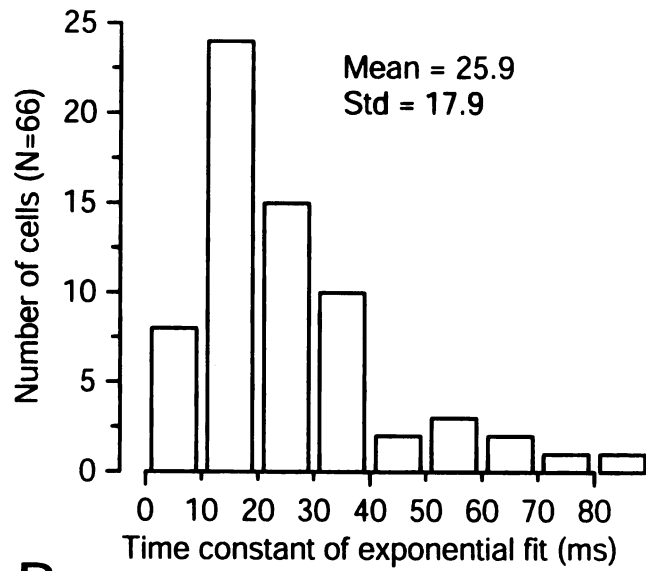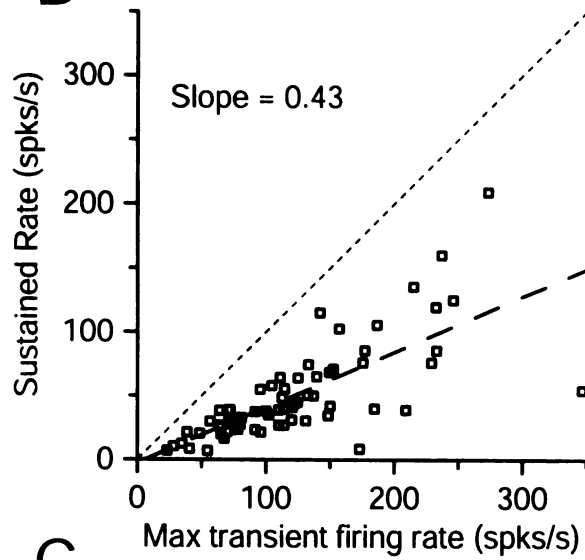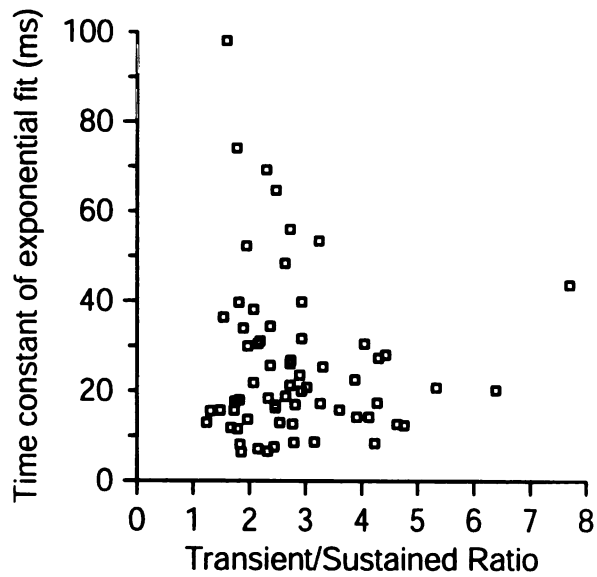
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A

Mean = 25.9
Std = 17.9

B

Slope = 0.43

C

Figure 2

Figure 2: Fit values of the transition from the transient to sustained firing. *A*: A histogram of the time constant of decay to the sustained rate of firing in our sample population. *B*: The peak transient firing rate (f_{max}) and the sustained firing rate (f_{sus}) for each neuron are shown by each square. There was a statistically significant relationship between these two values (PCA, (Sokal and Rohlf, 1995)), which is indicated by the thick dashed line. The thin line indicates a slope of 1. *C*: The time constant of the decay is not related to the transient-to-sustained ratio of the neurons in our population. Each neuron is indicated by a square. One neuron is not included in this plot because it had an extraordinarily high transient-to-sustained ratio (21). The time constant of that neuron was 21 ms.

Are neurons in area MT well described by a Poisson Process?

We now turn to the question of whether the transition from the transient period of high firing to the sustained period of reduced firing of an MT neuron can be explained by mechanisms intrinsic to the recorded neuron. As described by Hodgkin and Huxley, after neurons fire an action potential, they enter a period of absolute refractoriness due to the inactivation of sodium channels and latent activity of potassium channels (Hodgkin and Huxley, 1952). The neurons then must charge their membranes back to threshold in order to respond again with successive action potentials. In addition, spike-activated hyperpolarizing currents (i.e. I_{AHP}) may also open, increasing the time for the neuron to reach threshold.

Although such spike-dependent interactions are found in neural responses, almost all cortical neurons are also well-described by models of firing that do not include any interactions between spikes (Softky and Koch 1992). A Poisson process is defined by each event being independent of other events. A neuron spiking in a Poisson manner would spike independent of its history of response, unlike the spike-dependent processes described above. Refractory periods violate the assumption of a Poisson process because the spikes are not independent of the history of spiking, as a neuron cannot spike during the absolute refractory period.

We tested whether the neurons in our sample population are well-described by a Poisson process. One characteristic of a Poisson process is the variability of the occurrence of events. A metric of the variability of neural response is the Fano factor (de Ruyter van Steveninck et al., 1997). For a neuron described by a Poisson process, the mean spike count and variance of the spike count are equal and
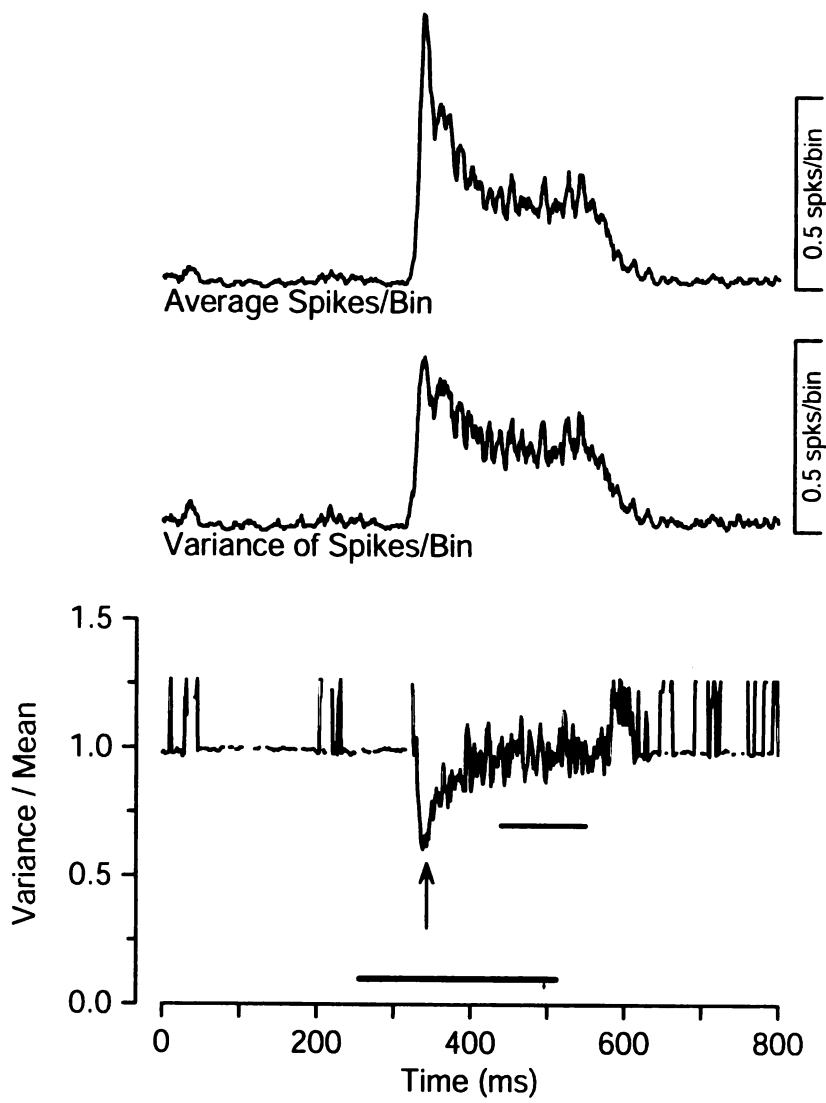
Figure 3

Figure 3: The variability of an MT neuron. *A*: The top trace shows the average number of spikes per sliding 8 ms bin. The variance of the spike count is shown in the middle trace. The ratio between the mean and variance of the spike count (the Fano factor) is shown in the bottom trace. The period of visual motion is indicated by the thick line in the bottom trace. The arrow indicates the time of the peak response and the time used to determine the transient Fano factor. The thin horizontal line indicates the times used to determine the sustained Fano factor. In addition, this is the time period used for this neuron to compute the inter-spike interval histogram.

the Fano factor is 1. A Fano factor less than one indicates that the neuron is responding in a manner less variable than a Poisson process which may be due to interactions between successive spikes.

For the example neuron shown in Figure 1, the average number of spikes per bin and the variance of the spike count are shown in the top traces, while the ratio of these two quantities (the Fano factor) is shown in the bottom graph of Figure 3. The Fano factor of the example neuron is close to 1 when it is responding at a background level, but once the neuron begins to respond to the motion stimulus, during the initial transient firing, the Fano factor quickly drops to 0.65, indicating that the variability of the neuron's response is reduced to a value lower than a Poisson model of firing predicts. During the sustained portion of response, the Fano factor of the neuron is higher, but is still less than 1. In our sample population, we found that the Fano factor was lower during the transient period of response than the sustained period of response. In Figure 4, the Fano factors of the neurons in our population are shown for both the transient and sustained periods of response. The tendency for the Fano factor to be less than 1 across the population of neurons indicates that the response variability of these neurons is not that expected from a Poisson process. The reductions in the Fano factors of the MT neurons indicates that the responses are not well described by a Poisson process, and that there may be interactions between successive spikes fired by an MT neuron.
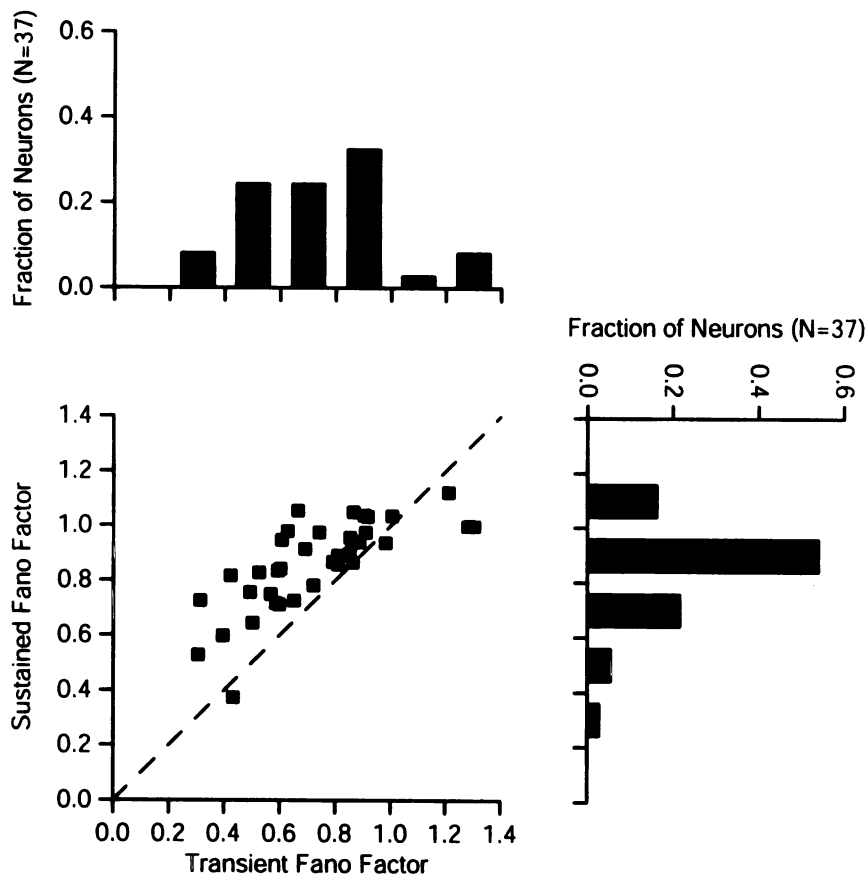
Figure 4

Figure 4: The variability of response in our sample population. The transient and sustained Fano factor is shown for each neuron in our sample population. The transient Fano factor was computed from the bin at the peak of the neurons' responses to motion. The sustained Fano factor was computed from the average Fano factor during the period 194 to 294 ms after the motion began, when the neurons were firing at a steady rate. Above the plot, a histogram of the transient Fano factor is shown. To the right is a histogram of the sustained Fano factor.

The contribution of the free firing rate to adaptation in MT neurons

The prior section established that the neurons are not simply responding in a Poisson manner, that is, their spikes are not independent of one another. We now reconstruct the "free firing rate" of MT neurons, defined as the firing rate the neurons would achieve during the sustained phase of response if each spike were independent of the time of occurrence of the prior spike. We will compare the free firing rate of the neuron during the sustained phase of response to the firing rate actually observed during the transient period. If the actual firing rate in the transient period and the sustained free firing rate are the same, then we will conclude that firing is based on the same Poisson statistics during both the transient and sustained firing, and that the depression of sustained firing relative to transient firing results from the spike-dependent adaptation, which is not included in the determination of sustained free firing rate (see below).

To extract the free firing rate during the sustained period, we built inter-spike interval (ISI) histograms for each of our neurons. This allowed us to define a range of small intervals over which the spike-dependent interactions affected the histograms, and a range of long-intervals that fell outside the time window of spike-dependent interactions. In Figure 5, for example, the neuron was in its absolute refractory period for intervals of less than 1 ms and therefore were no examples of such ISIs. There was a high probability of intervals with inter-spike intervals of 2, 3, and 4 ms, indicating bursting behavior, followed by a relative refractory period with a lower probability of intervals up to about 15 ms. For intervals greater than 15 ms, the neuron was affected less by its spiking history and approached what the ISI histogram
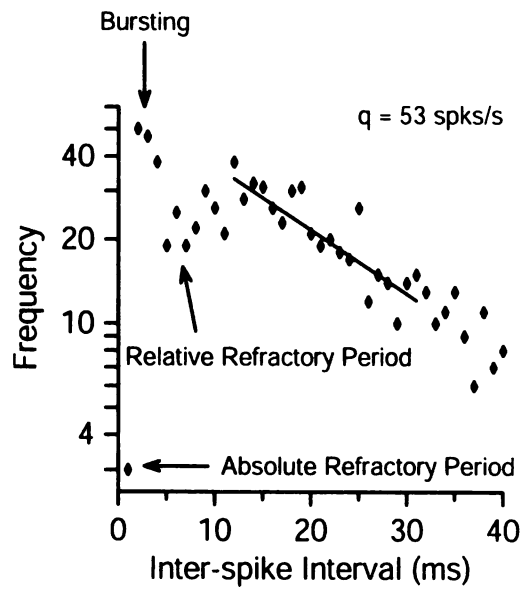
Figure 5

Figure 5: The inter-spike interval histogram of a neuron. The frequency of inter-spike intervals of different times is shown. The frequency is plotted in logarithmic coordinates. The thin line indicates an exponential fit of the intervals from 12 ms to 32 ms. The free firing rate, q, for this neuron was 53 spks/s. The observed sustained firing rate of the neuron was 37 spks/s.

of a neuron spiking according to a Poisson model would predict (Berry and Meister, 1998). The ISI histogram for such a Poisson model for a given firing rate is exponential, such that $P(\Delta) \propto \exp(-q\Delta)$, where q is the firing rate of the neuron, and Δ is the inter-spike interval. Thus, we can use q to estimate the the free firing rate of the neuron if we fit an exponential to the inter-spike interval histograms using only those ISIs that are beyond the time course of the absolute and relative refractory periods induced by the spiking of the neuron. For Figure 5, the mean firing rate of the neuron during this period was 37 spikes/s and the exponential fit to the ISI histograms indicated a free firing rate of 53 spikes/s.

The free firing rate of each neuron was estimated by fitting an exponential to later portions of the ISI histogram. A comparison of the observed sustained firing rate and the free firing rate of the neuron is shown in Figure 6A. Most of the points fall above the line of slope 1, indicating that the free firing rates of the neurons in our population were generally higher than the sustained firing rates. However, the increase was generally modest, and it was particularly noticable only for the small sample of neurons with higher sustained firing rates. The few neurons that lie below that unity slope line were neurons characterized by bursting. To summarize these data relative to the size of the transient responses, we computed a transient index, TI:

$$TI = \frac{q - R_{sus}}{R_{trans} - R_{sus}} \qquad (2)$$

where R_{sus} is the observed sustained response, q is the sustained free firing response and R_{trans} is the transient response of the neuron. A TI of 0 indicates that the observed and free sustained firing rates were the same, while a value of 1 indicates that the free firing rate is equal to the observed transient firing rate.

A

Sustained Free Firing Rate (spks/s) vs Observed Sustained Firing Rate (spks/s)

B

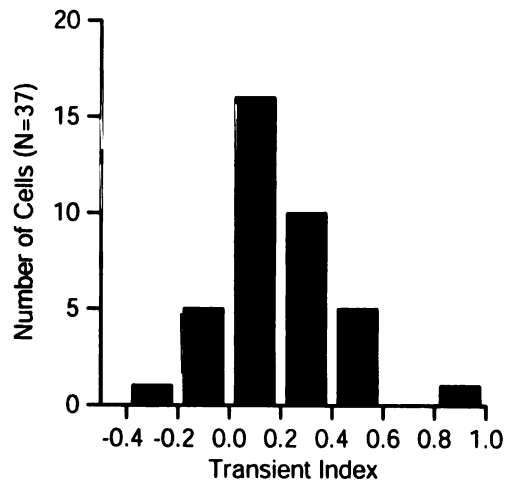Number of Cells (N=37) vs Transient Index
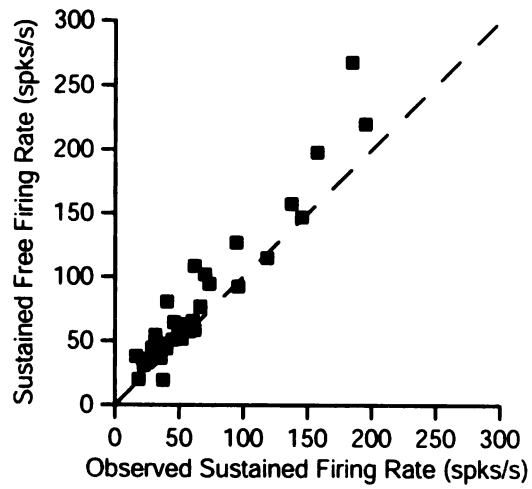
Figure 6

Figure 6: The sustained free firing rate of neurons in the population. *A*: Each filled square indicates the observed and free firing rate during the sustained period of response. The dashed line shows a slope of 1. Those neurons above this line had higher free firing rates than observed firing rates. *B*: The transient index (equation 2) of the neurons in our sample population.

A histogram of the TI for all of the neurons in our sample population is shown in Figure 6B. On average, the TI was 0.18, indicating that the spike-dependent interactions seen in the sustained period firing could account for only a small portion of the difference between transient and sustained firing rates.

Can the transient-to-sustained firing transition be accounted for by the measured spike-timing dependent interactions?

The preceding analysis assumed that the spike-timing dependent interactions only occurred during the sustained phase of firing and not during the transient response. However, spike-timing dependent mechanisms might also be important during the initial transient phase of firing. The adaptation observed in the sustained rate of firing might be due to the high transient rate of firing and would not be revealed unless the neuron spiked at a high rate. To test this hypothesis, we computed a recovery function that relates the change in the probability of a spike given the time of the last spike. From these recovery functions, we then made predictions about the contribution of spike-timing dependent mechanisms to the transient-to-sustained ratio observed in the responses of MT neurons by modeling the responses of the cells as Poisson processes with recovery functions after each spike.

The simplest assumption to make is that given a spike, the probability of spiking in the future is changed depending upon some underlying spike-dependent function $w(t-t_{last})$. The rate of the neuron can then be expressed in terms of the free firing rate of the neuron and this recovery function:

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$$R(t) = q(t) * w(t-t_{last}) \qquad\qquad (3)$$

The probability that time interval between successive spikes is Δ using this model is:

$$p(\Delta) = \exp(-\int_0^\Delta qw(\Delta')d\Delta')qw(\Delta) \qquad\qquad (4)$$

when q(t) is constant. When the ISI is long, then $w(\Delta)$ is 1 and the ISI

distribution approaches the exponential distribution expected from a Poisson model of

spiking. The first portion of equation 4 is the probability that there is no spike in a

time interval Δ. The recovery function of the neuron can therefore be extracted from

the probabilities function in the ISI histogram (Berry and Meister, 1998):

$$w(\Delta) = \frac{1}{q} \frac{p(\Delta)}{1 - \int_0^\Delta p(\Delta')d\Delta'} \qquad\qquad (5)$$

This weighting function is the probability of an interspike interval divided by

probability that there was no intervening spike. $w(\Delta)$ is a recovery function that

operates only between successive spikes; once a spike occurs, the recovery function is

reset. Therefore it only expresses the recovery of the neuron from the previous spike

and does not accumulate over multiple spikes.

The recovery functions of all of the MT neurons in our sample population

were computed using this technique. The form of the recovery functions was

variable. For example, the ISI histogram shown in Figure 7A generated the recovery

function shown in Figure 7D. The neuron had three phases of response. First it had

an absolute refractory period of 1 ms. Then, it had a bursting period for intervals of

2-3 ms followed by a longer relative refractory period, as shown before. The

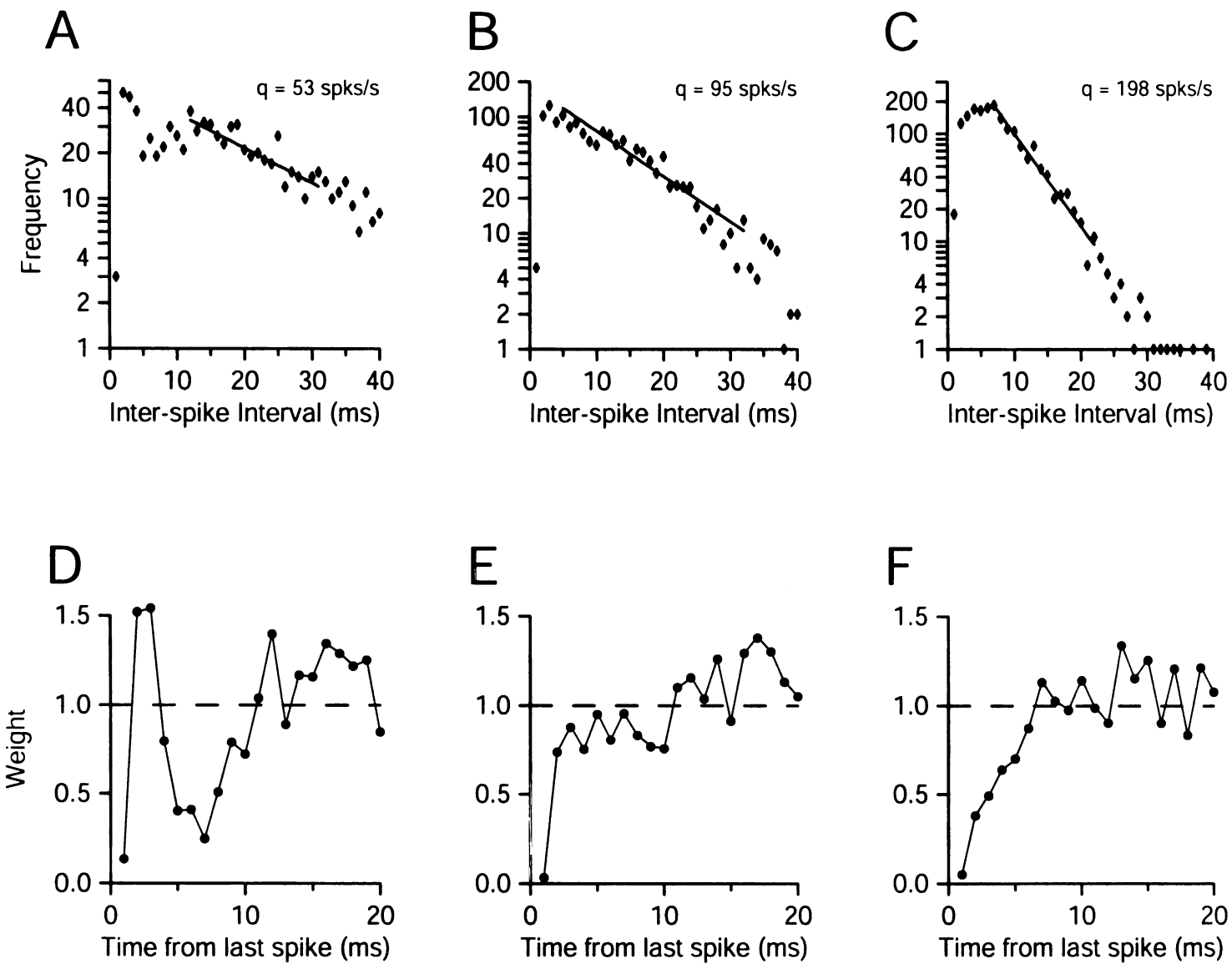recovery function for the neuron in Figure 7B is shown in Figure 7E. It had an

Figure 7

Figure 7: The estimation of the spike-dependent recovery functions. *A,B,C*: Each panel shows the frequency of the occurrence of inter-spike intervals for a different MT neuron. The intervals were measured from the sustained period of the neuron's response, between 150 to 280 ms after motion started. The lines in each figure are the exponential fits used to calculate the sustained free firing rate, q. *D,E,F*: Recovery functions were calculated from the inter-spike interval histograms shown in panels *A*, *B* and *C*. The weight is equivalent to the probability of a spike if a spike occurred at time 0.

absolute refractory period of 1 ms followed by a very small relative refractory period. Finally, there was evidence of long term refractoriness on the scale of 10 ms as shown in the example neuron in Figure 7C and Figure 7F. This neuron's recovery function did not return to 1 until 10 ms after the spike responded. In general, we did not find recovery functions that deviated from 1 beyond 15 ms.

Given the recovery functions extracted from the firing during the sustained phase of the neurons' responses to motion, we used simulations to determine their impact on the transient-to-sustained ratio observed in our recordings. The simulations were based upon equation 4, using the recovery function extracted for each neuron, $w(\Delta)$, while q was defined as follows:

$$q(t) = \begin{cases} R_{back} & for & t < 250 \\ R_{trans} & for & t > 256 & and & < 512 & or & 768 \\ R_{back} & for & t > 512 & or & 768 \end{cases} \quad (6)$$

R_{back} is the background firing rate of the neuron, while R_{trans} was the firing rate that produced the peak transient response of the neurons given the recovery function. R_{trans} was found iteratively for each neuron in our sample population, such that the peak response of the model matched the peak response of the neuron. R_{back} was usually small (less than 20 spikes/s). At each time step, the probability of firing was determined according to q(t) and the recovery from the last spike. A random number was picked to determine if the neuron spiked at each time in the simulation. Each trial lasted for 758 ms and was repeated 1000 times in order to extract predicted firing rates for each neuron.

The recovery function often produced transient and sustained responses in our model neurons. An example of the dynamic response of these neurons to changes in
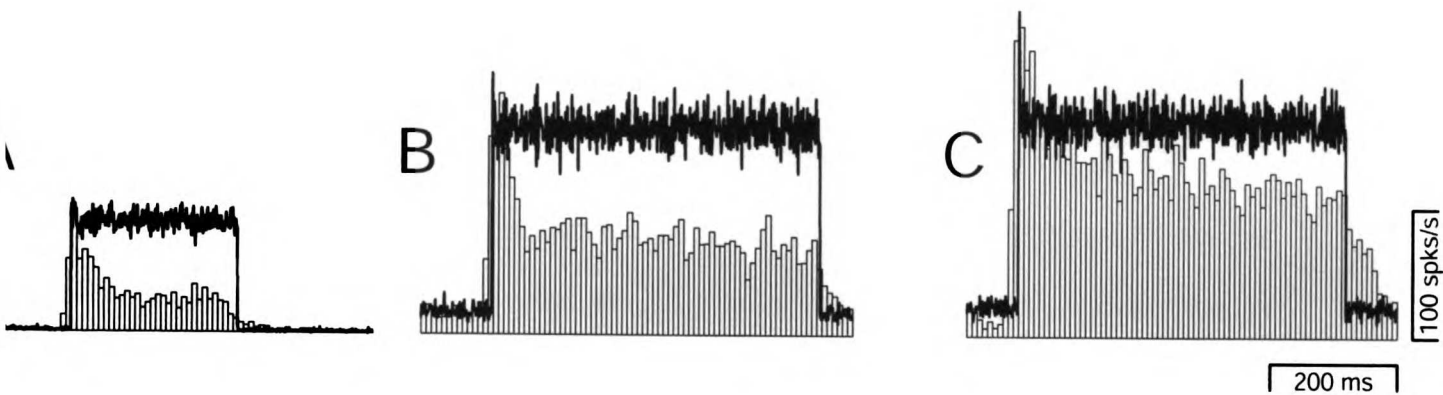
Figure 8

Figure 8: The predictions of a Poisson model with a recovery function. *A,B,C*: Each panel shows the prediction of a Poisson model with the recovery function shown in Figure 7 D, E and F with the thick dark line. The observed response of each neuron is shown by the histogram. For the neuron in panel A, the motion stimulus was on for 256 ms, while it was on for 512 ms for the other two neurons.

firing rate is shown Figure 8A, for the neuron shown in Figure 7A/D. The simulation

response to a change in firing rate (thick line) based upon the recovery function in

Figure 8A did produce a small transient that was quickly followed by a slightly lower

sustained rate of firing. In this same panel, the recorded neural response is shown by

the histogram. For this neuron, the recovery function does not account for the

adaptation of responses observed in the actual firing of the neuron. For the example

in Figure 8B, based on the recovery function in Figure 7E, the sustained component

of response was much lower in the actual response than in the simulation based upon

its recovery function. As before, the recovery function did not account for the

transient-to-sustained ratio observed in the response of the neuron. In addition, the

time course of the change from the transient to sustained mode of firing was very fast

in the simulation (<5 ms) while the actual decay of the neuron to the sustained rate of

firing for this neuron had a time constant of 25 ms. In the final example neuron, the

recovery function did cause a significant change in the response of the neuron,

although as in the first example, the transient-to-sustained ratio did not match the

ratio found from the actual neural response nor did the time course of the shift from

the transient to sustained rate match the time course of the actual neural response.

For all the neurons in our sample population for which we could extract recovery

functions, the predicted transient-to-sustained ratio from the model was computed.

We then compared the observed transient-to-sustained ratios to the modeled transient-

to-sustained ratio to assess the overall contribution of spike-timing dependent

mechanisms to the adaptation observed in area MT. In Figure 9A, the actual and

predicted values are plotted for each neuron. Although there was certainly an effect
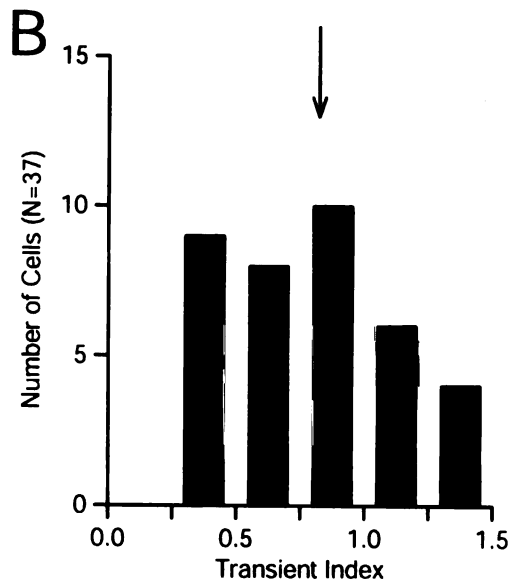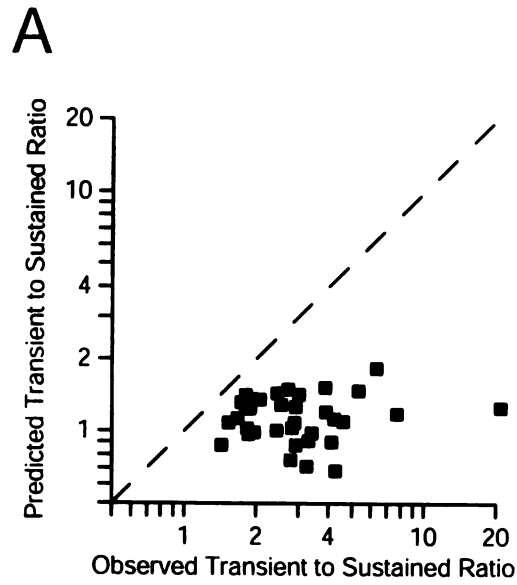
Figure 9

Figure 9: The effectiveness of the refractory period in accounting for the observed

adaptation of MT neurons. *A*: The observed transient-to-sustained ratio for each

neuron is shown relative to the transient-to-sustained ratio of the prediction based on

a Poisson model with a recovery function. The dashed line shows a slope of one

where the model reproduces the observed transient-to-sustained ratio. *B*: A

histogram of the transient index (equation 7) for each neuron is shown. The vertical

arrow indicates the mean transient index of the population.

of spike-dependent mechanisms, the recovery functions extracted from the neurons' responses cannot account for the observed transient-to-sustained ratio of the majority of neurons. To quantify the contribution of the spike-dependent recovery function, the transient index for each neuron was computed according to:

$$TI = \frac{R_{sim\_sus} - R_{sus}}{R_{trans} - R_{sus}}$$ (7)

where R_{sim_sus} is the sustained response measured from the simulations. When the TI is 1, the recovery function did not produce a reduction in firing. A TI of zero indicates that the neuron recovery function accounted completely for transition from transient to sustained response. The average transient index was 0.81. A few neurons had recovery functions that raised their sustained firing rate instead of reducing it, as indicated by values of the transient index greater than 1.

The effect of activity on subsequent responses

Our final test takes advantage of the variability of the initial transient responses to ask whether spike-timing dependent interactions are responsible for short-term adaptation in MT neurons. We began this analysis by defining a transient period like the one shown by the two vertical dashed lines in Figure 10A and measuring the number of spikes in the transient period for each trial used to accumulate the histogram of spike firing rate. Suppose that short-term adaptation results from activity-dependent interactions: then, an average of the trials with fewer spikes in the transient interval should reveal larger responses in the subsequent intervals. Suppose, instead, that short-term adaptation results from a process that
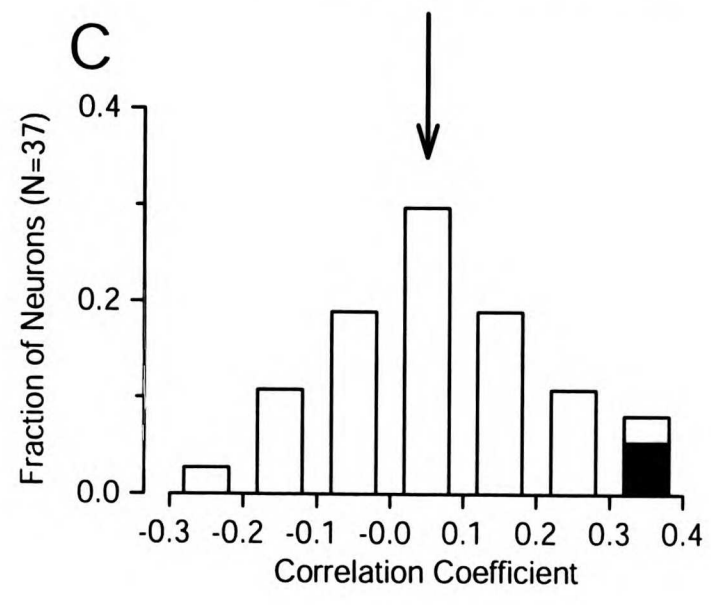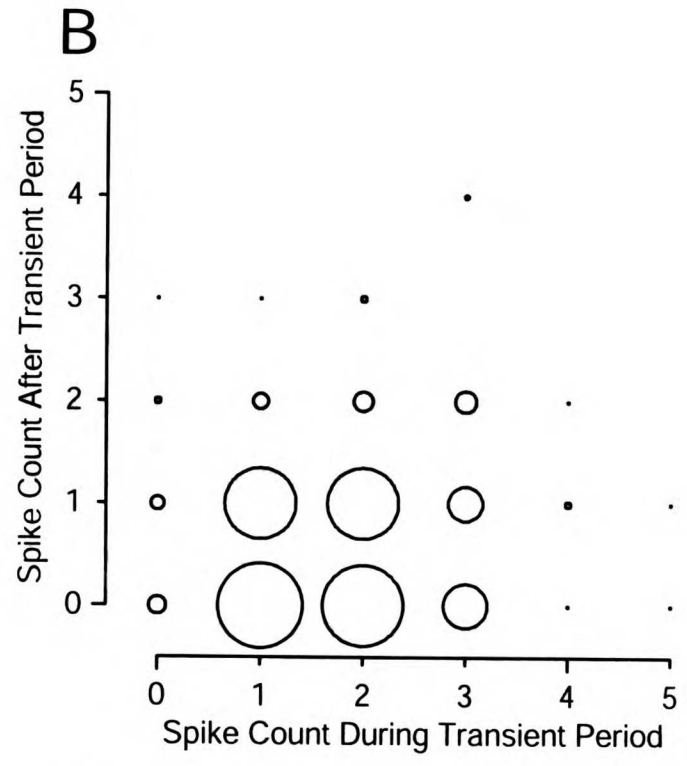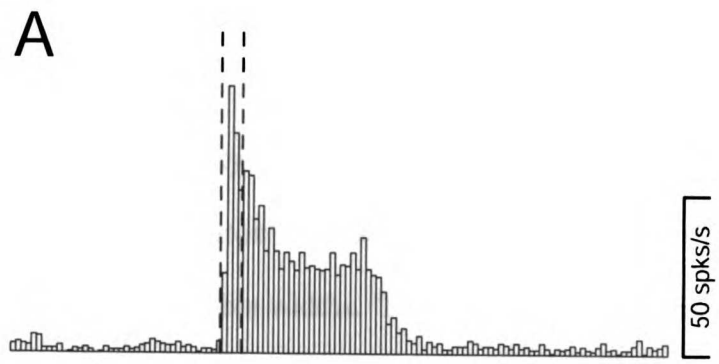
Figure 10

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Figure 10: The effect of activity during the transient period on subsequent responses. *A*: The response of an MT neuron to a step of motion is shown by the post stimulus time histogram with 8 ms size bin widths. The dashed lines indicate the period identified as the transient period. This period is not aligned with the bins of the histogram because the transient period was determined on a 1 ms time scale, not an 8 ms time scale. *B*: The frequency of spike counts during and after the transient period is indicated by the size of the circle at each point. The largest circle indicates that the combination of transient and sustained spike counts occurred in 45 different trials. *C*: The correlation coefficient for the 37 neurons in our sample population is shown as a histogram of values. The open bars indicate correlation coefficients that were not statistically significant (t-test, P>0.05). The filled bars indicate correlations coefficients that were significant (t-test, P<0.05). The arrow above the histogram indicates the mean correlation coefficient of the distribution (0.06).

goes on in the absence of activity: then, there should be no relation between the number of spikes in the transient intervals and the response in the subsequent intervals. For the neuron in Figure 10 A, we measured the number of spikes during the transient interval and directly after the transient interval. The frequency of the spike count for each period is shown in Figure 10B. There is not an obvious relationship between an increase in the number of spikes during the transient period and the number of spikes in the subsequent period. To measure quantitatively the relationship, we computed the correlation coefficient. For this neuron, the correlation coefficient was small (0.13) but was not statistically significant from zero (t-test, $P>0.05$, Sokal and Rohlf 1995). For the 37 neurons in our sample population the correlation coefficient was computed between the spike counts during and after the transient period. The mean correlation coefficient was 0.06, although there were only two cases with statistically significant correlations. A histogram of the coefficients of the sample population is shown in Figure 10C.

Although these correlation coefficients indicate that there is not a strong association between the firing during and after the transient period, it may be the case that a single spike during the transient period is able to switch neuron into the sustained phase of firing. We therefore wanted to examine the responses of neurons for trials in which the neuron does not respond at all during the transient period. For the neuron used to create Figure 10, 26 trials had zero spikes in the transient interval, and the remaining 239 trials had between 1 and 6 spikes, as shown in Figure 11A. We therefore separated the trials of the neuron into two groups, based on whether spikes occurred during the transient period. The histogram in Figure 11B shows the

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A

Number of Trials (N=265) / Number of Spikes

B

50 spks/s
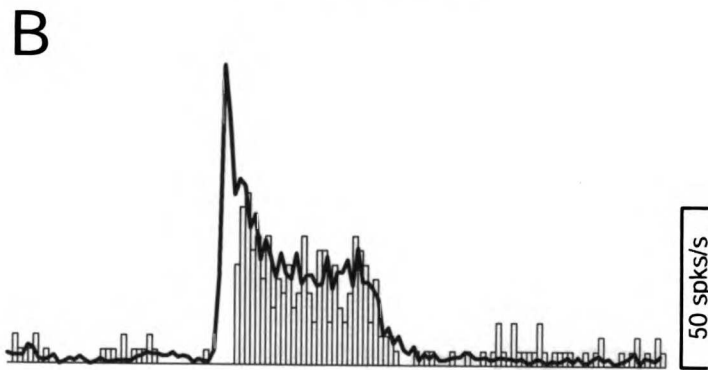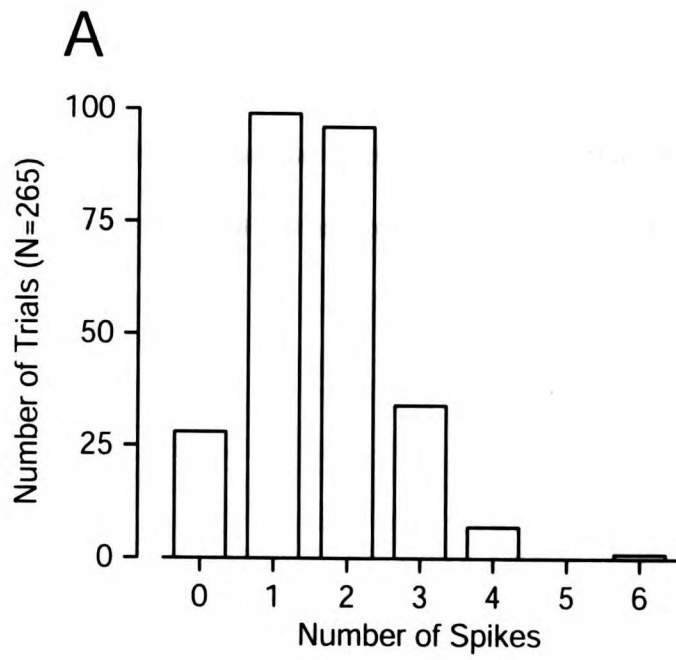
Figure 11

Figure 11: The lack of spiking during the transient period does not cause a delayed transient. *A*: The frequency of spike counts during the transient period is given for the same neuron in Figure 10A. *B*: The histogram shows the firing rate of the neuron for all trials in which there was no response during the transient period. The thick line indicates the response of the neuron when there was spiking during the transient period.

response of the neuron for trials lacking any spikes in the transient interval. The neuron has a delayed onset and a reduced transient. It rises to the average obtained for rest of the trials (bold, continuous trace) and follows it throughout the trial. We were able to perform this analysis for 68% of the neurons in our sample population (25/37). Each neuron was selected so that we had at least four trials in which no spiking was observed during the transient period. For each neuron, we divided trials into groups based upon whether or not there was spiking during the transient interval, and computed the mean response of each neuron for the period of 16 ms after the initial transient period separately for trials with and without firing in the transient period. A comparison between the responses immediately after the initial transient period in these two conditions is shown for each neuron in Figure 12. The absence of spikes during the transient interval did not lead to significantly different responses in the subsequent interval for the majority of neurons (22/25). The other 12% of the neurons did show a statistically significant effect on response during the interval following the transient period. These neurons had a higher firing rate during the interval after the transient period when there were spikes during the transient period.
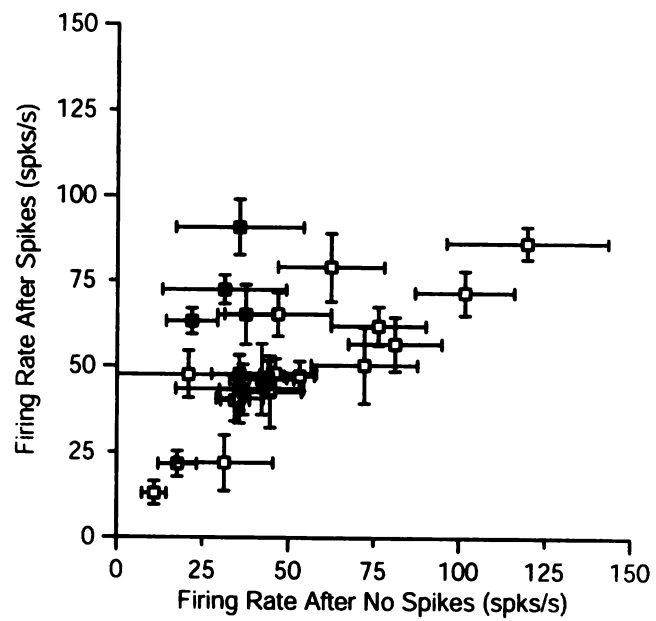
Figure 12

Figure 12: The effect of spiking on the adaptation of MT neurons. The firing rate of the neurons during the 16 ms immediately after the transient period is shown in this figure. For each neuron, the response when there was no spiking during the transient period is shown on the abscissa while the response when there was spiking is shown on the ordinate. The filled symbols indicate statistically different responses depending upon the presence of spiking in the transient period. Error bars show the standard error of the mean for the conditions of spiking or no spiking during the transient period.

Discussion

In this paper we have demonstrated that activity-dependent mechanisms of adaptation are not responsible for the adaptation observed in the response of MT neurons to visual motion. We used three methods to quantify the contribution of spike- and activity-dependent mechanisms. First, we estimated the change in the firing rate of each neuron during its sustained phase of firing if there were no interactions between spikes. This value, the sustained free firing rate q, was compared to the observed transient and sustained firing rate. We found that the sustained free firing rate was on average higher than the observed sustained free firing rate, but the free firing rate only accounted for 18% of the change it would need to have to reach the transient firing rate. We then assessed the impact of spike-dependent recovery functions on the firing of neurons by building a spiking model where the probability of a spike was determined by the firing rate of the neuron and the time from the previous spike. From the recovery function extracted from each neuron, we estimated the contribution of spike-timing dependent mechanisms to MT neuron adaptation to motion. The recovery functions did account for a portion of the transient-to-sustained response in some neurons, but they did not account for all of the adaptation observed in the MT neurons response. In addition, the modeled time course of decay to the sustained response was far shorter (<5 ms) than observed in MT neurons. Finally, we also measured the effect of a neuron's activity during the transient period on its response to a subsequent epoch and found little relation between responses in these two periods. These three techniques all led to the same

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conclusion: spike-timing and activity-dependent mechanisms do not lead to the adaptation observed in the firing of MT neurons.

The characteristics of the MT neuron recovery functions are compatible with a number of biophysical properties of cortical neurons. First, the absolute refractory period of the neurons is consistent with the inactivation of the ion channels that produce action potentials. The sodium channel is completely inactive for ~1 ms after an action potential, and the potassium channels also remain open after an action potential, thus hyperpolarizing the neuron (Hodgkin and Huxley, 1952). In addition, after firing an action potential, neurons must charge their membrane to reach threshold. The time constant for charging a membrane is usually reported as 10-20 ms, a period slightly longer than the relative refractory period observed in our neurons. The relative refractory period of these neurons may also be caused by a spike-activated hyperpolarizing current (I_{AHP}), although this current has a longer time constant (50-200 ms) (Hille, 1992).

Technical Considerations

Although spike-timing dependent interactions did not account for the transient-to-sustained responses of the majority of our MT neurons, some neurons, like the example in Figure 8C, had recovery functions that did account for the much of the transient-to-sustained response observed. These neurons had high firing rates, so that the time between spikes was small. The recovery functions for most neurons in our sample population return to the baseline value of 1 within 10 ms. Therefore there is a greater probability of an interaction between the recovery function and the

firing rate of the neurons when the response of the neurons is greater than 100 spikes/s. Because the amount of adaptation did not depend on the absolute firing rate of the neurons in our sample population, it is improbable that a spike-timing dependent mechanism could account for the adaptation observed unless the time course of the recovery function were much longer than we found.

Three significant assumptions were made in our modeling of the MT neuron responses with recovery functions. First, we assumed that the recovery function extracted during the sustained phase of the response is an attribute of the neuron, and does not depend on the absolute firing rate of the neuron. It may be the case that the recovery function during the transient period of response is different than during the sustained phase of response. For example, the propensity of neurons to burst may be higher during the initial transient period than during the sustained response. There should be a difference in this probability due to the difference in firing rate, but firing rate may not be the only factor controlling the probability of bursting. Second, we assumed that the important spike-timing dependent interactions occur between successive spikes. Once the neuron spikes, the recovery function is reset. Alternatively it may be the case that the effects of multiple spikes during a short period of time accumulate. The effect of multiple spikes may cause a more dramatic shift in the transient-to-sustained ratio. However, to extract the recovery function to model the effects of two spikes within the refractory period of the neuron requires much more data than we currently have. Finally, we modeled the responses of MT neurons as processes that had a background rate that was abruptly shifted to a higher rate to model the visual responses of neurons. The abrupt shift in rate is probably not

realistic, as neural responses tend to ramp up over a period of ~8-12 ms. Using a filtered version of the shift in rate would yield more realistic looking firing rates, but would not alter the effect of the spike-dependent mechanisms on the firing rate.

The calculations of the Fano factor, the recovery function, and activity-dependent interactions across multiple trials all depend on the excitability of the neuron remaining steady throughout the recording session. We discarded neurons which were not considered statistically stationary (see Methods) over the period of their sustained responses for all the repeats of the stimulus. Almost half of the neurons recorded were discarded by our standard. However, we noticed that a few neurons had enhanced responses during the 16 ms period after the transient period when there was a response during that period (Figure 11). Such a positive correlation between the firing in consecutive intervals is possibly evidence of a non-stationarity working on a short time scale that was not found when looking for changes in excitability across multiple trials.

Relationship to other studies

As others have found in the periphery of the visual system (Berry and Meister, 1998), auditory system (Teich and Lachs, 1979; Miller, 1985) and in primary visual cortex (Oram et al., 1999), the responses of neurons in area MT are less variable than might be expected from a Poisson process. Berry and Meister (1999) also computed recovery functions for retinal ganglion neurons and found that the recovery functions produced more precise responses as well as increased information rates. One might

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think that to extract the true relationship between stimulus and response, the free firing rate, q, of the neuron may be a more informative metric of the neuron's response than the observed firing rate of the neuron. The free firing rate is not subject to the saturating response non-linearities that constrain the observed firing rate. However, the free firing rate is not used by neurons to convey information and therefore any increases in information transmission by the free firing rate would be lost to downstream neurons.

The decrease in the variability of the response of MT neurons during the transient phase of firing is a byproduct of the recovery function, as has been suggested in somatosensory cortex (D. Blake, personal communication) and the auditory periphery (Teich and Lachs, 1979; Miller, 1985). At the peak firing rate of the neuron, there are more interactions between spikes. These interactions limit the number of spikes that can occur during a given time window. When the firing rate of a neuron is lower, as it is during the sustained phase firing, the variability of the neural response is higher. MT cortical responses are well modeled by a Poisson process at low firing rates when the spikes do not interact, but when the neurons are well driven by the stimulus the spikes do interact and cause more precise spiking than expected from the Poisson model.

This paper, along with the two companion papers, establishes that the mechanism for adaptation in area MT is not the result of a mechanism sensitive to the activity of the recorded neuron. Consistent with this finding, the speeds of motion that elicited the greatest suppression of response were not necessarily the speeds that elicited the largest response (Priebe and Lisberger A). Instead it appears that

adaptation is induced by interactions between MT neurons that may have different preferences for speed. In addition, after adaptation induced in one portion of an MT neuron receptive field, the response to motion in another portion of the receptive field often elicited small transients. If the mechanism for adaptation were simply the result of an activity-dependent mechanism, motion from other portions of the receptive field ought not to produce a second transient.

Through these experiments we have constrained the mechanism for adaptation in area MT to a mechanism based on specific interactions between neurons within area MT. Adaptation in MT neurons is tuned in terms of selectivity for space, directions and speeds in the same manner that the responses of MT neurons are tuned for these parameters. The function of this form of adaptation is not known, but we have been able to use this adaptation to shed light on the functional connectivity of MT neurons. Based on the properties of adaptation in MT neurons, we expect that neurons with the same preferences for direction and spatial location to interact strongly with each other, even if they have different preferred speeds. Neurons with the same direction tuning and different speed tunings also could interact to create an estimate of target acceleration (Lisberger and Movshon, 1999).

Some have suggested that the role of adaptation is to adjust the sensitivity of neurons to a state in which the transmission of information about the stimulus is most effective (Brenner et al., 2000). For example, the contrast response curve of neurons in V1 may be shifted by the continued presence of a high or low contrast stimulus (Ohzawa et al., 1985). The curve shifts so that it is most sensitive to the mean contrast in the environment. This class of adaptation is commonly referred to as

"gain control" because the overall gain of the neuron's sensitivity to the contrast is either turned up or down. Contrast gain control effectively changes the sensitivity of neurons so that the dynamic range of response matches the dynamic range of the stimulus. It is unclear whether the adaptation observed in area MT is an attempt by the cortex to match the input range to the output range, although the dynamic responses of MT neurons are well modeled by time-dependent changes in response gain (Lisberger and Movshon, 1999). The changes in sensitivity reported by Ohzawa et al. (1985) were over time scales much longer than the 30-50 ms shown here. A further analysis of the input to MT neurons over the period of the stimulus presentation will be necessary to determine if the observed change in response is an attempt to adjust the output range of MT neurons to the average input range.

References

Allman J, Miezin F, McGuinness E (1985) Direction- and velocity-specific responses from beyond the classical receptive field in the middle temporal visual area (MT). Perception 14:105-126.

Berry MJ, Meister M (1998) Refractoriness and neural precision. Journal of Neuroscience 18:2200-2211.

Brenner N, Bialek W, van Steveninck RD (2000) Adaptive rescaling maximizes information transmission. Neuron 26:695-702.

Churchland MM, Lisberger SG (2000) Apparent motion produces multiple deficits in visually guided smooth pursuit eye movements of monkeys. Journal of Neurophysiology 84:216-235.

de Ruyter van Steveninck RR, Lewen GD, Strong SP, Koberle R, Bialek W (1997) Reproducibility and variability in neural spike trains. Science 275:1805-1808.

Hille B (1992) Ionic channels of excitable membranes, 2nd Edition. Sunderland, Mass.: Sinauer Associates.

Hodgkin AL, Huxley AF (1952) A quantitative description of membrane current and its application to conduction and excitation in nerve. Journal of Physiology 117:500-544.

Lisberger S, Movshon J (1999) Visual motion analysis for pursuit eye movements in area MT of macaque monkeys. Journal of Neuroscience 19:2224-2246.

McCormick DA, Connors BW, Lighthall JW, Prince DA (1985) Comparative electrophysiology of pyramidal and sparsely spiny stellate neurons of the neocortex. Journal of Neurophysiology 54:782-806.

Merrill EG, Ainsworth A (1972) Glass-coated platinum-plated tungsten microelectrode. Med Biol Eng 10:495-504.

Mikami A, Newsome W, Wurtz R (1986) Motion selectivity in macaque visual cortex. II. Spatiotemporal range of directional interactions in MT and V1. Journal of Neurophysiology 55:1328-1339.

Miller MI (1985) Algorithms for removing recovery-related distortion from auditory-nerve discharge patterns. Journal of the Acoustical Society of America 77:1452-1464.

Muller JR, Metha AB, Krauskopf J, Lennie P (1999) Rapid adaptation in visual cortex to the structure of images. Science 285:1405-1408.

Nelson SB (1991) Temporal interactions in the cat visual system. I. Orientation-selective suppression in the visual cortex. Journal of Neuroscience 11:344-356.

Ohzawa I, Sclar G, Freeman RD (1985) Contrast gain control in the cat's visual system. Journal of Neurophysiology 54:651-667.

Oram MW, Wiener MC, Lestienne R, Richmond BJ (1999) Stochastic nature of precisely timed spike patterns in visual system neuronal responses. Journal of Neurophysiology 81:3021-3033.

Rieke F (1997) Spikes : exploring the neural code. Cambridge, Mass.: MIT Press.

Sokal RR, Rohlf FJ (1995) Biometry : the principles and practice of statistics in biological research, 3rd Edition. New York: W.H. Freeman.

Teich MC, Lachs G (1979) A neural-counting model incorporating refractoriness and

    spread of excitation. I. Application to intensity discrimination. Journal of the

    Acoustical Society of America 66:1738-1749.

Teich MC, Matin L, Cantor BI (1978) Refractoriness in the maintained discharge of

    the cat's retinal ganglion cell. Journal of the Optical Society of America

    68:386-402.

Tolhurst DJ, Walker NS, Thompson ID, Dean AF (1980) Non-linearities of temporal

    summation in neurones in area 17 of the cat. Experimental Brain Research

    38:431-435.

Wohlgemuth A (1911) On the aftereffect of seen movement. Journal of Psychology

    1:1-117.

Yarom Y, Sugimori M, Llinás R (1985) Ionic currents and firing patterns of

    mammalian vagal motoneurons in vitro. Neuroscience 16:719-737.

General Conclusions

In this thesis, we have made constraints on the mechanism of adaptation observed in the responses of MT neurons. The hypothesized mechanisms that could account for the adaptation of MT neuron response fall into three general classes: input mechanisms such as changes in the firing rate of V1 neurons or changes in the efficacy of the V1 synapses onto MT neurons, mechanisms intrinsic to the neurons such as spike rate adaptation, and finally interactions between neurons within area MT.

In the first chapter we measured the tuning of the adaptation mechanism in terms of direction and speed and found that adaptation was tuned to both the direction and speed of motion. The direction and speed tuning of adaptation is consistent with all of possible classes of adaptation listed above, but does make the constraint that a mechanisms based on interactions between neurons in area MT should be tuned. That is, the interactions between neurons in area MT should occur between neurons with correlated response properties. In the second chapter, we measured the spatial tuning of adaptation in area MT. We found that adaptation transferred over spatial distances larger than the size of a V1 receptive field. The transfer of adaptation over space would not be possible if an input-based mechanism for adaptation were responsible for the adaptation observed. Therefore, such a mechanism is not primarily responsible for the MT neuron adaptation. Finally, in the third chapter, we measured the effect that activity and spike-dependent mechanisms have on the subsequent responses of MT neurons. Since we found that there was no significant relationship

between activity of a neuron and the induction of adaptation, we conclude that mechanisms intrinsic to the neuron do not account for the adaptation of MT neuron responses.
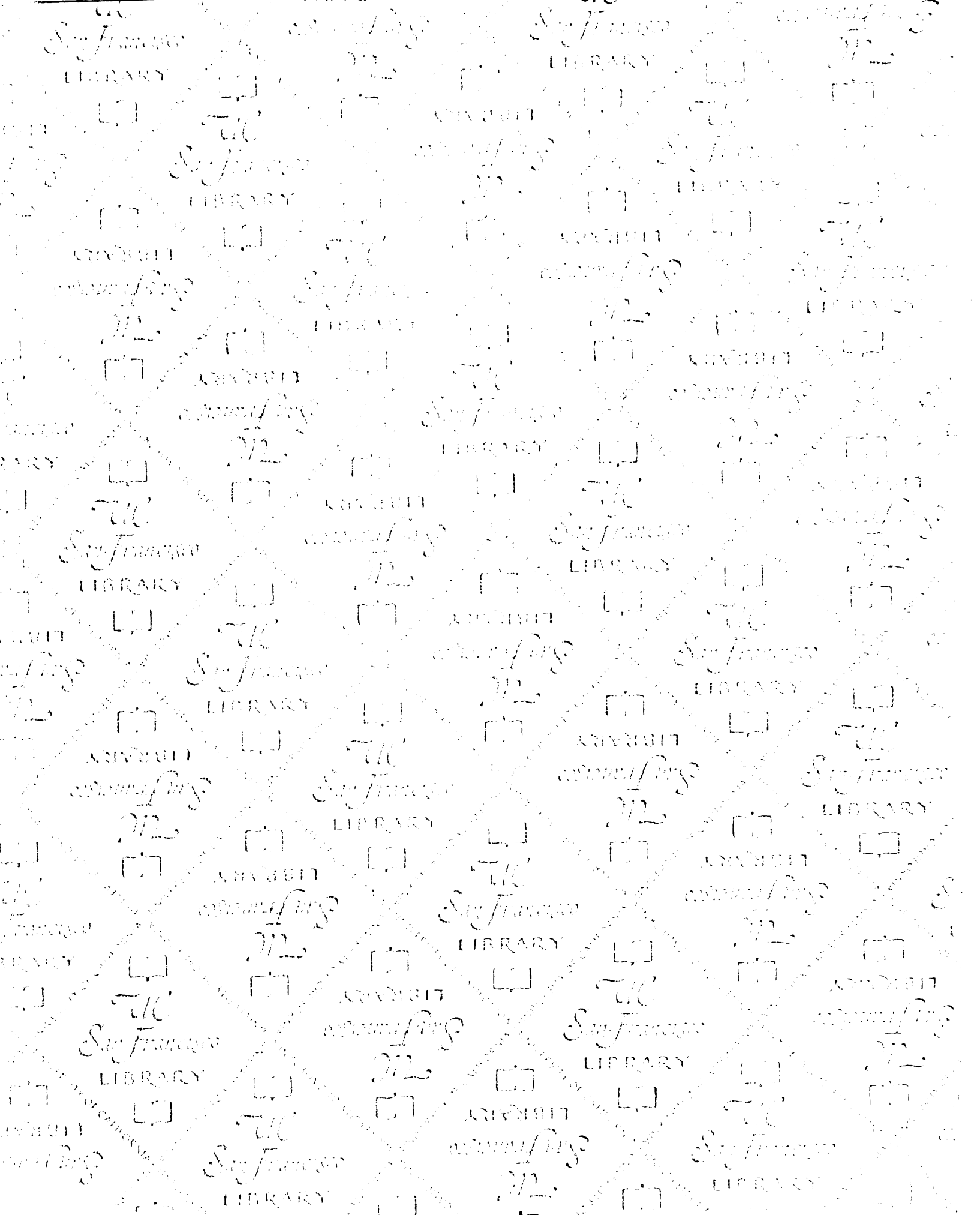
The mechanism of adaptation that is most consistent with our results is a network of interactions within MT, in which the interactions are based on the neurons' preferences for direction, speed and spatial location. The adaptation could be derived either from a loss of excitatory drive onto an MT neuron or from a gain of inhibitory input onto the neuron. With extracellular techniques we cannot distinguish between these two mechanisms. Correlation-based connectivity suggests that excitation occurs between neurons with similar tuning, while inhibition occurs between neurons that have opposite tuning (Troyer et al., 1998). MT neurons are often suppressed by motion opposite to their preferred direction (Maunsell and Van Essen, 1983; Heeger et al., 1999), consistent with this correlation-based connectivity hypothesis. Because the adaptation mechanism studied here has the same tuning as that of the neurons to single presentations of a stimulus, it seems more likely to be an effect of a loss of excitatory input from the network of neurons in MT than from inhibitory interactions between neurons of similar tuning.

Adaptation has long been used by psychophysicists to define different channels of information processing. As in our physiological experiments, the protocol used to induce adaptation is to present a conditioning stimulus and then to measure the subsequent response to a test stimulus. The degree to which the two components are commonly processed can then be estimated by the specificity and magnitude of the effect of the conditioning stimulus on the test response. In these

terms, we have attempted to uncover which "channels" overlap in the processing of motion information by measuring which conditioning motion affects the response to test motion. We find that the channels of overlap are similar to the tuning of the MT neurons. Motion that is correlated in terms of spatial position, direction and speed to the tuning of the neuron causes the greatest effect on the neuron's subsequent responses. We now know that MT neuron responses are not simply the result of the integration of the response properties of the input V1 neurons, but that interactions occurring within MT itself shape their response to motion. Because the interactions between neurons are tuned and actively used in generating the MT responses, our adaptation paradigm can be extended to measure the effect of a given conditioning direction or speed of motion on direction or speed tuning of the neurons. We expect a consistent change in the tuning of the neuron, depending on the direction or speed of the conditioning motion. Understanding the transformation of input at each cortical level provides us a base for uncovering the function of the cerebral cortex.

References

Heeger DJ, Boynton GM, Demb JB, Seidemann E, Newsome WT (1999) Motion

opponency in visual cortex. Journal of Neuroscience 19:7162-7174.

Maunsell JHR, Van Essen DC (1983) Functional properties of neurons in middle

temporal visual area of the macaque monkey. I. Selectivity for stimulus

direction, speed, and orientation. Journal of Neurophysiology 49:1127-1147.

Troyer TW, Krukowski AE, Priebe NJ, Miller KD (1998) Contrast-invariant

orientation tuning in cat visual cortex: Thalamocortical input tuning and

correlation-based intracortical connectivity. Journal of Neuroscience 18:5908-

5927.